Synthesis of Isosteric Analogues of Acylglycosylglycerols Active as Chemoprevention Agents

Federica Compostella,*[a] Diego Colombo,[a] Patrizia Ferraboschi,[a] Antonio Scala,[a] Lucio Toma,[b] and Fiamma Ronchetti[a]

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Monoacylated glycosylglycerols are known anti-tumor promoters: in order to study the role of the ester function in the modulation of their activity, we synthesized several analogues in which the acyloxy moiety was substituted with isosteric chains linked to the glycosylglycerol skeleton through an ether or a ketone functionality or simply by a C–C bond. Depending on the position of the chain, the key steps in the synthesis were either the coupling of suitable chiral synthons with the sugar, with complete stereocontrol over the anomeric configuration, or regioselective elaboration at position 6 of the sugar.

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Introduction

In the last decade, natural acyl mono- and diglycosylglycerols, generally galactolipids in which the sugar is linked to the 3-position of *sn*-glycerol, have attracted attention as anti-tumor-promoting compounds.[1−4] The search for effective chemopreventing agents is considered to be among the most promising cancer-control methods because of their potential in inhibiting promotion, the only reversible process during the multistages of carcinogenesis.[5] In this context, we started a research program based on the synthesis and biological evaluation of glycoglycerolipid analogues to clarify the structural features necessary for the anti-tumor promoting activity. Since the 2-*O*-isomers proved both to have activities comparable with those of the corresponding 1-*O*- and 3-*O*-isomers,[6] and to be easier to prepare, we decided to screen the role of acyl-2-*O*-β-D-glycosylglycerols. The structural features taken into consideration were: the nature of the saccharidic residue (glucose or galactose), the anomeric configuration of the glycosidic linkage (α or β), and the length, together with the position, of the acyl residue situated on one of the primary hydroxyls of the molecule.[7−11] We have found that the presence and the length of the acyl chain are essential requirements in determining the activity, which in general is higher for the acylated derivatives than for their nonesterified counterparts and, in particular, is more pronounced for analogues bearing a medium-length fatty acid (from C_4 to C_{10}), reaching a maximum for monohexanoyl derivatives. Figure 1 shows the structures of the three most active chemopreventing glycosylglycerols (**1a**−**3a**) found so far.[8,11]

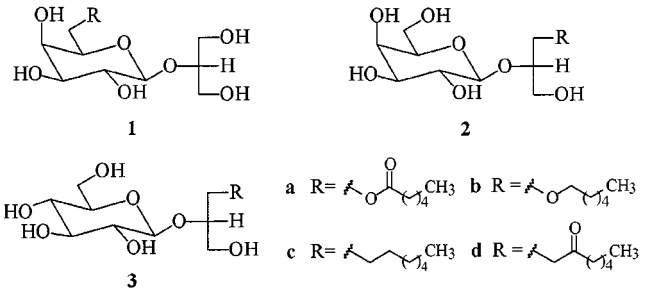


Figure 1. Structures of compounds **1**−**3**

Given the above considerations, we aimed at understanding the role of the ester function of such glycolipids in their properties and activities.

Therefore, the synthesis of analogues in which the lipophilic chain was linked to the glycosylglycerol skeleton through bonds chemically and enzymatically more stable than the ester linkage was planned. The designed analogues should be isosters of the reference acylglycosylglycerols, but with different functionalities in the part of the molecule corresponding to the ester linkage. We hence planned to link the chain to the skeleton through an ether or a ketone functionality, or simply through a C−C bond.

The anti-tumor promoting effect of such derivatives would clarify the role of the ester group in determining the activity; furthermore, these compounds would, if active, be more stable to digestive hydrolytic processes and so be candidates for possible therapeutic use by oral administration,

[a] Dipartimento di Chimica e Biochimica Medica, Università di Milano
Via Saldini 50, 20133 Milano, Italy
Fax: (internat.) + 39−02/50316036
E-mail: federica.compostella@unimi.it
[b] Dipartimento di Chimica Organica, Università di Pavia
Via Taramelli 10, 27100 Pavia, Italy

as acylglycosylglycerols have so far been successfully exploited only for topical application.[11]

In particular, we focused our attention on the most active glycosylglycerolipids **1a**−**3a**, each bearing a hexanoyl chain, and planned the synthesis of the analogues **1b**−**d**, **2b**−**d**, and **3b**−**d** with the hexanoate residue substituted by isosteric groups as depicted in Figure 1. A retrosynthetic analysis of the isosteric structures showed that two different approaches should be suitable for efficient synthesis of the desired derivatives; on the one hand the analogues at the sugar moiety **1b**−**d** should be easily accessible from alcohol **4** by alkylation, or by oxidation to aldehyde followed by Wittig olefination, while on the other hand, for the analogues at the glycerol moiety, it should be more convenient to synthesize the glycerol analogues **5a**−**c** first and then to couple them with the appropriate sugar derivative (Figure 2).

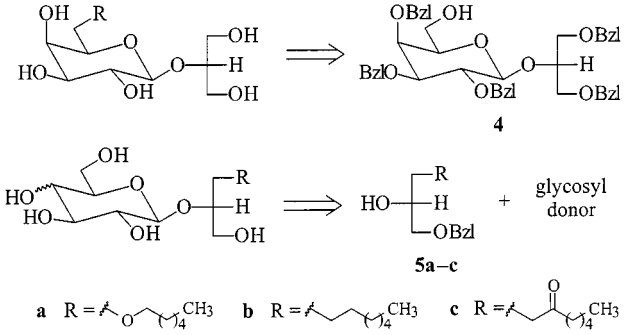


Figure 2. Retrosynthetic analysis of acylglycosylglycerol analogues

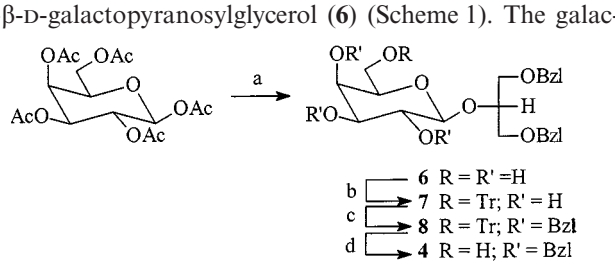
In a very recent paper[12] we reported the synthesis of the glycerol isosters **5a**−**c** and, as examples of their potential as carbohydrate acceptors, the synthesis of the glycoglycerolipid analogues **2d** and **3d**.

Here we describe the synthesis of the three analogues at the sugar part **1b**−**d**, and of compounds **2b**−**c** and **3b**−**c**, modified at the glycerol portion.

Results and Discussion

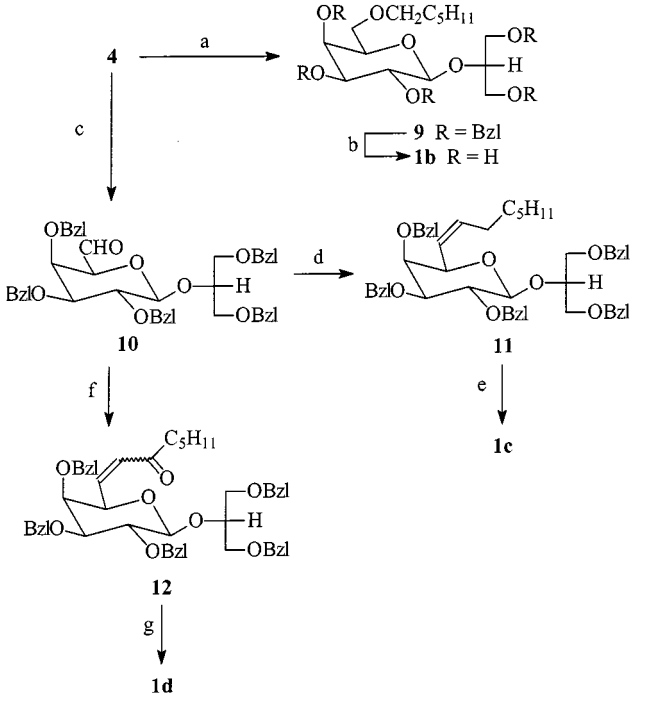
Synthesis of the 6′-*O*-Hexanoyl-2-*O*-β-D-galactopyranosylglycerol Analogues 1b−d

The key intermediate in the synthesis was the galactosylglycerol **4**, with all positions except 6′-OH protected as benzyl ethers; this was prepared by standard protection−deprotection strategies from 1,3-di-*O*-benzyl-2-*O*-β-D-galactopyranosylglycerol (**6**) (Scheme 1). The galactosyl derivative **6** was obtained through an efficient glycosylation reaction between β-D-galactose pentaacetate and 1-3-di-*O*-benzylglycerol in the presence of boron trifluoride−diethyl ether complex, followed by Zemplén deacetylation, with an overall yield of 90% and exclusive formation of the β-product. Compound **6** was then selectively tritylated at the primary hydroxy group in the carbohydrate, and the remaining hydroxyl groups were protected as benzyl ethers with benzyl chloride in pyridine to give **8**. By heating compound **8** under reflux in HCl/acetone, the trityl group was removed, and the key intermediate **4** was recovered in 70% overall yield from **6** (Scheme 1).



Scheme 1. a: 1,3-di-*O*-benzylglycerol, $BF_3{\cdot}Et_2O$, CH_2Cl_2; then MeONa; b: TrCl, Py; c: BzlCl, DMF; d: HCl, acetone

Alcohol **4** was alkylated with sodium hydride and hexyl bromide to give compound **9** in good yields (85%); after the conventional debenzylation procedure, the ether analogue **1b** was obtained (Scheme 2).



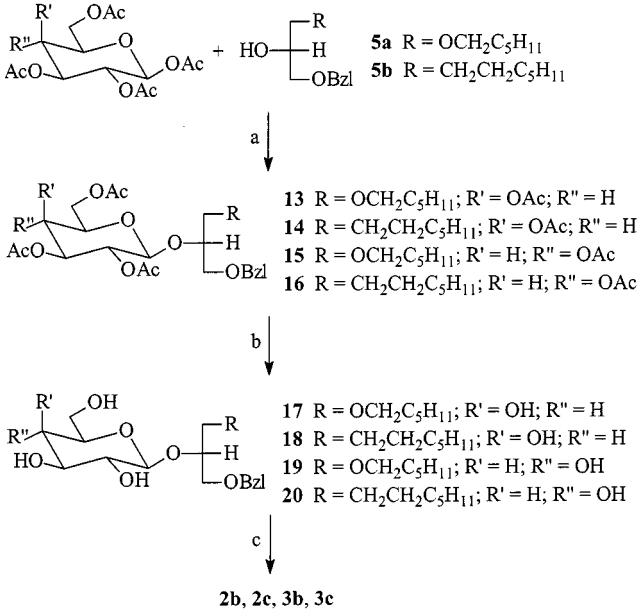
Scheme 2. a: $C_5H_{11}CH_2Br$, NaH, DMF; b: H_2, Pd/C; c: Swern oxidation; d: $C_5H_{11}CH_2CH_2PPh_3{}^+Br^-$, BuLi, THF; e: H_2, Pd/C; f: $C_5H_{11}COCHPPh_3$, THF; g: H_2, Pd/C

In turn, Swern oxidation of the key intermediate **4** gave the corresponding aldehyde **10**, which was subjected to two different Wittig olefinations. Firstly, **10** was coupled with heptylidenetriphenylphosphorane, formed in situ at −55 °C, to give the (*Z*) olefin **11**, as shown by the 11 Hz value of the ^1H NMR coupling constant for the olefinic protons.[13] Despite extensive efforts, the yields of this reaction (46%) could not be increased, due to the impossibility of isolating a non-stabilized ylide combined with the intrinsic instability of aldehyde **10** to basic conditions.[14] After hydrogenation, **11** gave the desired alkyl analogue **1c**. These reaction conditions, on the other hand, were more favorable for the synthesis of **1d**, the carbonyl analogue of this series; the stabilized 2-oxo-heptylidenetriphenylphosphorane was synthesized and isolated according to literature procedures,[15] and

the coupling with aldehyde **10** was performed under neutral conditions in THF at room temperature. The Wittig product **12** was recovered in 84% yield as an (*E*)/(*Z*) mixture. The mixture of the adducts was subjected to hydrogenation, yielding the wanted ketone **1d** (Scheme 2).

Synthesis of the 1-*O*-Hexanoyl-2-*O*-β-D-gluco- and -galactopyranosyl-*sn*-glycerol Analogues 2b−c and 3b−c

The building blocks **5a** and **5b**, crucial for the synthesis of the glycerol analogues **2b**, **2c**, **3b**, and **3c**, have already been described by us.[12] As noted in the introduction, these synthons were planned as common acceptors for the construction both of the glucosyl- and of the galactosylglycerol analogues, through glycosylation reactions. They have the primary hydroxy group protected as a benzyl ether and the secondary hydroxy group free for conjugation with a suitable sugar. The ether protection avoided migration from primary to secondary hydroxy group under the acid-catalyzed conditions for glycosylation. Glucose and galactose pentaacetate were chosen as glycosyl donors; these are convenient, commercially available starting materials with the necessary β-stereocontrolling ester group at their 2-positions. The glycosylation reactions, affording compounds **13−16** with the desired anomeric β-configuration, as depicted in Scheme 3, were carried out in dichloromethane at room temperature in the presence of boron trifluoride−diethyl ether complex, using acceptors **5a−b** as limiting reagents, except in the case of the gluco derivative **16** (1.5 equiv. of acceptor/1 equiv. donor). The β configuration of the glycosidic bond was indicated by the characteristic value (8 Hz) of the *trans*-diaxial $J_{1,2}$ coupling constants. The yields, all in the 80% range, illustrate the high efficiency of the glycosylation procedure with these kind of substrates, demonstrating the good pattern of reactivity between donor and acceptor.



Scheme 3. a: $BF_3{\cdot}Et_2O$, CH_2Cl_2; b: MeONa; c: H_2, Pd/C

The glycosylations were followed by deprotection steps: the acetyl groups were first removed under Zemplén conditions, and catalytic hydrogenolysis with Pd/C catalyst in methanol then afforded the desired analogues **2b**, **2c**, **3b**, and **3c** almost quantitatively.

Conclusion

We have synthesized compounds **1b−d**, **2b**, **2c**, **3b**, and **3c**, which are metabolically more stable isosteric analogues of the three most active chemopreventing acylated glycosylglycerols so far found (**1a−3a**), in order to study the influence of the ester function in modulating the anti-tumor promoting activity.

A preliminary screening of compounds **1b−d**, **2b−d**, and **3b−d** for their antitumor-promoting activity by a short-term in vitro assay for Epstein−Barr virus activation in Raji cells induced by 12-*O*-tetradecanoylphorbol-13-acetate (TPA)[1] has indicated that they are very active, although their inhibitory potentials are slightly lower than those of the reference acylated glycosylglycerols **1a**, **2a**, and **3a**. Complete data, together with a careful examination of the results in comparison with the data previously obtained by us from other glycolipid analogues, will be reported in due course.

Experimental Section

General: Optical rotations were determined on a Perkin−Elmer 241 polarimeter in a 1 dm cell at 20 °C. Uncorrected melting points were determined on a Büchi apparatus. Mass experiments were performed by chemical ionization mass spectrometry (CI−MS) as described by Colombo et al.[16] All NMR spectra were recorded at 303 K with a Bruker AM 500 spectrometer equipped with an Aspect 3000 computer, a process controller, and an array processor in $CDCl_3$ solutions unless otherwise noted; chemical shifts of NMR spectra are reported as δ (ppm) relative to tetramethylsilane as internal standard, except those of compound **1d**, which were referenced to HDO (δ = 4.55) for ^1H NMR and to dioxane (δ = 68.9) for ^{13}C NMR. Solvents were purified and dried in the usual way. All reactions were monitored by TLC on Silica Gel 60 F-254 plates (Merck) with detection by spraying with 50% H_2SO_4 solution and heating at 110 °C. Flash column chromatography was performed on Silica Gel 60 (230−400 mesh, Merck). All evaporations were carried out under reduced pressure at 40 °C. β-D-Galactose pentaacetate and 1,3-di-*O*-benzylglycerol were purchased from Fluka; β-D-glucose pentaacetate was purchased from Aldrich. Compounds **5a−b** were obtained as described in ref.[12] NaH was washed three times with hexane to remove the oil prior to use.

1,3-Di-*O*-benzyl-2-*O*-(β-D-galactopyranosyl)glycerol (6): Boron trifluoride−diethyl ether (4.3 mL, 33.1 mmol) was added dropwise, at 0 °C under argon, to a solution of β-D-galactose pentaacetate (6.54 g, 16.8 mmol) and 1,3-di-*O*-benzylglycerol (8.5 mL, 33.4 mmol) in dry dichloromethane (100 mL). The reaction mixture was allowed to warm to room temperature, stirred for an additional 3 h, and then quenched by addition of saturated $NaHCO_3$ solution (100 mL). The aqueous layer was extracted with dichloromethane (3 × 50 mL). The combined organic layers were then washed with

brine and dried, and the solvents were evaporated under reduced pressure. A solution of the crude material in MeOH (15 mL) was treated with sodium methoxide in dry methanol (1 M solution, 33 mL) for 2 h. The mixture was neutralized with an ion-exchange resin (Dowex 50 × 8, H^+) and filtered, and the filtrate was concentrated. The residue was purified by flash chromatography (EtOAc/MeOH, 95:5, then 9:1) to afford compound **6** (6.56 g, 90%) as a foam. $[\alpha]_D^{20}$ = +2.3 (*c* = 1.1, $CHCl_3$). ^1H NMR (CD_3OD): δ = 3.45−3.53 (m, 2 H, 3,5-H), 3.59 (dd, $J_{1,2}$ = 7.5 Hz, $J_{2,3}$ = 10.0 Hz, 1 H, 2-H), 3.62−3.80 (m, 6 H, 6a,6b-H and CH_2CHCH_2), 3.85 (br. d, $J_{3,4}$ = 3.5 Hz, 1 H, 4-H), 4.12 (m, 1 H, CH_2CHCH_2), 4.44 (d, 1 H, 1-H), 4.46−4.56 (m, 4 H, OCH_2Ph), 7.20−7.50 (m, 10 H, Ph). ^{13}C NMR (CD_3OD): δ = 62.5, 70.3, 71.0, 71.4, 72.7, 74.5 (2 C), 74.9, 76.7, 77.8, 104.5, 128.8−139.6 (C_6H_5). MS: *m*/*z* = 452 [M + NH_4]$^+$. $C_{23}H_{30}O_8$ (434.5): calcd. C 63.58, H 6.96; found C 63.75, H 6.83.

1,3-Di-*O*-benzyl-2-*O*-(6-*O*-trityl-β-D-galactopyranosyl)glycerol (7): A solution of **6** (5.48 g, 12.6 mmol) and trityl chloride (6.00 g, 21.6 mmol) in dry pyridine (38 mL) was stirred at 55 °C. After 4 h the mixture was diluted with ethyl acetate (120 mL), washed with 0.1 M HCl (2 × 50 mL) and water (3 × 100 mL), dried with sodium sulfate, and concentrated. The residue was purified by flash chromatography (hexane/EtOAc, 3:7, then EtOAc) to give **7** (6.80 g, 80%) as a white foam. $[\alpha]_D^{20}$ = −11.2 (*c* = 1.1, $CHCl_3$). ^1H NMR: δ = 2.28 (br. s, 1 H, OH exchange), 2.58 (br. s, 1 H, OH exchange), 3.28−3.42 (m, 3 H, 2 × 6-H and OH exchange), 3.48−3.67 (m, 7 H, 2,3,5-H and CH_2CHCH_2), 3.99 (m, 1 H, 4-H), 4.08 (m, 1 H, CH_2CHCH_2), 4.37 (d, $J_{1,2}$ = 8.0 Hz, 1 H, 1-H), 4.47 (m, 2 H, OCH_2Ph), 4.51 (m, 2 H, OCH_2Ph), 7.10−7.60 (*m*, 25 H, Ph). ^{13}C NMR: δ = 63.2, 69.5, 71.0, 71.3, 72.2, 74.2 (3 C), 74.5, 77.5, 87.5, 104.1, 127.8−144.4 (C_6H_5). MS: *m*/*z* = 694 [M + NH_4]$^+$. $C_{42}H_{44}O_8$ (676.8): calcd. C 74.54, H 6.55; found C 74.40, H 6.75.

1,3-Di-*O*-benzyl-2-*O*-(2,3,4-tri-*O*-benzyl-6-*O*-trityl-β-D-galactopyranosyl)glycerol (8): Sodium hydride (1.90 g with the oil, 64.1 mmol) was added under anhydrous conditions at 0 °C to a solution of compound **7** (6.20 g, 9.2 mmol) in dry DMF (60 mL), and the foaming gray reaction mixture was then allowed to warm to room temperature. Benzyl chloride (10.5 mL, 91.6 mmol) was slowly added, and the slurry was then heated at 55 °C and vigorously stirred at this temperature for 30 min. After MeOH (30 mL) had been added to destroy the excess of NaH, the mixture was concentrated under reduce pressure, and then diluted with ethyl acetate (300 mL) and washed with water (300 mL). The aqueous layer was further extracted with ethyl acetate (2 × 200 mL). The combined extracts were dried (Na_2SO_4) and concentrated. The residue was purified by flash chromatography (hexane/EtOAc, 95:5) to give product **8** (8.20 g, 94%) as a thin yellow oil. $[\alpha]_D^{20}$ = +2.1 (*c* = 1.0, $CHCl_3$). ^1H NMR: δ = 3.18 (dd, $J_{5,6b}$ = 7.0 Hz, $J_{6a,6b}$ = 9.5 Hz, 1 H, 6b-H), 3.30 (m, 1 H, 5-H), 3.40−3.46 (m, 2 H, 3,6a-H), 3.58−3.64 (m, 2 H, $CH_aH_bCHCH_aH_b$), 3.68−3.76 (m, 3 H, 2-H and $CH_aH_bCHCH_aH_b$), 3.79 (br. d, $J_{3,4}$ = 3.0 Hz, 1 H, 4-H), 4.06 (m, 1 H, CH_2CHCH_2), 4.42−4.96 (m, 10 H, CH_2Ph), 4.51 (d, $J_{1,2}$ = 8.0 Hz, 1 H, 1-H), 7.04−7.50 (m, 40 H, Ph). ^{13}C NMR: δ = 63.5, 70.8, 71.2, 74.0 (2 C), 74.1, 74.4, 75.0 (2 C), 75.7, 78.2, 80.3, 82.9, 87.6, 104.4, 127.8−144.6 (C_6H_5). MS: *m*/*z* = 964 [M + NH_4]$^+$. $C_{63}H_{62}O_8$ (947.2): calcd. C 79.89, H 6.60; found C 80.19, H 6.70.

1,3-Di-*O*-benzyl-2-*O*-(2,3,4-tri-*O*-benzyl-β-D-galactopyranosyl)-glycerol (4): Compound **8** (8.12 g, 8.6 mmol) in 1 N HCl−acetone (1:10, 60 mL) was heated under reflux for 45 min. The acid was neutralized with an excess of sodium hydrogen carbonate, and the solvent was evaporated off. The residue was diluted with ethyl acetate (300 mL), washed with water (2 × 200 mL), dried with sodium sulfate, and concentrated. The product (5.55 g, 92%) was recovered after flash chromatography (hexane/EtOAc, 6:4) as an oil. $[\alpha]_D^{20}$ = −11.5 (*c* = 1.0, $CHCl_3$). ^1H NMR: δ = 3.31 (m, 1 H, 5-H), 3.42 (dd, $J_{6a,6b}$ = 11.0 Hz, $J_{5,6b}$ = 5.0 Hz, 1 H, 6b-H), 3.49 (dd, $J_{2,3}$ = 9.5 Hz, $J_{3,4}$ = 3.0 Hz, 1 H, 3-H), 3.62 (m, 2 H, $CH_aH_bCHCH_aH_b$), 3.65−3.74 (m, 4 H, 4,6a-H and $CH_aH_bCHCH_aH_b$), 3.81 (dd, $J_{1,2}$ = 7.5 Hz, 1 H, 2-H), 4.05 (m, 1 H, CH_2CHCH_2), 4.56 (d, 1 H, 1-H), 4.42−5.00 (m, 10 H, OCH_2Ph), 7.10−7.40 (m, 25 H, Ph). ^{13}C NMR: δ = 62.0, 70.4 (2 C), 73.2, 73.3−75.0 (CH_2Ph), 74.7, 77.8, 79.6, 82.3, 103.7, 127.4−139.5 (C_6H_5). MS: *m*/*z* = 722 [M + NH_4]$^+$. $C_{44}H_{48}O_8$ (704.9): calcd. C 74.98, H 6.86; found C 74.75, H 6.55.

1,3-Di-*O*-benzyl-2-*O*-(2,3,4-tri-*O*-benzyl-6-*O*-hexyl-β-D-galacto-pyranosyl)glycerol (9): NaH (0.039 g with the oil, 1.3 mmol) was added at 0 °C under argon to a solution of **4** (0.70 g, 1.0 mmol) in DMF (3.5 mL). After 30 min, 1-bromohexane (0.18 mL, 1.3 mmol) and tetra-*n*-butylammonium iodide (0.01 g) were added, and the resulting solution was allowed to warm to room temperature. After 4 h, additional NaH (0.02 g) and 1-bromohexane (0.02 mL) were added, and the mixture was stirred overnight. The reaction mixture was quenched with water (100 mL), and then extracted with ethyl acetate (3 × 70 mL). The combined organic layers were washed with brine, dried with sodium sulfate, and concentrated. The residue was purified by flash chromatography (hexane/EtOAc, 6:4) to give the desired **9** (0.66 g, 84%) as an oil. $[\alpha]_D^{20}$ = +4.0 (*c* = 1.0, $CHCl_3$). ^1H NMR: δ = 0.86 (t, 3 H, CH_3), 1.20−1.32 (m, 6 H, 3 CH_2), 1.47 (m, 2 H, CH_2), 3.26 (m, 1 H, $OCH_aH_bCH_2$), 3.34 (m, 1 H, $OCH_aH_bCH_2$), 3.38−3.52 (m, 4 H, 3,5,6a,6b-H), 3.63 (m, 2 H, $CH_aH_bCHCH_aH_b$), 3.71 (m, 2 H, $CH_aH_bCHCH_aH_b$), 3.79 (dd, $J_{1,2}$ = 8.0 Hz, $J_{2,3}$ = 9.5 Hz, 1 H, 2-H), 3.84 (br. d, $J_{3,4}$ = 3.0 Hz, 1 H, 4-H), 4.06 (m, 1 H, CH_2CHCH_2), 4.56 (d, 1 H, 1-H), 4.43−4.98 (m, 10 H, OCH_2Ph), 7.10−7.40 (m, 25 H, Ph). ^{13}C NMR: δ = 14.1, 22.6, 25.8, 29.7, 31.7, 69.1, 70.3, 70.5, 71.6, 73.1, 73.3−74.9 (CH_2Ph), 74.6, 77.5, 79.6, 82.3, 103.7, 127.3−140.0 (C_6H_5). MS: *m*/*z* = 806 [M + NH_4]$^+$. $C_{50}H_{60}O_8$ (789.0): calcd. C 76.11, H 7.66; found C 76.44, H 7.38.

2-*O*-(6-*O*-Hexyl-β-D-galactopyranosyl)glycerol (1b): Palladium on activated carbon (10% 0.065 g) was added to a solution of **9** (0.66 g, 0.84 mmol) in methanol (16 mL). This mixture was shaken under hydrogen atmosphere for 4 h (TLC: *i*PrOH/EtOAc/H_2O, 3:3:1), and then filtered through Celite. After evaporation of the solvent, the product (0.28 g) was recovered as an oil in quantitative yield. $[\alpha]_D^{20}$ = −1.6 (*c* = 1.0, CH_3OH). ^1H NMR (CD_3OD): 0.90 (t, 3 H, CH_3), 1.26−1.41 (m, 6 H, 3 CH_2), 1.57 (m, 2 H, OCH_2CH_2), 3.45−3.52 (m, 3 H, 3-H and OCH_2CH_2), 3.56 (dd, $J_{1,2}$ = 8.0 Hz, $J_{2,3}$ = 10.0 Hz, 1 H, 2-H), 3.60−3.70 (m, 7 H, 5,6a,6b-H and CH_2CHCH_2), 3.75 (m, 1 H, CH_2CHCH_2), 3.79 (br. d, $J_{3,4}$ = 3.0 Hz, 1 H, 4-H), 4.37 (d, 1 H, 1-H). ^{13}C NMR (CD_3OD): 14.3, 23.6, 26.9, 30.7, 32.8, 62.8, 63.5, 70.5, 71.1, 72.6, 72.7, 74.7, 75.1, 83.7, 105.0. MS: *m*/*z* = 356 [M + NH_4]$^+$. $C_{15}H_{30}O_8$ (338.4): calcd. C 53.24, H 8.94; found C 53.31, H 9.22.

1,3-Di-*O*-benzyl-2-*O*-[(6*Z*)-2,3,4-tri-*O*-benzyl-6,7,8,9,10,11,12,13-octadeoxy-β-D-*galacto*-tridec-6-enopyranosyl]glycerol (11): A solution of oxalyl chloride (0.22 mL, 2.6 mmol) in dry dichloromethane (3 mL) was added at −60 °C to a stirred solution of DMSO (0.36 mL, 5.1 mmol) in dry dichloromethane (3 mL). After 15 min, a solution of compound **4** (0.90 g, 1.3 mmol) in dry dichloromethane (6 mL) was added dropwise, and the pale mixture was stirred for 30 min at −50 °C. Triethylamine (1.1 mL, 6.4 mmol) was added, and the reaction mixture was warmed to −40 °C. After 45 min, a saturated aqueous NH_4Cl solution (15 mL) was added

and the mixture was separated. The aqueous layer was extracted with ethyl acetate (3 × 10 mL), and the combined organic extracts were washed with brine (20 mL), dried, and concentrated. The residual aldehyde **10** (0.90 g, TLC: petroleum ether/EtOAc, 6:4, R_f = 0.5) was used without further purification.

Heptylidenetriphenylphosphorane was prepared at −50 °C by addition of butyllithium (2 mL, 1.6 M solution in hexane) to a solution of heptyltriphenylphosphonium bromide (1.53 g, 3.5 mmol) in dry THF (18 mL). After 20 min, the deep red solution of the ylide was added to a solution of the crude aldehyde **10** in dry THF (8 mL). The mixture was stirred at −50 °C for 40 min and then quenched by addition of water (1 mL). The mixture was concentrated, and the residue was dissolved in ether (20 mL) and washed with water (20 mL). The aqueous layer was extracted with ether (2 × 20 mL), and the combined organic extracts were washed with brine, dried, and concentrated. Purification of the residue by flash chromatography (toluene/EtOAc, 92:8) afforded **11** (0.46 g, 46%) as an oil. $[\alpha]_D^{20}$ = −16.0 (*c* = 1.0, $CHCl_3$). ^{1}H NMR: δ = 0.86 (t, 3 H, CH_3), 1.16−1.36 (m, 8 H, 4 CH_2), 1.80−2.00 (m, 2 H, CH_2), 3.50 (dd, $J_{2,3}$ = 9.5 Hz, $J_{3,4}$ = 3.0 Hz, 1 H, 3-H), 3.59 (br. d, 1 H, 4-H), 3.63 (dd, *J* = 10.0 Hz, 1 H, *J* = 6.0 Hz, 1 H, 2 H, CH_aH_bCH-CH_aH_b), 3.73 (dd, *J* = 4.0 Hz, 2 H, $CH_aH_bCHCH_aH_b$), 3.81 (dd, $J_{1,2}$ = 7.5 Hz, 1 H, 2-H), 4.03 (m, 1 H, 5-H), 4.07 (m, 1 H, CH_2CHCH_2), 4.59 (d, 1 H, 1-H), 4.42−5.02 (m, 10 H, OCH_2Ph), 5.43 (m, 1 H, $CH{=}CHCH_2$), 5.59 (ddt, $J_{6,1'}$ = 11.0 Hz, $J_{5,6}$ = 7.5 Hz, J_{all} = 1.0 Hz, 1 H, $CH{=}HCH_2$), 7.10−7.40 (m, 25 H, Ph). ^{13}C NMR: δ = 14.8, 23.3, 28.8, 29.6, 30.1, 32.4, 71.0, 71.2, 71.7, 73.9, 74.0, 74.1, 75.3, 75.6, 77.6, 77.9, 80.1, 82.9, 104.2, 127.3, 133.6, 127.3−140.0 (C_6H_5). MS: *m*/*z* = 802 $[M + NH_4]^+$. $C_{51}H_{60}O_7$ (785.0): calcd. C 78.03, H 7.70; found C 78.00, H 7.82.

2-*O*-(6,7,8,9,10,11,12,13-Octadeoxy-β-D-*galacto*-tridecopyranosyl)-glycerol (1c): Palladium on activated carbon (10%, 0.04 g) and one drop of AcOH were added to a mixture of **11** (0.38 g, 0.48 mmol) in MeOH (10 mL). The mixture was shaken under hydrogen and monitored by TLC (*i*PrOH/EtOAc/H_2O, 8:8:1). After 24 h, an additional quantity of the catalyst (0.04 g) and one drop of AcOH were added, and stirring was continued for 48 h. The mixture was filtered through Celite, the solvent was evaporated, and the residue was subjected to flash chromatography (CH_2Cl_2/MeOH, 85:15) to afford compound **1c** (0.16 g, quant.) as an oil. $[\alpha]_D^{20}$ = +3.4 (*c* = 1.0, CH_3OH). ^{1}H NMR (CD_3OD): 0.90 (t, 3 H, CH_3), 1.22−1.52 (m, 12 H, 6 CH_2), 1.57 (m, 1 H, 6b-H), 1.74 (m, 1 H, 6a-H), 3.45 (dd, $J_{5,6a}$ = 8.5 Hz, $J_{5,6b}$ = 5.5 Hz, 1 H, 5-H), 3.48 (dd, $J_{2,3}$ = 9.5 Hz, $J_{3,4}$ = 3.0 Hz, 1 H, 3-H), 3.53 (dd, $J_{1,2}$ = 7.5 Hz, 1 H, 2-H), 3.62−3.71 (m, 5 H, CH_2CHCH_2 and 4-H), 3.74 (m, 1 H, CH_2CHCH_2), 4.34 (d, 1 H, 1-H). ^{13}C NMR (CD_3OD): 14.4, 23.7, 26.9, 30.4, 30.6, 30.7, 31.7, 33.0, 62.7, 63.1, 71.9, 72.8, 75.0, 76.2, 83.0, 104.9. MS: *m*/*z* = 354 $[M + NH_4]^+$. $C_{16}H_{32}O_7$ (336.4): calcd. C 57.12, H 9.59; found C 57.35, H 9.38.

1,3-Di-*O*-benzyl-2-*O*-(2,3,4-tri-*O*-benzyl-6,7,9,10,11,12,13-heptadeoxy-β-D-*galacto*-tridec-6-enopyran-8-ulosyl)glycerol (12): Compound **4** (1.00 g, 1.4 mmol) was oxidized as described previously, and the crude aldehyde was diluted with dry THF (5 mL) under anhydrous conditions. A solution of 1-triphenylphosphoranylidene-2-heptanone (0.67 g, 1.8 mmol) (prepared according to ref.[12] and purified by flash chromatography: EtOAc/*i*PrOH, 8:2) in dry THF (5 mL) was added dropwise, and the reaction mixture was stirred at room temperature for 16 h. The mixture was quenched with water (20 mL), and extracted with dichloromethane (3 × 40 mL). The combined organic extracts were washed with water and brine, and dried with sodium sulfate, and the solvents were evaporated under reduce pressure. Flash chromatography (petroleum ether/EtOAc, 85:15, then 8:2) of the residue allowed compound (*Z*)-**12** (0.57 g) to be recovered first as an oil, and then (*E*)-**12** (0.38 g) as a white solid (overall yield = 84%).

(*Z*)-12: $[\alpha]_D^{20}$ = −73.0 (*c* = 1.1, $CHCl_3$). ^{1}H NMR ($CDCl_3$ on Al_2O_3): 0.90 (t, 3 H, CH_3), 1.20−1.36 (m, 4 H, 2 CH_2), 1.52 (m, 2 H, CH_2), 2.26−2.44 (m, 2 H, $COCH_2$), 3.58−3.75 (m, 5 H, 3-H and CH_2CHCH_2), 3.82 (dd, $J_{1,2}$ = 7.5 Hz, $J_{2,3}$ = 9.5 Hz, 1 H, 2-H), 4.04 (m, 1 H, CH_2CHCH_2), 4.10 (br. d, $J_{3,4}$ = 3.0 Hz, 1 H, 4-H), 4.57 (d, 1 H, 1-H), 4.73 (d, $J_{5,6}$ = 6.5 Hz, 1 H, 5-H), 4.40−5.00 (m, 10 H, OCH_2Ph), 5.96 (br. d, $J_{6,1'}$ = 11.5 Hz, 1 H, $CH{=}CHCO$), 6.12 (dd, 1 H, 6-H), 7.10−7.50 (m, 25 H, Ph). ^{13}C NMR ($CDCl_3$ on Al_2O_3): 14.6, 23.1, 24.2, 32.0, 44.7, 71.0 (2 C), 73.5, 73.9, 74.0 (2 C), 75.2, 75.6, 77.0, 78.1, 80.0, 83.0, 103.8, 126.0, 127.9−139.8 (C_6H_5), 146.5, 201.9. MS: *m*/*z* = 816 $[M + NH_4]^+$. $C_{51}H_{58}O_8$ (799.0): calcd. C 76.66, H 7.32; found C 76.80, H 7.40.

(*E*)-12: M.p. 78 °C (from hexane). $[\alpha]_D^{20}$ = −4.0 (*c* = 1.0, $CHCl_3$). ^{1}H NMR: δ = 0.86 (t, 3 H, CH_3), 1.26 (m, 4 H, 2 CH_2), 1.55 (m, 2 H, CH_2), 2.38 (t, 2 H, $COCH_2$), 3.51 (dd, $J_{2,3}$ = 9.5 Hz, $J_{3,4}$ = 3.0 Hz, 1 H, 3-H), 3.60−3.80 (m, 5 H, 4-H and CH_2CHCH_2), 3.83 (dd, $J_{1,2}$ = 8.0 Hz, 1 H, 2-H), 3.90 (m, 1 H, 5-H), 4.11 (m, 1 H, CH_2CHCH_2), 4.63 (d, 1 H, 1-H), 4.40−5.04 (m, 10 H, OCH_2Ph), 6.26 (dd, $J_{6,1'}$ = 16.0 Hz, $J_{1',5}$ 1.0 Hz, 1 H, $CH{=}CHCO$), 6.54 (dd, $J_{5,6}$ = 4.0 Hz, 1 H, 6-H), 7.10−7.50 (m, 25 H, Ph). ^{13}C NMR: δ = 14.6, 23.1, 24.3, 32.1, 41.5, 71.1, 71.3, 74.0 (2 C), 74.4 (2 C), 75.0, 75.7, 76.2, 78.2, 79.9, 82.6, 104.1, 128.0−139.6 (C_6H_5), 130.6, 141.9, 200.7. MS: *m*/*z* = 816 $[M + NH_4]^+$. $C_{51}H_{58}O_8$ (799.0): calcd. C 76.66, H 7.32; found C 76.92, H 7.30.

2-*O*-(6,7,9,10,11,12,13-Heptadeoxy-β-D-*galacto*-tridecopyran-8-ulosyl)glycerol (1d): Palladium on activated carbon (10%, 0.035 g) and two drops of AcOH were added to a mixture of (*E*,*Z*)-**12** (0.35 g, 0.439 mmol) in MeOH (10 mL). The mixture was shaken under hydrogen for 24 h; an additional quantity of the catalyst (0.04 g) and one drop of AcOH were again added, and stirring continued for 48 h. The mixture was filtered through Celite, evaporated to dryness, and diluted with water. This solution was treated with Dowex 50 × 8 (H^+ form) under reduced pressure (12 Torr) at 50 °C for 10 min; after filtration the solution was lyophilized to afford the desired **1d** (0.15 g, quant.) as a foam. $[\alpha]_D^{20}$ = +9.0 (*c* = 1.0, H_2O). ^{1}H NMR (D_2O): 0.70 (t, 3 H, CH_3), 1.11 (m, 4 H, 2 CH_2), 1.38 (m, 2 H, CH_2), 1.64 (m, 1 H, 6b-H), 1.77 (m, 1 H, 6a-H), 2.38 (t, 2 H, CH_2CO), 2.53 (t, 2 H, CH_2CO), 3.31−3.40 (m, 2 H, 2,5-H), 3.45 (dd, $J_{2,3}$ = 10.0 Hz, $J_{3,4}$ = 3.0 Hz, 1 H, 3-H), 3.50−3.61 (m, 4 H, CH_2CHCH_2), 3.62 (br. d, 1 H, 4-H), 3.67 (m, 1 H, CH_2CHCH_2), 4.28 (d, $J_{1,2}$ = 8.0 Hz, 1 H, 1-H). ^{13}C NMR (D_2O): 14.0, 22.6, 24.1, 25.2, 31.5, 39.4, 43.2, 61.6, 62.2, 71.2, 71.7, 73.6, 74.7, 81.5, 103.4, 219.1. MS: *m*/*z* = 368 $[M + NH_4]^+$. $C_{16}H_{30}O_8$ (350.4): calcd. C 54.84, H 8.63; found C 54.98, H 8.75.

3-*O*-Benzyl-1-*O*-hexyl-2-*O*-(2,3,4,6-tetra-*O*-acetyl-β-D-galacto-pyranosyl)*sn*-glycerol (13): Boron trifluoride−diethyl ether (0.19 mL, 1.51 mmol) was added dropwise at 0 °C under argon to a solution of β-D-galactose pentaacetate (0.59 g, 1.5 mmol) and **5a** (0.20 g, 0.76 mmol) in dry dichloromethane (5 mL). The reaction mixture was allowed to warm to room temperature, stirred for an additional 1 h, and then quenched by addition of saturated $NaHCO_3$ solution (5 mL). The aqueous layer was extracted with dichloromethane (3 × 5 mL). The combined organic layers were then washed with brine and dried, and the solvents were evaporated under reduced pressure. The residue was purified by flash chromatography (petroleum ether/EtOAc, 7.5:2.5, then 7:3) to yield **13** (0.38 g, 84%) as an oil. $[\alpha]_D^{20}$ = −1.7 (*c* = 1.0, $CHCl_3$). ^{1}H NMR: δ = 0.87 (t, 3 H, CH_3), 1.22−1.36 (m, 6 H, 3 CH_2), 1.43 (m, 2 H, OCH_2CH_2), 1.96, 1.99, 2.01, and 2.12 (4 s, 12 H, CH_3CO), 3.38

(m, 2 H, OCH_2CH$_2$), 3.43 (dd, J = 10.5 Hz, J = 7.0 Hz, 1 H, CH_aH$_b$CHCH$_a$H$_b$), 3.51 (dd, J = 10.5 Hz, J = 6.0 Hz, 1 H, CH$_a$H$_b$CHCH_aH$_b$), 3.58 (dd, J = 3.5 Hz, 1 H, CH$_a$$H_b$CHCH$_aH_b$), 3.62 (dd, J = 4.5 Hz, 1 H, CH$_a$H$_b$CHCH$_a$$H_b$), 3.84 (m, 1 H, 5-H), 3.96 (m, 1 H, CH$_2$CHCH$_2$), 4.10 (m, 2 H, 2 × 6-H), 4.51 (s, 2 H, OCH$_2$Ph), 4.72 (d, $J_{1,2}$ = 8.0 Hz, 1 H, 1-H), 4.98 (dd, $J_{3,4}$ = 3.5 Hz, 1 H, 3-H), 5.17 (dd, $J_{2,3}$ = 10.5 Hz, 1 H, 2-H), 5.35 (br. d, 1 H, 4-H), 7.20−7.36 (m, 5 H, Ph). ^{13}C NMR: δ = 14.7, 21.3, 23.3, 26.5, 30.3, 32.6, 62.0, 67.8, 69.8, 70.8, 71.3, 71.7, 72.2, 72.4, 74.0, 79.0, 102.0, 128.3, 129.0, 170.0, 171.0. MS: m/z = 614 [M + NH$_4$]$^+$. C$_{30}$H$_{44}$O$_{12}$ (596.7): calcd. C 60.39, H 7.43; found C 60.61, H 7.15.

(2*R*)-1-*O*-Benzyl-2-*O*-(2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl)-decane-1,2-diol (14): This compound was obtained from β-D-galactose pentaacetate (0.47 g, 1.2 mmol) and **5b** (0.16 g, 0.6 mmol) as described for compound **13**. The reaction mixture was stirred at room temperature for 2 h. Purification by flash chromatography (petroleum ether/EtOAc, 7:3) gave **14** (0.28 g, 79%) as an oil. $[\alpha]_D^{20}$ = +7.0 (c = 1.0, CHCl$_3$). ^{1}H NMR: δ = 0.85 (t, 3 H, CH$_3$), 1.16−1.41 (m, 12 H, 6 CH$_2$), 1.46−1.64 (m, 2 H, CHCH_2CH$_2$), 1.95, 1.99, 2.01, and 2.12 (4 s, 12 H, OCOCH$_3$), 3.44 (dd, J = 9.5 Hz, J = 5.5 Hz, 1 H, CH$_a$$H_b$OBzl), 3.63 (dd, J = 4.5 Hz, 1 H, CH_aH$_b$OBzl), 3.69 (m, 1 H, CH$_2$CHCH$_2$), 3.83 (t, $J_{5,6b}$ = $J_{5,6a}$ = 6.5 Hz, 1 H, 5-H), 4.08 (m, 2 H, 2 × 6-H), 4.51 (s, 2 H, OCH$_2$Ph), 4.56 (d, $J_{1,2}$ = 8.0 Hz, 1 H, 1-H), 4.98 (dd, $J_{2,3}$ = 10.5 Hz, $J_{3,4}$ = 3.5 Hz, 1 H, 3-H), 5.18 (dd, 1 H, 2-H), 5.35 (br. d, 1 H, 4-H), 7.18−7.40 (*m*, 5 H, Ph). ^{13}C NMR: δ = 14.7, 21.3 (4 C), 23.3, 25.8, 29.9, 30.2, 30.4, 32.5, 32.8, 62.0, 67.8, 70.0, 71.3, 71.7, 73.5, 74.0, 81.6, 102.4, 128.3−139.0 (C$_6$H$_5$), 169.9−171.0 (*C*OCH$_3$). MS: m/z = 612 [M + NH$_4$]$^+$. C$_{31}$H$_{46}$O$_{11}$ (594.7): calcd. C 62.61, H 7.80; found C 62.26, H 7.65.

3-*O*-Benzyl-1-*O*-hexyl-2-*O*-(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl)-*sn*-glycerol (15): This compound was obtained from β-D-glucose pentaacetate (0.59 g, 1.5 mmol) and **5a** (0.20 g, 0.75 mmol) as described for **13**. The reaction mixture was stirred at room temperature for 1.5 h. After flash chromatography (petroleum ether/EtOAc, 7:3), **15** (0.37 g) was recovered in 83% yield as an oil. $[\alpha]_D^{20}$ = −9.2 (c = 1.0, CH$_3$OH). ^{1}H NMR: δ = 0.88 (t, 3 H, CH$_3$), 1.22−1.34 (m, 6 H, 3 CH$_2$), 1.53 (m, 2 H, OCH$_2$CH_2), 1.98, 2.00, 2.01, and 2.04 (4 s, 12 H, CH$_3$CO), 3.38 (m, 2 H, OCH_2CH$_2$), 3.41−3.66 (m, 5 H, 5-H and CH_2CHCH_2), 3.98 (m, 1 H, CH$_2$CHCH$_2$), 4.09 (dd, $J_{6a,6b}$ = 12.0 Hz, $J_{5,6b}$ = 2.0 Hz, 1 H, 6b-H), 4.20 (dd, $J_{5,6a}$ = 5.0 Hz, 1 H, 6a-H), 4.52 (s, 2 H, OCH$_2$Ph), 4.78 (d, $J_{1,2}$ = 8.0 Hz, 1 H, 1-H), 4.96 (dd, $J_{2,3}$ = 9.0 Hz, 1 H, 2-H), 5.05 (dd, $J_{3,4}$ = $J_{4,5}$ = 9.5 Hz, 1 H, 4-H), 5.18 (dd, 1 H, 3-H), 7.20−7.40 (m, 5 H, Ph). ^{13}C NMR: δ = 14.7, 21.2−21.4 (CO*C*H$_3$), 23.3, 26.5, 30.3, 32.3, 62.8, 69.3, 70.9, 72.2, 72.3, 72.4, 72.5, 73.6, 74.0, 78.9, 101.3, 128.2−139.0 (C$_6$H$_5$), 170.0−171.3 (*C*OCH$_3$). MS: m/z = 614 [M + NH$_4$]$^+$. C$_{30}$H$_{44}$O$_{12}$ (596.7): calcd. C 60.39, H 7.43; found C 60.67, H 7.30.

(2*R*)-1-*O*-Benzyl-2-*O*-(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl)-decane-1,2-diol (16): The reaction was carried out as described for the synthesis of compound **13**, starting from β-D-glucose pentaacetate (0.33 g, 0.84 mmol) and **5b** (0.11 g, 0.42 mmol). Compound **16** (0.15 g, 60%) was obtained after flash chromatography (petroleum ether/EtOAc, 8:2, then 7:3) as an amorphous white solid. $[\alpha]_D^{20}$ = −1.0 (c = 1.0, CHCl$_3$). ^{1}H NMR: δ = 0.86 (t, 3 H, CH$_3$), 1.16−1.60 (m, 14 H, 7 CH$_2$), 1.97, 1.99, 2.00, and 2.03 (4 s, 12 H, CH$_3$CO), 3.43 (dd, J = 10.0 Hz, J = 5.5 Hz, 1 H, CH$_a$$H_b$OBzl), 3.57−3.65 (m, 2 H, 5-H and CH_aH$_b$OBzl), 3.69 (m, 1 H, CH$_2$CHCH$_2$), 4.05 (dd, $J_{6a,6b}$ = 12.0 Hz, $J_{5,6b}$ = 2.0 Hz, 1 H, 6b-H), 4.17 (dd, $J_{5,6a}$ = 4.5 Hz, 1 H, 6a-H), 4.50 (s, 2 H, OCH$_2$Ph), 4.59 (d, $J_{1,2}$ = 8.0 Hz, 1 H, 1-H), 4.96 (dd, $J_{2,3}$ = 9.5 Hz, 1 H, 2-H), 5.04 (dd, $J_{4,5}$ = 9.5 Hz, $J_{3,4}$ = 9.5 Hz, 1 H, 4-H), 5.16 (dd, 1 H, 3-H), 7.18−7.36 (m, 5 H, Ph). ^{13}C NMR: δ = 14.7, 21.2−21.4 (CO*C*H$_3$), 23.3, 25.8, 29.9, 30.2, 30.3, 32.5, 32.8, 62.8, 69.2, 72.4 (2 C), 73.5, 73.7, 74.0, 81.5, 101.9, 128.2−140.0 (C$_6$H$_5$), 170.0−171.3 (*C*OCH$_3$). MS: m/z = 612 [M + NH$_4$]$^+$. C$_{31}$H$_{46}$O$_{11}$ (594.7): calcd. C 62.61, H 7.80; found C 62.85, H 7.70.

3-*O*-Benzyl-2-*O*-β-D-galactopyranosyl-1-*O*-hexyl-*sn*-glycerol (17): Sodium methoxide (0.8 M solution in MeOH, 2.3 mL) was added to a solution of **13** (0.37 g, 0.62 mmol) in methanol (8 mL). After 2 h at room temperature, the reaction mixture was neutralized with Dowex 50 × 8 (H$^+$ form) and then filtered. The solvent was removed under reduced pressure, to afford pure **17** (0.26 g, quant) as an oil. $[\alpha]_D^{20}$ = −5.0 (c = 1.0, CH$_3$OH). ^{1}H NMR (CD$_3$OD): 0.91 (t, 3 H, CH$_3$). 1.25−1.40 (m, 6 H, 3 CH$_2$), 1.56 (m, 2 H, OCH$_2$CH_2), 3.42−3.56 (m, 5 H, 2,3,5-H and OCH_2CH$_2$), 3.56−3.78 (m, 6 H, 6a,6b-H and CH_2CHCH_2), 3.82 (m, 1 H, 4-H), 4.07 (m, 1 H, CH$_2$CHCH$_2$), 4.42 (d, $J_{1,2}$ = 7.5 Hz, 1 H, 1-H), 4.56 (m, 2 H, OCH$_2$Ph), 7.05−7.08 (m, 5 H, Ph). ^{13}C NMR (CD$_3$OD): 14.4, 23.7, 26.9, 30.7, 32.8, 62.5, 70.2, 71.4 (2 C), 72.7 (2 C), 74.4, 74.8, 76.8, 77.8, 104.6, 128.7−139.6 (C$_6$H$_5$). MS: m/z = 446 [M + NH$_4$]$^+$. C$_{22}$H$_{36}$O$_8$ (428.5): calcd. C 61.66, H 8.47; found C 61.46, H 8.40.

(2*R*)-1-*O*-Benzyl-2-*O*-β-D-galactopyranosyldecane-1,2-diol (18): The procedure used to prepare **17** was utilized to convert a solution of **14** (0.27 g, 0.46 mmol) in 1 mL of methanol, into **18** in quantitative yield. Waxy solid. $[\alpha]_D^{20}$ = −4.0 (c = 1.0, CH$_3$OH). ^{1}H NMR (CD$_3$OD): 0.90 (t, 3 H, CH$_3$), 1.21−1.49 (m, 12 H, 6 CH$_2$), 1.52−1.69 (m, 2 H, CHCH_2CH$_2$), 3.42−3.53 (m, 3 H, 2,3,5-H), 3.56 (dd, J = 10.0 Hz, J = 5.0 Hz, 1 H, CH$_a$$H_b$OBzl), 3.65 (dd, J = 4.5 Hz, 1 H, CH_aH$_b$OBzl), 3.72 (m, 2 H, 2 6-H), 3.83 (br. d, $J_{3,4}$ = 3.0 Hz, 1 H, 4-H), 3.85 (m, 1 H, CH$_2$CHCH$_2$), 4.31 (d, $J_{1,2}$ = 7.5 Hz, 1 H, 1-H), 4.52 and 4.57 (2 d, J = 12.0 Hz, 2 H, OCH$_2$Ph), 7.04−7.08 (*m*, 5 H, Ph). ^{13}C NMR (CD$_3$OD): 14.4, 23.7, 26.1, 30.4, 30.6, 30.9, 32.6, 33.1, 62.4, 70.3, 72.7, 73.7, 74.3, 75.0, 76.6, 79.3, 104.5, 128.6−140.0 (C$_6$H$_5$). MS: m/z = 444 [M + NH$_4$]$^+$. C$_{23}$H$_{38}$O$_7$ (426.5): calcd. C 64.76, H 8.98; found C 64.92, H 8.70.

3-*O*-Benzyl-2-*O*-β-D-glucopyranosyl-1-*O*-hexyl-*sn*-glycerol (19): A solution of **15** (0.36 g, 0.60 mmol) in methanol (2 mL) was treated for 1.5 h at room temperature with the same procedure as used for **17** to give **19** quantitatively as an oil. $[\alpha]_D^{20}$ = −14.6 (c = 1.0, CH$_3$OH). ^{1}H NMR (CD$_3$OD): 0.91 (t, 3 H, CH$_3$), 1.23−1.40 (m, 6 H, 3 CH$_2$), 1.55 (m, 2 H, OCH$_2$CH_2), 3.20 (dd, $J_{1,2}$ = 8.0 Hz, $J_{2,3}$ = 8.5 Hz, 1 H, 2-H), 3.23−3.39 (m, 3 H, 3,4,5-H), 3.47 (m, 2 H, OCH_2CH$_2$), 3.57−3.70 (m, 5 H, 6b-H and CH_2CHCH_2), 3.85 (dd, $J_{5,6a}$ = 2.0 Hz, $J_{6a,6b}$ = 12.0 Hz, 1 H, 6a-H), 4.07 (m, 1 H, CH$_2$CHCH$_2$), 4.48 (d, 1 H, 1-H), 4.56 (*s*, 2 H, OCH$_2$Ph), 7.04−7.08 (m, 5 H, Ph). ^{13}C NMR (CD$_3$OD): 14.4, 23.7, 26.9, 30.7, 32.8, 62.8, 71.4 (2 C), 71.6, 72.7, 74.4, 75.2, 77.9 (2 C), 78.0, 103.8, 128.7−139.5 (C$_6$H$_5$). MS: m/z = 446 [M + NH$_4$]$^+$. C$_{22}$H$_{36}$O$_8$ (428.5): calcd. C 61.66, H 8.47; found C 61.94, H 8.39.

(2*R*)-1-*O*-Benzyl-2-*O*-β-D-glucopyranosyldecane-1,2-diol (20): This compound was obtained quantitatively as an oil from **16** (0.15 g, 0.25 mmol), as described for **17**. $[\alpha]_D^{20}$ = −13.0 (c = 1, CH$_3$OH). ^{1}H NMR (CD$_3$OD): 0.89 (t, 3 H, CH$_3$), 1.21−1.47 (m, 12 H, 6 CH$_2$), 1.52−1.68 (m, 2 H, CHCH_2CH$_2$), 3.18 (dd, $J_{1,2}$ = 8.0 Hz, $J_{2,3}$ = 9.0 Hz, 1 H, 2-H), 3.22−3.39 (m, 3 H, 3,4,5-H), 3.57 (dd, J = 10.5, J = 5.0 Hz, 1 H, CH$_a$$H_b$OBzl), 3.62−3.69 (m, 2 H, 6b-H and CH_aH$_b$OBzl), 3.81−3.89 (m, 2 H, 6a-H and CH$_2$CHCH$_2$), 4.35 (d, 1 H, 1-H), 4.54 and 4.58 (2 d, 2 H, OCH$_2$Ph), 7.03−7.09 (m, 5 H, Ph). ^{13}C NMR (CD$_3$OD): 14.4, 23.7, 26.1, 30.4, 30.6, 30.9, 32.6, 33.1, 62.9, 71.7, 73.7, 74.4, 75.2, 77.9, 78.0, 79.5, 103.8,

128.7−139.7 (C_6H_5). MS: m/z = 444 $[M + NH_4]^+$. $C_{23}H_{38}O_7$ (426.5): calcd. C 64.76, H 8.98; found C 64.60, H 9.02.

2-*O*-β-D-Galactopyranosyl-1-*O*-hexyl-*sn*-glycerol (2b): Palladium on activated carbon (10%, 0.026 g) and a few drops of AcOH were added to a solution of **17** (0.25 g, 0.58 mmol) in MeOH (6 mL). The mixture was shaken under hydrogen and monitored by TLC (EtOAc/MeOH, 8:2). After 24 h, an additional quantity of the catalyst (0.006 g) was added, and stirring was continued for 48 h. The mixture was filtered through Celite, the solvent was evaporated, and the residue was subjected to flash chromatography (EtOAc/MeOH, 8:2) to afford **2b** (0.18, 91%) as an oil. $[\alpha]_D^{20} = -14.0$ (c = 1.0, CH_3OH). ^1H NMR (CD_3OD): 0.91 (t, 3 H, CH_3), 1.25−1.40 (m, 6 H, 3 CH_2), 1.57 (m, 2 H, OCH_2CH_2), 3.45−3.50 (m, 3 H, 3-H and OCH_2CH_2), 3.51−3.79 (m, 8 H, 2,5,6a,6b-H and CH_2CHCH_2), 3.82 (br. d, $J_{3,4}$ = 3.0 Hz, 1 H, 4-H), 3.91 (m, 1 H, CH_2CHCH_2), 4.39 (d, $J_{1,2}$ = 7.5 Hz, 1 H, 1-H). ^{13}C NMR (CD_3OD): 14.4, 23.7, 26.9, 30.7, 32.8, 62.6, 63.7, 70.3, 71.4, 72.7 (2 C), 74.8, 76.8, 80.5, 104.6. MS: m/z = 356 $[M + NH_4]^+$. $C_{15}H_{30}O_8$ (338.4): calcd. C 53.24, H 8.94; found C 52.90, H 8.80.

(2*R*)-2-*O*-β-D-Galactopyranosyldecane-1,2-diol (2c): Palladium on activated carbon (10% 0.02 g) and one drop of AcOH were added to a solution of **18** (0.19 g, 0.45 mmol) in methanol (4.5 mL). The mixture was shaken under hydrogen for 20 h and then filtered through Celite. After evaporation of the solvent, pure **2c** was obtained quantitatively as an amorphous solid. $[\alpha]_D^{20} = -7.0$ (c = 1.0, CH_3OH). ^1H NMR (CD_3OD): 0.90 (t, 3 H, CH_3), 1.23−1.64 (m, 14 H, 7 CH_2), 3.48 (dd, $J_{2,3}$ = 10.0 Hz, $J_{3,4}$ = 3.0 Hz, 1 H, 3-H), 3.50−3.59 (m, 4 H, 2,5-H and CH_2OH), 3.66−3.79 (m, 3 H, 2 6-H and CH_2CHCH_2), 3.82 (br. d, 1 H, 4-H), 4.29 (d, $J_{1,2}$ = 7.5 Hz, 1 H, 1-H). ^{13}C NMR (CD_3OD): 14.4, 23.7, 26.4, 30.4, 30.7, 30.9, 32.6, 33.1, 62.5, 66.1, 70.3, 72.7, 74.9, 76.7, 82.8, 104.7. MS: m/z = 354 $[M + NH_4]^+$. $C_{16}H_{32}O_7$ (336.4): calcd. C 57.12, H 9.59; found C 56.87, H 9.40.

2-*O*-β-D-Glucopyranosyl-1-*O*-hexyl-*sn*-glycerol (3b): This compound was obtained quantitatively as an oil, starting from **19** (0.23 g, 0.54 mmol), as described for **2c**. $[\alpha]_D^{20} = -24.5$ (c = 1.0, CH_3OH). ^1H NMR (CD_3OD): 0.91 (t, 3 H, CH_3), 1.25−1.42 (m, 6 H, 3 CH_2), 1.57 (m, 2 H, OCH_2CH_2), 3.21 (dd, $J_{2,3}$ = 9.0 Hz, $J_{1,2}$ = 7.5 Hz, 1 H, 2-H), 3.25−3.39 (m, 3 H, 3,4,5-H), 3.48 (m, 2 H, OCH_2CH_2), 3.53−3.70 (m, 5 H, 6b-H and CH_2CHCH_2), 3.83−3.94 (m, 2 H, 6a-H and CH_2CHCH_2), 4.45 (d, 1 H, 1-H). ^{13}C NMR (CD_3OD): 14.4, 23.7, 26.9, 30.7, 32.8, 62.6, 63.6, 71.4, 71.5, 72.7, 75.1, 77.8, 77.9, 80.4, 104.0. MS: m/z = 356 $[M + NH_4]^+$. $C_{15}H_{30}O_8$ (338.4): calcd. C 53.24, H 8.94; found C 53.50, H 9.15.

(2*R*)-2-*O*-β-D-Glucopyranosyldecane-1,2-diol (3c): Palladium on activated carbon (10%, 0.01 g) and one drop of AcOH were added to a solution of **20** (0.094 g, 0.22 mmol) in MeOH (2.5 mL). The mixture was shaken under hydrogen and monitored by TLC (EtOAc/MeOH, 8:2). After 24 h, a further 0.006 g of the catalyst and a few drops of AcOH were added, and stirring was continued for additional 48 h. The mixture was filtered through Celite, and, after evaporation of the solvent, pure **3c** was obtained in quantitative yield as an amorphous solid. $[\alpha]_D^{20} = -16.0$ (c = 1.0, CH_3OH). ^1H NMR (CD_3OD): 0.90 (t, 3 H, CH_3), 1.21−1.63 (m, 14 H, 7 CH_2), 3.20 (dd, $J_{2,3}$ = 8.0 Hz, $J_{1,2}$ = 7.5 Hz, 1 H, 2-H), 3.25−3.40 (m, 2 H, 3,5-H), 3.52−3.74 (m, 5 H, 4,6b-H, CH_2CHCH_2, and CH_2OBzl), 3.89 (br. d, $J_{6a,6b}$ = 12.0 Hz, 1 H, 6a-H), 4.33 (d, 1 H, 1-H). ^{13}C NMR (CD_3OD): 14.5, 23.7, 26.4, 30.4, 30.6, 30.9, 32.6, 33.1, 62.6, 65.9, 71.6, 75.2, 77.8, 78.0, 82.9, 104.1. MS: m/z = 354 $[M + NH_4]^+$. $C_{16}H_{32}O_7$ (336.4): calcd. C 57.12, H 9.59; found C 57.20, H 9.90.

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