RSC Advances

PAPER

An unusual Wittig reaction with sugar derivatives: exclusive formation of a 4-deoxy analogue of α-galactosyl ceramide†

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The Wittig reaction of the pyrano-type reducing sugars undergoes an unexpected formation of dienes through the elimination of a benzyloxy group in the presence of t-BuOK. LiHMDS is used rather than t-BuOK to prevent alcohol elimination in the same sugar derivatives. Collectively, t-BuOK has unusual functions in the Wittig reaction that correspond with other bases such as LiHMDS, NaH, and n-BuLi. This unusual function of t-BuOK showed that a unique 4-deoxy-5-hydroxyl analogue **2** of α-galactosyl ceramide was formed exclusively.

Introduction

The Wittig reaction is one of the most commonly used methods for the synthesis of alkenes which has attracted substantial interest from the scientific community.[1] The mild reaction conditions, high yields, and the absence of migration for the formed bond are notable features of the Wittig reaction. The remarkable success of the Wittig reaction in synthetic organic chemistry originates from using phosphonium ylides with the formation of phosphonium oxide as a side product, which drives the reaction to completion. The chemistry of the Wittig reaction was initially applied to sugars by Kuhn and Brossmer in 1962, who reacted glyceraldehyde with (carbethoxy-methylene) triphenyl-phosphorane.[2] Thereafter, notable applications of this reaction were expanded in various directions for approximately 6 decades.[3] Usually the carbonyl olefin product is often achieved in normal condition of Wittig reaction. Interestingly, previous reports have demonstrated that 2-deoxy sugars undergoes base promoted β-elimination to form corresponding dienes.[4] It is worth mentioning here that there are few reports appeared recently describing the elimination reaction of pyrano-sugar derivatives[5] as well as α,β-elimination of anomeric form of pyranoses which provided the dienes under the influence of base[6] during the Wittig reaction.

The α-galactosyl ceramide **1** (ref. 7) (α-GalCer) is also referred to as KRN7000 (Fig. 1), and is a commonly known significant compound that is best characterized as an antigen for CD1d-reactive T cells in mice and humans.[8] The structure of the 4-deoxy-5-hydroxyl analog **2** (Fig. 1) of α-GalCer is composed of
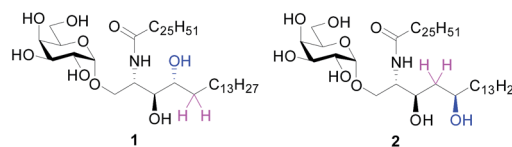
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† Electronic supplementary information (ESI) available. See DOI: 10.1039/c4ra03369h

Fig. 1 α-Galactosyl ceramide **1** and its 4-deoxy-5-hydroxyl analogue **2**.

an α-linked D-galacto-pyranoside with phytosphingosine-like ceramide. The hydroxyl groups of α-galactosyl ceramide (α-GalCer) **1** play significant role through hydrogen bonding with various proteins[9] that can be recognize with the help of X-ray crystallographic analysis.[20]

Kim *et al.* disclosed the role of the 4-hydroxyl group for CD1d-mediated NKT cell activation.[10] Van Calenbergh conducted synthesis and *in vitro* evaluation of α-GalCer epimers.[11] Because of its unique structure, no study has reported a method for the synthesis of analogue **2**. However, we herein report the straightforward synthesis of 4-deoxy-5-hydroxyl analogue **2** (Fig. 1) by applying an unusual Wittig reaction with reducing disaccharides.

Results and discussion

We recently published a concise synthesis of α-galactosyl ceramide from D-galactosyl iodide and D-lyxose[12a] and conducted a study to prepare the derivatives of α-galactosyl ceramide.[12b] However, we attempted to prepare α-GalCer analogues in the phytosphingolipid chain that contain one additional hydroxyl group compared to phytosphingosine. Kim and co-workers[10] reported the 3-deoxy and 4-deoxy analogues of α-GalCer with results of their biological evaluation but they

required additional steps to finalize the synthesis of related analogues by using different precursors (Fig. 2).

We began by stereoselectively and regioselectively preparing the key disaccharides (**5a**–**5c**) from a well-azeotroped solution of 2,3,4,6-tetra-*O*-benzyl-D-galactosyl iodide (**3**) and hexopyranoses (**4a**–**4c**).[12b] The galactosyl iodide **3** (ref. 13) was prepared *in situ* *via* the treatment of 2,3,4,6-tetra-*O*-benzyl-D-galactosyl acetate with iodo-trimethylsilane. The *in situ* generated **3** was then treated with hexopyranoses (**4a**–**4c**) in the presence of *N,N*-diisopropylethylamine (DIPEA, 1 equiv.) and tetra-*n*-butylammonium iodide (TBAI, 3 equiv.) in toluene for 1 h at 65 °C, followed by azeotropic distillation, provided α-linked disaccharides (**5a**–**5c**) containing protected D-galactose **4a**, D-glucose **4b**, and D-mannose **4c** (ref. 14) (Table 1) in good overall yields.[13]

The Wittig reaction was performed using the *in situ* generation of phosphorane[15] with addition of *t*-BuOK[16] to the well-stirred suspension of D-galactose hemiacetal **5a** and phosphonium salt at 0 °C, which produced the undesired product **6a** in 3 h in an excellent yield (96%, entry 1, Table 1). The effects of changing bases for the formation of eliminated (**6a**, **6b**) and expected (**7a**–**7c**) compounds during the Wittig reaction are shown in Table 1.

We initially expected to obtain the olefination product **7a** from the Wittig reaction of the hemiacetal of D-galactose **5a** by using *t*-BuOK, but ^{1}H NMR analysis of the reaction product indicated that one set of benzyl protons disappeared, and one additional double bond proton appeared in the olefin region of the proton spectrum. Moreover, the ^{13}C NMR spectrum showed one additional downfield peak at δ 154 ppm, which belongs to diene C-5 of the sphingosine chain of **6a**. The formation of **6a** and **6b** are probably due to initial base-promoted elimination in the ring-opened isomers of **5a** to **5c** and furnished the olefination products **6a** and **6b**. The change in the number of equivalent of *t*-BuOK from 4 to 3 in the similar reaction resulted in a decreased yield of product to 56% (entry 2, Table 1). Using sodium hydride formed only 4% of the desired product **7a** (entry 3, Table 1), and *n*-butyl lithium resulted in trace amounts of the desired single olefination compound **7a** on the TLC plate (entry 4, Table 1). It is worth mentioning here that when we have employed some stronger bases, such as NaH[16] and *n*-BuLi,[17] we didn't obtain the unexpected diene derivative. However, the expected olefination products were obtained in very low yields (Table 1).

We then applied the similar Wittig reaction exhibiting the D-galactosyl hemiacetal **5a** by using the hindered strong base LiHMDS.[18] We obtained the expected olefination compound **7a**, in an excellent yield (90%, entry 5, Table 1). This Wittig reaction of hemiacetal **5a** with LiHMDS takes 24 hours, because the hemiacetal cannot consume before 24 hours. The Similar
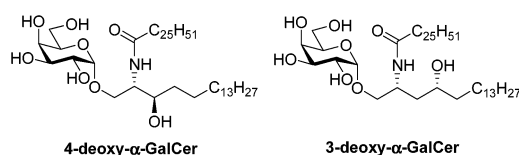
Table 1 Effect of various bases on Wittig reaction of disaccharides

Entry	SM	Base	Product (yield)
1	**5a**	4 equiv. *t*-BuOK	**6a** (96%)
2	**5a**	3 equiv. *t*-BuOK	**6a** (56%)
3	**5a**	3 equiv. NaH	**7a** (04%)
4	**5a**	2.5 equiv. *n*-BuLi	**7a** (trace)
5	**5a**	6 equiv. LiHMDS	**7a** (90%)
6	**5b**	4 equiv. *t*-BuOK	**6b** (66%)
7	**5b**	6 equiv. LiHMDS	**7b** (72%)
8	**5c**	4 equiv. *t*-BuOK	**6b** (84%)
9	**5c**	6 equiv. LiHMDS	**7c** (72%)

results were observed during the Wittig reaction of the hemiacetal of D-glucose **5b** and D-mannose **5c** when using the base LiHMDS, wherein we formed the expected single olefination compounds **7b** and **7c** in favorable yields (entry 7 and entry 9, Table 1). Moreover, using *t*-BuOK in the Wittig reactions of the hemiacetal of D-glucose **5b** and D-mannose **5c** produced the same unexpected dienes **6b** in moderate to favorable yields (entry 6 and entry 8, Table 1). Conversely, this unexpected formation of 4-deoxy sugars occurred through the elimination of the benzyloxy group at the C-3 position during the Wittig reaction of sugar derivatives (**5a**–**5c**).

For further study of these unusual Wittig products, we have carried out the Wittig reaction of hexapyranose sugars **8** as shown in Table 2. In this regard, first, we have treated galactosyl hemiacetal **8a** with *t*-BuOK and phosphonium salt in THF at 0 °C (entry 1, Table 2) which provided eliminated compound **9a** in 71% isolated yield. Similarly, the reaction of glucosyl hemiacetal **8b** (entry 3, Table 2) and mannosyl hemiacetal **8c** (entry 5, Table 2) with phosphonium salt and *t*-BuOK in THF at 0 °C produced eliminated compound **9b** in 90 and 79% yield respectively. We have also employed talosyl pyrano-reducing sugar **8d** for such kind of transformation under same reaction conditions, which provided eliminated diene **9a** and expected olefin **10d** in good yields (entry 7 and entry 8, Table 2).


Fig. 2 α-GalCer analogues reported by Kim *et al.*[10]

Table 2 Effect of various bases on Wittig reaction of hexopyranoses

8a, gal, R¹=R⁴=OBn, R²=R³=H, R⁵=Bn
8b, glc, R¹=R³=OBn, R²=R⁴=H, R⁵=Bn
8c, man, R²=R³=OBn, R¹=R⁴=H, R⁵=Bn
8d, tal, R²=R⁴=OBn, R¹=R³=H, R⁵=Bn

9a, R³=H, R⁴=OBn, R⁵=Bn
9b, R³=OBn, R⁴=H, R⁵=Bn

10a, R¹=R⁴=OBn, R²=R³=H, R⁵=Bn
10b, R¹=R³=OBn, R²=R⁴=H, R⁵=Bn
10c, R²=R³=OBn, R¹=R⁴=H, R⁵=Bn
10d, R²=R⁴=OBn, R¹=R³=H, R⁵=Bn

Entry	SM	Base	Product (yield)
1	8a	4 equiv. t-BuOK	9a (71%)
2	8a	6 equiv. LiHMDS	10a (65%)
3	8b	4 equiv. t-BuOK	9b (90%)
4	8b	6 equiv. LiHMDS	10b (72%)
5	8c	4 equiv. t-BuOK	9b (79%)
6	8c	6 equiv. LiHMDS	10c (64%)
7	8d	4 equiv. t-BuOK	9a (80%)
8	8d	6 equiv. LiHMDS	10d (87%)

We have also proposed a plausible mechanism for these interesting unexpected transformations as shown in Scheme 1. First, hemiacetal **5a** underwent Wittig reaction with phosphonium ylide to provide the olefin **7a** via oxa-phosphetane intermediate **11b** (pathway a). We assumed that olefin **7a** can further undergo β-elimination to provide the diene **6a**. In this regard, we have treated olefin **7a** with 4 equiv. of t-BuOK and phosphonium salt in THF but we could not obtained any product as the olefin **7a** was intact. Therefore, we have proposed alternative scenario where the aldehyde form of **5a** can be transformed into α,β-unsaturated aldehyde **11c** in presence of t-BuOK, which will
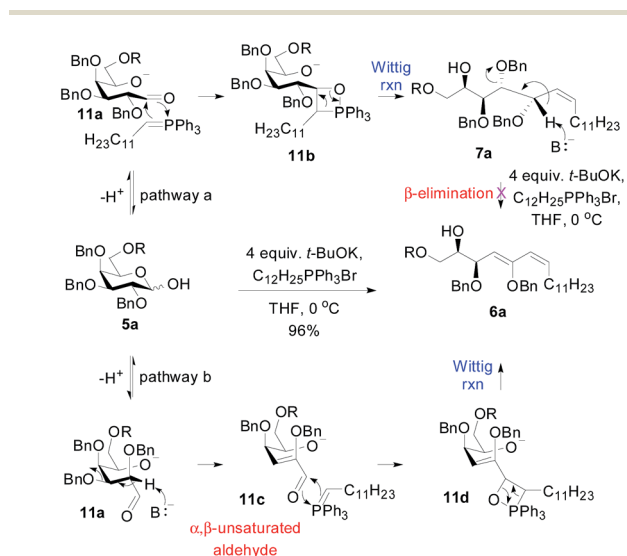
be the real reaction partner for the Wittig reaction with phosphonium salt, could provide the unexpected diene **6a** according to pathway b.[4a]

We decided to synthesize α-GalCer derivative with diene **6a** because of their structural similarities from positions C-2 to C-4 in the α-GalCer **1** and analogue **6a** (Scheme 2). We applied Mitsunobu conditions[19] to obtain the azido displacement product **12** at the C-2 position, which successfully produced an excellent 96% yield. Because the olefin was reacted with the azido group during intramolecular cycloaddition, we purified azide **12** without data collection and performed the next step directly. The azido compound **12** was used first to form an amine by using the Staudinger reaction followed by an amide bond formation to produce the compound **13** in an 80% yield. Finally, global deprotection obtained an 85% crude yield of the final 4-deoxy-5-hydroxyl analogue **2** by using a palladium catalyst in a chloroform and methanol mixture of solvent at room temperature. At last, the crude product was purified by performing flash column chromatography on silica gel to afford compound **2** in a 62% yield.

The SAR studies on the crystal structure of α-GalCer complexed with CD1d reveals that the analogue lacking the 4-hydroxyl group on the phytosphingosine exhibits slightly reduced activity as compared to α-GalCer.[20] However, the activity of analogue **2** lacking the 4-hydroxyl group, which contains an additional hydroxyl group at the C-5 position of the phytosphingosine chain, remains worthy of investigation. Examining the binding activity of these newly formed compounds with CD1d molecules to stimulate NKT cells would be interesting. Many studies have reported on the biological activities of numerous derivatives with different functional groups at various positions of α-GalCer.[20] Based on computer modeling, Henon et al. suggested that the 4-OH group in the sphingosine chain of α-GalCer could form hydrogen bond with Asp80 of CD1d molecule and was important for the recognition of mouse NKT cells.[21] However, whether the 4-OH and 5-OH-bonds play a role to anchor the ligand into the binding groove of CD1d molecule is unclear. Moreover, removing the 3-OH and 2-OH groups on the sphingosine chain of α-GalCer caused no response of splenocytes when stimulated with glycolipid-loaded dendritic cells.[22] These data suggested that the hydroxyl group on the sphingosine chain of α-GalCer is very important.

Scheme 1 Plausible mechanism of unusual Wittig reaction.
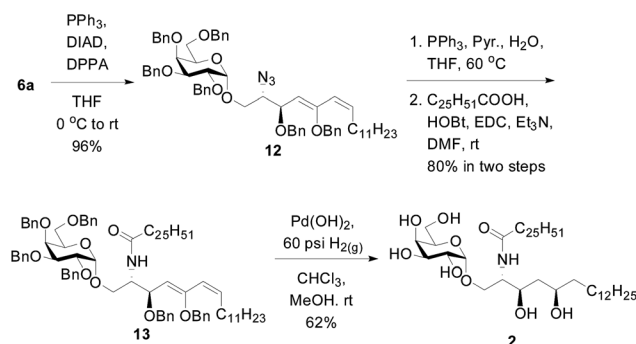
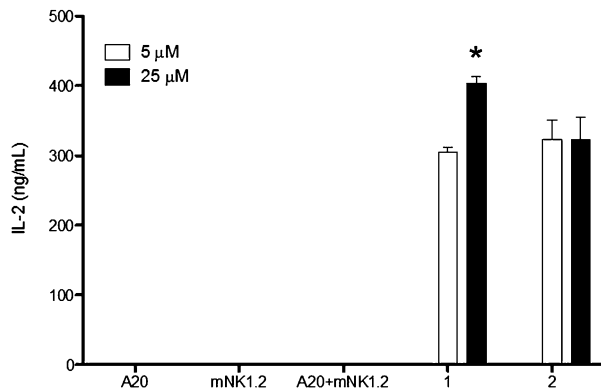**Scheme 2** Preparation of α-galactosyl ceramide analogue **2**.

Fig. 3 Biological activity of α-GalCer analogue **2**. The indicated glycolipids (5 μM and 25 μM) were loaded onto A20-mCD1d cells and co-cultured with mNK1.2 cells. Three days after incubation, supernatants were harvested to determine the production of IL-2 by ELISA. Data were presented as means ± SD. * $p < 0.05$ vs. 25 μM of α-GalCer by one-way ANOVA with Tukey's multiple comparison test.

To evaluate the biological activities of α-GalCer and analog **2** (Fig. 3), B lymphoma cells overexpressing mouse CD1d/A20-mCD1d was loaded with these glycolipids to stimulate the Vα14-expressing mNK1.2 cells to produce IL-2 and the level of IL-2 was determined by ELISA. As shown in Fig. 2, α-GalCer induced the production of IL-2 in a dose-dependent manner (5 μM: 305 ± 7.3 and 25 μM: 404 ± 9.7). IL-2 induction by analog **2** at 5 μM (323.4 ± 27.4) was comparable to α-GalCer, but significantly lower than α-GalCer at 25 μM (322.9 ± 32.3, $p < 0.05$ by one-way ANOVA with Tukey's multiple comparison test).

These results suggested that the hydroxyl group at the 4th position of the sphingosine chain of α-GalCer is important for the CD1d α-GalCer complex to stimulate the NKT cells. Whether such modification at the sphingosine chain of α-GalCer could influence the Th1/Th2 polarization awaits future investigation.

Conclusion

In conclusion, the Wittig reaction can be applied to extend the sphingosine chain of α-GalCer. The unexpected formation of a diene analogue enables preparing unique type of α-GalCer **2** derivative. Using the base LiHMDS rather than *t*-BuOK prevents the formation of unexpected olefination compounds. Otherwise, elimination occurs, and diene is the only product in various pyrano-type reducing sugar derivatives. The mechanism in which *t*-BuOK influences the outcome of the reaction has been proposed. This unusual effect of *t*-BuOK has been extended to the hexopyranoses of various sugar derivatives. The hydroxyl group at 4th position of the sphingosine chain in α-GalCer plays an important role for the interaction between CD1d–glycolipid complex and T-cell receptor of NKT cells.

Experimental section

General information

Some reactions were conducted in flame-dried glassware, under nitrogen atmosphere. Dichloromethane, tetrahydrofuran,

toluene and *N*,*N*-dimethylformamide were purified and dried from a safe purification system containing activated Al_2O_3. All reagents obtained from commercial sources were used without purification, unless otherwise mentioned. Flash column chromatography was carried out on Silica Gel 60 (230–400 mesh, E. Merck). TLC was performed on pre-coated glass plates of Silica Gel 60 F254 (0.25 mm, E. Merck); detection was executed by spraying with a solution of $Ce(NH_4)_2(NO_3)_6$ (0.5 g), $(NH_4)_6Mo_7O_{24}$ (24 g) and H_2SO_4 (28 mL) in water (500 mL) and subsequent heating on a hot plate. Optical rotations were measured at 589 nm (Na) at ∼27 °C. ^1H, ^{13}C NMR, DEPT, ^1H–^1H COSY, ^1H–^{13}C COSY, and ^1H–^1H NOESY spectra were recorded with 400 and 600 MHz instruments. Chemical shifts are in ppm from Me_4Si, generated from the $CDCl_3$ lock signal at δ 7.24 ppm. IR spectra were taken with a FT-IR spectrometer using KBr plates. Mass spectra were analyzed on a Finnigan LTQ-Orbi-trapxL instrument with an ESI source.

2,3,4-Tri-*O*-benzyl-6-*O*-(2,3,4,6-tetra-*O*-benzyl-α-D-galactopyra-nosyl)-D-galactopyranose (5a). To a solution of 1-*O*-acetyl-2,3,4,6-tetra-*O*-benzyl-β-D-galactopyranoside **3** (760 mg, 1.31 mmol) in anhydrous dichloromethane (8 mL) was added iodo-trimethylsilane (232 μL, 1.63 mmol) at 0 °C under nitrogen atmosphere. After the reaction was stirred for 30 min, the mixture was evaporated *in vacuo*. Toluene (7 mL) was added to the residue and evaporated *in vacuo* for three times. In another round bottom flask, a mixture of acceptor **4a** (600 mg, 1.33 mmol), diisopropylethylamine (227 μL, 1.31 mmol), tetrabutyl-ammonium iodide (1.44 g, 3.92 mmol) and 4 Å molecular sieves in anhydrous toluene (7 mL) was stirred for 10 min at 65 °C under nitrogen atmosphere. A solution of iodo-residue in toluene (7 mL) was transferred into the reaction flask which contains acceptor, the mixture was kept stirring for 1 h, and ethyl acetate (20 mL) was added to the reaction flask to remove white precipitate and molecular sieves by filtration through celite. The resulting mixture was extracted with aqueous $Na_2S_2O_3$ (3 × 15 mL) and brine (15 mL), and the organic layers were dried over anhydrous $MgSO_4$, filtered, and concentrated *in vacuo*. The residue was purified by column chromatography on silica gel to afford the desired product **5a** (960 mg, 75%). R_f 0.5 (EtOAc/Hex = 1/2); $[\alpha]_D^{29}$ +38.9 (*c* 1.2, $CHCl_3$); IR ($CHCl_3$) ν 3445, 3030, 1454, 1098 cm^{-1}; α-form: ^1H NMR (400 MHz, $CDCl_3$) δ 7.39–7.23 (m, 35H, ArH), 5.18 (d, J = 2.4 Hz, 1H, H-1), 4.91 (d, J = 10.4 Hz, 1H, CH$_2$Ph), 4.90 (d, J = 11.6 Hz, 1H, CH$_2$Ph), 4.89 (d, J = 10.4 Hz, 1H, CH$_2$Ph), 4.88 (d, J = 12.0 Hz, 1H, CH$_2$Ph), 4.78 (d, J = 11.6 Hz, 2H, CH$_2$Ph), 4.75 (d, J = 3.2 Hz, 1H, H-1'), 4.60 (d, J = 10.4 Hz, 2H, CH$_2$Ph), 4.53 (d, J = 11.6 Hz, 2H, CH$_2$Ph), 4.46 (d, J = 11.6 Hz, 1H, CH$_2$Ph), 4.42 (d, J = 12.0 Hz, 1H, CH$_2$Ph), 4.35 (d, J = 11.6 Hz, 1H, CH$_2$Ph), 4.30 (d, J = 11.6 Hz, 1H, CH$_2$Ph), 4.13 (m, 1H, H-3'), 4.03–3.89 (m, 7H, H-2, H-2', H-3, H-4, H-4', H-5, H-5'), 3.62–3.48 (m, 4H, H-6a, H-6b, H-6a', H-6b'), 3.41 (s, 1H, OH); ^{13}C NMR (150 MHz, $CDCl_3$) δ 138.62 (C), 138.58 (C), 138.5 (C), 138.2 (C × 2), 138.2 (C), 137.5 (C), 128.4 (CH × 2), 128.3 (CH × 4), 128.23 (CH × 2), 128.19 (CH × 2), 128.15 (CH × 4), 128.1 (CH × 2), 128.04 (CH × 2), 128.01 (CH × 2), 127.96 (CH × 2), 127.9 (CH × 2), 127.8 (CH), 127.61 (CH), 127.57 (CH), 127.5 (CH × 2), 127.4 (CH × 2), 127.34 (CH × 2), 127.30 (CH × 2), 98.4 (CH), 91.5 (CH), 78.9 (CH), 78.6 (CH), 76.4 (CH), 76.3

(CH), 75.2 (CH), 74.6 (CH), 74.4 (CH_2), 73.5 (CH_2), 73.43 (CH_2), 73.39 (CH_2), 73.3 (CH_2), 73.0 (CH_2), 72.9 (CH_2), 72.8 (CH_2), 69.7 (CH), 69.3 (CH), 68.9 (CH_2); β-form: ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.37–7.23 (m, 35H, ArH), 4.82–4.63 (m, 15H, H-1′, CH$_2$Ph), 4.56 (d, J = 8.4 Hz, 1H, H-1), 4.03–3.89 (m, 4H, H-2′, H-3, H-3′, H-4′), 3.82–3.68 (m, 4H, H-2, H-5, H-6a, H-6a′), 3.64–3.48 (m, 4H, H-4, H-5′, H-6b, H-6b′), 3.41 (s, 1H, OH); ^{13}C NMR (150 MHz, CDCl$_3$) δ 138.62 (C), 138.58 (C), 138.5 (C), 138.4 (C × 2), 138.2 (C), 137.5 (C), 128.4 (CH × 2), 128.3 (CH × 4), 128.23 (CH × 2), 128.19 (CH × 2), 128.15 (CH × 4), 128.1 (CH × 2), 128.04 (CH × 2), 128.01 (CH × 2), 127.96 (CH × 2), 127.9 (CH × 2), 127.8 (CH), 127.61 (CH), 127.57 (CH), 127.5 (CH × 2), 127.4 (CH × 2), 127.34 (CH × 2), 127.30 (CH × 2), 98.2 (CH), 97.6 (CH), 81.9 (CH), 80.6 (CH), 79.0 (CH), 76.2 (CH), 74.8 (CH_2), 74.3 (CH), 74.3 (CH), 74.0 (CH), 73.5 (CH_2), 73.43 (CH_2), 73.39 (CH_2), 73.3 (CH_2), 73.0 (CH_2), 72.9 (CH_2), 72.8 (CH_2), 69.4 (CH), 68.4 (CH_2); HRMS (ESI, M + Na$^+$) calcd for $C_{61}H_{64}O_{11}$Na 995.4341, found 995.4380.

2,3,4-Tri-*O*-benzyl-6-*O*-(2,3,4,6-tetra-*O*-benzyl-α-D-galactopyranosyl)-D-glucopyranose (5b). To a solution of 1-*O*-acetyl-2,3,4,6-tetra-*O*-benzyl-β-D-galactopyranoside 3 (1.90 g, 3.26 mmol) in anhydrous dichloromethane (20 mL) was added iodo-trimethylsilane (578 µL, 4.08 mmol) at 0 °C under nitrogen atmosphere. After the reaction was stirred for 30 min, the mixture was evaporated *in vacuo*. Toluene (17 mL) was added to the residue and evaporated *in vacuo* for three times. In another round bottom flask, a mixture of acceptor 4b (1.50 g, 3.33 mmol), diisopropylethylamine (567 µL, 3.26 mmol), tetrabutyl-ammonium iodide (3.60 g, 9.78 mmol) and 4 Å molecular sieves in anhydrous toluene (17 mL) was stirred for 10 min at 65 °C under nitrogen atmosphere. A solution of iodo-residue in toluene (17 mL) was transferred into the reaction flask which contains acceptor, the mixture was kept stirring for 1 h, and ethyl acetate (30 mL) was added to the reaction flask to remove white precipitate and molecular sieves by filtration through celite. The resulting mixture was extracted with aqueous Na$_2$S$_2$O$_3$ (3 × 20 mL) and brine (20 mL), and the organic layers were dried over anhydrous MgSO$_4$, filtered, and concentrated *in vacuo*. The residue was purified by column chromatography on silica gel to afford the desired product 5b (2.33 g, 72%). R_f 0.5 (EtOAc/Hex = 1/2); $[α]_D^{29}$ +39.0 (*c* 1.3, CHCl$_3$); IR (CHCl$_3$) ν 3431, 3030, 1454, 1096 cm^{-1}; α-form: ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.37–7.24 (m, 35H, ArH), 5.09 (d, J = 2.8 Hz, 1H, H-1), 4.97 (d, J = 3.2 Hz, 1H, H-1′), 4.95–4.53 (m, 12H, CH$_2$Ph), 4.42 (d, J = 12.0 Hz, 1H, CH$_2$Ph), 4.35 (d, J = 12.4 Hz, 1H, CH$_2$Ph), 4.07–4.00 (m, 2H, H-2′, H-5), 3.97–3.83 (m, 4H, H-3, H-3′, H-4′, H-6a′), 3.75–3.68 (m, 1H, H-6b′), 3.54 (m, 4H, H-4, H-5′, H-6a, H-6b), 3.40 (dd, J = 9.2, 3.6 Hz, 1H, H-2); ^{13}C NMR (150 MHz, CDCl$_3$) δ 138.64 (C), 138.59 (C), 138.5 (C), 138.4 (C), 138.1 (C), 137.9 (C), 137.7 (C), 128.3 (CH × 2), 128.24 (CH × 2), 128.18 (CH × 2), 128.11 (CH × 2), 128.09 (CH × 2), 128.07 (CH × 2), 128.0 (CH), 127.82 (CH × 2), 127.78 (CH × 2), 127.74 (CH × 2), 127.72 (CH × 2), 127.71 (CH × 2), 127.69 (CH × 2), 127.67 (CH × 2), 127.65 (CH × 2), 127.6 (CH), 127.54 (CH), 127.49 (CH), 127.42 (CH), 127.37 (CH), 127.31 (CH), 98.2 (CH), 90.7 (CH), 81.6 (CH), 80.1 (CH), 78.2 (CH), 77.9 (CH), 76.5 (CH), 75.5 (CH_2), 74.84 (CH_2), 74.83 (CH), 74.58 (CH_2), 74.56 (CH_2), 73.2 (CH_2), 72.8 (CH_2), 72.7 (CH_2), 70.3 (CH), 69.3 (CH), 68.9 (CH_2), 67.3 (CH_2); β-form: ^{1}H

NMR (400 MHz, CDCl$_3$) δ 7.37–7.24 (m, 35H, ArH), 5.00 (d, J = 3.6 Hz, 1H, H-1′), 4.97–4.53 (m, 13H, CH$_2$Ph, H-1), 4.44 (d, J = 11.2 Hz, 1H, CH$_2$Ph), 4.30 (d, J = 11.6 Hz, 1H, CH$_2$Ph), 4.07–3.39 (m, 11H, H-2′, H-3, H-3′, H-4, H-4′, H-5, H-5′, H-6a, H-6b, H-6a′, H-6b′), 3.27 (dd, J = 8.4, 8.0 Hz, 1H, H-2); ^{13}C NMR (150 MHz, CDCl$_3$) δ 138.64 (C), 138.59 (C), 138.5 (C), 138.4 (C), 138.2 (C), 138.1 (C), 137.5 (C), 128.3 (CH × 2), 128.24 (CH × 2), 128.18 (CH × 2), 128.11 (CH × 2), 128.09 (CH × 2), 128.07 (CH × 2), 128.0 (CH), 127.82 (CH × 2), 127.78 (CH × 2), 127.74 (CH × 2), 127.72 (CH × 2), 127.71 (CH × 2), 127.69 (CH × 2), 127.67 (CH × 2), 127.65 (CH × 2), 127.6 (CH), 127.54 (CH), 127.49 (CH), 127.42 (CH), 127.37 (CH), 127.31 (CH), 98.1 (CH), 97.1 (CH), 84.3 (CH), 83.2 (CH), 78.4 (CH), 77.6 (CH), 75.3 (CH_2), 75.2 (CH), 74.8 (CH), 74.7 (CH_2), 74.5 (CH), 74.3 (CH_2), 73.3 (CH_2), 73.0 (CH_2), 72.7 (CH_2), 71.9 (CH_2), 71.6 (CH), 69 (CH_2), 67.9 (CH_2); HRMS (ESI, M + Na$^+$) calcd for $C_{61}H_{64}O_{11}$Na 995.4341, found 995.4343.

2,3,4-Tri-*O*-bezyl-6-*O*-(2,3,4,6-tetra-*O*-benzyl-α-D-galactopyranosyl)-D-mannopyranoside (5c). To a solution of 1-*O*-acetyl-2,3,4,6-tetra-*O*-benzyl-β-D-galactopyranoside 3 (200 mg, 0.34 mmol) in anhydrous dichloromethane (2 mL) was added iodo-trimethylsilane (62 µL, 0.43 mmol) at 0 °C under nitrogen atmosphere. After the reaction was stirred for 30 min, the mixture was evaporated *in vacuo*. Toluene (2 mL) was added to the residue and evaporated *in vacuo* for three times. In another round bottom flask, a mixture of acceptor 4c (170 mg, 0.38 mmol), diisopropylethylamine (60 µL, 0.34 mmol), tetrabutyl-lammonium iodide (380 mg, 1.02 mmol) and 4 Å molecular sieves in anhydrous toluene (2 mL) was stirred for 10 min at 65 °C under nitrogen atmosphere. A solution of iodo-residue in toluene (2 mL) was transferred into the reaction flask which contains acceptor, the mixture was kept stirring for 1 h, and ethyl acetate (10 mL) was added to the reaction flask to remove white precipitate and molecular sieves by filtration through celite. The resulting mixture was extracted with aqueous Na$_2$S$_2$O$_3$ (3 × 5 mL) and brine (5 mL), and the organic layers were dried over anhydrous MgSO$_4$, filtered, and concentrated *in vacuo*. The residue was purified by column chromatography on silica gel to afford the desired product 5c (229 mg, 69%). R_f 0.5 (EtOAc/Hex = 1/2); $[α]_D^{29}$ +36.7 (*c* 0.9, CHCl$_3$); IR (CHCl$_3$) ν 3422, 3030, 1454, 1097 cm^{-1}; ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.37–7.22 (m, 35H, ArH), 5.13 (s, 1H, H-1), 5.01 (d, J = 3.2 Hz, 1H, H-1′), 4.92 (d, J = 11.6 Hz, 1H, CH$_2$Ph), 4.86 (d, J = 10.8 Hz, 1H, CH$_2$Ph), 4.79 (d, J = 11.6 Hz, 1H, CH$_2$Ph), 4.74–4.59 (m, 7H, CH$_2$Ph), 4.55 (d, J = 10.8 Hz, 1H, CH$_2$Ph), 4.53 (d, J = 11.6 Hz, 1H, CH$_2$Ph), 4.42 (d, J = 11.6 Hz, 1H, CH$_2$Ph), 4.35 (d, J = 12.0 Hz, 1H, CH$_2$Ph), 4.07–4.00 (m, 3H, H-2′, H-4, H-5′), 3.96–3.93 (m, 2H, H-3, H-6a), 3.87 (m, 2H, H-3′, H-4′), 3.78–3.71 (m, 3H, H-2, H-5, H-6b), 3.53 (dd, J = 9.6, 6.4 Hz, 1H, H-6a′), 3.42 (dd, J = 9.6, 6.4 Hz, 1H, H-6b′); ^{13}C NMR (100 MHz, CDCl$_3$) δ 138.8 (C), 138.6 (C), 138.51 (C), 137.46 (C), 138.4 (C), 138.3 (C), 137.6 (C), 128.5 (CH × 2), 128.43 (CH × 2), 128.36 (CH × 5), 128.3 (CH × 4), 128.2 (CH × 2), 128.1 (CH × 2), 128.02 (CH × 2), 128.01 (CH × 2), 127.94 (CH × 2), 127.88 (CH × 2), 127.8 (CH), 127.7 (CH × 2), 127.61 (CH × 2), 127.56 (CH × 2), 127.50 (CH × 2), 127.47 (CH), 98.1 (CH), 92.6 (CH), 79.9 (CH), 78.7 (CH), 76.7 (CH), 75.4 (CH), 75.1 (CH), 75.02 (CH), 74.96 (CH_2), 74.7 (CH_2), 73.4 (CH_2), 73.2 (CH_2), 73.0 (CH_2), 72.8 (CH_2), 72.2 (CH_2), 72.0

(CH), 69.4 (CH), 69.3 (CH$_2$), 68.50 (CH$_2$); HRMS (ESI, M + Na$^+$) calcd for C$_{61}$H$_{64}$O$_{11}$Na 995.4341, found 995.4331.

(2S,3S,4Z,6Z)-3,5-di-O-benzyl-1-O-(2,3,4,6-tetra-O-benzyl-α-D-galactopyranosyl)-octadec-4,6-dien-1,2,3,5-tetraol (6a). A mixture of disaccharide **5a** (980 mg, 1.00 mmol), tridecanyl-triphenylphosphonium bromide (2.06 g, 4.03 mmol) and potassium *tert*-butoxide (452 mg, 4.03 mmol) in anhydrous THF (10 mL) was stirred at 0 °C under nitrogen. After the reaction mixture was kept stirring for 3 h at 0 °C, water (20 mL) was added to quench the reaction and the mixture was extracted with EtOAc (3 × 30 mL). The combined organic layers were washed with brine, dried over anhydrous MgSO$_4$, filtered, and concentrated under vacuum to give a residue. The residue was purified by column chromatography to give the only diene **6a** (979 mg, 96%) as colorless oil. R_f 0.5 (EtOAc/Hex = 1/3); $[\alpha]_D^{29}$ +12.9 (*c* 1.6, CHCl$_3$); IR (CHCl$_3$) *ν* 3063, 2924, 1652, 1454, 1099 cm^{-1}; ^{1}H NMR (400 MHz, CDCl$_3$) *δ* 7.36–7.20 (m, 30H, ArH), 5.83 (d, *J* = 12.0 Hz, 1H, H-6), 5.76–5.70 (m, 1H, H-7), 4.90 (d, *J* = 11.6 Hz, 1H, CH$_2$Ph), 4.80 (d, *J* = 3.6 Hz, 1H, H-1′), 4.75 (d, *J* = 12.0 Hz, 1H, CH$_2$Ph), 4.73–4.66 (m, 5H, CH$_2$Ph, H-4), 4.59 (d, *J* = 12.0 Hz, 1H, CH$_2$Ph), 4.54 (d, *J* = 11.6 Hz, 1H, CH$_2$Ph), 4.49–4.37 (m, 4H, CH$_2$Ph, H-3), 4.20 (d, *J* = 11.6 Hz, 1H, CH$_2$Ph), 4.06 (t, *J* = 6.4 Hz, 1H, H-5′), 4.01 (dd, *J* = 9.6, 3.6 Hz, 1H, H2′), 3.90–3.87 (m, 2H, H-3′, H-4′), 3.74–3.69 (m, 1H, H-2), 3.66–3.62 (dd, 1H, H-1a), 3.54 (dd, *J* = 11.2, 3.2 Hz, 1H, H-1b), 3.50 (d, *J* = 6.8 Hz, 2H, H-6a′, H-6b′), 3.04 (d, *J* = 4.4 Hz, 1H, 2-OH), 2.27–2.21 (m, 2H, CH$_2$), 1.40–1.23 (m, 18H, CH$_2$), 0.87 (t, *J* = 6.8 Hz, 3H, CH$_3$); ^{13}C NMR (100 MHz, CDCl$_3$) *δ* 154.0 (C), 138.9 (C), 138.73 (C), 138.68 (C), 138.5 (C), 138.0 (C), 137.6 (CH), 137.4 (C), 128.4 (CH × 2), 128.30 (CH × 2), 128.26 (CH × 2), 128.2 (CH × 2), 128.1 (CH × 2), 128.00 (CH × 2), 127.98 (CH × 2), 127.9 (CH × 2), 127.8 (CH × 2), 127.7 (CH × 2), 127.61 (CH × 2), 127.55 (CH × 2), 127.5 (CH × 2), 127.33 (CH × 2), 127.29 (CH × 2), 123.2 (CH), 110.5 (CH), 98.1 (CH), 79.1 (CH), 76.4 (CH), 75.0 (CH), 74.7 (CH$_2$), 73.8 (CH), 73.4 (CH$_2$), 73.2 (CH$_2$), 73.0 (CH$_2$), 72.9 (CH), 70.9 (CH$_2$), 70.1 (CH$_2$), 70.0 (CH$_2$), 69.2 (CH), 68.8 (CH$_2$), 31.9 (CH$_2$), 29.64 (CH$_2$), 29.63 (CH$_2$), 29.61 (CH$_2$), 29.60 (CH$_2$), 29.5 (CH$_2$), 29.4 (CH$_2$), 29.3 (CH$_2$), 29.2 (CH$_2$), 22.9 (CH$_2$), 14.1 (CH$_3$); HRMS (ESI, M + Na$^+$) calcd for C$_{66}$H$_{80}$O$_9$Na 1039.5695, found 1039.5717.

(2S,3R,4Z,6Z)-3,5-Di-O-benzyl-1-O-(2,3,4,6-tetra-O-benzyl-α-D-galactopyranosyl)-octadec-4,6-dien-1,2,3,5-tetraol (6b). A mixture of disaccharide **5c** (522 mg, 0.54 mmol), tridecanyl-triphenylphosphonium bromide (1.09 g, 2.15 mmol) and potassium *tert*-butoxide (240 mg, 2.15 mmol) in anhydrous THF (5 mL) at 0 °C under nitrogen was stirred. After the reaction mixture was kept stirring for 3 h at 0 °C, water (10 mL) was added to quench the reaction and the mixture was extracted with EtOAc (3 × 20 mL). The combined organic layers were washed with brine, dried over anhydrous MgSO$_4$, filtered, and concentrated under vacuum to give a residue. The residue was purified by column chromatography to give the diene **6b** (457 mg, 84%) as colorless oil. R_f 0.5 (EtOAc/Hex = 1/3); $[\alpha]_D^{24}$ +35.13 (*c* 0.8, CHCl$_3$); IR (CHCl$_3$) *ν* 3063, 2924, 1608, 1454, 1059 cm^{-1}; ^{1}H NMR (600 MHz, CDCl$_3$) *δ* 7.36–7.20 (m, 30H, ArH), 5.83 (d, *J* = 12.0 Hz, 1H, H-6), 5.73 (dt, *J* = 12.0, 7.2 Hz, 1H, H-7), 4.91 (d, *J* = 11.4 Hz, 1H, CH$_2$Ph), 4.80–4.71 (m, 6H, CH$_2$Ph, H-1′, H-4),

4.67 (d, *J* = 12.0 Hz, 1H, CH$_2$Ph), 4.65 (d, *J* = 10.2 Hz, 1H, CH$_2$Ph), 4.55 (d, *J* = 11.4 Hz, 1H, CH$_2$Ph), 4.46–4.42 (m, 3H, CH$_2$Ph, H-3), 4.37 (d, *J* = 12.0 Hz, 1H, CH$_2$Ph), 4.21 (d, *J* = 12.0 Hz, 1H, CH$_2$Ph), 4.06–4.01 (m, 2H, H-2′, H-5′), 3.93–3.85 (m, 3H, H-2, H-3′, H-4′), 3.70–3.62 (m, 2H, H-1a, H-1b), 3.49 (d, *J* = 6.6 Hz, 2H, H-6a′, H-6b′), 3.04 (bs, 1H, 2-OH), 2.28–2.24 (m, 2H, H-8a, H-8b), 1.41–1.20 (m, 18H, CH$_2$), 0.87 (t, *J* = 7.2 Hz, 3H, CH$_3$); ^{13}C NMR (150 MHz, CDCl$_3$) *δ* 154.1 (C), 138.8 (C), 138.7 (C), 138.6 (C), 138.3 (C), 137.9 (C), 137.5 (C × 1, CH × 1), 128.34 (CH × 2), 128.31 (CH × 3), 128.19 (CH × 2), 128.15 (CH × 3), 128.04 (CH × 2), 127.96 (CH × 2), 127.82 (CH × 2), 127.77 (CH × 2), 127.64 (CH × 2), 127.61 (CH × 2), 127.5 (CH × 2), 127.4 (CH × 2), 127.33 (CH × 2), 127.25 (CH × 2), 123.2 (CH), 111.1 (CH), 98.2 (CH), 79.1 (CH), 76.3 (CH), 74.8 (CH), 74.7 (CH$_2$), 73.9 (CH), 73.5 (CH$_2$), 73.3 (CH$_2$), 72.9 (CH$_2$), 72.3 (CH), 71.1 (CH$_2$), 70.3 (CH$_2$), 70.0 (CH$_2$), 69.3 (CH), 68.7 (CH$_2$), 31.9 (CH$_2$), 29.62 (CH$_2$ × 2), 29.59 (CH$_2$ × 2), 29.55 (CH$_2$ × 2), 29.4 (CH$_2$), 29.3 (CH$_2$), 29.2 (CH$_2$), 14.1 (CH$_3$); HRMS (ESI, M + Na$^+$) calcd for C$_{66}$H$_{80}$O$_9$Na 1039.5695, found 1039.5732.

(2R,3S,4R,5S)-3,4,5-Tri-O-benzyl-1-O-(2,3,4,6-tetra-O-benzyl-α-D-galactopyranosyl)-octadec-6-en-1,2,3,4,5-pentaol (7a). A mixture of disaccharide **5a** (1.00 g, 1.03 mmol) and tridecanyl-triphenylphosphonium bromide (3.15 g, 6.17 mmol) in anhydrous tetrahydrofuran (10 mL) was cooled to 0 °C under nitrogen. A 1.0 M solution of lithium hexamethyldisilylamide in THF (6.2 mL, 6.17 mmol) was added to the reaction mixture and the reaction solution was stirred for 24 h at 0 °C. Water (20 mL) was added to quench the reaction and the mixture was extracted with EtOAc (3 × 30 mL). The combined organic layers were washed with brine, dried over anhydrous MgSO$_4$, filtered, and concentrated under vacuum to give a residue. The residue was purified by column chromatography to give the olefin **7a** (1.05 g, 90%, *cis*–*trans* = 1.2 : 1.6) as colorless oil. R_f 0.3 (EtOAc/Hex = 1/4); $[\alpha]_D^{28}$ +46.8 (*c* 1.6, CHCl$_3$); IR (CHCl$_3$) *ν* 3483, 2925, 2360, 1497, 1061 cm^{-1}; ^{1}H NMR (400 MHz, CDCl$_3$) *δ* 7.34–7.15 (m, 70H), 5.72 (dt, *J* = 15.6, 6.8 Hz, 1H), 5.58 (dt, *J* = 11.6, 7.2 Hz, 1H), 5.50–5.44 (m, 2H), 4.91 (d, *J* = 11.2 Hz, 2H), 4.83 (d, *J* = 4.8 Hz, 2H), 4.18–4.64 (m, 11H), 4.60 (d, *J* = 12.0 Hz, 3H), 4.54 (d, *J* = 11.2 Hz, 2H), 4.47–4.44 (m, 3H), 4.41 (d, *J* = 11.2 Hz, 3H), 4.35 (d, *J* = 11.6 Hz, 2H), 4.27 (d, *J* = 11.6 Hz, 3H), 4.14–4.07 (m, 2H), 4.05 (m, 5H), 3.93–3.89 (m, 4H), 3.81–3.71 (m, 6H), 3.57 (dd, *J* = 10.4, 5.6 Hz, 2H), 3.48 (d, *J* = 6.4 Hz, 4H), 3.26–3.21 (m, 2H), 2.09–1.95 (m, 4H), 1.38–1.95 (m, 36H), 0.88 (t, *J* = 6.0 Hz, 6H); ^{13}C NMR (100 MHz, CDCl$_3$) *δ* 138.8 (C × 2), 138.6 (C × 2), 138.51 (C × 2), 138.48 (C × 2), 138.33 (C), 137.32 (C), 138.26 (C), 138.2 (C), 137.92 (C), 137.90 (C), 136.0 (CH), 135.0 (CH), 128.36 (CH × 5), 128.35 (CH × 5), 128.3 (CH × 7), 128.24 (CH × 5), 128.21 (CH × 3), 128.19 (CH × 3), 128.15 (CH × 3), 128.07 (CH × 3), 127.06 (CH × 3), 127.9 (CH × 3), 127.8 (CH × 3), 127.7 (CH × 3), 127.60 (CH × 3), 127.57 (CH × 3), 127.52 (CH × 3), 127.48 (CH × 3), 127.45 (CH × 3), 127.42 (CH × 3), 127.35 (CH × 3), 127.3 (CH × 3), 98.12 (CH), 98.06 (CH), 82.06 (CH), 82.04 (CH), 79.9 (CH), 79.2 (CH), 79.1 (CH), 77.40 (CH), 76.3 (CH), 75.3 (CH$_2$), 75.2 (CH$_2$), 74.9 (CH × 3), 74.78 (CH$_2$), 74.76 (CH$_2$), 73.9 (CH), 73.5 (CH$_2$), 73.44 (CH$_2$ × 2), 73.40 (CH$_2$), 73.34 (CH$_2$), 73.32 (CH$_2$), 73.0 (CH$_2$), 72.9 (CH$_2$), 70.4 (CH$_2$), 70.3 (CH$_2$), 69.80 (CH$_2$), 69.78 (CH$_2$), 69.5 (CH), 69.42 (CH × 2), 69.37 (CH), 68.9

(CH$_2$), 68.8 (CH$_2$), 32.4 (CH$_2$), 32.0 (CH$_2$ × 3), 29.7 (CH$_2$ × 5), 29.59 (CH$_2$), 29.55 (CH$_2$), 29.5 (CH$_2$), 29.4 (CH$_2$), 29.39 (CH$_2$), 29.3 (CH$_2$), 29.2 (CH$_2$), 28.1 (CH$_2$), 22.7 (CH$_2$ × 3), 14.2 (CH$_3$ × 2); HRMS (ESI, M + Na$^+$) calcd for C$_{73}$H$_{88}$O$_{10}$Na 1147.6270, found 1147.6261.

(2R,3R,4R,5S,6Z)-3,4,5-Tri-O-benzyl-1-O-(2,3,4,6-tetra-O-benzyl-α-D-galactopyranosyl)-octadec-6-en-1,2,3,4,5-pentaol (7b). A mixture of disaccharide **5b** (730 mg, 0.75 mmol) and tridecanyltriphenylphosphonium bromide (2.30 g, 4.50 mmol) in anhydrous tetrahydrofuran (7 mL) was cooled to 0 °C under nitrogen. A 1.0 M solution of lithium hexamethyldisilylamide in THF (4.50 mL, 4.50 mmol) was added to the mixture and the reaction solution was stirred for 24 h at 0 °C. Water (10 mL) was added to quench the reaction and the mixture was extracted with EtOAc (3 × 20 mL). The combined organic layers were washed with brine, dried over anhydrous MgSO$_4$, filtered, and concentrated under vacuum to give a residue. The residue was purified by column chromatography to give the olefin **7b** (610 mg, 72%) as colorless oil. R_f 0.3 (EtOAc/Hex = 1/4); $[\alpha]_D^{27}$ +51.2 (c 1.1, CHCl$_3$); IR (CHCl$_3$) ν 3463, 3030, 2925, 1497, 1061 cm^{-1}; ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.38–7.22 (m, 35H, ArH), 5.68–5.58 (m, 1H, H-7), 5.40 (t, J = 10.8 Hz, 1H, H-6), 4.92 (d, J = 11.4 Hz, 1H, CH$_2$Ph), 4.86 (d, J = 3.6 Hz, 1H, H-1′), 4.82–4.51 (m, 11H, CH$_2$Ph, H-5), 4.42 (d, J = 11.6 Hz, 1H, CH$_2$Ph), 4.37 (d, J = 12.0 Hz, 1H, CH$_2$Ph), 4.34 (d, J = 12.0 Hz, 1H, CH$_2$Ph), 4.04 (dd, J = 9.6, 3.6 Hz, 1H, H-2′), 4.01–3.97 (m, 2H, H-2, H-5′), 3.95–3.90 (m, 2H, H-3, H-4), 3.81–3.68 (m, 4H, H-1a, H-1b, H-3′, H-4), 3.55–3.44 (m, 2H, H-6a′, H-6b′), 2.08–1.85 (m, 2H, H-8a, H-8b), 1.31–1.17 (m, 18H, CH$_2$), 0.88 (t, J = 6.8 Hz, 3H, CH$_3$); ^{13}C NMR (100 MHz, CDCl$_3$) δ 138.7 (C), 138.63 (C), 138.60 (C), 138.57 (C × 2), 138.3 (C), 137.8 (C), 135.8 (CH), 128.4 (CH), 128.3 (CH × 5), 128.21 (CH), 128.19 (CH × 2), 128.16 (CH × 4), 128.1 (CH × 5), 128.00 (CH), 127.98 (CH × 2), 127.9 (CH), 127.79 (CH), 127.76 (CH × 2), 127.68 (CH), 127.66 (CH), 127.53 (CH), 127.49 (CH), 127.44 (CH), 127.38 (CH × 3), 127.33 (CH), 127.30 (CH), 126.7 (CH), 98.7 (CH), 81.8 (CH), 79.01 (CH), 78.84 (CH), 76.4 (CH), 75.5 (CH), 74.9 (CH$_2$), 74.8 (CH), 74.7 (CH$_2$), 73.5 (CH$_2$), 73.4 (CH$_2$), 73.0 (CH$_2$), 72.9 (CH$_2$), 70.7 (CH$_2$), 70.2 (CH$_2$), 70.1 (CH), 70.0 (CH), 68.8 (CH$_2$), 31.9 (CH$_2$), 29.7 (CH$_2$), 29.64 (CH$_2$), 29.63 (CH$_2$), 29.61 (CH$_2$), 29.5 (CH$_2$), 29.43 (CH$_2$), 29.3 (CH$_2$), 28.2 (CH$_2$), 22.7 (CH$_2$), 14.1 (CH$_3$); HRMS (ESI, M + Na$^+$) calcd for C$_{73}$H$_{88}$O$_{10}$Na 1147.6270, found 1147.6296.

(2R,3R,4R,5R,6Z)-3,4,5-Tri-O-benzyl-1-O-(2,3,4,6-tetra-O-benzyl-α-D-galactopyranosyl)-octadec-6-en-1,2,3,4,5-pentaol (7c). A mixture of disaccharide **5c** (903 mg, 0.92 mmol) and tridecanyltriphenylphosphonium bromide (2.84 g, 5.57 mmol) in anhydrous tetrahydrofuran (10 mL) was cooled to 0 °C under nitrogen. A 1.0 M solution of lithium hexamethyldisilylamide in THF (5.6 mL, 5.6 mmol) was added to the mixture and the reaction solution was stirred for 24 h at 0 °C. Water (10 mL) was added to quench the reaction and the mixture was extracted with EtOAc (3 × 20 mL). The combined organic layers were washed with brine, dried over anhydrous MgSO$_4$, filtered, and concentrated under vacuum to give a residue. The residue was purified by column chromatography to give the olefin **7c** (726 mg, 70%) as colorless oil. R_f 0.3 (EtOAc/Hex = 1/4); $[\alpha]_D^{27}$ +42.6 (c 1.1, CHCl$_3$); IR (CHCl$_3$) ν 3400, 3089, 2924, 1455, 1095 cm^{-1}; ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.34–7.16 (m, 35H, ArH), 5.81–5.75 (m, 1H, H-7), 5.45 (dd, J = 11.2, 9.6 Hz, 1H, H-6), 4.91 (d, J = 11.6 Hz, 1H, CH$_2$Ph), 4.87 (d, J = 3.6 Hz, 1H, H-1′), 4.82 (d, J = 11.6 Hz, 1H, CH$_2$Ph), 4.73 (d, J = 11.6 Hz, 1H, CH$_2$Ph), 4.67 (d, J = 12.0 Hz, 1H, CH$_2$Ph), 4.66 (d, J = 12.0 Hz, 1H, CH$_2$Ph), 4.63–4.53 (m, 6H, CH$_2$Ph), 4.50 (t, J = 9.2 Hz, 1H, H-5), 4.42 (d, J = 12.0 Hz, 1H, CH$_2$Ph), 4.34 (d, J = 12.0 Hz, 1H, CH$_2$Ph), 4.13 (d, J = 11.6 Hz, 1H, CH$_2$Ph), 4.06–4.00 (m, 4H, H-2′, H-3′, H-4′, H-5′), 3.95–3.82 (m, 2H, H-2, H-3), 3.81–3.75 (m, 3H, H-1a, H-1b, H-4), 3.51–3.44 (m, 2H, H-6a′, H-6b′), 2.20–2.01 (m, 2H, H-8a, H-8b), 1.40–1.25 (m, 18H, CH$_2$), 0.88 (t, J = 6.4 Hz, 3H, CH$_3$); ^{13}C NMR (100 MHz, CDCl$_3$) δ 138.67 (C), 138.66 (C × 2), 138.54 (C), 138.52 (C), 138.1 (C), 137.8 (C), 136.7 (CH), 128.37 (CH × 3), 128.3 (CH × 3), 128.19 (CH × 6), 128.18 (CH × 4), 128.1 (CH), 128.0 (CH × 4), 127.8 (CH), 127.70 (CH × 3), 127.65 (CH), 127.60 (CH × 3), 127.54 (CH), 127.48 (CH), 127.41 (CH × 2), 127.38 (CH), 127.33 (CH), 127.26 (CH), 99.1 (CH), 80.6 (CH), 79.3 (CH), 78.8 (CH), 76.4 (CH), 74.7 (CH$_2$ × 1, CH × 1), 74.5 (CH$_2$), 73.9 (CH$_2$), 73.7 (CH$_2$), 73.6 (CH), 73.4 (CH$_2$), 72.9 (CH$_2$), 71.4 (CH$_2$), 69.73 (CH), 69.69 (CH), 69.4 (CH$_2$), 68.8 (CH$_2$), 31.9 (CH$_2$), 29.66 (CH$_2$), 29.64 (CH$_2$), 29.63 (CH$_2$), 29.61 (CH$_2$), 29.5 (CH$_2$), 29.4 (CH$_2$), 29.3 (CH$_2$), 28.1 (CH$_2$), 22.7 (CH$_2$), 14.1 (CH$_3$); HRMS (ESI, M + Na$^+$) calcd for C$_{73}$H$_{88}$O$_{10}$Na1147.6270, found 1147.6305.

(2R,3R,4Z,6Z)-1,3,5-Tri-O-benzyl-octadec-4,6-diene-1,2,3,5 pentaol (9a). Method A: a solution of hemiacetal **8a** (100 mg, 0.19 mmol) and dodecyltriphenylphosphonium bromide (378 mg, 0.74 mmol) in anhydrous tetrahydrofuran (1 mL) was cooled to 0 °C, followed by quick addition of potassium tert-butoxide (83 mg, 0.74 mmol). After stirring for 1 h at this temperature, the reaction mixture was treated with water (2 mL) and extracted with ethyl acetate (3 × 2 mL). The combined organic layers were dried over anhydrous MgSO$_4$, filtered, and concentrated. The residue was purified by column chromatography to afford olefin **9a** (77 mg, 71%) as a colorless oil. **Method B:** a solution of hemiacetal **8d** (110 mg, 0.20 mmol) and dodecyltriphenylphosphonium bromide (416 mg, 0.81 mmol) in anhydrous tetrahydrofuran (1.1 mL) was cooled to 0 °C, followed by quick addition of potassium tert-butoxide (91 mg, 0.81 mmol). After stirring for 1 h at this temperature, the reaction mixture was treated with water (1.2 mL) and extracted with ethyl acetate (3 × 2 mL). The combined organic layers were dried over anhydrous MgSO$_4$, filtered, and concentrated. The residue was purified by column chromatography to afford olefin **9a** (95 mg, 80%) as a colorless oil. R_f 0.56 (EtOAc/Hex = 1/3); $[\alpha]_D^{22}$ −9.1 (c 0.8, CH$_2$Cl$_2$); IR (CH$_2$Cl$_2$) ν 2925, 2854, 1729, 1652, 1497, 1455 cm^{-1}; ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.61–7.24 (m, 15H, ArH), 5.86 (d, J = 11.6 Hz, 1H, H-6), 5.76 (dt, J = 11.6, 7.2 Hz, 1H, H-7), 7.41 (s, 2H, CH$_2$Ph), 4.67 (d, J = 9.2 Hz, 1H, H-4), 4.54 (d, J = 12.0 Hz, 1H, CH$_2$Ph), 4.49 (d, J = 12.0 Hz, 1H, CH$_2$Ph), 4.44 (d, J = 11.6 Hz, 1H, CH$_2$Ph), 4.45–4.41 (m, 1H, H-3), 4.25 (d, J = 11.6 Hz, 1H, CH$_2$Ph), 3.72 (dddd, J = 10.4, 7.2, 3.6, 3.6 Hz, 1H, H-2), 3.50 (dd, J = 10.0, 3.6 Hz, 1H, H-1a), 3.43 (dd, J = 10.0, 6.8 Hz, 1H, H-1b), 2.78 (d, J = 3.6 Hz, 1H, 2-OH), 2.26–2.20 (m, 2H, CH$_2$), 1.40–1.24 (m, 18H, CH$_2$), 0.88 (t, J = 6.8 Hz, 3H, CH$_3$); ^{13}C NMR (100 MHz, CDCl$_3$) δ 154.3 (C), 138.5 (C), 138.3 (C), 137.9 (CH), 137.3 (C), 128.4 (CH × 2), 128.3 (CH × 2), 128.2 (CH × 2), 128.1 (CH × 2), 127.9 (CH), 127.8 (CH × 2), 127.7 (CH × 2),

127.5 (CH × 2), 123.1 (CH), 110.4 (CH), 73.8 (CH), 73.5 (CH), 73.4 (CH$_2$), 71.2 (CH$_2$), 71.0 (CH$_2$), 70.1 (CH$_2$), 31.9 (CH$_2$), 29.65 (CH$_2$), 29.64 (CH$_2$ × 2), 29.56 (CH$_2$), 29.54 (CH$_2$), 29.4 (CH$_2$), 29.3 (CH$_2$), 29.2 (CH$_2$), 22.7 (CH$_2$), 14.1 (CH$_3$); HRMS (ESI, M + Na$^+$) calcd for C$_{39}$H$_{52}$O$_4$Na 607.3758, found 607.3762.

(2R,3S,4Z,6Z)-1,3,5-Tri-O-benzyl-octadec-4,6-diene-1,2,3,5-tetraol (9b). Method A: a solution of hemiacetal **8b** (100 mg, 0.19 mmol) and dodecyltriphenylphosphonium bromide (378 mg, 0.74 mmol) in anhydrous tetrahydrofuran (5 mL) was cooled to 0 °C, followed by quick addition of potassium *tert*-butoxide (83 mg, 0.74 mmol). After stirring for 4 h at this temperature, the reaction mixture was treated with water (2 mL) and extracted with ethyl acetate (3 × 2 mL). The combined organic layers were dried over anhydrous MgSO$_4$, filtered, and concentrated. The residue was purified by column chromatography to afford the olefin **9b** (98 mg, 90%) as a colorless oil. **Method B:** a solution of hemiacetal **8c** (200 mg, 0.37 mmol) and dodecyltriphenyl-phosphonium bromide (760 mg, 1.48 mmol) in anhydrous tetrahydrofuran (2 mL) was cooled to 0 °C, followed by quick addition of potassium *tert*-butoxide (170 mg, 1.48 mmol). After stirring for 2 h at this temperature, the reaction mixture was treated with water (5 mL) and extracted with ethyl acetate (3 × 5 mL). The combined organic layers were dried over anhydrous MgSO$_4$, filtered, and concentrated. The residue was purified by column chromatography to afford the olefin **9b** (170 mg, 79%) as a colorless oil. R_f 0.55 (EtOAc/Hex = 1/3); $[\alpha]_D^{23}$ +15.3 (*c* 0.5, CH$_2$Cl$_2$); IR (CH$_2$Cl$_2$) ν 3567, 3463, 3064, 3031, 2925, 2854, 1651, 1496, 1457 cm^{-1}; ^{1}H NMR (600 MHz, CDCl$_3$) δ 7.35–7.22 (m, 15H, ArH), 5.76 (d, *J* = 11.4 Hz, 1H, H-6), 5.77 (dt, *J* = 12.0, 7.8 Hz, 1H, H-7), 4.87 (d, *J* = 9.6 Hz, 1H, H-4), 4.80 (s, 2H, CH$_2$Ph), 4.59 (dd, *J* = 9.6, 4.2 Hz, 1H, H-3), 4.52–4.48 (m, 3H, CH$_2$Ph), 4.29 (d, *J* = 12.0 Hz, 1H, CH$_2$Ph), 3.92–3.89 (m, 1H, H-2), 3.69 (d, *J* = 4.8 Hz, 1H, 2-OH), 3.56 (dd, *J* = 9.6, 4.2 Hz, 1H, H-1a), 3.50 (dd, *J* = 9.6, 6.0 Hz, 1H, H-1b), 2.35–2.31 (m, 2H, CH$_2$), 1.42–1.40 (m, 2H, CH$_2$), 1.31–1.26 (m, 16H, CH$_2$), 0.88 (t, *J* = 7.2 Hz, 3H, CH$_3$); ^{13}C NMR (150 MHz, CDCl$_3$) 155.0 (C), 140.3 (C), 139.8 (C), 138.8 (C), 137.6 (CH), 129.1 (CH × 2), 128.9 (CH × 2), 128.8 (CH × 2), 128.7 (CH × 2), 128.5 (CH), 128.3 (CH × 2), 128.2 (CH × 2), 128.0 (CH), 127.8 (CH), 124.6 (CH), 112.1 (CH), 75.3 (CH), 73.6 (CH), 73.5 (CH), 72.7 (CH), 71.9 (CH$_2$), 70.5 (CH$_2$), 32.6 (CH$_2$), 30.34 (CH$_2$), 30.29 (CH$_2$), 30.16 (CH$_2$), 30.11 (CH$_2$), 30.0 (CH$_2$), 29.8 (CH$_2$), 29.4 (CH$_2$), 23.3 (CH$_2$), 14.3 (CH$_3$); HRMS (ESI, M + Na$^+$) calcd for C$_{39}$H$_{52}$O$_4$Na 607.3758, found 607.3738.

(2S,3S,4R,5S,6Z)-1,3,4,5-Tetra-O-benzyl-octadec-6-ene-1,2,3,4,5-pentaol (10a). A solution of hemiacetal **8a** (100 mg, 0.19 mmol) and dodecyltriphenylphosphonium bromide (567 mg, 1.11 mmol) in anhydrous tetrahydrofuran (1 mL) was cooled to 0 °C, followed by slow addition of lithium hexamethyldisilazane (1 M in tetrahydrofuran, 1.1 mL, 1.11 mmol). After stirring for 24 h at this temperature, the reaction mixture was treated with water (1 mL) and extracted with ethyl acetate (3 × 2 mL). The combined organic layers were dried over anhydrous MgSO$_4$, filtered, and concentrated. The residue was purified by column chromatography to afford the olefin **10a** (83 mg, 65%, Z/E = 2.4/1) as a colorless oil. **10a-Z:** R_f 0.48 (EtOAc/Hex = 1/4); $[\alpha]_D^{22}$ −3.5 (*c* 0.1, CH$_2$Cl$_2$); IR (CH$_2$Cl$_2$) ν 3468, 2925, 2854, 1648, 1496, 1210 cm^{-1}; ^{1}H NMR (600 MHz, CDCl$_3$) δ 7.36–7.23 (m, 18H, ArH), 7.17–7.16

(m, 2H, ArH), 5.65 (dt, *J* = 10.8, 7.2 Hz, 1H, H-7), 5.44 (dd, *J* = 11.4, 9.6 Hz, 1H, H-6), 4.79 (d, *J* = 10.8 Hz, 1H, CH$_2$Ph), 4.74 (d, *J* = 10.8 Hz, 1H, CH$_2$Ph), 4.63 (d, *J* = 12.0 Hz, 1H, CH$_2$Ph), 4.48 (d, *J* = 12.0 Hz, 1H, CH$_2$Ph), 4.44 (dd, *J* = 9.0, 3.6 Hz, 1H, H-5), 4.41 (d, *J* = 12.0 Hz, 1H, CH$_2$Ph), 4.40 (d, *J* = 11.4 Hz, 1H, CH$_2$Ph), 4.37 (d, *J* = 11.4 Hz, 1H, CH$_2$Ph), 4.31 (d, *J* = 12.0 Hz, 1H, CH$_2$Ph), 4.10–4.07 (m, 1H, H-2), 3.79–3.76 (m, 2H, H-3, H-4), 3.51 (dd, *J* = 9.6, 6.6 Hz, 1H, H-1a), 3.47 (dd, *J* = 9.0, 6.6 Hz, 1H, H-1b), 3.13 (d, *J* = 4.8 Hz, 1H, 2-OH), 2.06–1.95 (m, 2H, CH$_2$), 1.32–1.25 (m, 18H, CH$_2$), 0.88 (t, *J* = 7.2 Hz, 3H, CH$_3$); ^{13}C NMR (150 MHz, CDCl$_3$) δ 138.4 (C), 138.22 (C), 138.15 (C), 138.0 (C), 135.5 (CH), 128.3 (CH × 8), 128.1 (CH × 2), 127.99 (CH × 2), 127.97 (CH × 2), 127.7 (CH × 3), 127.6 (CH), 127.53 (CH), 127.50 (CH), 127.0 (CH), 82.5 (CH), 76.6 (CH), 75.4 (CH$_2$), 74.3 (CH), 73.11 (CH$_2$), 73.06 (CH$_2$), 71.2 (CH$_2$), 69.9 (CH$_2$), 69.8 (CH), 31.9 (CH$_2$), 29.7 (CH$_2$ × 3), 29.6 (CH$_2$), 29.5 (CH$_2$), 29.42 (CH$_2$), 29.36 (CH$_2$), 28.1 (CH$_2$), 22.7 (CH$_2$), 14.1 (CH$_3$); HRMS (ESI, M + Na$^+$) calcd for C$_{46}$H$_{60}$O$_5$Na 715.4333, found 715.4348. **10a-E:** R_f 0.44 (EtOAc/Hex = 1/4); $[\alpha]_D^{23}$ −0.1 (*c* 0.1 CH$_2$Cl$_2$); IR (CH$_2$Cl$_2$) ν 3361, 2925, 2853, 1649, 1497, 1209 cm^{-1}; ^{1}H NMR (600 MHz, CDCl$_3$) δ 7.36–7.25 (m, 18H, ArH), 7.18–7.17 (m, 2H, ArH), 5.70 (dt, *J* = 15.0, 6.6 Hz, 1H, H-7), 5.40 (dd, *J* = 15.6, 9.0 Hz, 1H, H-6), 4.78 (d, *J* = 11.4 Hz, 1H, CH$_2$Ph), 4.75 (d, *J* = 11.4 Hz, 1H, CH$_2$Ph), 4.62 (d, *J* = 11.4 Hz, 1H, CH$_2$Ph), 4.47 (d, *J* = 12.0 Hz, 1H, CH$_2$Ph), 4.43 (d, *J* = 11.4 Hz, 1H, CH$_2$Ph), 4.39 (d, *J* = 12.0 Hz, 1H, CH$_2$Ph), 4.35 (d, *J* = 10.8 Hz, 1H, CH$_2$Ph), 4.33 (d, *J* = 11.4 Hz, 1H, CH$_2$Ph), 4.11–4.08 (m, 1H, H-2), 4.01 (dd, *J* = 8.4, 5.4 Hz, 1H, H-5), 3.8 (dd, *J* = 4.8, 4.8 Hz, 1H, H-4), 3.76–3.75 (m, 1H, H-3), 3.51 (dd, *J* = 9.0, 6.0 Hz, 1H, H-1a), 3.47 (dd, *J* = 9.6, 6.6 Hz, 1H, H-1b), 3.19 (d, *J* = 4.8 Hz, 1H, 2-OH), 2.04–1.98 (m, 2H, CH$_2$), 1.33–1.25 (m, 18H, CH$_2$), 0.88 (t, *J* = 7.2 Hz, 3H, CH$_3$); ^{13}C NMR (150 MHz, CDCl$_3$) δ 138.5 (C), 138.3 (C), 138.2 (C), 138.0 (C), 136.6 (CH), 128.3 (CH × 8), 128.12 (CH × 2), 128.07 (CH × 2), 127.9 (CH × 2), 127.70 (CH), 127.66 (CH × 2), 127.62 (CH), 127.53 (CH), 127.46 (CH), 127.0 (CH), 82.5 (CH), 80.6 (CH), 76.3 (CH), 75.4 (CH$_2$), 73.1 (CH$_2$), 72.8 (CH$_2$), 71.1 (CH$_2$), 69.9 (CH$_2$), 69.7 (CH), 32.4 (CH$_2$), 31.9 (CH$_2$), 29.70 (CH$_2$), 29.66 (CH$_2$ × 2), 29.5 (CH$_2$), 29.4 (CH$_2$), 29.3 (CH$_2$), 29.0 (CH$_2$), 22.7 (CH$_2$), 14.1 (CH$_3$); HRMS (ESI, M + Na$^+$) calcd for C$_{46}$H$_{60}$O$_5$Na 715.4333, found 715.4350.

(2S,3R,4R,5S,6Z)-1,3,4,5-Tetra-O-benzyl-octadec-6-ene-1,2,3,4,5-pentaol (10b). A solution of hemiacetal **8b** (100 mg, 0.19 mmol) and dodecyltriphenylphosphonium bromide (567 mg, 1.11 mmol) in anhydrous tetrahydrofuran (1.5 mL) was cooled to 0 °C, followed by slow addition of lithium hexamethyldisilazane (1 M in tetrahydrofuran, 1.11 mL, 1.11 mmol). After stirring for 24 h at this temperature, the reaction mixture was treated with water (1 mL) and extracted with ethyl acetate (3 × 2 mL). The combined organic layers were dried over anhydrous MgSO$_4$, filtered, and concentrated. The residue was purified by column chromatography to afford olefin **10b** (94 mg, 72%) as a colorless oil. R_f 0.38 (EtOAc/Hex = 1/6); $[\alpha]_D^{23}$ +26.5 (*c* 0.7, CH$_2$Cl$_2$); IR (CH$_2$Cl$_2$) ν 3565, 3475, 3088, 2925, 2854, 1600, 1496, 1457 cm^{-1}; ^{1}H NMR (600 MHz, CDCl$_3$) δ 7.37–7.19 (m, 20H, ArH), 5.67 (dt, *J* = 10.8, 7.2 Hz, 1H, H-7), 5.47 (dd, *J* = 11.4, 9.6 Hz, 1H, H-6), 4.80 (d, *J* = 11.4 Hz, 1H, CH$_2$Ph), 4.74–4.68 (m, 2H, CH$_2$Ph), 4.62 (d, *J* = 11.4 Hz, 1H, CH$_2$Ph), 4.58–4.46 (m, 4H, CH$_2$Ph, H-5), 4.37

(d, J = 12.0 Hz, 1H, CH$_2$Ph), 4.01 (bs, 1H, H-2), 3.77–3.72 (m, 2H, H-4, H-3), 3.61–3.56 (m, 2H, H-1a, H-1b), 2.98 (d, J = 4.2 Hz, 1H, 2-OH), 2.07–2.01 (m, 2H, CH$_2$), 1.30–1.16 (m, 18H, CH$_2$), 0.88 (t, J = 7.2 Hz, 3H, CH$_3$); ^{13}C NMR (150 MHz, CDCl$_3$) δ 138.45 (C), 138.38 (C), 138.35 (C), 138.1 (C), 135.6 (CH), 128.55 (CH), 128.48 (CH), 128.4 (CH), 128.3 (CH × 7), 128.2 (CH × 2), 127.9 (CH × 2), 127.8 (CH × 2), 127.7 (CH), 127.6 (CH), 127.5 (CH), 127.4 (CH), 127.0 (CH), 126.9 (CH), 81.8 (CH), 78.3 (CH), 74.9 (CH), 74.7 (CH$_2$), 73.3 (CH$_2$), 73.1 (CH$_2$), 71.2 (CH$_2$), 70.5 (CH), 70.2 (CH$_2$), 31.9 (CH$_2$), 29.7 (CH$_2$), 29.6 (CH$_2$ × 2), 29.5 (CH$_2$), 29.4 (CH$_2$), 29.3 (CH$_2$), 28.1 (CH$_2$), 22.7 (CH$_2$), 14.1 (CH$_3$); HRMS (ESI, M + Na$^+$) calcd for C$_{46}$H$_{60}$O$_5$Na 715.4333, found 715.4349.

(2S,3R,4R,5R)-1,3,4,5-Tetra-O-benzyl-octadec-6-ene-1,2,3,4,5-pentaol (10c). A solution of hemiacetal **8c** (100 mg, 0.18 mmol) and dodecyltriphenylphosphonium bromide (567 mg, 1.11 mmol) in anhydrous tetrahydrofuran (1 mL) was cooled to 0 °C, followed by slow addition of lithium hexamethyldisilazane (1 M in tetrahydrofuran, 1.1 mL, 1.11 mmol). After stirring for 12 h at this temperature, the reaction mixture was treated with water (2 mL) and extracted with ethyl acetate (3 × 2 mL). The combined organic layers were dried over anhydrous MgSO$_4$, filtered, and concentrated. The residue was purified by column chromatography to afford olefin **10c** (82 mg, 64%) as a colorless oil. R_f 0.68 (EtOAc/Hex = 1/3); $[\alpha]_D^{23}$ −7.3 (c 4.8, CH$_2$Cl$_2$); IR (CHCl$_3$) ν 3565, 3475, 3064, 3031, 2925, 2854, 1599, 1495, 1457 cm^{-1}; ^{1}H NMR (600 MHz, CDCl$_3$) δ 7.38–7.18 (m, 20H, ArH), 5.83–5.77 (m, 1H, H-7), 5.54–5.48 (m, 1H, H-6), 4.72–4.04 (m, 9H, CH$_2$Ph, H-5), 4.00 (bs, 1H, H-2), 3.89–3.56 (m, 1H, H-3), 3.84–3.83 (m, 1H, H-4), 3.65–3.55 (m, 2H, H-1), 2.61 (bs, 1H, 2-OH), 2.17–2.05 (m, 2H, CH$_2$), 1.37–1.25 (m, 18H, CH$_2$), 0.89–0.87 (m, 3H, CH$_3$); ^{13}C NMR (150 MHz, CDCl$_3$) δ 138.6 (C), 138.51 (C), 138.47 (C), 138.4 (C), 136.7 (CH), 128.3 (CH × 8), 128.21 (CH), 128.16 (CH), 128.13 (CH), 128.09 (CH), 127.8 (CH), 127.7 (CH × 2), 127.6 (CH × 2), 127.5 (CH), 127.44 (CH), 127.41 (CH), 127.37 (CH), 80.8 (CH), 79.9 (CH), 74.4 (CH$_2$), 74.3 (CH$_2$), 73.93 (CH$_2$), 73.6 (CH), 73.2 (CH$_2$), 71.3 (CH$_2$), 70.07 (CH), 69.4 (CH$_2$), 31.9 (CH$_2$), 29.65 (CH$_2$), 29.62 (CH$_2$), 29.60 (CH$_2$), 29.51 (CH$_2$), 29.47 (CH$_2$), 29.4 (CH$_2$), 29.32 (CH$_2$), 28.1 (CH$_2$), 14.1 (CH$_3$); HRMS (ESI, M + Na$^+$) calcd for C$_{46}$H$_{60}$O$_5$Na 715.4333, found 715.4343.

(2S,3S,4R,5R,6Z)-1,3,4,5-Tetra-O-benzyl-octadec-6-ene-1,2,3,4,5-pentaol (10d). A solution of hemiacetal **8d** (168 mg, 0.31 mmol) and dodecyltriphenylphosphonium bromide (954 mg, 1.86 mmol) in anhydrous tetrahydrofuran (1.7 mL) was cooled to 0 °C, followed by slow addition of lithium hexamethyldisilazane (1 M in tetrahydrofuran, 1.9 mL, 1.86 mmol). After stirring for 18 h at this temperature, the reaction mixture was treated with water (2 mL) and extracted with ethyl acetate (3 × 2 mL). The combined organic layers were dried over anhydrous MgSO$_4$, filtered, and concentrated. The residue was purified by column chromatography to afford olefin **10d** (188 mg, 87%, E/Z = 1/2) as a colorless oil. **10d-Z**: R_f 0.65 (EtOAc/Hex = 1/4); $[\alpha]_D^{26}$ −39.1 (c 1.0, CH$_2$Cl$_2$); IR (CH$_2$Cl$_2$) ν 3058, 3064, 3031, 2925, 2854, 1496, 1456, 1092, 1066, 1027 cm^{-1}; ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.29–7.22 (m, 20H, ArH), 5.77 (dt, J = 11.2, 7.6 Hz, 1H, H-7), 5.48 (dd, J = 10.4, 10.0 Hz, 1H, H-6), 4.73 (d, J = 11.2 Hz, 1H, CH$_2$Ph), 4.66 (d, J = 11.2 Hz, 1H, CH$_2$Ph), 4.59 (d, J = 11.6 Hz, 1H, CH$_2$Ph), 4.58 (d, J = 11.6 Hz, 1H, CH$_2$Ph), 4.50 (d, J = 11.6 Hz, 1H,

CH$_2$Ph), 4.49–4.41 (m, 3H, CH$_2$Ph, H-5), 4.33 (d, J = 11.6 Hz, 1H, CH$_2$Ph), 4.17 (dddd, J = 8.0, 6.0, 6.0, 2.0 Hz, 1H, H-2), 3.90 (dd, J = 4.8, 4.8 Hz, 1H, H-4), 3.80 (dd, J = 4.8, 2.0 Hz, 1H, H-3), 3.54 (d, J = 6.0 Hz, 2H, H-1a, H-1b), 3.44 (d, J = 4.4 Hz, 1H, 2-OH), 2.06–1.88 (m, 2H, CH$_2$), 1.30–1.20 (m, 18H, CH$_2$), 0.88 (t, J = 7.2 Hz, 3H, CH$_3$); ^{13}C NMR (100 MHz, CDCl$_3$) δ 138.3 (C), 138.2 (C), 138.1 (C), 137.9 (C), 136.6 (CH), 128.3 (CH × 8), 128.1 (CH × 2), 127.9 (CH × 2), 127.8 (CH × 2), 127.7 (CH × 2), 127.66 (CH), 127.61 (CH), 127.51 (CH), 127.47 (CH), 126.5 (CH), 81.9 (CH), 77.2 (CH), 74.4 (CH$_2$), 74.1 (CH), 73.2 (CH$_2$), 72.7 (CH$_2$), 71.1 (CH$_2$), 70.1 (CH), 70.0 (CH$_2$), 31.9 (CH$_2$), 29.7 (CH$_2$), 29.63 (CH$_2$ × 2), 29.60 (CH$_2$), 29.5 (CH$_2$), 29.4 (CH$_2$), 29.3 (CH$_2$), 28.2 (CH$_2$), 22.7 (CH$_2$), 14.1 (CH$_3$); HRMS (ESI, M + Na$^+$) calcd for C$_{46}$H$_{60}$O$_5$Na 715.4333, found 715.4331. **10d-E**: R_f 0.59 (EtOAc/Hex = 1/4); $[\alpha]_D^{27}$ −29.6 (c 1.0 CH$_2$Cl$_2$); IR (CH$_2$Cl$_2$) ν 3509, 3061, 3031, 2925, 2854, 1496, 1456, 1209, 1097, 1065, 1027, 973 cm^{-1}; ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.32–7.19 (m, 20H, ArH), 5.63 (dt, J = 15.6, 6.4 Hz, 1H, H-7), 5.51 (dd, J = 15.6, 8.4 Hz, 1H, H-6), 4.80 (d, J = 10.8 Hz, 1H, CH$_2$Ph), 4.66 (d, J = 11.2 Hz, 1H, CH$_2$Ph), 4.59 (d, J = 12.0 Hz, 1H, CH$_2$Ph), 4.56 (d, J = 10.8 Hz, 1H, CH$_2$Ph), 4.51 (d, J = 12.0 Hz, 1H, CH$_2$Ph), 4.47 (d, J = 12.0 Hz, 1H, CH$_2$Ph), 4.44 (d, J = 12.0 Hz, 1H, CH$_2$Ph), 4.32 (d, J = 12.0 Hz, 1H, CH$_2$Ph), 4.16–4.11 (m, 1H, H-2), 4.00 (dd, J = 8.4, 4.8 Hz, 1H, H-5), 3.91 (dd, J = 5.2, 5.2 Hz, 1H, H-4), 3.73 (dd, J = 6.0, 2.0 Hz, 1H, H-3), 3.53 (d, J = 6.4 Hz, 2H, H-1a, H-1b), 3.20 (d, J = 5.6 Hz, 1H, 2-OH), 2.11–2.06 (m, 2H, CH$_2$), 1.40–1.26 (m, 18H, CH$_2$), 0.88 (t, J = 6.8 Hz, 3H, CH$_3$); ^{13}C NMR (100 MHz, CDCl$_3$) δ 138.4 (C), 138.2 (C), 138.1 (C), 138.0 (C), 137.6 (CH), 128.31 (CH × 2), 128.29 (CH × 4), 128.27 (CH × 2), 128.1 (CH × 2), 128.0 (CH × 2), 127.8 (CH × 2), 127.7 (CH × 4), 127.5 (CH), 127.4 (CH), 126.5 (CH), 81.7 (CH), 80.6 (CH), 77.1 (CH), 74.3 (CH$_2$), 73.2 (CH$_2$), 73.0 (CH$_2$), 71.1 (CH$_2$), 69.9 (CH), 69.8 (CH$_2$), 32.5 (CH$_2$), 31.9 (CH$_2$), 29.7 (CH$_2$), 29.6 (CH$_2$ × 2), 29.5 (CH$_2$), 29.35 (CH$_2$), 29.29 (CH$_2$), 29.20 (CH$_2$), 22.7 (CH$_2$), 14.1 (CH$_3$); HRMS (ESI, M + Na$^+$) calcd for C$_{46}$H$_{60}$O$_5$Na 715.4333, found 715.4340.

(2S,3S,4Z,6Z)-2-Hexacosanoylamino-3,5-di-O-benzyl-1-O-(2,3,4,6-tetra-O-benzyl-α-D-galactopyranosyl)-octadec-4,6-dien-1,3,5-triol (13). To a solution of compound **6a** (150 mg, 0.15 mmol) and triphenylphosphine (105 mg, 0.40 mmol) in anhydrous THF (2 mL) at 0 °C was added diisopropyl azodicarboxylate (DIAD, 95 μL, 0.43 mmol) followed by dropwise addition of diphenylphosphoryl azide (DPPA, 78 μL, 0.40 mmol) to the reaction flask. After complete addition, the temperature was brought to room temperature by removing ice bath and the reaction was stirred for 1 h. Upon completion of the reaction, the mixture was diluted with EtOAc, and the resulting mixture was washed by water. The organic layer was dried over anhydrous MgSO$_4$, filtered, and concentrated *in vacuo*. Purification of this residue by column chromatography gives the compound **12** (147 mg, 97%). The compound **12** (686 mg, 0.66 mmol) was added to a round bottom flask followed by the addition of triphenylphosphine (313 mg, 1.19 mmol), pyridine (2.0 mL), water (700 μL), and tetrahydrofuran (7.0 mL). Then, the mixture was warmed up to 60 °C and stirred for 12 h. The solvent was evaporated in vacuum to get a crude amine. This crude amine was dissolved in anhydrous dichloromethane (7.0 mL) at room

temperature, 1-[3-(di-methylamino)propyl]-3-ethylcarbodiimide hydrochloride (EDC, 205 mg, 1.07 mmol), hexaeicosanoic acid (306 mg, 0.77 mmol) and HOBt (145 mg, 1.07 mmol) were sequentially added to the solution, and the mixture was continuously stirred for 12 h. The reaction solution was diluted with EtOAc, and the resulting mixture was washed by water. The organic layer was dried over anhydrous MgSO$_4$, filtered, and concentrated *in vacuo*. This resulting residue was purified by column chromatography to give the amide compound **13** (730 mg, 80%). R_f 0.4 (EtOAc/Hex = 1/5); $[\alpha]_D^{29}$ +10.2 (*c* 1.3, CHCl$_3$); mp = 79 °C; IR (CHCl$_3$) ν 3428, 2918, 2360, 1645, 1454, 1116 cm^{-1}; ^{1}H NMR (600 MHz, CDCl$_3$) δ 7.37–7.19 (m, 30H, ArH), 5.91 (d, J = 9.1 Hz, 1H, NH), 5.78 (d, J = 11.8 Hz, 1H, H-6), 5.73–5.69 (m, 1H, H-7), 4.90 (d, J = 11.4 Hz, 1H, CH$_2$Ph), 4.87 (d, J = 3.6 Hz, 1H, H-1′), 4.79 (d, J = 11.4 Hz, 1H, CH$_2$Ph), 4.73 (d, J = 12.0 Hz, 3H, CH$_2$Ph), 4.69 (d, J = 9.6 Hz, 1H, H-4), 4.65 (d, J = 11.4 Hz, 2H, CH$_2$Ph), 4.61 (dd, J = 8.4, 9.0 Hz, 1H, H-3), 4.55 (d, J = 11.4 Hz, 1H, CH$_2$Ph), 4.45 (d, J = 11.4 Hz, 1H, CH$_2$Ph), 4.372 (d, J = 11.4 Hz, 1H, CH$_2$Ph), 4.367 (d, J = 11.4 Hz, 1H, CH$_2$Ph), 4.18–4.12 (m, 2H, CH$_2$Ph, H-2), 4.04 (dd, J = 9.9, 3.6 Hz, 1H, H-2′), 3.94–3.89 (m, 4H, H-1a, H-3′, H-4′, H-5′), 3.72 (dd, J = 10.8, 3.0 Hz, 1H, H-1b), 3.50–3.43 (m, 2H, H-6a′, H-6b′), 2.22–2.11 (m, 2H, H-8a, H-8b), 1.98–1.86 (m, 2H, CH$_2$), 1.51–1.46 (m, 2H, CH$_2$), 1.34–1.23 (m, 62H, CH$_2$), 0.88 (t, J = 6.6 Hz, 6H, CH$_3$ × 2); ^{13}C NMR (150 MHz, CDCl$_3$) δ 172.6 (C), 153.7 (C), 138.8 (C), 138.7 (C), 138.6 (C), 138.5 (C), 137.8 (C), 137.7 (C), 137.5 (CH), 128.33 (CH × 4), 128.29 (CH × 4), 128.24 (CH), 128.17 (CH × 3), 127.7 (CH), 127.82 (CH × 3), 127.77 (CH × 3), 127.7 (CH), 127.5 (CH × 3), 127.4 (CH × 3), 127.3 (CH × 3), 127.2 (CH), 123.0 (CH), 112.4 (CH), 98.8 (CH), 79.0 (CH), 76.5 (CH), 74.73 (CH), 74.70 (CH$_2$), 73.4 (CH$_2$), 73.0 (CH$_2$), 72.9 (CH$_2$), 72.3 (CH), 70.8 (CH$_2$), 70.3 (CH$_2$), 69.4 (CH), 68.8 (CH$_2$), 68.0 (CH$_2$), 52.3 (CH), 36.7 (CH$_2$), 31.9 (CH$_2$ × 3), 29.7 (CH$_2$ × 20), 29.50 (CH$_2$), 29.45 (CH$_2$), 29.4 (CH$_2$), 29.3 (CH$_2$ × 2), 29.2 (CH$_2$), 25.6 (CH$_2$), 22.7 (CH$_2$ × 3), 14.1 (CH$_3$ × 2); HRMS (ESI, M + H$^+$) calcd for C$_{92}$H$_{131}$O$_9$NNa 1416.9716, found 1416.9722.

(2S,3S,5S)-2-Hexacosanoylamino-1-O-(α-d-galactopyranosyl)-octadec-1,3,5-triol (2). Compound **13** (118 mg, 0.08 mmol) was dissolved in MeOH/CHCl$_3$ (3/1 ratio, 2 mL) at room temperature. Pd(OH)$_2$/C (118 mg, Degussa type) was added to the reaction mixture, the reaction vessel was purged with hydrogen, and the mixture was stirred under 60 psi pressure at the same temperature for 1 day. The resulting solution was filtered through celite, the filtrate was concentrated *in vacuo*, and the residue was purified by flash column chromatography on silica gel to afford the compound **2** (43 mg, 62%). Compound **2** was unable to dissolve in d-solvents such as pure CDCl$_3$, CD$_3$OD or d-DMSO but it was slightly dissolved in d5-pyridine. R_f 0.6 (MeOH/DCM = 1/7); mp = 144–148 °C; $[\alpha]_D^{24}$ +39.7 (*c* 0.3, CHCl$_3$); IR (CHCl$_3$) ν 3280, 2850, 1148, 1454 cm^{-1}; ^{1}H NMR (400 MHz, d5-Pyridine) δ 8.38 (d, J = 8.8 Hz, 1H, NH), 5.39 (d, J = 4.0 Hz, 1H, H-1′), 4.69–4.62 (m, 2H, H-2, H-2′), 4.56 (d, J = 3.3 Hz, 1H, H-4′), 4.50–4.38 (m, 6H, H-3, H-3′, H-5, H-5′, H-6a′, H-6b′), 4.09 (dd, J = 10.4, 5.6 Hz, 1H, H-1a), 3.89 (dd, J = 10.4, 5.6 Hz, 1H, H-1b), 2.69 (t, J = 7.2 Hz, 2H, CH$_2$), 2.45 (t, J = 7.6 Hz, 2H, CH$_2$), 2.41–2.38 (m, 2H, CH$_2$), 2.31–2.04 (m, 4H, CH$_2$), 1.89–1.78 (m, 2H, CH$_2$), 1.65–1.55 (m, 2H, CH$_2$), 1.40–1.23 (m, 60H, CH$_2$), 0.87–

0.83 (m, 6H, CH$_3$); ^{13}C NMR (150 MHz, d5-Pyridine 100 °C) δ 173.4 (C), 101.8 (CH), 73.1 (CH), 72.1 (CH$_2$), 71.9 (CH × 2), 71.3 (CH × 2), 70.8 (CH), 63.1 (CH$_2$), 50.0 (CH), 43.2 (CH$_2$ × 2), 39.8 (CH$_2$), 37.1 (CH$_2$), 32.3 (CH$_2$ × 4), 30.1 (CH$_2$ × 13), 30.0 (CH$_2$ × 5), 29.9 (CH$_2$ × 5), 26.9 (CH$_2$), 26.4 (CH$_2$), 24.5 (CH$_2$), 23.0 (CH$_2$ × 3), 14.2 (CH$_3$ × 2). HRMS (ESI, M − H$^+$) calcd for C$_{50}$H$_{98}$O$_9$N 856.7236, found 856.7222.

General procedure for ELISA

Supernatant was collected three days after incubation and the production of IL-2 was quantified with DuoSet ELISA Development System (R&D System, MN, USA). Briefly, capture antibody was coated on the plate overnight at 4 °C. The plates were washed and blocked with blocking buffer (1% BSA in PBS). Then, samples were added and incubated for 2 hours at room temperature, washed three times with wash buffer (0.05% Tween 20 in PBS), added the detection antibody, and incubated for 2 hours at room temperature. After washing, the plates were added streptavidin–HRP and incubated for 20 minutes at room temperature. After incubation, the plates were washed, then added substrate solution to each well, and incubated for 20 minutes at room temperature. Finally, added stop solution (2.0 N H$_2$SO$_4$) and determined the optical density (OD450) by using a microplate reader (SpectraMax M2, Molecular device, CA, USA).

Acknowledgements

Notes and references

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