Asymmetric Allylboration and Ring Closing Alkene Metathesis: A Novel Strategy for the Synthesis of Glycosphingolipids

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A novel strategy for the synthesis of D,L-glucosylceramide **1**, a member of the glycosphingolipid class of natural products is described. Reagent-controlled asymmetric Brown allylboration gave excellent stereochemical control in the construction of adjacent stereocenters in the sphingoid base portion of the molecule. The *trans*-configured double bond was obtained as a single geometrical isomer by use of silicon-tethered olefin metathesis employing the Schrock carbene $[(CF_3)_2MeCO]_2Mo(=CHCMe_2Ph)(=NC_6H_3\text{-}2,6\text{-}i\text{-}Pr_2)$ and in situ PhLi-induced ring-opening of the intermediate 5,6-dihydro-2*H*-1,2-oxasiline followed by protodesilylation with TBAF in DMSO. The synthesis was completed by long chain amide formation and global deprotection.

Introduction

Glycosphingolipids are central components of a wide variety of tissues and organs in biological systems.[1] They serve as structural support and shape determinants of the cell membrane and, via protein binding, act as mediators of biological events such as activation, cell agglutination, intracellular communication, cell death, and cell growth. Such cellular recognition events are common to cancer, allergy, viral infection, inflammation, and autoimmune disease.[2,3] Each of these events is executed by a specific glycosphingolipid such as a ganglioside, tumor antigen, or viral receptor.[3,4] This exquisite degree of specificity suggests that glycosphingolipid analogues could be suitable candidates for new drugs,[3] thus necessitating efficient synthetic routes to pure glycosphingolipids and their derivatives.

The key synthetic concerns in synthesis of glycosphingolipids are the stereo- and regioselective construction of the polysaccharide moiety (glycosyl donor) via *O*-glycosylation, stereoselective construction of the sphingoid base (glycosyl acceptor), in which the asymmetric constructions of the *anti*-amino alcohol and *trans*-olefin units are of chief importance and the stereoselective and regioselective coupling of the glycosyl acceptor to the glycosyl donor. Excellent reviews address these concerns, especially stereoselective *O*-glycosylations and *anti*-amino alcohol construction related to sphingosine synthesis.[5,6] However, the incorporation of the sphingoid *trans*-disubstituted double bond remains nontrivial, as its installation does not typically proceed with high *trans* selectivity and the starting materials require prior derivatization.[6a,7] We envisioned that the *trans*-disubstituted double bond could be installed via alkene metathesis using the molybdenum metathesis catalyst, **2**, developed by Schrock,[8] or the ruthenium-based catalyst **3** developed by Grubbs.[9] We have recently published two efficient routes to *trans*-disubstituted homoallylic alcohols employing the tandem use of Brown's asymmetric allylboration technology and alkene metathesis.[10,11] We now report the extension of this work to the synthesis of D,L-glucosylceramide, **1**,[12] a simple member of the glycosphingolipid class of compounds.

Results and Discussion

Alkene metathesis has been shown to be amenable to both cross metathesis[13] and ring closing metathesis[14] in

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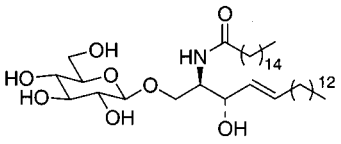
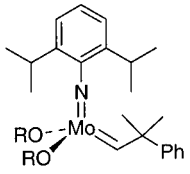
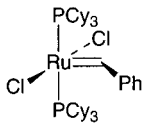


1

D,L-glucosylceramide



2; R = $C(CH_3)(CF_3)_2$

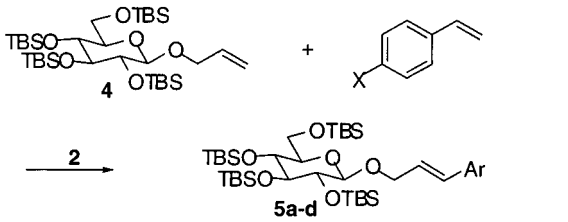


3; Cy = cyclohexyl

sugar systems. However, when we started our work on glycosphingolipids, the use of alkene cross-metathesis on carbohydrate substrates was unknown. Thus we initially sought to examine allyl 2,3,4,6-tetra-*O*-*tert*-butyldimethylsilyl-β-D-glucose **4** as a suitable model system. Glucoside **4** was readily prepared from allyl β-D-glucopyranoside[15] by reaction with *tert*-butyldimethylsilyl trifluoromethanesulfonate, in the presence of 2,6-lutidine. To optimize the cross-metathesis selectivities in this preliminary set of experiments, styrene was chosen as the other metathetic partner, as it undergoes self-metathesis only very slowly.[16] Treatment of glucopyranoside **4** with styrene in the presence of carbene **2** (1 mol %) provided cinnamyl glucopyranoside **5a**, exclusively as the *trans* isomer, in 72% yield (Table 1). Cross metathesis of glucopyranoside **4** with 4-substituted styrenes provided adducts **5b**−**d**, demonstrating the generality of the method. The variation in chemical yield, and thus the cross-metathesis selectivity of the reaction, reflects the degree of styrene activation, as previously observed.[16] In all cases only the *trans* cinnamyl-glucopyranoside was observed. In the case of 4-methoxystyrene (entry 4), the yield of the corresponding product **5d** was optimized by conducting the cross-metathesis in the presence of only 2 equiv of 4-methoxystyrene. With these results in hand, we felt confident to embark upon our synthesis of ceramide **1**.

Ozonolysis of alkene **4** in ethanol solution afforded aldehyde **6** in excellent yield (Scheme 1).[17] Brown asymmetric allylboration by slow addition of a THF solution of aldehyde **6** to a cold (−85 °C) THF solution of [(*Z*)-γ-(methoxoymethoxy)allyl]diisopinocampheylborane[18] followed by oxidative workup provided the expected MOM protected *syn*-diol **7** as a single diastereomer in 65% chemical yield after chromatography. To install the *anti*-amino alcohol subunit of ceramide **11**, the homoallylic alcohol present in alcohol **7** required activation then substitution by ammonia or an equivalent nucleophile. Activation of alcohol **7** with trifluoromethanesulfonic anhydride in the presence of pyridine, followed by direct treatment with sodium azide in DMF,[19] gave the *anti* azido-ether **8** in 78% yield. Benzyl ether **9** was also prepared from alcohol **7** for use in cross-metathesis experiments. Subsequent reduction of azide **8** could be accomplished with either triphenylphosphine[20] or samarium(II) iodide[21] to give amine **10** which was *N*-acylated using stearoyl chloride in the presence of triethylamine to provide amide **11** in excellent yield.

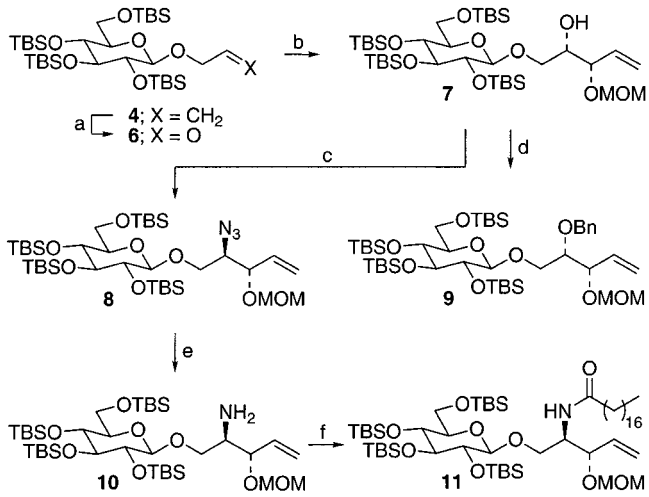
Table 1. Cross-Metathesis of Substituted Styrenes with Allyl Glycoside 4[a]



entry	X	product	no. equiv of styrene	time (h)	yield (%)[b]
1	H	**5a**	10	2	72
2	Me	**5b**	10	2	77
3	Cl	**5c**	10	2	50
4	OMe	**5d**	2	3	72

[a] All reactions performed in CH_2Cl_2. [b] Isolated yield after chromatography.

Scheme 1[a]



[a] Reagents and conditions: (a) (i) O_3, EtOH, Sudan Red, −78 °C, 10 min; (ii) Me_2S, EtOH (85%); (b) (i) (*Z*)-(+)-Ipc_2BCH_2-$CH{=}CHOCH_2OCH_3$, THF, −85 °C, 18 h; (ii) MeOH, $NaBO_3{\cdot}xH_2O$ (65%); (c) (i) Tf_2O, pyridine, CH_2Cl_2, −10 °C, 30 min; (ii) NaN_3, DMF, −10 °C − 25 °C, 12 h (78%); (d) $PhCH_2Br$, NaH, THF-DMF, 25 °C, 18 h (47%); (e) PPh_3, H_2O (1.5 equiv), THF, 25 °C, 5 d (75%) or SmI_2, THF-EtOH, 25 °C, 2 h (55−65%); (f) $CH_3(CH_2)_{16}COCl$, Et_3N, CH_2Cl_2, 0 °C, 3 h (88%).

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(15) Allyl β-D-glucopyranoside was prepared according to known methodologies from 2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranosyl bromide and allyl alcohol, followed by Zemplen methanolysis. See (a) Tietze, L. F.; Eicher, T. H. *Reactions and Syntheses in the Organic Chemistry Laboratory*; University Science Books: Mill Valley, CA, 1989; p 494. (b) Rodriguez, E. B.; Stick, R. V. *Aust. J. Chem.* **1990**, *43*, 665. (c) Schroeder, L. R.; Green, J. W. *J. Chem. Soc. C* **1966**, 530.

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(17) The neat alcoholic solvent rendered the expected blue ozone saturation endpoint difficult to observe. To avoid overoxidation of the product, Sudan Red 7B was concurrently utilized as an indicator. See: Veysoglu, T.; Mitscher, L. A.; Swayze, J. K. *Synthesis* **1980**, 807.

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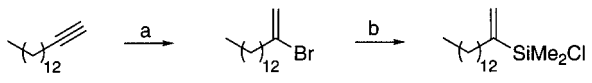
Scheme 2[a]



12 **13**

[a] Reagents and conditions: (a) (i) 9-Br−BBN, Et_2O, −78 °C; (ii) AcOH; (iii) H_2O_2, NaOH, H_2O (86%); (b) (i) *t*-BuLi, Et_2O, −78 °C; (ii) Me_2SiCl_2, Et_2O, −78 °C (67%).

We initially sought to prepare ceramide **1** via alkene cross metathesis between 1-pentadecene and amide **11** with catalysis by the Schrock carbene **2**. To ascertain the cross-metathesis selectivities, styrene was again chosen as the reaction partner. However, to our dismay attempted cross metathesis between azide **8**, ether **9**, or amide **11** with styrene or 1-pentadececene using catalytic or stoichiometric quantities of carbenes **2** or **3** at 25 °C to 60 °C in benzene-d_6, dichloromethane, or toluene solution were all unsuccessful. It was soon evident that an alternative protocol was necessary. We next considered whether recently published work on silicon-tethered ring closing metathesis by our group[11] and others[22] could be employed to circumvent this problem. Unlike cross metathesis[13a,16b] where both *E* and *Z* isomers can form, our silicon tether ring-closing metathesis strategy[11] gives products with *E* double bond configuration exclusively after the ring closing metathesis event and silicon tether removal. The required silicon tether was synthesized from 1-pentadecyne via regioselective bromoboration using *B*-bromo-9-borabicyclo[3.3.1]nonane followed by in situ protodeboration[23] to give 2-bromo-1-pentadecene, **12** (Scheme 2). Conversion to chloro(dimethyl)(1-pentadecen-2-yl)silane, **13**, was brought about by bromine−lithium exchange using *tert*-butyllithium followed by condensation with dichloro(dimethyl)silane.

Alcohol **7** was found to undergo only slow silylation with silyl chloride **13** in the presence of amine bases. In consequence, the corresponding silyl triflate **14** was generated in situ using silver(I) triflate[24] and added immediately to a premixed solution of alcohol **7** and 2,6-lutidine resulting in an excellent yield of the desired diene **15** (Scheme 3). Attempted ring closing metathesis of diene **15** using the Grubbs catalyst **3** was unsuccessful; such low reactivity has been observed for similar homoallylic vinyl siladienes.[11] Treatment of diene **15** with the molybdenum carbene **2** was then examined, initially in dichloromethane solution. Much to our delight, ring closing metathesis did occur to give the desired cyclic ether **16**, although significant quantities of an unidentified side product were also observed by ^{1}H NMR spectroscopy. In contrast, we found that upon treatment of diene **15** with carbene **2** in heptane at 45 °C, ring closing metathesis proceeded essentially quantitatively (>95% as assessed by ^{1}H NMR) to give the siloxacycle **16** which was not isolated but directly treated in situ with phenyllithium to generate alkenylsilane **17** in excellent yield over two steps. Siloxacycle **16** could be isolated and in a subsequent step treated with phenyllithium[25] to give alkenylsilane **17**, but higher yields were obtained with the in situ procedure. As anticipated due to the cyclic nature of the intermediate ring closing metathesis reaction product, alkenylsilane **17** was generated exclusively as the (*Z*)-isomer. The desired *anti*-amino alcohol entity was installed via the Mitsunobu reaction using diphenylphosphoryl azide[26] (DPPA), generating azide **18** in essentially quantitative yield. This procedure was found to be a great improvement over activation with trifluoromethanesulfonic anhydride and in situ displacement with sodium azide in DMF as used previously for the conversion of alcohol **7** into azide **8**. Azide **18** was treated with tetrabutylammonium fluoride in DMSO in order to bring about both the protodesilylation of the alkenyl(dimethyl)phenylsilane[27] and silyl ether deprotection. In situ reprotection of the β-glucopyranoside moiety using acetic anhydride generated the peracetylated azide **19** in excellent yield. We were pleased to observe that azide **19** was formed as the (*E*)-isomer only, thereby demonstrating that the phenyldimethylsilane moiety was cleaved with complete retention of the double bond geometry. Azide **19** was reduced to the corresponding amine, using triphenylphosphine and water. Subsequent in situ *N*-acylation, this time using palmitoyl chloride in the presence of triethylamine provided amide **20** in excellent yield. Saponification using 5% KOH in methanol and acidification using 1% HCl in methanol gave glucosylceramide, **1**, in excellent yield.[28]

Conclusions

We have demonstrated a concise and high-yielding synthesis of D,L-glucosylceramide, **1**,[29] a member of the glycosphingolipid class of natural products. Excellent control of both stereochemistry and alkene geometry in the sphingoid base portion of the molecule have been achieved using our previously reported allylboration-ring closing metathesis-ring opening protocol.[11] This route has the potential to be extremely flexible as variation in the amide or hydrocarbon chain areas of the molecule should be easily controlled late in the side chain assembly.

Experimental Section

General. All reactions, except those involving alkene metathesis catalysts **2** or **3**, were run in oven-dried glassware under a nitrogen atmosphere. Reactions involving alkene metathesis catalysts **2** or **3** were performed in a glovebox under a nitrogen atmosphere or using a Schlenk line. THF and Et_2O were distilled from Na/Ph_2CO. CH_2Cl_2, DMF, pyridine, and Et_3N were distilled from CaH_2. For reactions involving alkene metathesis catalysts **2** or **3** solvents were degassed prior to use by the freeze−pump−thaw method. *n*-BuLi, *sec*-BuLi, and *tert*-BuLi were titrated against diphenylacetic acid or by acid−base titration. Acid chlorides and dichloro(dimethyl)silane

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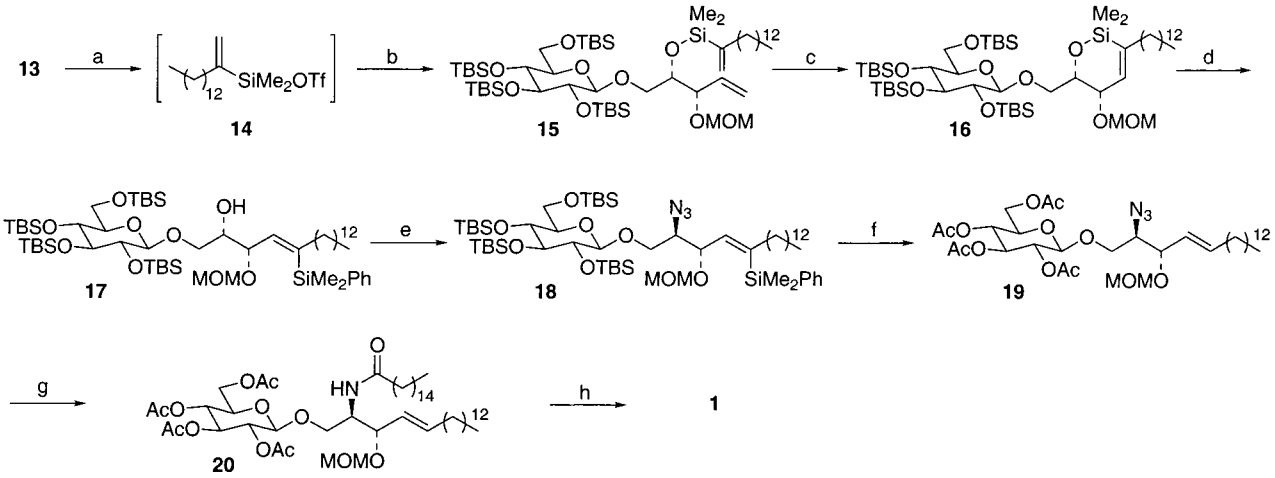
(29) We were unable to obtain an authentic sample of D,L-glucosylceramide in order to unequivocally confirm the identity of our material; however, all the characterizing data is consistent with the published data (ref 12).

Scheme 3[a]



[a] Reagents and conditions: (a) AgOTf, CH_2Cl_2; (b) 2,6-lutidine, **7**, CH_2Cl_2, 0−25 °C (79%); (c) **2**, C_7H_{16}, 45 °C; (d) PhLi, THF, 0 °C (83%); (e) DEAD, PPh_3, $PH_2P(O)N_3$, THF, 45 °C (100%); (f) Bu_4NF, DMSO, 60 °C; (ii) Ac_2O, DMAP, pyridine (80%); (g) (i) PPh_3, H_2O, THF, 45 °C; (ii) $ClCO(CH_2)_{14}CH_3$, Et_3N, CH_2Cl_2 (90%); (h) (i) 5% KOH in MeOH; Dowex-50W; (ii) 1% HCl in MeOH, 45 °C; Ag_2CO_3 (64%).

were distilled before use. All other reagents were purchased from commercial sources and used without further purification. Analytical thin-layer chromatography (TLC) was performed on precoated glass-backed plates (Merck Kieselgel 60 F_{254}) and visualized with ultraviolet light (254 nm) or potassium permanganate as appropriate. Column chromatography was performed under medium pressure using Merck Kieselgel 60 (230−400) mesh. Molybdenum carbene **2**,[8] ruthenium carbene **3**,[9] allyl β-D-glucoside,[15] and allyl methoxymethyl ether[30] were synthesized according to literature procedures with minor modifications where necessary.

1-*O*-Allyl 2,3,4,6-tetra-*O*-*tert*-butyldimethylsilyl-β-D-glucopyranoside (4). To a cooled (0 °C) mixture of β-D-allyl glucopyranoside (2.55 g, 12 mmol) and 2,6-lutidine (14.7 g, 137 mmol) in CH_2Cl_2 (15 mL) was added *t*-$BuMe_2SiOTf$ (24 g, 91 mmol). The reaction mixture was stirred for 12 h at 40 °C, allowed to cool, diluted with CH_2Cl_2 (50 mL), and washed with aqueous $CuSO_4$ (50% w/v). The organic phase was dried (Na_2SO_4), concentrated in vacuo, and chromatographed (1:49 Et_2O:hexanes) to give **4** (7.1 g, 93%) as a colorless oil: R_f (1:24 Et_2O:hexanes) 0.5; $[\alpha]^{25}_D$ +17 (*c* 1.1, $CHCl_3$); IR (thin film) 3082, 3017, 1640 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 5.99−5.90 (1H, m), 5.27 (1H, dq, *J* = 17.2, 1.6 Hz), 5.15 (1H, dq, *J* = 10.4, 1.5 Hz), 4.74 (1H, d, *J* = 6.8 Hz), 4.38 (1H, dt, *J* = 12.3, 5.3, 1.4 Hz), 3.98 (1H, ddt, *J* = 12.4, 6.3, 1.3 Hz), 3.93 (1H, d, *J* = 2.6 Hz), 3.82−3.71 (4H, m), 3.60 (1H, d, *J* = 6.6 Hz), 0.89−0.86 (36H, m), 0.09−0.04 (24H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 134.4, 116.9, 100.9, 82.4, 79.1, 77.7, 70.1, 70.0, 64.1, 26.0, 25.9, 25.9, 25.8, 18.3, 18.0, 18.0, 17.8, −4.2, −4.4, −4.6, −4.8, −5.1, −5.3. MS (CI^+, NH_3) *m*/*z* 694 $(M + NH_4)^+$. HRMS (CI^+, NH_3) Calcd for $C_{33}H_{76}NO_6Si_4$ $(M + NH_4)^+$; 694.4750. Found; 694.4743. Anal. Calcd for $C_{33}H_{72}O_6Si_4$: C, 58.52; H, 10.72. Found: C, 58.37; H, 10.70.

General Procedure for the Cross Metathesis of 4 with Styrenes Furnishing Glucopyranosides 5a−d. To catalyst **2** in CH_2Cl_2 (1 mol %, 20 μL CH_2Cl_2) was added a solution of the appropriate styrene (4.55 mmol) in CH_2Cl_2 (0.2 mL), and after 15 min, glycoside **4** (149 mg, 0.022 mmol) in CH_2Cl_2 (0.2 mL) was added dropwise. After 2 h, the mixture was removed from the glovebox, diluted with CH_2Cl_2, and filtered through silica. The resultant light yellow solution was concentrated in vacuo and the crude oil chromatographed.

***trans*-Cinnamyl 2,3,4,6-tetra-*O*-*tert*-butyldimethylsilyl-β-D-glucopyranoside (5a).** Colorless oil (0.113 g, 72%): R_f (3:247 EtOAc:hexane) 0.25; $[\alpha]^{25}_D$ −27 (*c* 2.00, $CHCl_3$); IR (thin film) 3054 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.33−7.15 (5H, m), 6.56 (1H, d, *J* = 15.9 Hz), 6.25 (1H, dt, *J* = 15.9, 5.8 Hz), 4.75 (1H, d, *J* = 6.8 Hz), 4.48 (1H, dd, *J* = 5.7, 12.4 Hz), 4.11 (1H, dd, *J* = 6.6, 12.4 Hz), 3.88 (1H, d, *J* = 2.4 Hz), 3.79−3.68 (4H, m), 3.58 (1H, d, *J* = 6.7 Hz), 0.84−0.80 (36H, m), 0.05 to −0.01 (24H, m); ^{13}C NMR (75 MHz, $CDCl_3$) δ 137.0, 132.4, 128.5, 127.5, 126.5, 125.8, 100.8, 82.5, 79.2, 77.8, 70.1, 69.6, 64.1, 26.0, 25.9, 25.8, 18.3, 18.1, 17.8, −4.0, −4.4, −4.5, −4.7, −4.9, −5.3; MS (CI^+, NH_3), *m*/*z* 770 $(M + NH_4)^+$. Anal. Calcd for $C_{39}H_{76}O_6Si_4$: C, 62.18; H, 10.17. Found: C, 62.37; H, 10.17.

***trans*-3-(4-Methylphenyl)-2-propenyl 2,3,4,6-tetra-*O*-*tert*-butyldimethylsilyl-β-D-glucopyranoside (5b).** Colorless oil (0.141 g, 77%): R_f (1:499 Et_2O:hexane) 0.25; $[\alpha]^{25}_D$ −25 (*c* 1.2, $CHCl_3$); IR (thin film) 3070, 3022 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.17 (2H, d, *J* = 8.0 Hz), 7.02 (2H, d, *J* = 8.0 Hz), 6.48 (1H, d, *J* = 15.9 Hz), 6.16 (1H, dt, *J* = 15.9, 6.1 Hz), 4.71 (1H, d, *J* = 6.7 Hz), 4.46−4.39 (1H, m), 4.08−4.02 (1H, m), 3.84 (1H, d, *J* = 2.6 Hz), 3.72−3.63 (4H, m), 3.53 (1H, d, *J* = 6.7 Hz), 2.24 (3H, s), 0.80−0.76 (36H, m), 0.00 to −0.06 (24H, m); ^{13}C NMR (75 MHz, $CDCl_3$) δ 137.3, 134.2, 132.4, 129.2, 126.4, 124.8, 100.8, 82.4, 79.2, 77.8, 70.1, 69.7, 64.1, 26.0, 26.0, 25.9, 25.8, 21.2, 18.3, 18.1, 18.0, 17.8, −4.0, −4.4, −4.5, −4.7, −5.0, −5.3; MS (CI^+, NH_3) *m*/*z* 784 $(M + NH_4)^+$. Anal. Calcd for $C_{40}H_{78}O_6Si_4$: C, 62.61; H, 10.25. Found: C, 62.31; H, 10.28.

***trans*-3-(4-Chlorophenyl)-2-propenyl 2,3,4,6-tetra-*O*-*tert*-butyldimethylsilyl-β-D-glucopyranoside (5c).** Colorless oil (0.126 g, 50%): R_f (3:497 Et_2O:hexane) 0.2. $[\alpha]^{25}_D$ −25 (*c* 1.4, $CHCl_3$): IR (thin film) 3032 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.19−7.16 (4H, m), 6.47 (1H, d, *J* = 16.0 Hz), 6.18 (1H, dt, *J* = 15.9, 6.2 Hz), 4.70 (1H, d, *J* = 6.8 Hz), 4.42 (1H, ddd, *J* = 1.4, 5.6, 12.7 Hz), 4.06 (1H, ddd, *J* = 1.2, 6.5, 12.7 Hz), 3.84 (1H, d, *J* = 2.5 Hz), 3.72−3.63 (4H, m), 3.53 (1H, d, *J* = 6.7 Hz), 0.80−0.76 (36H, m), 0.00 to −0.05 (24 H, m); ^{13}C NMR (75 MHz, $CDCl_3$) δ 135.8, 133.5, 131.4, 129.0, 128.0, 126.9, 101.2, 82.9, 79.5, 78.1, 70.4, 69.7, 64.4, 26.32, 26.30, 26.2, 18.7, 18.4, 18.2, −3.7, −4.0, −4.2, −4.4, −4.6, −4.9; MS (CI^+, NH_3) *m*/*z* 804 $(M + NH_4)^+$. Anal. Calcd for $C_{39}H_{75}ClO_6Si_4$: C, 59.46; H, 9.60. Found: C, 59.37; H, 9.31.

***trans*-3-(4-Methoxyphenyl)-2-propenyl 2,3,4,6-tetra-*O*-*tert*-butyldimethylsilyl-β-D-glucopyranoside (5d).** Colorless oil (45 mg, 72%): R_f (1:49 Et_2O:hexane) 0.25; $[\alpha]^{27}_D$ −35 (*c* 1.1, $CHCl_3$); IR (thin film) 3034, 1609 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.25 (2H, d, *J* = 8.7 Hz), 6.79 (2H, d, *J* = 8.7 Hz), 6.49 (1H, d, *J* = 15.9 Hz), 6.12 (1H, dt, *J* = 15.9, 6.5 Hz), 4.75 (1H, d, *J* = 6.8 Hz), 4.44 (1H, ddd, *J* = 1.3, 5.9, 12.1 Hz), 4.08 (1H, ddd, *J* = 1.0, 6.8, 12.1 Hz), 3.89 (1H, d, *J* = 2.5 Hz), 3.78−3.68 (7H, m), 3.57 (1H, d, *J* = 6.7 Hz), 0.84−0.80 (36H, m), 0.04 to −0.03 (24H, m); ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.6, 132.5, 130.2, 128.0, 124.0, 114.3, 101.1, 82.8, 79.6, 78.2, 70.5,

(30) Gras, J.-L.; Chang, Y.-Y. K. W.; Guerin, A. *Synthesis* **1985**, 74.

70.1, 64.5, 55.6, 26.4, 26.3, 26.1, 18.7, 18.5, 18.4, 18.2, −3.6, −4.0, −4.2, −4.4, −4.6, −4.9; MS (CI, NH_3) *m/z* 800 (M + NH_4)$^+$.

2-Oxoethyl 2,3,4,6-tetra-*O*-*tert*-butyldimethylsilyl-*β*-D-glucopyranoside (6). Ozone was bubbled through a solution of glycoside **4** (1.56 g, 2.30 mmol) in EtOH (100 mL) and Sudan Red (0.03 mol % in EtOH, 20μL) at −78 °C until the pink color was discharged (ca. 5 min). Oxygen was bubbled through the colorless solution to remove excess ozone (ca. 2 min), and Me_2S (2.5 mL) was added. The solution was allowed to warm to room temperature, stirred for 4 h, evaporated, and chromatographed, providing **6** (1.2 g, 85%) as a colorless oil: R_f (1:24 Et_2O:hexane) = 0.15; $[\alpha]^{25}_D$ +16 (*c* 1.3, $CHCl_3$); IR (thin film) 2955, 2929, 1737 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.79 (1H, dd, *J* = 1.3, 1.5 Hz), 4.75 (1H, d, *J* = 6.5 Hz), 4.20 (1H, dd, *J* = 1.8, 17.3 Hz), 4.09 (1H, dd, *J* = 1.1, 17.3 Hz), 3.92 (1H, d, *J* = 2.9 Hz), 3.81−3.63 (5H, m), 0.90−0.87 (36H, m), 0.11−0.04 (24H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 201.9, 102.7, 82.5, 78.8, 77.5, 74.5, 70.0, 63.9, 25.9, 25.9, 25.8, 25.8, 18.3, 18.1, 18.0, 17.8, −4.2, −4.4, −4.6, −4.76, −4.79, −4.9, −5.3; MS (CI$^+$, NH_3) *m/z* 696 (M + NH_4)$^+$. Anal. Calcd for $C_{32}H_{70}O_7Si_4$: C, 56.59; H, 10.38. Found: C, 56.51; H, 10.13.

1-*O*-((2*S*,3*S*)-2-Hydroxy-3-methoxymethoxy-4-penten-1-yl) 2,3,4,6-Tetra-*O*-*tert*-butyldimethylsilyl-*β*-D-glucopyranoside (7). *sec*-BuLi (4.0 mL, 5.2 mmol, 1.3 M in cyclohexane) was added dropwise to solution of $MeOCH_2OCH_2CH{=}CH_2$ (0.529 g, 5.19 mmol) in THF (2 mL) at −85 °C. After 3 h at −85 °C (+)-diisopinocampheylmethoxyborane (1.68 g, 5.31 mmol) in THF (2 mL) was added dropwise maintaining the internal temperature at −85 °C. The resulting cloudy, white solution was stirred at this temperature for 3 h and treated with $BF_3{\cdot}OEt_2$ (0.363 g, 2.51 mmol). After 15 min, aldehyde **6** (1.71 g, 2.51 mmol) in THF (4 mL) was added over 1 h, via syringe pump, maintaining the internal temperature at −85 °C. The mixture was stirred at −85 °C for 18 h and quenched with MeOH (2 mL). After 15 min, aqueous saturated sodium perborate (15 mL) was added, and the mixture was allowed to warm to room temperature and stirred for 24 h. The organics were removed by evaporation, and the resulting aqueous layer was extracted with EtOAc. The combined organic layers were washed with H_2O and brine and dried (Na_2SO_4). Evaporation and chromatography (1:49 Et_2O:hexane) gave alcohol **7** (1.2 g, 65%) as a colorless oil: R_f (9:241 Et_2O:toluene) 0.2; $[\alpha]^{30}_D$ +7 (*c* 1, $CHCl_3$); IR (thin film) 3463, 3081, 1640 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.91−5.82 (1H, m), 5.33−5.27 (2H, m), 4.70 (1H, d, *J* = 6.8 Hz), 4.67 (1H, d, *J* = 6.6 Hz), 4.59 (1H, d, *J* = 6.7 Hz), 4.10 (1H, dd, *J* = 4.2, 7.3 Hz), 3.93 (1H, dd, *J* = 2.3, 11.4 Hz), 3.90−3.86 (2H, m), 3.86−3.84 (1H, m), 3.77 (1H, d, *J* = 3.1 Hz), 3.70 (2H, d, *J* = 7.4 Hz), 3.64 (1H, dd, *J* = 8.2, 11.4 Hz), 3.58 (1H, d, *J* = 6.6 Hz), 3.47 (1H, q, *J* = 7.1 Hz), 3.37 (3H, s), 0.89−0.86 (36H, m), 0.09−0.02 (24H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 134.6, 118.6, 103.2, 94.1, 82.4, 78.9, 77.9, 77.6, 74.1, 73.0, 69.9, 65.8, 63.8, 55.6, 25.9, 25.8, 25.8, 18.2, 18.0, 17.9, 17.8, −4.2, −4.4, −4.6, −4.7, −4.8, −5.0, −5.4; MS (CI, NH_3) *m/z* 798 (M + NH_4)$^+$. Anal. Calcd for $C_{37}H_{80}O_9Si_4$: C, 56.87; H, 10.32. Found: C, 57.15; H, 10.09.

1-*O*-((2*R*,3*S*)-2-Azido-3-methoxymethoxy-4-penten-1-yl) 2,3,4,6-Tetra-*O*-*tert*-butyldimethylsilyl-*β*-D-glucopyranoside (8). Tf_2O (0.57 g, 2.0 mmol) was added to alcohol **7** (1.20 g, 1.54 mmol) and pyridine (0.36 g, 4.6 mmol) in CH_2Cl_2 (5 mL) at −10 °C over 10 min. After 30 min at −10 °C, DMF (30 mL) and NaN_3 (0.75 g, 11.5 mmol) were added. The mixture was allowed to warm to room temperature over 12 h. The resulting yellow solution was diluted in Et_2O, poured into water, and extracted with further portions of Et_2O. The combined organic layers were washed with water and brine, dried (Na_2SO_4), concentrated, and chromatographed to give azide **8** (0.97 g, 78%) as a colorless oil: R_f (2:123 EtOAc:hexane) 0.15; $[\alpha]^{28}_D$ +12 (*c* 1.4, $CHCl_3$); IR (thin film) 2127, 2097 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.81−5.73 (1H, m), 5.37−5.32 (2H, m), 4.70 (1H, d, *J* = 6.8 Hz), 4.69 (1H, d, *J* = 6.2 Hz), 4.58 (1H, d, *J* = 6.7 Hz), 4.16 (1H, dd, *J* = 3.9, 7.8 Hz), 3.90−3.71 (7H, m), 3.59 (1H, d, *J* = 6.1 Hz), 3.40 (1H, m), 3.38 (3H, s), 0.89−0.88 (36H, m), 0.11−0.05 (24H, m); ^{13}C NMR (125 MHz, $CDCl_3$) δ 133.3, 120.6, 102.3, 93.7, 82.1, 78.7, 77.5, 77.4, 70.1, 68.0, 65.2, 64.2, 55.6, 25.9, 25.8, 25.8, 18.3, 18.03, 18.0, 17.9, −4.2, −4.4, −4.4, −4.5, −4.7, −5.1, −5.2; MS (CI$^+$, NH_3) *m/z* 823 (M + NH_4)$^+$. Anal. Calcd for $C_{37}H_{79}N_3O_8Si_4$: C, 55.11; H, 9.87; N, 5.21. Found: C, 55.14; H, 9.81; N, 5.13.

1-*O*-((2*R*,3*S*)-2-Amino-3-methoxymethoxy-4-penten-1-yl) 2,3,4,6-Tetra-*O*-*tert*-butyldimethylsilyl-*β*-D-glucopyranoside (10). Azide **8** (0.98 g, 1.2 mmol) was added to SmI_2 (25 mL, 0.1 M in THF) in degassed EtOH (2.4 mL) at room temperature. The blue solution was stirred for 10 min at room temperature before the color discharged. An additional portion of SmI_2 (25 mL, 0.1 M in THF) was added. The reaction was quenched after 30 min by the addition of ice-cold, saturated aqueous K_2CO_3 (2 mL), and the mixture was stirred at room temperature for 3 h. The organic solvents were removed by evaporation, and the residual aqueous layer was extracted with EtOAc. The combined organic layers were washed with brine, dried (Na_2SO_4), concentrated, and chromatographed (3:17 EtOAc:hexane) to provide amine **10** (0.66 g, 70%) as a colorless oil: R_f (1:4 EtOAc:hexane) 0.25; $[\alpha]^{26}_D$ +7 (*c* 1.7, $CHCl_3$); IR (thin film) 3393, 3080, 1643 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.78−5.65 (1H, m), 5.27−5.22 (2H, m), 4.63 (1H, d, *J* = 6.6 Hz), 4.62 (1H, d, *J* = 6.3 Hz), 4.50 (1H, d, *J* = 6.6 Hz), 4.00 (1H, dd, *J* = 5.3, 7.4 Hz), 3.85−3.81 (2H, m), 3.75−3.64 (4H, m), 3.52 (1H, d, *J* = 6.2 Hz), 3.34 (1H, m), 3.3 (3H, s), 3.12 (1H, m), 1.73 (2H, br s), 0.82−0.81 (36H, m), 0.03 to −0.02 (24H, m); ^{13}C NMR (75 MHz, $CDCl_3$) δ 134.9, 119.4, 102.4, 94.1, 82.1, 79.0, 78.9, 76.6, 71.5, 70.2, 64.2, 55.6, 54.4, 30.3, 26.0, 25.9, 25.8, 18.4, 18.0, 17.9, −4.1, −4.2, −4.5, −4.7, −4.8, −5.3; MS (CI$^+$, NH_3) *m/z* 780 (M + H)$^+$. HRMS (CI$^+$, NH_3) Calcd for $C_{37}H_{82}NO_8Si_4$ (M + H)$^+$: 780.5118. Found: 780.5108. Anal. Calcd for $C_{37}H_{81}NO_8Si_4$: C, 56.95; H, 10.46; N, 1.79. Found: C, 56.77; H, 10.23; N, 1.97.

1-*O*-((2*S*,3*S*)-2-Benzyloxy-3-methoxymethoxy-4-penten-1-yl) 2,3,4,6-Tetra-*O*-*tert*-butyldimethylsilyl-*β*-D-glucopyranoside (9). Alcohol **7** (72 mg, 0.09 mmol) in DMF:THF (2:1, 0.2 mL total) was added to a suspension of NaH (7 mg, 0.2 mmol) in DMF (0.5 mL). The mixture was stirred at room temperature for 45 min and then treated with $PhCH_2Br$ (16 mg, 0.093 mmol), stirred for 18 h at room temperature, and quenched by addition of water (0.5 mL). The mixture was poured into water and extracted with Et_2O, and the combined organic extracts were washed with water and brine, dried (Na_2SO_4), evaporated, and chromatographed (1:99 EtOAc:hexane) to give benzyl ether **9** (37 mg, 47%) as a colorless oil: R_f (1:49 EtOAc:hexane) 0.5; $[\alpha]^{25}_D$ +2 (*c* 1.3, $CHCl_3$); IR (thin film) 3085 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.32−7.18 (5H, m), 5.86−5.75 (1H, m), 5.26−5.15 (2H, m), 4.72 (1H, d, *J* = 11.8 Hz), 4.66−4.50 (4H, m), 4.17 (1H, m), 3.87−3.80 (2H, m), 3.70−3.58 (6H, m), 3.51 (1H, d, *J* = 6.3 Hz), 3.29 (3H, s), 0.83−0.78 (36H, m), 0.03 to −0.04 (24H, m); ^{13}C NMR (75 MHz, $CDCl_3$) δ 138.8, 135.0, 128.1, 128.0, 127.4, 118.0, 102.4, 94.4, 82.1, 80.6, 78.9, 77.7, 76.9, 73.1, 70.2, 69.3, 64.3, 55.6, 26.0, 25.9, 18.4, 18.1, 18.0, 17.9, −4.1, −4.3, −4.5, −4.7, −4.9, −5.2; MS (CI$^+$, NH_3) *m/z* 888 (M + NH_4)$^+$. Anal. Calcd for $C_{44}H_{86}O_9Si_4$: C, 60.64, H, 9.95. Found: C, 60.40, H, 9.66.

1-*O*-((2*S*,3*S*)-3-Methoxymethoxy-2-octadecanamido-4-penten-1-yl) 2,3,4,6-Tetra-*O*-*tert*-butyldimethylsilyl-*β*-D-glucopyranoside (11). Stearoyl chloride (0.5 g, 1.6 mmol) was added to amine **10** (0.63 g, 0.81 mmol) and Et_3N (0.25 g, 3.2 mmol) in CH_2Cl_2 (7.5 mL) at 0 °C. After 3 h at 0 °C 3-dimethylaminopropylamine (8 mg, 0.81 mmol) was added, and the mixture was allowed to warm to room temperature and stirred for 15 min. The white precipitous mixture was diluted with $CHCl_3$ and poured into aqueous citric acid (0.25 M). The aqueous layer was extracted with $CHCl_3$, and the combined organic layers were washed with brine, dried (Na_2SO_4), concentrated, and chromatographed (1:19 EtOAc:hexane) to afford amide **11** (0.75 g, 88%) as a colorless oil: R_f (3:47 EtOAc:hexane) 0.3; $[\alpha]^{26}_D$ +10 (*c* 1.3, $CHCl_3$); IR (thin film) 3340, 3078, 1663 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.37 (1H, d, *J* = 7.9 Hz), 5.77−5.65 (1H, m), 5.21−5.15 (2H, m), 4.62 (1H, d, *J* = 6.8 Hz), 4.59 (1H, d, *J* = 6.9 Hz), 4.51 (1H, d, *J* = 6.5 Hz), 4.11−4.06 (3H, m), 3.83 (1H, d, *J* = 3.0 Hz), 3.77−3.50 (6H, m), 3.30 (3H, s), 2.11−1.99 (2H, m), 1.18 (30H, s),

0.84−0.81 (39H, m), 0.05 to −0.02 (24H, m). ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.6, 133.9, 117.2, 101.4, 92.6, 80.7, 77.2, 75.8, 75.4, 68.2, 67.9, 62.3, 53.8, 49.6, 35.1, 30.0, 27.8, 27.6, 27.5, 27.5, 27.4, 24.0, 24.0, 24.0, 23.9, 23.8, 20.8, 16.4, 16.1, 15.9, 12.2, −6.1, −6.2, −6.4, −6.7, −6.8, −7.2; MS (CI^+, NH_3) *m/z* 1046 $(M + H)^+$. Anal. Calcd for $C_{55}H_{115}NO_9Si_4$: C, 63.10; H, 11.07; N, 1.34. Found: C, 62.88; H, 11.13; N, 1.33.

2-Bromo-1-pentadecene (12). To a solution of *B*-bromo-9-borobicyclo[3.3.1]nonane (27 mL, 1.0 M in CH_2Cl_2) was added CH_2Cl_2 (150 mL). The solution was cooled to 0 °C, and a solution of 1-pentadecyne (4.35 g, 21 mmol) in CH_2Cl_2 (10 mL) was added slowly via cannula with stirring. The mixture was stirred at 0 °C for 3.5 h, AcOH (15 mL) was added, and the reaction was stirred for 1 h at 0 °C. Aqueous NaOH (3 M, 180 mL) was added, followed by H_2O_2 (26 mL, 35 wt %). The mixture was stirred at room temperature for 30 min and extracted with hexane. The combined organic layer was washed with water, aqueous $NaHCO_3$, water, dried ($MgSO_4$), evaporated, and chromatographed (hexane) to give **12** (5.24 g, 86%) as a colorless oil: R_f (hexane) 0.62; IR (thin film) 2925, 2854, 1630, 1466 cm^{-1}; ^{1}H NMR (250 MHz, $CDCl_3$) δ 5.55 (1H, m), 5.38 (1H, d, J = 1.4 Hz), 2.41 (2H, dt, J = 0.9, 6.9 Hz), 1.54 (2H, m), 1.26 (20H, br m), 0.88 (3H, t, J = 6.6 Hz); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 135.0, 116.1, 41.4, 31.9, 29.6, 29.5, 29.3, 29.3, 28.4, 27.9, 22.6, 14.1; MS (EI^+) *m/z* 290 ($M^{+\cdot}$), 288 ($M^{+\cdot}$). HRMS (EI^+) Calcd for $C_{15}H_{29}{}^{81}Br$ ($M^{+\cdot}$): 290.1432. Found: 290.1419. Calcd for $C_{15}H_{29}{}^{79}Br$ ($M^{+\cdot}$): 288.1453. Found: 288.1436. Anal. Calcd for $C_{15}H_{29}Br$: C, 62.28; H, 10.10. Found: C, 61.97; H, 9.93.

Chloro(dimethyl)(1-pentadecen-2-yl)silane (13). *t*-BuLi (1.66 M in pentane, 29 mL) was added to a stirred solution of vinyl bromide **12** (5.0 g, 24 mmol) in Et_2O (150 mL) at −65 °C. The resulting cloudy solution was stirred at −65 °C for 45 min and transferred via insulated cannula to Me_2SiCl_2 (6.52 g, 60 mmol) in Et_2O (30 mL) at −78 °C. The mixture was allowed to warm to room temperature over the course of 3.5 h. The solvent was removed under vacuum (Schlenk line), and the crude mixture was redissolved in pentane and filtered. The solvent was evaporated and the resultant oil distilled to give silyl chloride **13** (4.7 g, 67%) as a colorless liquid: bp 55−58 °C (5 mmHg); IR (thin film) 2925, 2854 cm^{-1}; ^{1}H NMR (250 MHz, $CDCl_3$) δ 5.70 (1H, m), 5.53 (1H, m), 2.21 (2H, m), 1.45 (2H, m), 1.26 (20 H, m), 0.88 (3H, app t, J = 6.6 Hz), 0.50 (6H, s); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 149.0 126.8, 34.9, 31.9, 31.2, 29.7, 29.5, 29.4, 28.9, 27.3, 26.3, 22.7, 14.1, 1.7. The moisture sensitive silyl chloride was further characterized as methoxy(dimethyl)(1-pentadecen-2-yl)silane by quenching with excess MeOH and Et_3N: R_f (1:39 EtOAc:hexane) 0.30; IR (thin film) 3049, 1598 cm^{-1}; ^{1}H NMR (250 MHz, $CDCl_3$) δ 5.66−5.63 (1H, m), 5.43−5.41 (1H, m), 3.41 (3H, s), 2.13 (2H, m), 1.44−1.38 (2H, m), 1.26 (20H, m), 0.88 (3H, m), 0.19 (6H, s); ^{13}C NMR (62.5 MHz, $CDCl_3$) δ 150.1, 125.8, 50.4, 35.7, 31.9, 29.6, 29.5, 29.3, 28.9, 22.7, 14.1, −2.7; MS (CI^+, NH_3) *m/z* 316 $(M + NH_4)^+$. HRMS (CI^+, NH_3) Calcd for $C_{18}H_{42}NOSi$ $(M + NH_4)^+$: 316.3036. Found: 316.3040. Anal. Calcd for $C_{18}H_{38}OSi$: C, 72.41; H, 12.83. Found: C, 72.56; H, 12.63.

1-*O*-[(2*S*,3*S*)-2-Dimethyl(pentadecen-2-yl)siloxy-3-methoxymethoxy-4-penten-1-yl] 2,3,4,6-Tetra-*O*-*tert*-butyldimethylsilyl-*β*-D-glucopyranoside (15). Silyl chloride **13** (770 mg, 2.5 mmol) in CH_2Cl_2 (2 mL) was added to a vigorously stirred suspension of silver triflate (520 mg, 2.0 mmol) in CH_2Cl_2 (2 mL) and stirred vigorously for 20 min at room temperature. The mixture was transferred via filter cannula to alcohol **7** (1.23 g, 1.6 mmol) and 2,6-lutidene (1.2 mL, 10.1 mmol) in CH_2Cl_2 (4 mL) at 0 °C. A further portion of CH_2Cl_2 (2 mL) was used to wash the silver chloride and ensure complete transfer of silyl triflate. The mixture was allowed to warm to room temperature and stirred for 3 h, and MeOH (5 mL) was added to quench the reaction. The solvent was evaporated and the crude oil redissolved in hexane. Filtration and reconcentration afforded a crude oil that was chromatographed (1:99 CH_2Cl_2:hexane followed by 1:40 EtOAc:hexane) to give **15** (1.3 g, 79%) as a colorless oil: R_f (1:9 EtOAc:hexane) 0.54; $[\alpha]^{26}{}_D$ = −4 (*c* 1.0, $CHCl_3$); IR (thin film) 3174, 1644, 1601 cm^{-1}; ^{1}H NMR ($CDCl_3$, 250 MHz) δ 5.83 (1H, ddd, J = 6.9, 10.4, 17.4 Hz), 5.61−5.5.60 (1H, m) 5.46 (1H, d, J = 3.0 Hz), 5.32−5.20 (2H, m), 4.69 (1H, d, J = 6.6 Hz), 4.63 (1H, d, J = 8.7 Hz), 4.61 (1H, d, J = 6.6 Hz), 4.16 (1H, dd, J = 4.1, 6.8 Hz), 3.96−3.88 (2H, m), 3.76−3.64 (6H, m), 3.55 (1H, d, J = 6.3 Hz), 3.36 (3H, s), 2.14 (2H, m), 1.40 (2H, m), 1.26 (20H, s), 0.89−0.85 (39H, m), 0.21 (6H, s), 0.09−0.04 (24H, m); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 150.7, 135.5, 125.5, 117.5, 102.6, 94.5, 82.1, 78.8, 77.7, 77.6, 74.4, 70.6, 70.1, 64.2, 55.5, 35.3, 31.9, 29.7, 29.6, 29.3, 28.9, 26.0, 25.8, 22.7, 18.3, 18.0, 17.9, 17.8, 14.1, −1.1, −1.3, −4.2, −4.4, −4.6, −4.7, −4.8, −4.9, −5.3; MS ($EI^{+\cdot}$) *m/z* 1046 (M^+). Anal. Calcd for $C_{54}H_{114}O_9Si_5$: C, 61.89; H, 10.97. Found C, 62.13; H, 11.13.

((5*S*,6*S*)-22-Dimethyl-5-methoxymethoxy-3-tridecyl-5,6-dihydro-2*H*-1,2-oxasilin-6-yl)methyl 2,3,4,6-tetra-*O*-*tert*-butyldimethylsilyl-*β*-D-glucopyranoside (16). Molybdenum carbene **2** (9.1 mg, 12 μmol, 25 mol %) was added to a stirred solution of diene **15** (50 mg, 0.05 mmol) in heptane (1 mL) and stirred at 45 °C for 24 h. The solvent was evaporated to give a crude a yellow oil which was chromatographed (1:39 EtOAc:hexane) to give **16** (164 mg, 70%) as a colorless oil: R_f (1:9 EtOAc:hexane) 0.53; IR (thin film) 1604 cm^{-1}; ^{1}H NMR (250 MHz, $CDCl_3$) 6.50 (1H, d, J = 5.6 Hz), 4.75 (1H, d, J = 6.7 Hz), 4.71 (1H, d, J = 6.5 Hz), 4.69 (1H, d, J = 6.6 Hz), 4.16−4.08 (2H, m), 3.88 (1H, d, J = 2.8 Hz), 3.79−3.66 (6H, m), 3.56 (1H, d, J = 6.3 Hz), 3.35 (3H, s), 2.09 (2H, m), 1.25 (22H, m), 0.88 (39H, m), 0.25 (3H, s) 0.18 (3H, s), 0.09−0.04 (24H, m); ^{13}C NMR ($CDCl_3$, 62.5 MHz) δ 144.9, 139.2, 102.7, 95.9, 82.2, 79.1, 73.0, 71.8, 70.6, 70.2, 64.2, 55.3, 35.1, 31.9, 29.7, 29.5, 29.4, 29.1, 26.0, 25.9, 25.8, 22.7, 18.3, 18.0, 17.9, 14.1, −0.6, −1.4, −4.1, −4.3, −4.5, −4.7, −4.9, −5.3; MS (ES^+, NaI) *m/z* 1042.2 $(M + Na)^+$. The sensitive oxasiline **17** was used directly in the next step without further purification.

(+)-1-*O*-[(2*S*,3*S*,4*Z*)-2-Hydroxy-3-methoxymethoxy-5-dimethylphenylsilyl-octadec-4-en-1-yl] 2,3,4,6-tetra-*O*-*tert*-butyldimethylsilyl-*β*-D-glucopyranoside (17). PhLi (1.8 M in cyclohexane/Et_2O; 18 μL) was added to oxasiline **16** in THF (0.5 mL) at 0 °C. The reaction mixture was allowed to warm slowly to room temperature over 18 h after which solid NH_4Cl (50 mg) was added to quench the reaction. After filtration and concentration by rotary evaporation, the crude product was chromatographed (1:39 EtOAc:hexane, then 1:19 EtOAc:hexane) to give **17** (19 mg, 83%) as a colorless oil: R_f (1:4 EtOAc:hexane) 0.57; $[\alpha]^{26}{}_D$ = +24 (*c* 1.0, $CHCl_3$); IR (thin film) 3462 cm^{-1}; ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.55−7.51 (2H, m), 7.36−7.32 (3H, m), 6.05 (1H, d, J = 10.0 Hz), 4.57 (1H, d, J = 6.7 Hz), 4.56 (1H, d, J = 6.8 Hz), 4.43 (1H, d, J = 6.7 Hz), 4.02 (1H, m), 3.90−3.85 (3H, m), 3.77 (1H, d, J = 3.9 Hz), 3.68 (2H, d, J = 6.7 Hz), 3.53 (1H, d, J = 6.7 Hz), 3.38 (3H, m), 3.27 (3H, s), 2.15 (2H, m), 1.31 (2H, m), 1.25 (20H, m), 0.90−0.87 (39H, m), 0.48 (3H, s), 0.42 (3H, s), 0.09−0.02 (24H, m); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 144.3, 139.8, 139.5, 133.9, 129.1, 127.8, 103.2, 93.0, 82.4, 79.0, 78.0, 75.0, 74.1, 73.6, 69.9, 63.8, 55.1, 38.2, 31.9, 30.5, 29.6, 29.5, 29.3, 25.9, 25.8, 25.8, 22.7, 22.4, 18.2, 18.0, 18.0, 17.8, 14.0, −1.2, −1.7, −4.1, −4.5, −4.7, −4.8, −5.0, −5.4; MS (CI^+, NH_3) *m/z* 1114 $(M + NH_4)^+$. Anal. Calcd for $C_{58}H_{116}O_9Si_5$: C, 63.45; H, 10.65. Found: C, 63.51; H, 10.73.

(+)-1-*O*-[(2*R*,3*S*,4*Z*)-2-Azido-3-methoxymethoxy-5-dimethylphenylsilyl-octadec-4-en-1-yl] 2,3,4,6-tetra-*O*-*tert*-butyldimethylsilyl-*β*-D-glucopyranoside (18). PPh_3 (26 mg, 100 μmol) and DEAD (16 μL, 100 μmol) were added to a stirred solution of alcohol **17** (55 mg, 50 μmol) in THF (0.5 mL). DPPA (22 μL, 100 μmol) was added, and the mixture stirred for 18 h. The solvent was evaporated and the resultant crude reaction mixture chromatographed (1:39 EtOAc:hexane then 1:19 EtOAc:hexane) to give **18** (56 mg, 100%) as a colorless oil: R_f (1:9 EtOAc:hexane) 0.67; $[\alpha]^{26}{}_D$ = +23 (*c* 1.0, $CHCl_3$); IR (thin film) 2099 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.55−7.52 (2H, m), 7.37−7.34 (3H, m), 5.90 (1H, d, J = 10.0 Hz, 4.65 (1H, d, J = 6.2 Hz), 4.51 (1H, d, J = 6.7 Hz), 4.40 (1H, d, J = 6.7 Hz), 4.22 (1H, dd, J = 4.0, 9.9 Hz), 3.94 (1H, d, J = 2.7 Hz), 3.79−3.71 (5H, m), 3.59 (1H, d, J = 6.2 Hz), 3.52 (1H, dt, J = 3.77, 9.2 Hz), 3.37−3.27 (1H, m), 3.31 (3H, s), 2.14−2.08 (2H, m), 1.33−1.23 (22H, m), 0.94−0.87 (39H, m), 0.48 (3H, s), 0.45 (3H, s), 0.10−0.06 (24H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 146.6,

138.8, 138.0, 133.9, 129.1, 127.9, 102.4, 93.3, 82.0, 78.8, 77.3, 74.6, 70.0, 68.1, 65.5, 64.0, 55.3, 38.2, 31.9, 31.6, 30.4, 29.7, 29.6, 29.5, 29.4, 29.3, 25.9, 25.8, 25.8, 22.7, 22.6, 18.3, 18.0, 18.0, 17.8, 14.1, −1.1, −1.2, −4.4, −4.4, −4.5, −4.7, −5.1, −5.3, −5.3; MS (CI^+, NH_3) *m/z* 1139 $(M + NH_4)^+$. Anal. Calcd for $C_{58}H_{115}N_3O_8Si_5$: C, 62.03; H, 10.32; N, 3.74. Found: C, 62.19; H, 10.30; N, 3.64.

(+)-1-*O*-[(2*R*,3*S*,4*E*)-2-Azido-3-methoxymethoxy-octadec-4-en-1-yl] 2,3,4,6-tetra-*O*-acetyl-*β*-D-glucopyranoside (19). Bu_4NF (1.0 M in THF containing ∼5% water, 164 μL, 164 μmol) was added to a stirred solution of azide **18** (23 mg, 20 μmol) in DMSO (0.2 mL). The mixture was heated to 60 °C and stirred for 3 h. The mixture was allowed to cool to room temperature, DMAP (10 mg, 82 μmol) was added followed by pyridine (0.2 mL) and Ac_2O (0.1 mL), and the resultant mixture was stirred at room temperature for 19 h. The mixture was diluted with Et_2O (20 mL) and poured into a saturated aqueous $NaHCO_3$ and stirred vigorously for 30 min. The organic layer was separated and the aqueous layer extracted with Et_2O. The combined organic layers were washed with aqueous $CuSO_4$ (0.5 M), water, and brine and dried ($MgSO_4$). Filtration and concentration yielded the crude product which was chromatographed (1:19 EtOAc:hexane then 1:1 EtOAc:hexane) to give **19** as a white solid (11 mg, 80%): R_f (1:1 EtOAc:hexane) 0.47; mp 56−58 °C; $[\alpha]^{26}_D = +20$ (*c* 1.0, $CHCl_3$); IR (thin film) 2100, 1759 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 5.73 (1H, dt, *J* = 15.2, 6.9 Hz), 5.30 (1H, dd, *J* = 8.5, 15.4 Hz), 5.21 (1H, t, *J* = 9.5 Hz), 5.10 (1H, t, *J* = 9.6 Hz), 5.03 (1H, dd, *J* = 8.0, 9.5 Hz), 4.68 (1H, d, *J* 6.8 Hz), 4.58 (1H, d, *J* = 8.0 Hz), 4.50 (1H, d, *J* = 6.7 Hz), 4.27 (1H, dd, *J* = 4.5 and 12.3 Hz), 4.13 (1H, dd, *J* = 2.3 and 12.3 Hz), 4.06−4.01 (2H, m), 3.72−3.68 (2H, m), 3.48 (1H, dd, *J* = 9.0 and 10.2 Hz), 3.33 (3H, s), 2.06 (3H, s), 2.05 (3H, s), 2.02 (3H, s), 2.00 (3H, s), 2.08−2.00 (2H, m), 1.36 (2H, m),1.29−1.24 (20H, m), 0.87 (3H, t, *J* = 6.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.6, 170.3 169.4, 169.4, 138.5, 124.6, 101.0, 93.2, 76.1, 72.8, 71.8, 71.0, 69.6, 68.3, 64.8, 61.8, 55.6, 32.3, 31.9, 29.6, 29.4, 29.3, 29.1, 28.9, 22.7, 20.7, 20.6, 20.6, 14.1. MS (CI^+, NH_3) *m/z* 717 $(M + NH_4)^+$. Anal. Calcd for $C_{34}H_{57}N_3O_{12}$: C, 58.35; H, 8.21; N, 6.00. Found: C, 58.47; H, 8.34; N, 6.06.

(+)-1-*O*-[(2*R*,3*S*,4*E*)-2-*n*-Hexadecanamido-3-methoxymethoxy-octadec-4-en-1-yl] 2,3,4,6-tetra-*O*-acetyl-*β*-D-glucopyranoside (20). PPh_3 (12 mg, 47 μmol) and water (6 μL) were added to a stirred solution of azide **19** (11 mg, 15.7 μmol) in THF (1 mL), and the mixture was heated to 45 °C for 24 h. After rotary evaporation, the residue was redissolved in CH_2Cl_2 (1 mL) and cooled to 0 °C. Et_3N (11 μL, 78 μmol) and palmitoyl chloride (14 μL, 47 μmol) were added. The reaction mixture was allowed to warm to room temperature while stirring for 16 h. The solvent was evaporated and the crude solid chromatographed (2:3 EtOAc:hexane) to give amide **20** (13 mg, 90%) as a white solid: R_f (1:1 EtOAc:hexane) 0.31; mp 94−96 °C; $[\alpha]^{26}_D = +8$ (*c* 1.0, $CHCl_3$); IR (thin film) 1750, 1643 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 5.73 (1H, d, *J* = 9.3 Hz), 5.61 (1H, dt, *J* = 6.7, 5.3 Hz), 5.26 (1H, dd, *J* = 8.8, 15.4 Hz), 5.20 (1H, t, *J* = 9.5 Hz), 5.07 (1H, t, *J* = 9.7 Hz), 5.02 (1H, dd, *J* = 8.1, 9.6 Hz), 4.67 (1H, d, *J* = 6.6 Hz), 4.52 (1H, d, *J* = 8.0 Hz), 4.46 (1H, d, *J* = 6.6 Hz), 4.27 (1H, dd, *J* = 4.8, 12.3 Hz), 4.17−4.09 (2H, m), 3.93 (1H, t, *J* = 8.4 Hz), 3.92−3.84 (2H, m), 3.69 (1H, ddd, *J* = 2.2, 4.8, 10.0 Hz), 3.33 (3H, s), 2.32−1.93 (4H, m), 2.08 (3H, s), 2.07 (3H, s), 2.02 (3H, s), 2.01 (3H, s), 1.56 (2H, m), 1.24 (46H, s), 0.87 (6H, t, 6.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.5, 170.6, 170.2, 169.5, 169.4, 137.8, 126.4, 100.9, 93.4, 75.8, 72.6, 71.9, 71.2, 68.5, 68.3, 61.8, 55.6, 51.1, 36.9, 32.3, 31.9, 29.7, 29.54, 29.50, 29.44, 29.35, 29.28, 29.19, 29.09, 25.7, 22.7, 20.7, 20.6, 14.1; MS (EI^+) *m/z* 911 ($M^{+\cdot}$). HRMS (EI^+) Calcd for $C_{50}H_{89}NO_{13}$ ($M^{+\cdot}$); 911.6334. Found; 911.6311.

D,L-Glucosylceramide (1). Amide **20** (72 mg, 79 μmol) was dissolved in MeOH (3.5 mL) and treated with 5% KOH−MeOH (3.5 mL) with stirring for 30 min at room temperature. The mixture was neutralized with Dowex 50W × 8 resin (H^+ form), filtered, and concentrated. The crude product was redissolved in MeOH (3.5 mL) and treated with 2% HCl−MeOH (3.5 mL) at 45 °C for 5 h. The mixture was then neutralized using Ag_2CO_3, filtered, concentrated, and chromatographed (1:9 MeOH:$CHCl_3$) to give **1** (38 mg, 69%) as a white solid: R_f (1:9 MeOH:$CHCl_3$) 0.09; mp 184 °C (lit.[12b] 182−183 °C); $[\alpha]^{26}_D = -9$ (*c* 1.0, 1:1 $CHCl_3$:MeOH); IR (thin film) 3273, 2917, 2849, 1651, 1557, 1465 cm^{-1}; ^1H NMR (400 MHz, 9:1 $CDCl_3$:CD_3OD) δ 6.90 (1H, d, *J* = 8.1 Hz), 5.64 (1H, dt, *J* = 15.2, 6.8 Hz), 5.38 (1H, dd, *J* = 6.8, 15.2 Hz), 4.20 (1H, d, *J* = 7.8 Hz), 4.03 (1H, t, *J* = 6.3 Hz), 3.95−3.86 (1H, m), 3.85−3.72 (3H, m), 3.67 (1H, dd, *J* = 4.3, 12.2 Hz), 3.40−3.27 (2H, m), 3.25−3.14 (2H, m), 2.10 (2H, t, *J* = 7.6 Hz), 1.97−1.92 (2H, m), 1.56−1.45 (2H, m), 1.30−1.10 (46H, m), 0.81 (6H, app t); ^{13}C NMR (100 MHz, 9:1 $CDCl_3$:CD_3OD) δ 174.3, 134.1, 128.7, 103.3, 76.2, 75.9, 73.3, 72.4, 69.8, 69.2, 61.5, 53.3, 36.4, 32.2, 31.8, 29.6, 29.4, 29.3, 29.2, 29.1, 25.7, 22.5, 13.9; MS (FAB +ve) *m/z* 722$(M + Na)^+$. HRMS (FAB +ve) Calcd for $C_{40}H_{77}NO_8Na$ $(M + Na)^+$: 722.5547. Found: 722.5567.

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Supporting Information Available: ^{13}C NMR spectra available for **1**, **7**−**11**, and **15**−**20**. ^1H NMR, DEPT 90, DEPT 135, COSY, and HETCOR spectra available for **1** and **20**. This material is available free of charge via the Internet at http://pubs.acs.org.

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