Total Synthesis and Biological Evaluation of Glycolipids Plakosides A, B and Their Analogs

by **Kyriacos C. Nicolaou**[a])*, **Jim Li**[a]), and **Gerhard Zenke**[b])

[a]) Department of Chemistry and The Skaggs Institute for Chemical Biology, The Scripps Research Institute, 10550 North Torrey Pines Road, La Jolla, California 92037, USA, and Department of Chemistry and Biochemistry, University of California, San Diego, 9500 Gilman Drive, La Jolla, California 92093, USA
[b]) *Novartis Pharma AG*, Transplantation Research, WSJ-386.127, CH-4002, Basel

Dedicated to Professor *Albert Eschenmoser* on the occasion of his 75th birthday for his outstanding contributions to organic and bioorganic chemistry

The total synthesis of plakosides A (**1**) and B (**2**), and their designed analogs **3**–**10** was accomplished. The convergent strategy employed involved construction of the individual building blocks employing the *Sharpless* asymmetric dihydroxylation and the *Charette* asymmetric cyclopropanation reactions to introduce the desired configuration, followed by their couplings and final elaboration. Thus, key intermediates **12**–**14** were prepared in their optically active forms and joined through a glycosidation reaction and amide-bond formation to yield the target molecules after appropriate elaboration and final deprotection. The synthesized compounds **1**–**10** were evaluated for their immunosuppressive properties *in vitro* and found to be only modestly active.

Introduction. – Plakosides A and B (**1** and **2**, *Fig. 1*) are two naturally occurring glycosphingolipids (GSLs) whose structures and biological properties have recently been reported [1]. Isolated from the marine sponge *Plakortis simplex*, these glycosphingolipids are novel among many members of their class, since they are the first found to include a cyclopropane ring in their sphingosine chain and a prenylated 2-*O*-substituent on their carbohydrate moiety. Interestingly, the latter functionality has been associated with the immunosuppressive properties exhibited by these compounds [1–3]. The potent immunosuppressive activity reported for plakosides A (**1**) and B (**2**) stands in contrast to other related glycosphingolipids, which are either inactive or immunostimulating [4–6]. To further investigate the biological properties of these new, but scarce, natural products, we initiated a program aimed at their total synthesis and the synthesis of selective analogs. In this article, we describe an efficient and stereocontrolled total synthesis that delivers not only plakosides A (**1**) and B (**2**), but also their analogs **3**–**10** (*Fig. 1*), as well as their biological evaluation as potential immunosuppressive agents.

Results and Discussion. – *Retrosynthetic Analysis.* The structures of plakosides A (**1**) and B (**2**) render themselves to the obvious retrosynthetic disconnections shown in *Fig. 2*. The disassembly at the strategic glycosidic, amide, and prenyl ether bonds reveal primary alcohols **13** (plakoside A) or **14** (plakoside B), galactosyl fluoride **11**, and prenyl bromide (1-bromo-3-methylbut-2-ene; **15**) as the key building blocks required for the total synthesis. It was envisioned that the absolute configuration of the

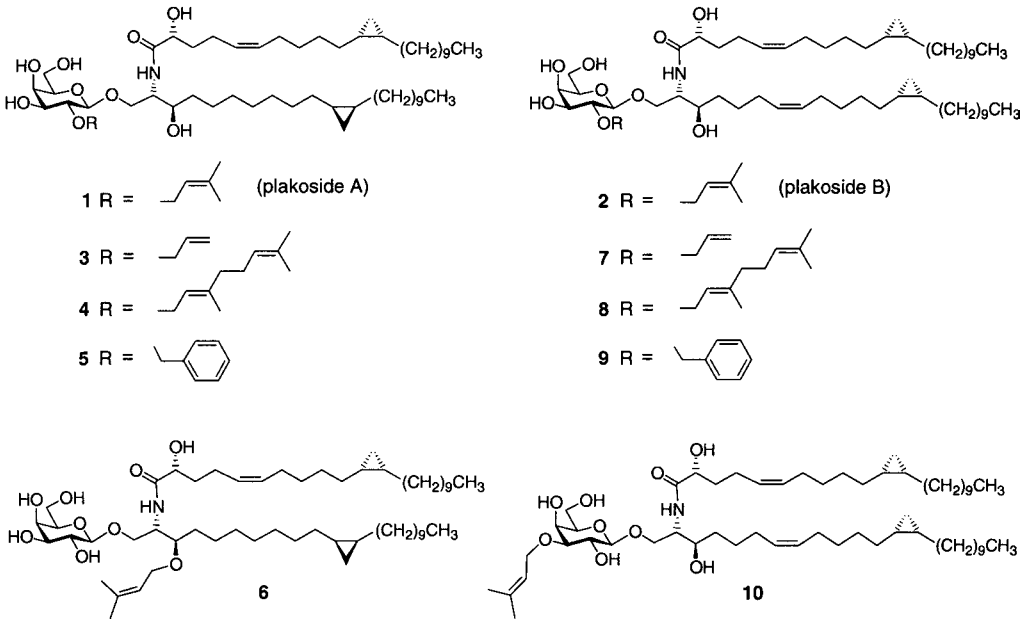


Fig. 1. *Structures of plakosides A* (**1**), *B* (**2**) *and their analogs* **3**–**10**

cyclopropane rings would arise from a *Charette* cyclopropanation [7]. The O-bearing stereogenic centers of the side chains would be generated by two *Sharpless* asymmetric dihydroxylation (AD) processes [8]. Selective conversion of the *syn*-diol resulting from the latter reaction into the hydroxy azide would then produce a precursor to the required amino-alcohol moiety on the sphingosine chain. The installation of a pivaloate group at the 2-*O* on the galactosyl fluoride was the designed element by which we were hoping to direct the glycosidation reaction in the desired sense (β-configuration) [9–11]. The two-stage activation procedure [10] for the glycosidation step was reserved for the key coupling of the galactose moiety with the azide-containing sphingosine equivalent.

Synthesis of Galactosyl Fluoride **11**. Galactosyl fluoride **11** was obtained from commercially available galactose pentaacetate **16** in six steps as shown in *Scheme 1*. The exposure of **16** to thiophenol in the presence of a catalytic amount of $SnCl_4$ provided thiogalactoside **17** in excellent yield and selectivity (94%, $\beta/\alpha > 15:1$). Chromatographically purified β-thiogalactoside **17** was exposed to a catalytic amount of MeONa in MeOH to provide tetraol **18**, which was selectively monosilylated at the primary position (TBDPSCl and imidazole in DMF; for abbreviations of reagents and protecting groups, see legends in the *Schemes*) to afford triol **19** in 97% overall yield from **17**. Engagement of the 3,4-diol system of **19** as an acetonide was accomplished by treatment with 2,2-dimethoxypropane in the presence of CSA to furnish compound **20** (89% yield). The remaining OH group was reacted with pivaloyl chloride and 4-DMAP in refluxing pyridine to give pivaloate ester **21** in 99% yield. Finally, exposure of **21** to DAST in the presence of the activator DMTST led to the desired galactosyl fluoride **11** in 94% yield and a *ca.* 11:1 ratio of β/α-anomers [12]. This mixture was directly used for the glycosidation step without further separation.

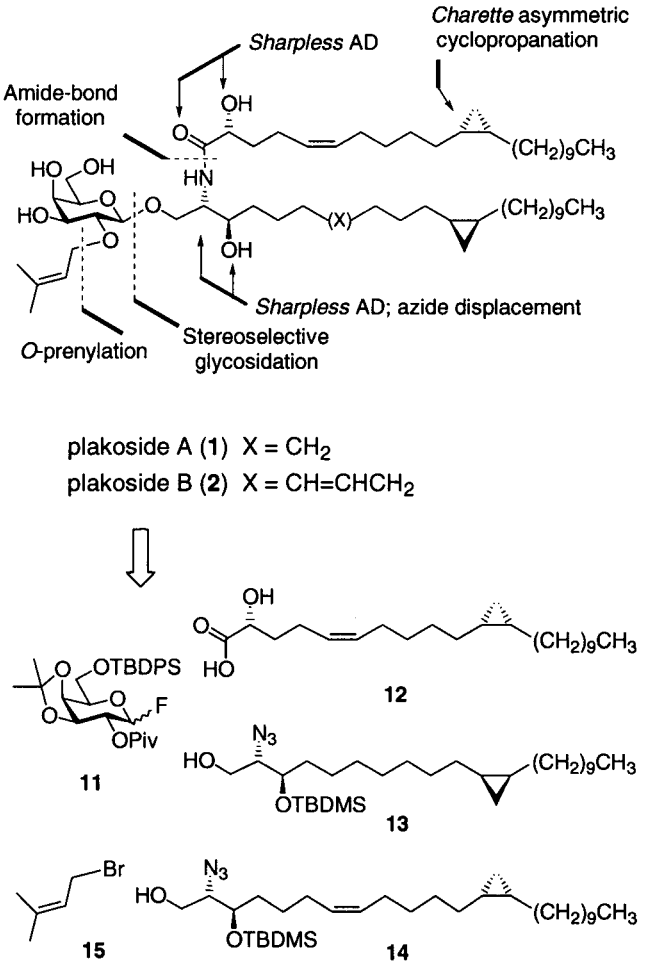
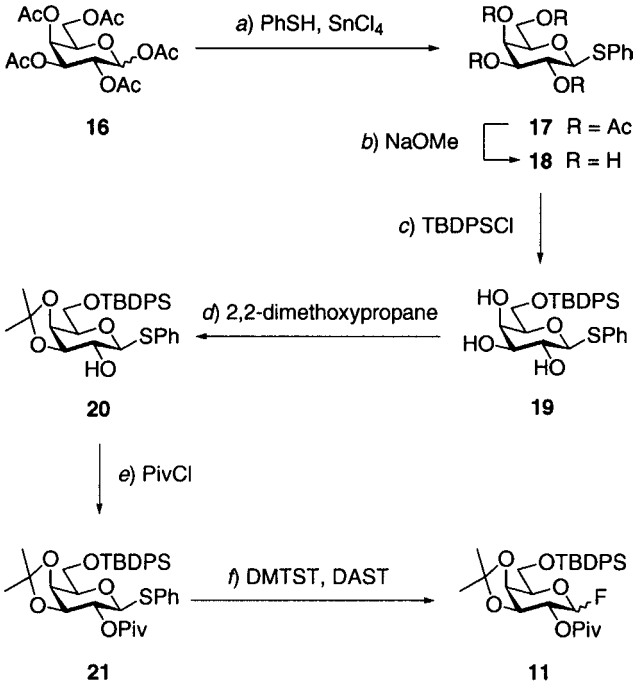


Fig. 2. *Retrosynthetic analysis of plakosides A* (**1**) *and B* (**2**). Piv = pivaloyl; TBDMS = (*t*-Bu)Me_2Si; TBDPS = (*t*-Bu)Ph_2Si.

Synthesis of Azides **13** *and* **14**. Employing the *Sharpless* [8] and *Charette* [7] methodologies, enantioselective syntheses of the requisite azides **13** (*Scheme 2*) and **14** (*Scheme 3*) were developed. Starting from commercially available tridec-2-yn-1-ol (**22**), the (*Z*)-alcohol **23** was obtained in 96% yield by selective hydrogenation (H_2, 5% Pd on $BaSO_4$) [13]. *Charette* asymmetric cyclopropanation [7] of **23** using bis(iodomethyl)zinc · DME complex and (*R*,*R*)-dioxaborolane **24** resulted in the formation of **25** in 96% yield and 84% ee[1]). Exposure of alcohol **25** to Ph_3P and I_2 in the presence of

[1]) The ee value [%] was determined from comparison of $[\alpha]_D$ values of cyclopropanemethanol **25** prepared as shown in *Scheme 2* and the following procedure. From known (+)-(1*S*,2*R*)-2-(benzyloxymethyl)cyclopropanemethanol (93% ee) [7b], conversion of the alcohol to the iodide and followed by coupling with *Grignard* reagent from 1-bromononane in the presence of Li_2CuCl_4 catalyst, and finally removal of the $PhCH_2$ group afforded **25**.

Scheme 1. *Synthesis of Galactosyl Fluoride* **11**

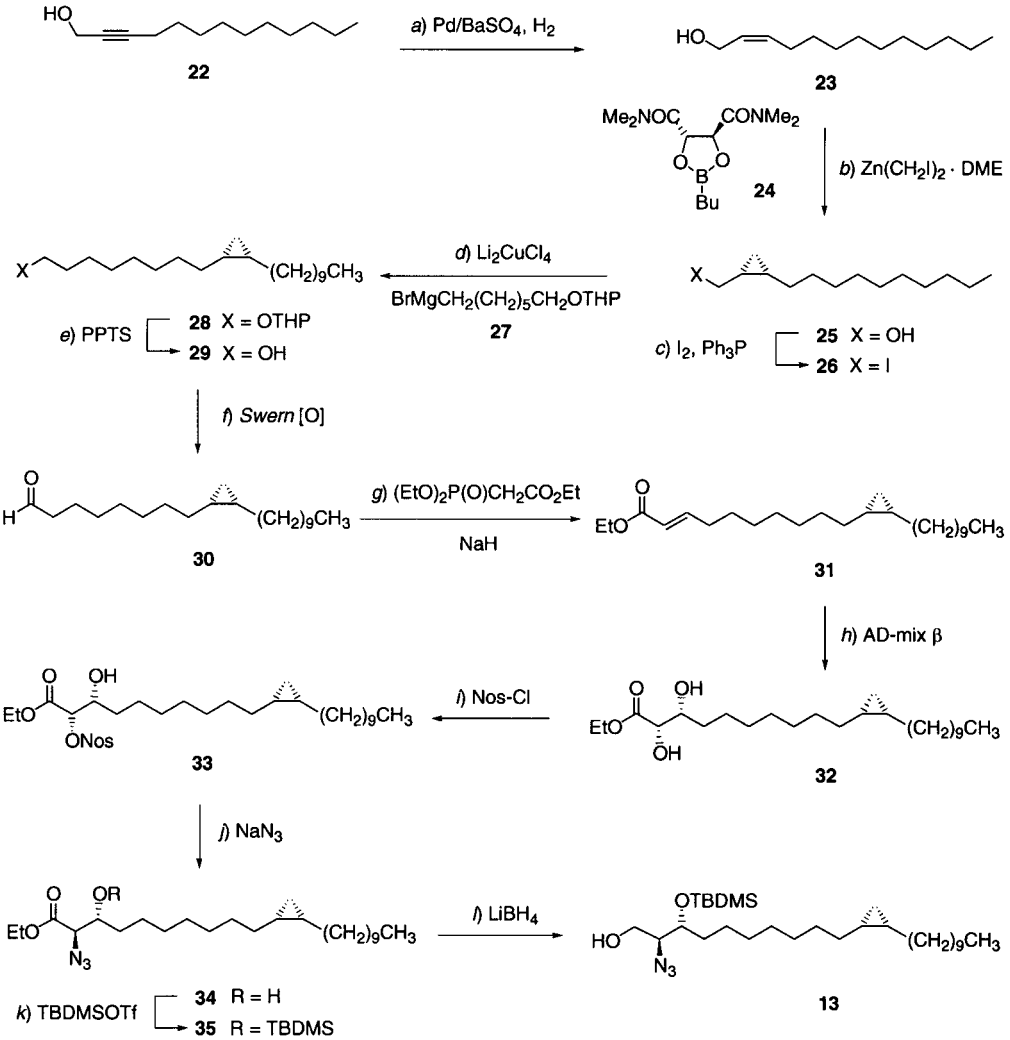


a) PhSH (1.2 equiv.), $SnCl_4$ (0.1 equiv.), CH_2Cl_2, $-15°$, 3.5 h; 94%. *b*) MeONa (0.2 equiv.), MeOH, 25°, 1 h. *c*) TBDPSCl (1.3 equiv.), imidazole (1.3 equiv.), DMF, 0°, 1.5 h; 97% for 2 steps. *d*) 2,2-Dimethoxypropane (2.0 equiv.), CSA (0.1 equiv.), 25°, 8 h; 89%. *e*) PivCl (2.0 equiv.), 4-DMAP (0.05 equiv.), pyridine, reflux, 2 h; 99%. *f*) DMTST (1.2 equiv.), DAST (3.0 equiv.), CH_2Cl_2, $0 \rightarrow 25°$, 3 h; 94% (α/β *ca.* 1:11). Abbreviations: Ac = acetyl, DAST = (diethylamino)sulfur trifluoride, DMF = *N*,*N*-dimethylformamide, 4-DMAP = 4-(dimethylamino)pyridine, DMTST = dimethyl(methylthio)sulfonium triflate, Piv = pivaloyl, TBDPS = (*t*-Bu)Ph_2Si.

imidazole furnished the corresponding iodo derivative **26** in 96% yield, which was cross-coupled with the *Grignard* reagent **27**, derived from the THP ether of 7-bromoheptan-1-ol in the presence of Li_2CuCl_4 catalyst, to afford product **28** in 87% yield [14]. Aldehyde **30** was then derived from acidic cleavage of the THP ether from **28** (PPTS, 98% yield), followed by *Swern* oxidation [15] (96% yield) of the resulting primary alcohol **29**. Olefination of aldehyde **30** ($(EtO_2P(O)CH_2CO_2Et$, NaH) led to the α,β-unsaturated ester **31** (94% yield, $(E)/(Z) > 95:5$). Asymmetric dihydroxylation (AD) of **31** with AD mix-β in the presence of $MeSO_2NH_2$ proceeded smoothly to afford the *syn*-dihydroxy ester **32** in 96% isolated yield [8b]. Selective nosylation [16] (nosyl (4-nitrobenzenesulfonyl) chloride, pyridine) of the α-OH group of the latter compound gave nosylate **33** in 90% yield. Displacement of the nosylate group in **33** with azide [16] (NaN_3, DMF, 25°) then led smoothly to the α-azido-β-hydroxy ester **34** (94% yield), which was silylated (TBDMSOTf, 2,6-lutidine) to afford silyl ether **35** in quantitative yield. Finally, reduction of the ester group in **35** with $LiBH_4$ in THF at 0° furnished the desired primary alcohol **13** in 95% yield.

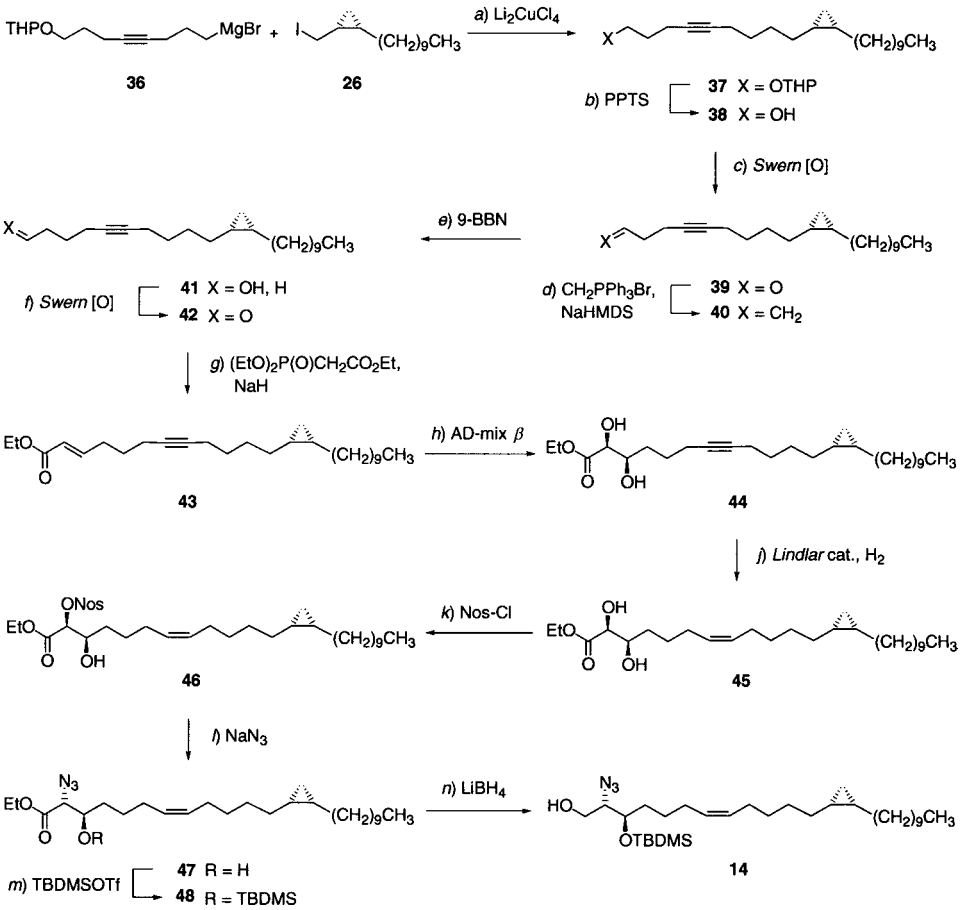
The construction of the α-azidosphingosine **14** required for the synthesis of plakoside B (**2**) is summarized in *Scheme 3*. The strategy involved introduction of the

Scheme 2. *Synthesis of Azidosphingosine* **13**



a) Pd/$BaSO_4$ (10% *w*/*w*), H_2 (1 atm), pyridine, 25°, 10 h; 96%. *b*) $Zn(CH_2I)_2 \cdot$ DME (3.0 equiv.), dioxaborolane (**24**) (1.2 equiv.), 4-Å molecular sieves, CH_2Cl_2, $-15 \rightarrow 25°$, 6 h; 96%. *c*) I_2 (1.5 equiv.), Ph_3P (1.3 equiv.), imidazole (1.4 equiv.), Et_2O/MeCN 5:3 (*v*/*v*), 0°, 1 h; 96%. *d*) Li_2CuCl_4 (0.006 equiv.), $BrMgCH_2(CH_2)_5CH_2OTHP$ (**27**) (1.3 equiv.), THF, 0°, 30 min; 87%. *e*) PPTS (0.2 equiv.), MeOH, 55°, 4 h; 98%. *f*) DMSO (2.0 equiv.), $(COCl)_2$ (1.5 equiv.), Et_3N (5.0 equiv.), CH_2Cl_2, $-78 \rightarrow 25°$, 1 h, 96%. *g*) $(EtO)_2P(O)CH_2CO_2Et$ (1.5 equiv.), NaH (1.5 equiv.), THF, 0°, 45 min; 94% ((*E*)/(*Z*) > 95:5). *h*) AD-mix *β* (1.4 g/mmol), $MeSO_2NH_2$ (1.0 equiv.), *t*-BuOH/H_2O 1:1 (*v*/*v*), 0°, 8 h; 96%. *i*) Nos-Cl (1.15 equiv.), pyridine, 0°, 7.5 h; 90%. *j*) NaN_3 (6.0 equiv.), DMF, 25°, 36 h; 94%. *k*) TBDMSOTf (1.05 equiv.), 2,6-lutidine (2.5 equiv.), CH_2Cl_2, $-78 \rightarrow 25°$, 30 min; 100%. *l*) $LiBH_4$ (2.5 equiv.), THF, 0°, 3.5 h; 95%. Abbreviations: AD-mix *β* = reagent for *Sharpless* AD containing $(DHQD)_2PHAL$ ligand, DME = dimethoxyethane, DMF = *N*,*N*-dimethylformamide, DMSO = dimethyl sulfoxide, PPTS = pyridinium 4-toluenesulfonate, THP = tetrahydro-2*H*-pyran-2-yl, Nos = 4-nitrobenzenesulfonyl, TBDMS = (*t*-Bu)Me_2Si.

Scheme 3. *Synthesis of Azidosphingosine* **14**



a) Li_2CuCl_4 (0.006 equiv.), THF, 0°, 30 min; 84%. *b*) PPTS (0.2 equiv.), MeOH, 55°, 4 h; 100%. *c*) DMSO (2.0 equiv.), $(COCl)_2$ (1.5 equiv.), Et_3N (5.0 equiv.), CH_2Cl_2, $-78 \rightarrow 25°$, 1 h; 97%. *d*) CH_2PPh_3Br (1.6 equiv.), NaHMDS (1.4 equiv.), THF, 0°, 1 h; 97%. *e*) 9-BBN (1.1 equiv.), H_2O_2 (1.1 equiv.), $NaHCO_3$, THF, $0 \rightarrow 25°$; 84%. *f*) DMSO (2.0 equiv.), $(COCl)_2$ (1.5 equiv.), Et_3N (5.0 equiv.), CH_2Cl_2, $-78 \rightarrow 25°$, 1 h; 97%. *g*) $(EtO)_2P(O)CH_2CO_2Et$ (1.5 equiv.), NaH (1.5 equiv.), THF, 0°, 30 min; 96% ($(E)/(Z) > 98:2$). *h*) AD-mix β (1.4 g/mmol), $MeSO_2NH_2$ (1.0 equiv.), *t*-BuOH/H_2O 1:1 (*v*/*v*), 0°, 8 h; 97%. *j*) *Lindlar* cat. (10% *w*/*w*), H_2 (1 atm), EtOH, 25°, 40 min; 100%. *k*) Nos-Cl (1.15 equiv.), pyridine, 0°, 6.5 h; 84%. *l*) NaN_3 (2.0 equiv.), DMF, 25°, 36 h; 95%. *m*) TBDMSOTf (1.05 equiv.), 2,6-lutidine (2.5 equiv.), CH_2Cl_2, $-78 \rightarrow 25°$, 30 min; 100%. *n*) $LiBH_4$ (2.5 equiv.), THF, 0°, 10 h; 92%. Abbreviations: AD-mix β = reagent for *Sharpless* AD containing $(DHQD)_2PHAL$ ligand, 9-BBN = 9-borabicyclo[3.3.1]nonane, DME = dimethoxyethane, DMF = *N*,*N*-dimethylformamide, DMSO = dimethyl sulfoxide, NaHMDS = sodium bis(trimethylsilyl)amide, PPTS = pyridinium 4-toluenesulfonate, THP = tetrahydro-2*H*-pyran-2-yl, Nos = 4-nitrobenzenesulfonyl, TBDMS = (*t*-Bu)Me_2Si.

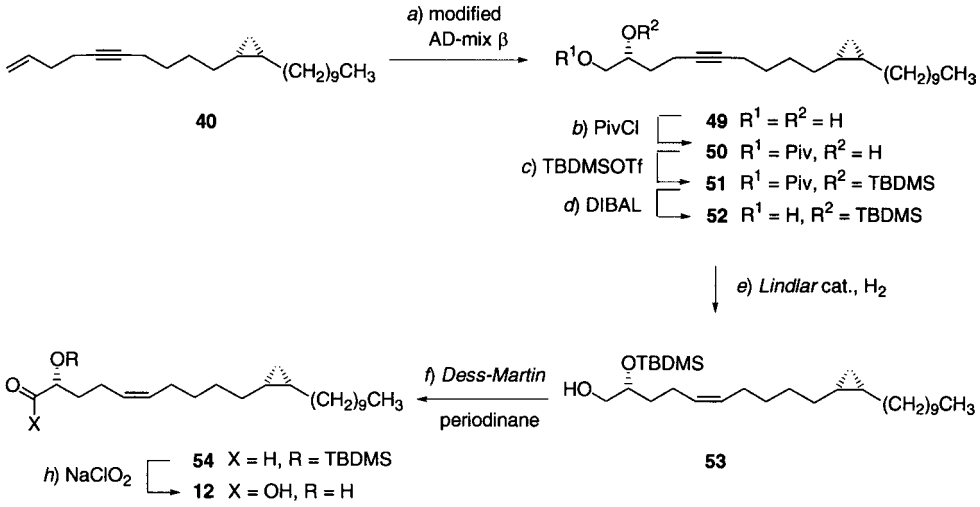
(*Z*)-olefin, masked as an acetylenic linkage, after the asymmetric dihydroxylation (**43** → **44**), at which stage *Lindlar* [17] hydrogenation generated compound **45**. The *Grignard* reagent **36** was derived from the corresponding bromide (generated from the THP ether of pent-4-yn-1-ol and 1,3-dibromopropane) [18] and was coupled with iodide **26** in the presence of Li_2CuCl_4 catalyst to afford alkyne **37** (84% yield). Removal

of the THP group from **37** (PPTS, 100% yield), followed by *Swern* oxidation (97% yield), led to aldehyde **39** *via* alcohol **38**.

The required C_1 homologation of aldehyde **39** was accomplished by a *Wittig* olefination (CH_2=PPh_3, **40**, 97% yield), followed by regioselective hydroboration [19] (9-BBN, **41**, 84% yield). *Swern* oxidation of the resulting primary alcohol **41** furnished aldehyde **42** (97% yield). Olefination of **42** with $(EtO)_2P(O)CH_2CO_2Et$ and NaH gave the α,β-unsaturated ester **43** in 96% yield ((*E*)/(*Z*) *ca.* 98:2). Asymmetric dihydroxylation of **43** with AD-mix β and $MeSO_2NH_2$ gave the *syn*-dihydroxy ester **44** (97% yield), which was selectively and quantitatively hydrogenated (H_2, *Lindlar* catalyst) to afford **45**. Selective nosylation of **45** (nosyl chloride, pyridine, **46**, 84% yield), followed by reaction with NaN_3 in DMF, furnished azide **47** (95% yield), from which silyl ether **48** was generated quantitatively (TBDMSOTf, 2,6-lutidine). The targeted α-azido-β-(silyloxy)sphingosine **14** was then obtained in 92% yield by $LiBH_4$ reduction of **48**.

Synthesis of α-Hydroxy Carboxylic Acid **12**. The construction of the remaining fragment, α-hydroxy acid **12**, proceeded as shown in *Scheme 4*. Thus, asymmetric dihydroxylation of the intermediate **40** with ($(DHQD)_2AQN$, $K_2Os_2(OH)_4$, $K_2Fe(CN)_6$, and K_2CO_3) resulted in the formation of diol **49** in 91% yield [26]. Selective pivaloate formation proceeded smoothly with **49** in the presence of stoichiometric amounts of freshly distilled PivCl in pyridine at 0°, leading to **50** (91% yield) [21]. The secondary OH group in **50** was silylated (TBDMSOTf, 2,6-lutidine, **51**, 100% yield), and the pivaloate group was cleaved by treatment with DIBAL,

Scheme 4. *Synthesis of α-Hydroxy Acid* **12**

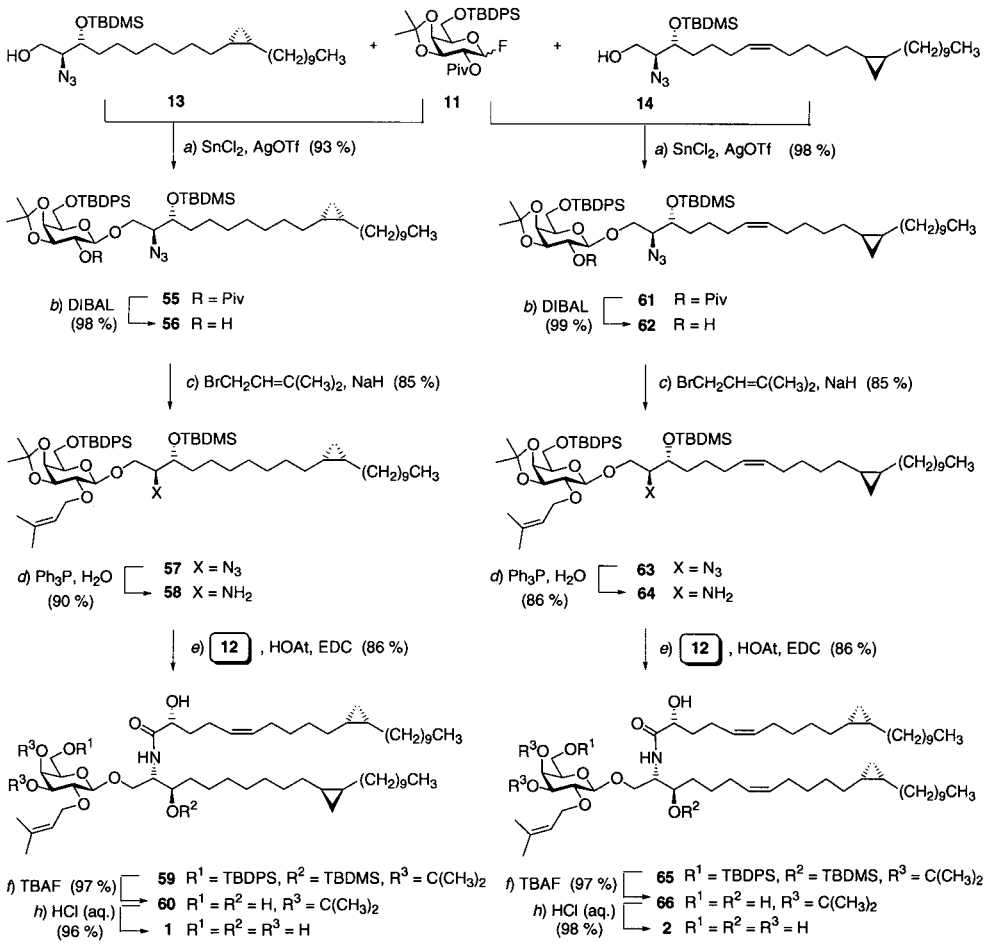


a) $(DHQD)_2AQN$ (0.01 equiv.), $K_2Fe(CN)_6$ (3.0 equiv.), $K_2Os_2(OH)_4$ (0.004 equiv.), K_2CO_3 (3.0 equiv.), *t*-BuOH/H_2O 1:1 (*v*/*v*), 0°, 8 h; 91%. *b*) PivCl (1.0 equiv.), pyridine, 0°, 40 min; 91%. *c*) TBDMSOTf (1.01 equiv.), 2,6-lutidine (2.5 equiv.), CH_2Cl_2, $-78\rightarrow25°$, 30 min; 100%. *d*) DIBAL (2.0 equiv.), CH_2Cl_2, $-78°$, 20 min; 100%. *e*) *Lindlar* cat. (0.1 equiv.), H_2 (1 atm), EtOH, 25°, 30 min; 100%. *f*) *Dess-Martin* periodinane (1.2 equiv.), CH_2Cl_2, $0\rightarrow25°$, 40 min; 96%. *g*) $NaClO_2$ (2.5 equiv.), NaH_2PO_4(12.0 equiv.), 2-methylbut-2-ene (20.0 equiv.), *t*-BuOH/H_2O 5:1 (*v*/*v*), 0°, 30 min; >95%. Abbreviations: AD-mix β = reagent for *Sharpless* AD, in this case containing 1,4-bis(dihydroquinidinyl)anthraquinone ($(DHQD)_2AQN$) ligand, DIBAL = diisobutylaluminium hydride, Piv = pivaloyl, TBDMS = (*t*-Bu)Me_2Si.

furnishing primary alcohol **52** in quantitative yield from compound **51**. The C≡C bond in **52** was then selectively reduced with H_2 and *Lindlar* catalyst to afford the (*Z*)-olefin **53** in quantitative yield. Finally, stepwise oxidation of **53** furnished first aldehyde **54** (*Dess-Martin* periodinane, 96% yield) [22] and then the desired hydroxy carboxylic acid **12** ($NaClO_2$, >95%) [23].

Synthesis of Plakosides A and B. With all the required fragments in hand, we proceeded to assemble the final targets, plakosides A (**1**) and B (**2**), as shown in *Scheme 5*. The stereoselective glycosidation of azidosphingosine **13** with galactosyl

Scheme 5. *Total Synthesis of Plakosides A* (**1**) *and B* (**2**)



a) $SnCl_2$ (3.0 equiv.), AgOTf (3.0 equiv.), DTBMP (1.2 equiv.), 4-Å MS, CH_2Cl_2, $0 \rightarrow 25°$. *b*) DIBAL (1.5 equiv.), CH_2CH_2, $-78°$. *c*) Prenyl bromide (1.5 equiv.), NaH (1.2 equiv.), DMF, 0°. *d*) Ph_3P (2.0 equiv.), H_2O (2.0 equiv.), benzene, 45°. *e*) HOAt (3.1 equiv.), EDC (3.0 equiv.), THF, 0°. *f*) TBAF (5.0 equiv.), THF, 25°. *h*) aq. 1N HCl (cat.), MeOH, 37°. Abbreviations: DIBAL = diisobutylaluminium hydride, EDC = 1-[3-(dimethylamino)propyl]3-ethylcarbodiimide, DTBMP = 2,6-di-(*tert*-butyl)-4-methylpyridine, HOAt = 1-hydroxy-7-azabenzotriazole, TBDMS = (*t*-Bu)Me_2Si, TBDPS = (*t*-Bu)Ph_2Si, TBAF = Bu_4NF.

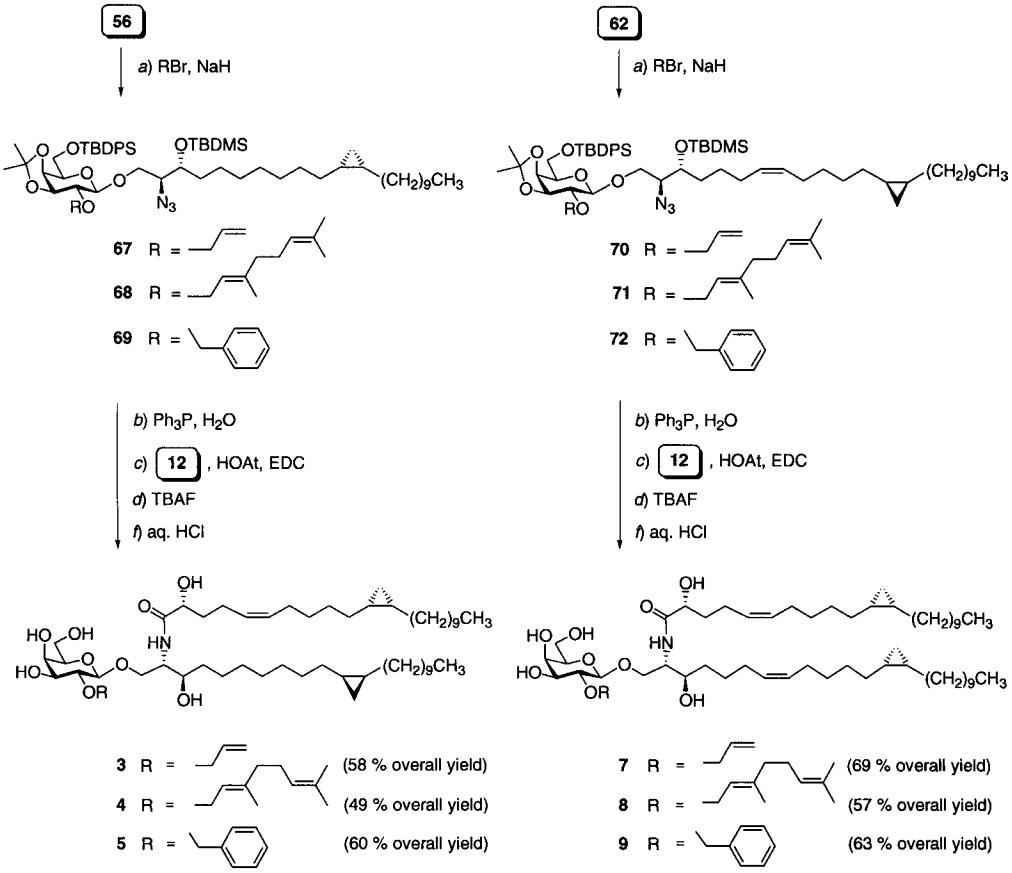
fluoride **11** proceeded in the presence of $SnCl_2$, AgOTf, 2,6-di-(*tert*-butyl)-4-methylpyridine and 4-Å molecular sieves to afford exclusively the expected β-galactoside **55** in 93% yield [12]. Removal of the pivaloate from **55** with DIBAL furnished hydroxy compound **56** (98% yield) onto which the prenyl group was installed (NaH, $BrCH_2CH{=}C(CH_3)_2$) to afford compound **57** (89% yield). *Staudinger* reduction [12][24] of the azido group in **57** (Ph_3P, H_2O, 45°) led to amine **58** in 90% yield, which was then coupled with the acid **12** in the presence of EDC and HOAt to furnish the desired plakoside A skeleton **59** (85% yield). Finally plakoside A (**1**) was released from **59** by sequential treatment with TBAF (97% yield of diol **60**) and aqueous HCl (96% yield of **1**). Compound **14** was converted to plakoside B (**2**) *via* a similar path and in similar yields (see *Scheme 5*). Both **1** and **2** exhibited spectroscopic data identical to those reported for natural plakosides A (**1**) and B (**2**) [1].

Synthesis of Plakoside Analogs **3**–**10**. The plakoside analogs **3**–**5** and **7**–**9** were synthesized (*Scheme 6*) starting from glycosides **56** and **62**, respectively, and utilizing the synthetic technology developed for the construction of the natural plakosides A (**1**) and B (**2**). Thus, *O*-alkylation of **56** with allyl, geranyl, or benzyl bromide in the presence of NaH furnished the corresponding ethers (**67**, **68**, and **69**, resp.). The N_3 groups of these compounds were reduced to afford the expected amines in high overall yields. Attachments of the α-hydroxy-carboxylic-acid side chain through amide-bond formation were then followed by the two-step deprotection sequence described above, affording analogs **3**, **4**, and **5** in high overall yields (58, 49, and 60% overall yields, resp.). Analogs **7**, **8**, and **9** were similarly prepared (69, 57, and 63% overall yields, resp.) as summarized in *Scheme 6*.

The syntheses of analogs **6** and **10** followed similar paths as shown in *Scheme 7*. Compound **6** was assembled in 58% overall yield from α-hydroxy carboxylic acid **12**, 3-*O*-prenylated azidosphingosine **73**, and galactosyl fluoride **74** through glycosidation, azide reduction, amide-bond formation, and sequential removal of protecting groups. Coupling of 3-*O*-prenylated galactosyl fluoride **76**, α-hydroxy carboxylic acid **12**, and azidosphingosine **13** in similar fashion gave compound **10** (60% overall yield).

Biological Evaluation of Plakosides A (**1**), *B* (**2**), *and Analogs* **3**–**10**. With the synthetic plakosides A, B, and their analogs in hand, we proceeded to evaluate their biological activities in three *in vitro* assays. We used the mixed-lymphocyte-reaction (MLR) proliferation assay as an *in vitro* model for an allogeneic immune response, the concanavalin A (Con A) response as a model for T cell proliferation in response to mitogen, and the murine bone marrow cell proliferation assay as a culture system of primary, non-lymphoid cells. The combination of these assays provided information not only about the immunosuppressive activity (MLR and Con A response), but also about the potential cytotoxic and cytostatic effects (bone marrow cell proliferation) of these compounds. In the MLR assay, spleen cells from CBA and BALB/c mice were used. The Con A response assay, was performed with Con A-stimulated CBA spleen cells, and the murine bone marrow cell proliferation assay was performed with bone marrow cells from CBA mice and conditioned media from the myelomonocytic cell line WEHI-3 and the fibroblast-like cell line L-929 as a source of growth factors. In all assays, proliferation was measured by [^{3}H]thymidine incorporation. Proliferation of BALB/c spleen cells alone, of CBA spleen cells without Con A, and of CBA bone marrow cells

Scheme 6. *Synthesis of Plakoside Analogs* **2**–**4** *and* **7**–**9**

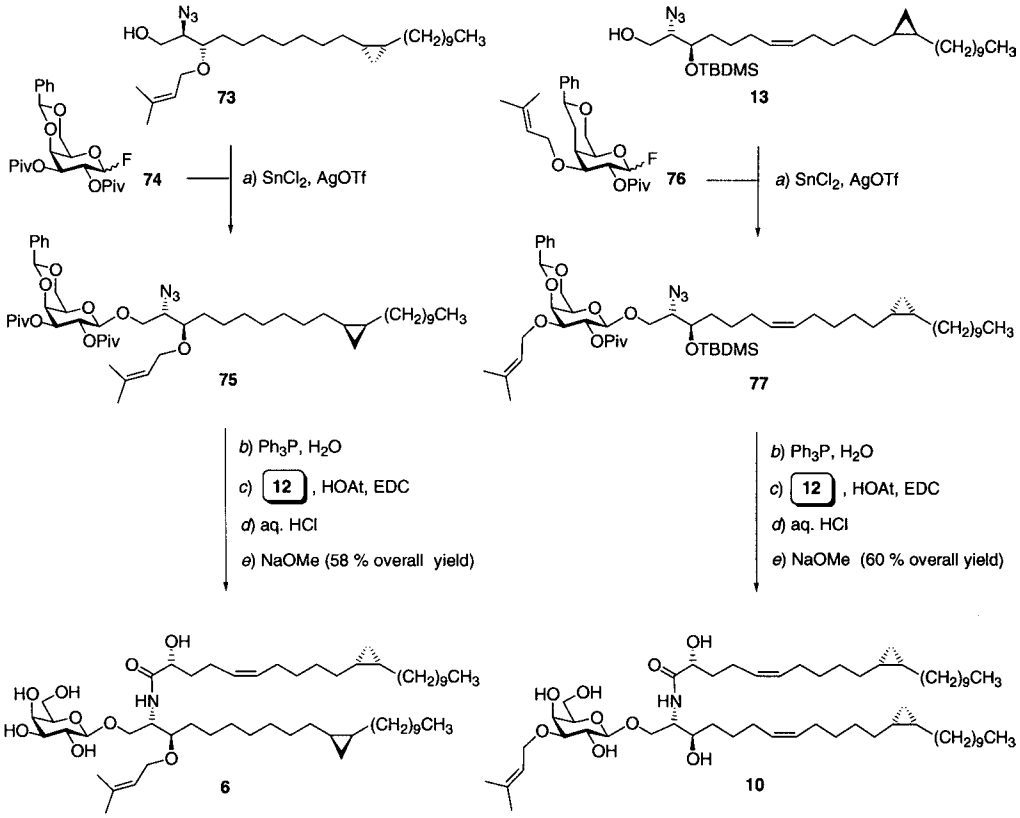


a) DIBAL (1.5 equiv.), CH_2Cl_2, −78°. *b*) Alkyl bromide (1.5 equiv.), NaH (1.2 equiv.), DMF, 0°. *c*) Ph_3P (2.0 equiv.), H_2O (2.0 equiv.), benzene, 45°. *d*) HOAt (3.1 equiv.), EDC (3.0 equiv.), THF, 0°. *e*) TBAF (5.0 equiv.), THF, 25°. *f*) aq. 1N HCl (cat.), MeOH, 37°. Abbreviations: DIBAL = diisobutylaluminium hydride, EDC = 1-[3-(dimethylamino)propyl]-3-ethylcarbodiimide hydrochloride, DTBMP = 2,6-di(*tert*-butyl)-4-methylpyridine, HOAt = 1-hydroxy-7-azabenzotriazole, TBDMS = (*t*-Bu)Me_2Si, TBDPS = (*t*-Bu)Ph_2Si, TBAF = Bu_4NF

without conditoned media was taken as background (low control) in the MLR, the Con A response, and the bone marrow proliferation assays, respectively.

[^{3}H]Thymidine uptakes for the high and low controls were measured at 200,000 cpm and 2,200 cpm in the MLR, at 440,000 cpm and 20,000 cpm in the Con A response, and at 43,000 cpm and 600 cpm in the bone marrow cell proliferation assay, resulting in signal-to-noise ratios of 90, 22, and 70, respectively. The IC_{50} values of the reference compounds cyclosporine A (CsA) [25], a T-cell-selective immunosuppressant, and azathioprine [26], a nucleotide analogue, which interferes with DNA synthesis and thus generally inhibits cell proliferation, are shown in the *Table*. CsA showed a T-cell-selective activity profile; it inhibited the MLR and the Con A response

Scheme 7. *Synthesis of Plakoside Analogs* **6** *and* **10**



a) $SnCl_2$ (3.0 equiv.), AgOTf (3.0 equiv.), DTBMP (1.2 equiv.), 4-Å molecular sieves, CH_2Cl_2, $0 \rightarrow 25°$, 6.5 h. *b*) Ph_3P (2.0 equiv.), H_2O (2.0 equiv.), benzene, 45°, 3.5 h. *c*) HOAt (3.1 equiv.), EDC (3.0 equiv.), THF, 0°, 6 h. *d*) aq. 1N HCl (cat.), MeOH, 37°, 3 h. *e*) NaOMe (0.2 equiv.), MeOH, 25°, 30 min. Abbreviations: EDC = 1-[3-(dimethylamino)propyl]-3-ethylcarbodiimide hydrochloride, DTBMP = 2,6-di-(*tert*-butyl)-4-methylpyridine, HOAt = 1-hydroxy-7-azabenzotriazole, TBDMS = (*t*-Bu)Me_2Si, TBDPS = (*t*-Bu)Ph_2Si

with IC_{50} values of 0.014 and 0.14 μM, respectively, and had no effect on the proliferation of bone marrow cells ($IC_{50} > 1$ μM). In contrast, the anti-proliferative compound azathioprine was active in all three assays (IC_{50} values of 0.028 μM for MLR, 0.15 μM for the Con A response, and 0.050 μM for bone marrow cell proliferation).

None of the plakosides showed any selective activity in the MLR and/or the Con A response (*Table*). With the exception of compound **3**, all plakosides were either inactive ($IC_{50} > 50$ μM) or showed only marginal activity (IC_{50} of 18–50 μM). Compound **3** showed an IC_{50} value of 7.1 μM in the MLR and of 30 μM in the Con A response. However, bone marrow cell proliferation was inhibited as well with an IC_{50} value of 3.3 μM.

Plakosides A (**1**) and B (**2**) have been suggested in the literature to be immunosuppressive on activated T cells based on results obtained in a T-cell proliferation assay where murine lymph node cells were activated with Con A [1]. In

Table. *Inhibitory Effects of Plakosides A* (**1**), *B* (**2**), *and Their Analogs* **3**–**10** *in the MLR*[a]), *the Con A Response*[b]), *and the Bone Marrow Cell*[c]) *Proliferation Assays*

Compound	IC_{50} [μM]		
	MLR	Con A Response	Bone marrow cell proliferation
CsA	0.014	0.14	> 1
Azathioprine	0.028	0.15	0.050
1	> 50	> 50	50
2	⩾ 50	> 50	> 50
3	7.1	30	3.3
4	28	> 50	18
5	> 50	> 50	⩾ 50
6	28	30	24
7	> 50	> 50	40
8	> 50	> 50	> 50
9	> 50	> 50	50
10	> 50	> 50	29

[a]) Equal amounts of spleen cells from CBA and BALB/c mice (1.6×10^5 from each strain, 3.2×10^5 in total) suspended in 200 μl RPMI 1640 medium containing 10% FCS, 100 units/ml penicillin, 100 μg/ml streptomycin, 2 mM L-glutamine, and 50 μM 2-mercaptoethanol (complete RPMI medium) were plated on a 96-well plate. The cultures were incubated for four days at 37° in 5% CO_2. [b]) Spleen cells from CBA mice (2×10^5 cells per well) were incubated for two days in complete RPMI medium in the presence of concanavalin A (2 μg/ml). [c]) Bone marrow cells (2.5×10^4 cells per well) prepared from CBA mice were incubated in complete RPMI medium for four days. Supernatants from the myelomonocytic cell line WEHI-3 and the fibroblast-like cell line L929 were added as a source of growth factors. In all assays seven 5-fold dilution steps in duplicates per test compound were added into each well. Proliferation was determined by pulsing the cultures for 5 h with 1 μCi [^{3}H]thymidine. The concentrations required for 50% inhibition (IC_{50}) were determined by using a four-parameter logistic function.

constrast to our results, both compounds significantly inhibited this assay at all doses tested (0.01–10 μg/ml) with 50% inhibition at *ca.* 0.1 μg/ml. However, the dose-response curves of plakoside A (**1**) and B (**2**) were rather flat over a 1000-fold concentration range and reached a plateau at 60–70% inhibition. Moreover, a maximal [^{3}H]-thymidine incorporation of only 575 cpm was observed [1]. Based on our observations, we consider these compounds to be at best modest immunosuppressive agents.

Conclusion. – In conclusion, the total synthesis of β-galactosylceramides plakosides A (**1**), B (**2**) and the synthesis of their analogs **3**–**10** were accomplished through an efficient and convergent strategy. These homogenous pure compounds were evaluated by a MLR, a Con A response, and a murine bone marrow cell proliferation assay, and found to be only marginally active, except compound **3**, which exhibited modest immunosuppressive properties, but which was also found to be cytotoxic. Nevertheless, plakosides A (**1**) and B (**2**) with the prenyl residue on the carbohydrate moiety may interfere with some biological process that still remains to be shown.

Experimental Part

General. All reactions were carried out under an Ar atmosphere with dry, freshly distilled solvents under anh. conditions, unless otherwise noted. Anh. solvents were also obtained by passing them through commercially available alumina columns. Yields refer to the chromatographically and spectroscopically (^{1}H- and ^{13}C-NMR) homogeneous materials, unless otherwise stated. Reagents were purchased at highest commercial quality and used without further purification unless otherwise stated. Reactions were monitored by TLC carried out on 0.25-mm *E. Merck* silica gel plates (*60F-254*) with UV light as visualizing agent or *p*-anisaldehyde soln. and heat as developing agents. Flash column chromatography (FC) was performed with *E. Merck* silica gel (*60*, particle size 0.040–0.063 mm). M.p.: *Thomas Hoover Unimelt* cap. melting-point apparatus; uncorrected. Optical rotations were recorded on a *Perkin-Elmer 241* polarimeter. IR Spectra were recorded on a *Perkin-Elmer 1600* series FT-IR spectrometer. NMR Spectra: *Bruker DRX-600*, *AMX-500*, or *AMX-400* instruments at 295 K, unless otherwise noted, and calibrated using residual undeuterated solvent as an internal reference. High-resolution mass spectra (HR-MS): *VG ZAB-ZSE* mass spectrometer under fast-atom-bombardment (FAB) conditions. Matrix-assisted laser-desorption-ionization (MALDI-FT-MS) MS: *PerSeptive Biosystems Voyager™ IonSpec* mass spectrometer. Electrospray (ESI) MS: *API 100 Perkin-Elmer* mass spectrometer. GC/MS: *Hewlett Packard 5971A* spectrometer.

Phenyl 6-O-*[(*tert-*butyl)diphenylsilyl]-3,4*-O-*isopropylidene-1-thio-β*-D-*galactopyranoside* (**20**). To a stirred soln. of triol **19** (2.72 g, 5.33 mmol) in DMF (15 ml) at 25° was added camphorsulfonic acid (0.12 g, 0.53 mmol). The mixture was then stirred for 8 h before it was neutralized with Et_3N (0.74 ml, 0.53 mmol). The mixture was concentrated *in vacuo*. The crude oil was purified by FC (12% AcOEt in hexanes) to afford **20** (82.61 g, 89%). Colorless oil. R_f 0.44 (silica gel; 30% AcOEt in hexanes). $[\alpha]_D = +9.7$ ($c = 1.2$, $CHCl_3$); Ft-IR (neat): 3402, 2932, 2872, 1429, 1380, 1219, 1081, 1032, 871, 701. ^{1}H-NMR (600 MHz, $CDCl_3$): 7.72–7.70 (*m*, 4 arom. H); 7.58–7.52 (*m*, 2 arom. H); 7.44–7.35 (*m*, 6 arom. H); 7.27–7.23 (*m*, 3 arom. H); 4.45 (*d*, $J = 10.2$, H–C(1)); 4.28 (*dd*, $J = 2.1, 5.4$, H–C(4)); 4.10–4.08 (*dd*, $J = 5.5, 6.9$, H–C(3)); 3.99–3.87 (*m*, H–C(5), CH_2(6)); 3.57 (*dt*, $J =$ 2.1, 7.9, H–C(2)); 2.58 (*d*, $J = 2.4$, OH); 1.44 (*s*, Me); 1.33 (*s*, Me); 1.06 (*s*, *t*-Bu). ^{13}C-NMR (150 MHz, $CDCl_3$): 135.6; 135.6; 135.6; 135.6; 133.2; 133.2; 132.3; 132.3; 129.7; 129.7; 129.7; 128.9; 128.9; 127.8; 127.7; 127.7; 127.6; 127.6; 110.0; 88.2; 78.9; 76.8; 73.2; 71.5; 62.8; 28.1; 26.7; 26.7; 26.7; 26.3; 19.2. HR-MS (MALDI-FT): 573.2106 ($[M + Na]^+$, $C_{31}H_{38}NaO_5SSi^+$; calc. 573.2101).

Phenyl 6-O-*[(*tert-*butyl)diphenylsilyl]-3,4*-O-*isopropylidene-1-thio-2*-O-*(trimethylacetyl)-β*-D-*galactopyranoside* (**21**). To a stirred soln. of **20** (2.00 g, 3.63 mmol) and 4-(dimethylamino)pyridine (22 mg, 0.18 mmol) in pyridine (20 ml) at 0° was carefully added PivCl (0.89 ml, 7.26 mmol). The mixture was then refluxed for 2 h before it was allowed to cool, and then H_2O (1 ml) was carefully added. The mixture was diluted with AcOEt (50 ml) and extracted with sat. aq. $CuSO_4$ soln. (25 ml), H_2O (25 ml), sat. $NaHCO_3$ (3×15 ml) and brine (25 ml). The org. layer was dried ($MgSO_4$) and concentrated *in vacuo*. The crude syrup was purified by FC (20% AcOEt in hexanes) to afford **21** (2.29 g, 99%). White foam. R_f 0.79 (silica gel; 30% AcOEt in hexanes). $[\alpha]_D = -0.9$ ($c = 2.9$, $CHCl_3$). FT-IR (neat): 3422, 2964, 1730, 1479, 1283, 1150, 1109, 1050, 702, 503. ^{1}H-NMR (600 MHz, $CDCl_3$): 7.70–7.69 (*m*, 4 arom. H); 7.48–7.46 (*m*, 2 arom. H); 7.43–7.33 (*m*, 6 arom. H); 7.23–7.21 (*m*, 3 arom. H); 5.03 (*dd*, $J = 7.1, 10.2$, H–C(2)); 4.62 (*d*, $J = 10.3$, H–C(1)); 4.27 (*dd*, $J = 1.9, 5.3$, H–C(4)); 4.16 (*d*, $J = 5.5, 6.8$, H–C(3)); 4.00–3.89 (*m*, H–C(5), CH_2(6)); 1.50 (*s*, Me); 1.32 (*s*, Me); 1.26 (*s*, *t*-Bu); 1.06 (*s*, *t*-Bu). ^{13}C-NMR (150 MHz, $CDCl_3$): 176.8; 135.6; 135.6; 135.6; 135.6; 134.1; 133.2; 133.2; 131.6; 131.6; 129.7; 129.7; 128.9; 128.9; 127.7; 127.7; 127.6; 127.6; 127.5; 110.0; 86.5, 77.2; 76.9; 73.4; 70.9; 63.0; 38.7; 27.7; 27.1; 27.1; 27.1; 26.7; 26.7; 26.7; 26.4; 19.2. HR-MS (MALDI-FT): 657.2684 ($[M + Na]^+$, $C_{36}H_{46}NaO_6SSi^+$; calc. 657.2677).

6-O-*[(*tert-*Butyl)diphenylsilyl]-3,4*-O-*isopropylidene-2*-O-*(trimethylacetyl)-α*-D-*galactopyranosyl Fluoride* (**11a**) *and 6*-O-*[(*tert-*Butyl)diphenylsilyl]-3,4*-O-*isopropylidene-2*-O-*(trimethylacetyl)-β*-D-*galactopyranosyl Fluoride* (**11b**). To a stirred soln. of **21** (0.98 g, 1.54 mmol) in CH_2Cl_2 (3 ml) at 0° was added diethylaminosulfur trifluoride (0.76 ml, 5.76 mmol), followed by dropwise addition of dimethyl(methylthio)sulfonium triflate (0.59 g, 2.31 mmol) in CH_2Cl_2 (2 ml) *via* syringe. The mixture was stirred at 0° for 1 h before it was slowly warmed up to 25° over a period of 3 h. The mixture was quenched with cold sat. aq. $NaHCO_3$ soln. (5 ml) and was diluted with AcOEt (30 ml). The layers were separated, and the org. layer was washed with sat. aq. $NaHCO_3$ soln. (15 ml), H_2O (15 ml), and brine (15 ml). The org. layer was dried ($MgSO_4$) and concentrated *in vacuo*. The crude oil was purified by FC (6% AcOEt in hexanes) to afford the β-anomer **11b** (765 mg, 91%) and the α-anomer **11a** (34 mg, 3%) as faintly yellow oils.

Data of the β-Anomer (**11b**): R_f 0.53 (silica gel; 17% AcOEt in hexanes). $[\alpha]_D = +16.4$ ($c = 0.5$, $CHCl_3$). FT-IR (neat): 2935, 1740, 1475, 1389, 1218, 1107, 802, 702, 503. ^{1}H-NMR (500 MHz, $CDCl_3$): 7.72–7.65

(*m*, 4 arom. H); 7.48–7.36 (*m*, 6 arom. H); 5.34 (*dd*, *J* = 4.7, 55.3, H–C(1)); 5.03 (*m*, H–C(2)); 4.50 (*d*, *J* = 6.8, H–C(4)); 4.23 (*dd*, *J* = 4.5, 6.7, H–C(3)); 4.05–3.99 (*m*, H–C(5), H–C(6a)); 3.96–3.91 (*m*, H–C(6b)); 1.53 (*s*, Me); 1.36 (*s*, Me); 1.23 (*s*, *t*-Bu); 1.07 (*s*, *t*-Bu). ^{13}C-NMR (150 MHz, $CDCl_3$): 176.7; 135.6; 135.6; 135.5; 135.5; 133.2; 133.1; 129.8; 129.7; 127.9; 127.7; 127.7; 127.6; 127.6; 110.4; 105.4 (*d*, *J*(C,F) = 867.6, C(1)); 73.4 (*d*, *J*(C,F) = 14.5, C(F)); 71.9 (C(3)); 71.3 (C(4)); 69.6 (*d*, *J*(C,F) = 110.5, C(2)); 62.6 (C(6)); 38.8; 27.0; 27.0; 27.0; 26.7; 26.7; 26.7; 26.2; 19.2. HR-MS (MALDI-FT): 567.2548 $[M + Na]^+$ ($C_{30}H_{41}FNaO_6Si^+$; calc. 567.2554).

Data of α-Anomer (**11a**): R_f 0.61 (silica gel; 17% AcOEt in hexanes). $[\alpha]_D = +40.3$ (*c* = 1.5, $CHCl_3$). FT-IR (neat): 2935, 1737, 1476, 1380, 1220, 1070, 920, 820, 703, 505. ^{1}H-NMR (500 MHz, $CDCl_3$): 7.72–7.67 (*m*, 4 arom. H), 7.47–7.33 (*m*, 6 arom. H); 5.60 (*dd*, *J* = 2.9, 54.1, H–C(1)); 4.96 (*ddd* , *J* = 3.0, 7.0, 22.7, H–C(2)); 4.50–4.38 (*m*, H–C(3), H–C(4)); 4.33 (*m*, H–C(5)); 4.01–3.88 (*m*, CH_2(6)); 1.49 (*s*, Me); 1.36 (*s*, Me); 1.24 (*s*, *t*-Bu); 1.05 (*s*, *t*-Bu). ^{13}C-NMR (150 MHz, $CDCl_3$): 177.7; 135.6; 135.6; 135.5; 135.5; 133.2; 133.2; 129.7; 129.7; 127.7; 127.7; 127.6; 127.6; 109.9; 104.3 (*d*, *J*(C,F) = 900.0, C(1)); 72.7 (C(3)); 70.2 (C(4)); 70.2 (*d*, *J*(C,F) = 100.0, C(2)); 70.1 (*d*, *J*(C,F) = 25.0, C(5)); 62.3 (C(6)); 38.8; 27.6; 27.0; 27.0; 27.0; 26.7; 26.7; 26.7; 26.1; 19.2. HR-MS (MALDI-FT): 567.2570 $[M + Na]^+$ ($C_{30}H_{41}FNaO_6Si^+$; calc. 567.2554).

(2Z)-Tridec-2-en-1-ol (**23**). A mixture of *tridec-2-yn-1-ol* (**22**) (10.3 g, 51.75 mmol) and 5% Pd on $BaSO_4$ (0.71 g) in pyridine (200 ml) was stirred at 25° under 1 atm H_2 for 10 h. The catalyst was removed through a pad of *Celite* and rinsed with AcOEt (100 ml). The filtrate was concentrated *in vacuo* at 50°. The residue was taken up in AcOEt (400 ml) and extracted with sat. aq. $CuSO_4$ soln. (100 ml), H_2O (2 × 100 ml), and brine (100 ml). The org. layer was dried ($MgSO_4$) and concentrated *in vacuo* to give the crude product as a faintly yellow liquid. The crude product was then purified by FC (silica gel; 10% AcOEt in hexanes) to afford **23** (9.99 g, 96%). Clear liquid. R_f 0.44 (silica gel; 25% AcOEt in hexanes). FT-IR (neat): 3331, 3015, 2922, 2853, 1464, 1378, 1016, 721. ^{1}H-NMR (500 MHz, $CDCl_3$): 5.63–5.50 (*m*, 2 H); 4.17 (*t*, *J* = 4.4, 2 H); 2.05 (*q*, *J* = 5.8, 2 H); 1.34–1.24 (*m*, 13 H); 0.86 (*t*, *J* = 6.8, 3 H). ^{13}C-NMR (125 MHz, $CDCl_3$): 134.2; 129.1; 59.5; 32.8; 30.5 (3 C); 30.3; 30.2; 30.1; 28.3; 23.5; 15.0. GS/MS: 198 M^+ ($C_{13}H_{26}O^+$; calc. 198).

[(1R,2S)-2-Decylcyclopropyl]methanol (**25**). To a mixture of dioxaborolane **24** (18.77 g, 62.92 mmol), **23** (10.40 g, 52.44 mmol), and activated 4-Å molecular sieves (2.00 g) in CH_2Cl_2 at −15° was dropwise added a freshly prepared soln. of $Zn(CH_2I)_2 \cdot DME$ complex *via* cannula kept at −15° over a period of 1 h at a rate to keep the internal temp. below −10°. The mixture was stirred at −10° for 2 h and then allowed to warm to 25° slowly over a period of 4 h. A sat. aq. NH_4Cl soln. (100 ml) was added to the mixture, and the layers were separated. The aq. layer was further extracted with Et_2O (3 × 250 ml). The combined org. layers were stirred vigorously with 5N aq. KOH soln. (300 ml) at 25° for 12 h. The biphasic mixture was separated, and the org. layer was successively extracted with 1N aq. HCl soln. (2 × 100 ml), sat. aq. $NaHCO_3$ soln. (2 × 100 ml), H_2O (100 ml), brine (100 ml), dried ($MgSO_4$), and concentrated *in vacuo*. The oily residue was purified by FC (silica gel; 15% AcOEt in hexanes) to afford **24** (10.67 g, 96%). Clear liquid. R_f 0.43 (silica gel; 25% AcOEt in hexanes). $[\alpha]_D = +19.7$ (*c* = 5.7, $CHCl_3$); FT-IR (neat): 3346, 3063, 2993, 2934, 2854, 1462, 1380, 1028, 721. ^{1}H-NMR (500 MHz, $CDCl_3$): 3.65–3.52 (*m*, 2 H); 1.45–1.33 (*m*, 3 H); 1.32–1.16 (*m*, 16 H); 1.11–1.03 (*m*, 1 H); 0.85 (*t*, *J* = 6.5, 3 H); 0.85–0.81 (*m*, 1 H); 0.69–0.65 (*m*, 1 H); −0.07 (*m*, 1 H). ^{13}C-NMR (125 MHz, $CDCl_3$): 63.3; 31.9; 30.2; 29.6 (3 C); 29.5; 29.3; 28.5; 22.7; 18.1; 16.1; 14.1; 9.4. HR-MS (FAB): 235.2041 ($[M + Na]^+$, $C_{14}H_{28}NaO^+$; calc. 235.2038).

10-[(1S,2R)-2-(Iodomethyl)cyclopropyl]decane (**26**). To a soln. of **25** (17.01 g, 80.10 mmol), imidazole (7.47 g, 109.73 mmol), and Ph_3P (27.31 g, 104.12 mmol) in a mixture of MeCN/E_2O (270 ml, 3 : 5 (*v* : *v*)) at 0° was added I_2 (30.49 g, 120.12 mmol) in five portions over 30 min under Ar in the dark. The resulting yellow mixture was stirred at 0° for 30 min before it was diluted with Et_2O (300 ml) and washed successively with sat. aq. $Na_2S_2O_3$ soln. (2 × 125 ml), aq. $CuSO_4$ soln. (2 × 100 ml), H_2O (100 ml), and brine (100 ml). The org. layer was dried ($MgSO_4$) and concentrated *in vacuo* in the dark. The crude residue was purified by FC in the dark (silica gel; 6% Et_2O in hexanes) to afford **26** (24.79 g, 96%). Clear liquid. R_f 0.88 (silica gel; 9% Et_2O in hexanes). $[\alpha]_D = +0.2$ (*c* = 4.6, $CHCl_3$). FT-IR (neat): 2923, 2852, 1461, 1377, 1170, 1024, 721, 600. ^{1}H-NMR (500 MHz, $CDCl_3$): 3.29 (*dd*, *J* = 8.0, 14.0, 1 H); 3.18 (*dd*, *J* = 8.0, 14.0, 1 H); 1.55–1.48 (*m*, 1 H); 1.42–1.33 (*m*, 3 H); 1.32–1.19 (*m*, 13 H); 1.17–1.09 (*m*, 1 H); 1.07–0.99 (*m*, 1 H); 0.85 (*t*, *J* = 6.5, 3 H); 0.85–0.81 (*m*, 1 H); 0.69–0.65 (*m*, 1 H); −0.07 (*m*, 1 H). ^{13}C-NMR (125 MHz, $CDCl_3$): 31.9; 30.1; 29.7 (3 C); 29.5; 29.3; 27.5; 22.7; 21.8; 20.4; 16.1; 14.1; 9.7. HR-MS (MALDI-FT): 195.2114 ($[M - I]^+$, $C_{14}H_{27}^+$; calc. 195.2113).

10-{(1S,2R)-2-[8-(Tetrahydro-2H-pyran-2-yl)-octyl]cyclopropyl}decane (**28**). To a soln. of **26** (9.53 g, 29.55 mmol) in THF (75 ml) at 0° in the dark was added *via* cannula the *Grignard* reagent **27**, prepared from $THPOCH_2(CH_2)_5CH_2Br$ (13.18 g, 44.33 mmol) and Mg (1.33 g, 54.67 mmol) in THF (100 ml). The mixture was stirred at 0° for 5 min before addition of a soln. of Li_2CuCl_4, prepared from LiCl (7.5 mg, 0.18 mmol) and anh. $CuCl_2$ (11.9 mg, 0.09 mmol) in dry THF (1 ml). The resulting mixture was stirred at 0° for additional 30 min

before quenching with H_2O (2 ml). The mixture was diluted with Et_2O (400 ml), and extracted successively with 1N aq. HCl soln. (125 ml), H_2O (100 ml), and brine (100 ml). The org. layer was dried ($MgSO_4$) and concentrated *in vacuo*. The crude residue was then purified by FC (silica gel; 100% hexanes) to afford **28** (10.13 g, 87%). Clear liquid. R_f 0.21 (silica gel; 100% hexanes). $[\alpha]_D = +0.3$ ($c = 1.1$, $CHCl_3$); FT-IR (neat): 2925, 2854, 1460, 1124, 1073, 1034. ^{1}H-NMR (600 MHz, $CDCl_3$): 4.55 (t, $J = 3.1$, 1 H); 3.87–3.83 (m, 1 H); 3.73–3.69 (m, 1 H); 3.49–3.46 (m, 1 H); 3.37–3.34 (m, 1 H); 1.83–1.78 (m, 1 H); 1.72–1.68 (m, 1 H); 1.60–1.45 (m, 6 H); 1.40–1.15 (m, 28 H); 1.15–1.09 (m, 2 H); 0.86 (t, $J = 7.0$, 3 H); 0.65–0.60 (m, 2 H); 0.58–0.52 (m, 1 H); −0.34 (m, 1 H). ^{13}C-NMR (150 MHz, $CDCl_3$): 98.8; 67.7; 62.3; 31.9; 30.8; 30.2; 30.2; 29.8; 29.7; 29.7; 29.7; 29.7; 29.7; 29.6; 29.6; 29.5; 29.4; 28.7; 28.7; 26.2; 25.5; 22.7; 19.7; 15.8; 14.1; 10.9. LR-MS (ESI): 417 ($[M + Na]^+$, $C_{26}H_{50}NaO_2^+$; calc. 417).

*8-[(1*R*,2*S*)-2-Decylcyclopropyl]octan-1-ol* (**29**). To a soln. of **18** (7.60 g, 19.26 mmol) in MeOH (300 ml) was added pyridinium toluene-4-sulfonate (0.97 g, 3.85 mmol). The mixture was then heated at 55° for 5 h before it was cooled and concentrated *in vacuo*. The residue was then taken up in Et_2O (250 ml), and washed with sat. aq. $NaHCO_3$ soln. (100 ml), and brine (100 ml). The org. layer dried ($MgSO_4$) and concentrated *in vacuo*. The crude product was purified by FC (silica gel; 10% AcOEt in hexanes) to afford **29** (5.86 g, 98%). White, waxy solid. R_f 0.39 (silica gel; 10% AcOEt in hexanes). M.p. 59–60° (Et_2O). $[\alpha]_D = +0.3$ ($c = 0.9$, $CHCl_3$). FT-IR ($CHCl_3$): 3333, 2924, 2853, 1698, 1651, 1558, 1458, 1422, 1052, 751. ^{1}H-NMR (600 MHz, $CDCl_3$): 3.62 (t, $J = 6.6$, 2 H); 1.58–1.52 (m, 2 H); 1.42–1.18 (m, 29 H); 1.17–1.14 (m, 2 H); 0.86 (t, $J = 7.0$, 3 H); 0.65–0.60 (m, 2 H); 0.58–0.52 (m, 1 H); −0.38 (m, 1 H). ^{13}C-NMR (150 MHz, $CDCl_3$): 63.1; 32.8; 31.9; 30.2; 30.2; 29.7 (5 C); 29.6; 29.4; 29.4; 28.7; 28.7; 25.7; 22.7; 15.8; 15.7; 14.1; 10.9. HR-MS (FAB): 311.3310 ($[M + H]^+$, $C_{21}H_{42}O^+$; calc. 311.3314).

*8-[(1*R*,2*S*)-2-Decylcyclopropyl]octanal* (**30**). To a soln. of oxalyl chloride (1.87 ml, 21.01 mmol) in CH_2Cl_2 (75 ml) at −78° was dropwise added a soln. of DMSO (1.99 ml, 28.01 mmol) in CH_2Cl_2 (15 ml). The mixture was stirred at −78° for 30 min before the dropwise addition of **29** (4.35 g, 14.01 mmol) in CH_2Cl_2 (20 ml) *via* cannula. The mixture was stirred further at −78° for 30 min and then Et_3N (9.76 ml, 70.05 mmol) was dropwise added. The mixture was stirred for 30 min at −78° before it was allowed to warm to 25° over a period of 30 min. The mixture was diluted with Et_2O (150 ml) and washed with sat. aq. NH_4Cl soln. (2 × 75 ml), H_2O (75 ml), and brine (75 ml). The org. layer was dried ($MgSO_4$) and concentrated *in vacuo*. The crude residue was purified by FC (silica gel; 5% Et_2O in hexanes) to afford **30** (4.18 g, 96%). Clear liquid. R_f 0.36 (silica gel; 10% Et_2O in hexanes). $[\alpha]_D = +0.4$ ($c = 1.3$, $CHCl_3$). FT-IR (neat): 30.58, 2922, 2853, 2711, 1729, 1465, 1388, 1020, 722. ^{1}H-NMR (500 MHz, $CDCl_3$): 9.73 (t, $J = 2.0$, 1 H); 3.39 (dt, $J = 5.0$, 10.0, 2 H); 1.64–1.55 (m, 2 H); 1.42–1.15 (m, 26 H); 1.17–1.07 (m, 2 H); 0.84 (t, $J = 7.5$, 3 H); 0.65–0.58 (m, 2 H); 0.55–0.52 (m, 1 H); −0.37 (m, 1 H). ^{13}C-NMR (125 MHz, $CDCl_3$): 202.8; 43.9; 31.9; 30.2; 30.1; 29.7 (4 C); 29.4; 29.4; 29.3; 29.1; 28.7; 28.6; 22.7; 22.1; 15.7; 15.7; 14.1; 10.9. HR-MS (FAB): 331.2975 ($[M + Na]^+$, $C_{21}H_{40}NaO^+$; calc. 331.2977).

Ethyl (E)*-10-[(1*R*,2*S*)-2-Decylcyclopropyl]dec-2-enoate* (**31**). To a soln. of triethyl phosphonoacetate (1.76 ml, 7.05 mmol) in THF (10 ml) at 0° was added NaH (60% in mineral oil; 0.28 g, 7.05 mmol). The resulting mixture was stirred for 15 min at 0° before the dropwise addition of **30** (1.45 g, 4.69 mmol) in THF (15 ml) *via* syringe. The mixture was stirred further for 25 min at 0° before it was quenched with sat. aq. NH_4Cl soln. (3 ml). The mixture was diluted with Et_2O (150 ml) and washed with sat. aq. NH_4Cl soln. (75 ml), H_2O (75 ml), and brine (75 ml). The org. layer was dried ($MgSO_4$) and concentrated *in vacuo*. The crude residue was then purified by FC (silica gel; 5% Et_2O in hexanes) to afford the desired (*E*)-ester **31** (1.66 g, 94%) and a trace of the less polar undesired (*Z*)-ester (0.08 g, 4%) as clear oils. **31**: R_f 0.36 (silica gel; 10% Et_2O in hexanes). $[\alpha]_D = -0.1$ ($c = 1.5$, $CHCl_3$). FT-IR (neat): 2924, 2855, 1723, 1654, 1459, 1368, 1307, 1265, 1180, 1045, 980, 720 cm^{-1}; ^{1}H-NMR (600 MHz, $CDCl_3$): 6.97–6.93 (m, 1 H); 5.80–5.78 (m, 1 H); 4.17 (q, $J = 7.1$, 10.0, 2 H); 2.19–2.15 (m, 2 H); 1.50–1.39 (m, 2 H); 1.39–1.15 (m, 29 H); 1.17–1.07 (m, 2 H); 0.86 (t, $J = 7.0$, 3 H); 0.65–0.58 (m, 2 H); 0.55–0.52 (m, 1 H); −0.35 (m, 1 H). ^{13}C-NMR (150 MHz, $CDCl_3$): 166.8; 149.5; 121.2; 60.1; 32.2; 31.9; 30.2; 30.2; 29.7 (4 C); 29.5; 29.4; 29.4; 29.2; 28.7; 28.7; 28.0; 22.7; 15.8; 15.7; 14.3; 14.1; 10.9. HR-MS (FAB): 379.3568 ($[M + H]^+$, $C_{25}H_{46}O_2^+$; calc. 379.3576).

*Ethyl (2*S*,3*R*)-10-[(1*R*,2*S*)-2-Decylcyclopropyl]-2,3-dihydroxydecanoate* (**32**). To a mixture of ^{t}BuOH (30 ml) and H_2O (30 ml) at 25° were added $K_2Os_2(OH)_4$ (4.4 mg), $(DHQD)_2$-PHAL (47 mg), $K_3Fe(CN)_6$ (5.96 g), K_2CO_3 (2.50 g), and $MeSO_2NH_2$ (0.58 g, 6.08 mmol). The resulting mixture was stirred to produce a biphasic mixture before cooling to 0° and subsequent addition of **31** (2.30 g, 6.08 mmol). The mixture was then stirred at 0° for 8 h. Na_2SO_3 (9.00 g) was added to the mixture at 0° before it was allowed to warm to 25° and was stirred for additional 40 min. The mixture was diluted with AcOEt (150 ml), and the aq. layer was further extracted with AcOEt (2 × 75 ml). The combined org. layers were extracted with 2N aq. KOH soln. (75 ml), H_2O (75 ml), and brine (75 ml), and dried ($MgSO_4$) and concentrated *in vacuo* to give the crude product, which

was purified by FC (silica gel; 20% AcOEt in hexanes) to afford **32** (2.31 g, 92%). Waxy white solid. R_f 0.29 (silica gel; 20% AcOEt in hexanes). M.p. 58–61° (AcOEt). $[\alpha]_D = +7.2$ ($c = 1.0$, $CHCl_3$). FT-IR ($CHCl_3$ soln.): 3357, 2916, 2849, 1717, 1465, 1383, 1291, 1130, 1036, 602. ^{1}H-NMR (500 MHz, $CDCl_3$): 4.28 (q, $J = 7.0$, 2 H); 4.07 (br. s, 1 H); 3.88 (t, $J = 2.2$,1 H); 3.02 (br. s, OH); 1.83 (br. s, OH); 1.63–1.55 (m, 2 H); 1.50–1.41 (m, 1 H); 1.41–1.15 (m, 30 H); 1.15–1.07 (m, 2 H); 0.87 (t, $J = 7.0$, 3 H); 0.65–0.58 (m, 2 H); 0.55–0.52 (m, 1 H); −0.34 (m, 1 H). ^{13}C-NMR (125 MHz, $CDCl_3$): 164.2; 72.9; 72.5; 62.1; 33.9; 31.9; 30.2; 30.2; 29.7 (3 C); 29.6; 29.6; 29.6; 29.5; 29.4; 28.7; 28.7; 25.7; 22.7; 15.7; 15.7; 14.2; 14.1; 10.9. HR-MS (FAB): 435.3456 ($[M+H]^+$; $C_{25}H_{48}O_4^+$; calc. 435.3450).

*Ethyl (2*S*,3*R*)-10-[(1*R*,2*S*)-2-Decylcyclopropyl]-3-hydroxy-2-[(4-nitrophenylsulfonyl)oxy]decanoate* (**33**). To a soln. of **32** (1.32 g, 3.20 mmol) in pyridine (30 ml) at 0° was added 4-nitrobenzenesulfonyl chloride (0.79 g, 3.20 mmol) in one portion. The resulting mixture was stirred at 0° for 7.5 h before it was quenched with icy cold H_2O (2 ml). The mixture was diluted with cold Et_2O (200 ml) and extracted with cold sat. aq. $CuSO_4$ soln. (50 ml), cold H_2O (2 × 100 ml), and cold brine (100 ml). The org. layer was dried ($MgSO_4$) and concentrated *in vacuo* below 10°. The crude residue was then purified by FC (silica gel; 12% chilled AcOEt in hexanes) to afford **33** (1.59 g, 90%) as a clear oil, which solidified to a white solid upon standing. R_f 0.30 (silica gel; 20% AcOEt in hexanes). $[\alpha]_D = +1.0$ ($c = 2.7$, $CHCl_3$). FT-IR (neat): 3532, 2924, 2853, 1759, 1537, 1465, 1372, 1350, 1313, 1188, 1095, 1024, 855, 740. ^{1}H-NMR (500 MHz, $CDCl_3$): 8.38 (dd, $J = 2.0$, 7.0, 2 H); 8.16 (dd, $J = 2.0$, 7.0, 2 H); 4.97 (d, $J = 3.0$, 1 H); 4.15 (q, $J = 7.0$, 2 H); 4.10–4.07 (m, 1 H); 1.76 (d, $J = 9.0$, 1 H); 1.60–1.40 (m, 3 H); 1.41–1.15 (m, 31 H); 1.15–1.07 (m, 1 H); 0.86 (t, $J = 7.0$, 3 H); 0.65–0.58 (m, 2 H); 0.55–0.52 (m, 1 H); −0.35 (m, 1 H). ^{13}C-NMR (125 MHz, $CDCl_3$): 166.8; 150.7; 141.9; 129.5; 129.5; 124.2; 124.2; 80.9; 71.7; 62.4; 33.1; 31.9; 30.2; 30.1; 29.7 (3 C); 29.5; 29.5; 29.3; 29.3; 28.7; 28.6; 25.3; 22.7; 15.7; 15.7; 14.1; 14.1; 14.0; 10.9. HR-MS (FAB): 620.3216 ($[M+Na]^+$, $C_{31}H_{51}O_8NNaS^+$; calc. 620.3233).

*Ethyl (2*R*,3*R*)-2-Azido-10-[(1*R*,2*S*)-2-decylcyclopropyl]-3-hydroxydecanoate* (**34**). A mixture of **33** (0.50 g, 0.91 mmol) and NaN_3 (0.37 g, 5.61 mmol) in DMF (5 ml) was stirred at 25° for 36 h. The mixture was diluted with Et_2O (25 ml) and washed with H_2O (2 × 10 ml) and brine (100 ml). The org. layer was dried ($MgSO_4$) and concentrated *in vacuo*. The crude residue was then purified by FC (silica gel; 20% Et_2O in hexanes) to afford **34** (0.37 g, 94%). Clear oil. R_f 0.80 (silica gel; 20% AcOEt in hexanes). $[\alpha]_D = +3.7$ ($c = 1.6$, $CHCl_3$). FT-IR (neat): 3422, 2924, 2853, 2109, 1736, 1465, 1384, 1255, 1190, 1022, 855. ^{1}H-NMR (400 MHz, $CDCl_3$): 4.28 (dq, $J = 0.8$, 7.0, 2 H); 3.94–3.88 (m, 2 H); 2.23 (d, $J = 6.2$, 1 H); 1.60–1.40 (m, 3 H); 1.41–1.15 (m, 30 H); 1.15–1.07 (m, 2 H); 0.85 (t, $J = 6.7$, 3 H); 0.65–0.58 (m, 2 H); 0.55–0.52 (m, 1 H); −0.35 (m, 1 H). ^{13}C-NMR (100 MHz, $CDCl_3$): 169.0; 71.9; 66.2; 62.1; 33.1; 31.9; 30.2; 30.2; 29.7 (3 C); 29.5; 29.5; 29.4; 29.4; 28.7; 28.6; 25.4; 22.7; 15.7; 15.7; 14.2; 14.1; 14.0; 10.9. HR-MS (FAB): 460.3507 ($[M+Na]^+$, $C_{25}H_{47}N_3NaO_3^+$; calc. 460.3515).

*Ethyl (2*R*,3*R*)-2-Azido-3-[(*tert*-butyl)dimethylsilyloxy]-10-[(1*R*,2*S*)-2-decylcyclopropyl]decanoate* (**35**). To a stirred soln. of **34** (0.79 g, 1.81 mmol) and 2,6-lutidine (0.53 ml, 4.51 mmol) in CH_2Cl_2 (8 ml) at −78° was added dropwise TBDMSOTf (0.44 ml, 1.90 mmol) *via* syringe. The mixture was allowed to warm to 25° and was stirred further for 30 min before it was diluted with Et_2O (25 ml) and extracted successively with sat. aq. $CuSO_4$ soln. (5 ml), H_2O (10 ml), and brine (5 ml). The org. layer was dried ($MgSO_4$) and concentrated *in vacuo* to afford **35** (1.00 g, 100%). Faintly yellow oil. R_f 0.72 (silica gel; 10% AcOEt in hexanes). $[\alpha]_D = -8.01$ ($c = 2.8$, $CHCl_3$). FT-IR (neat): 2926, 2855, 2108, 1748, 1464, 1373, 1256, 1187, 1113, 1027, 837, 777. ^{1}H-NMR (600 MHz, $CDCl_3$): 4.22 (dq, $J = 0.8$, 7.1, 2 H); 4.09–4.06 (m, 1 H); 3.95 (d, $J = 5.0$, 1 H); 1.64–1.59 (m, 1 H); 1.50–1.40 (m, 1 H); 1.39–1.15 (m, 33 H); 1.15–1.07 (m, 2 H); 0.89–0.84 (m, 12 H); 0.65–0.58 (m, 2 H); 0.55–0.52 (m, 1 H); 0.08 (s, 5 H); −0.35 (m, 1 H). ^{13}C-NMR (150 MHz, $CDCl_3$): 168.6; 73.3; 66.4; 61.7; 33.2; 32.0; 30.3; 30.2; 29.7 (3 C); 29.6; 29.5; 29.5; 29.4; 28.7; 28.6; 25.7; 25.7; 25.7; 24.7; 22.7; 18.0; 15.7; 15.7; 14.2; 14.1; 14.1; 10.9; −4.5, −4.7. HR-MS (MALDI-FT): 574.4389 ($[M+Na]^+$, $C_{31}H_{63}N_3NaO_3Si^+$; calc. 574.4380).

*(2*S*,3*R*)-1-Azido-3-[(*tert*-butyl)dimethylsilyloxy]-10-[(1*R*,2*S*)-2-decylcyclopropyl]decan-1-ol* (**13**). To a stirred soln. of **35** (0.28 g, 0.50 mmol) in THF (8 ml) at 0° was added dropwise a soln. of $LiBH_4$ (2.0M in THF, 1 ml, 2.00 mmol). The mixture was stirred at 0° for 1.5 h before it was allowed to warm to 25° over a period of 2 h. The mixture was quenched carefully with MeOH (1 ml), diluted with AcOEt (10 ml), and was washed successively with H_2O (5 ml) and brine (5 ml). The org. layer was dried ($MgSO_4$) and concentrated *in vacuo*. The crude residue was then purified by FC (silica gel; 17% AcOEt in hexanes) to afford **13** (0.25 g, 95%). Faintly yellow liquid. R_f 0.38 (silica gel; 10% AcOEt in hexanes). $[\alpha]_D = -2.9$ ($c = 2.0$, $CHCl_3$). FT-IR (neat): 3372, 2926, 2855, 2101, 1464, 1368, 1256, 1080, 1042, 837, 776. ^{1}H-NMR (500 MHz, $CDCl_3$): 3.82–3.70 (m, 2 H); 3.50–3.45 (m, 1 H); 2.20–2.15 (m, 1 H); 1.64–1.56 (m, 1 H); 1.50–1.40 (m, 1 H); 1.39–1.15 (m, 29 H); 1.15–1.07 (m, 2 H); 0.89–0.84 (m, 12 H); 0.65–0.58 (m, 2 H); 0.55–0.52 (m, 1 H); 0.10 (s, 3 H); 0.07 (s, 3 H); −0.35 (m, 1 H). ^{13}C-NMR (125 MHz, $CDCl_3$): 73.4; 66.5; 62.2; 33.9; 31.9; 30.2; 30.1; 29.7 (3 C); 29.5; 29.5; 29.4; 28.7;

28.7; 25.8; 25.8; 25.8; 24.8; 22.8; 24.9; 22.7; 18.0; 15.7; 15.7; 14.1; 10.9; −4.5; −4.6. HR-MS (FAB): 642.3418 ($[M+Cs]^+$, $C_{29}H_{59}CsN_3O_2Si^+$; calc. 642.3431).

*9-[(1*R,*2*S*)-2-Decylcyclopropyl]-1-[(tetrahydo-2*H*-pyran-2-yl)oxy]non-4-yne* (**37**). To a soln. of **26** (8.68 g, 26.92 mmol) in THF (75 ml) at 0° in the dark was added *via* cannula the *Grignard* reagent **36**, prepared from $THPOCH_2(CH_2)_2C{\equiv}C(CH_2)_2CH_2Br$ (11.67 g, 40.38 mmol) and Mg (1.21 g, 49.80 mmol) in THF (100 ml). The mixture was stirred at 0° for 5 min before the addition of a soln. of Li_2CuCl_4, prepared from LiCl (6.8 mg, 0.16 mmol) and anh. $CuCl_2$ (11 mg, 0.08 mmol) in dry THF (1 ml). The resulting mixture was stirred at 0° for additional 30 min before quenching with H_2O (2 ml). The mixture was diluted with Et_2O (400 ml) and extracted successively with 1N aq. HCl soln. (125 ml), H_2O (100 ml), and brine (100 ml). The org. layer was dried ($MgSO_4$) and concentrated *in vacuo*. The crude residue was then purified by FC (silica gel; 100% hexanes) to afford **37** (9.16 g, 84%). Clear oil. R_f 0.51 (silica gel; 10% Et_2O in hexanes). $[\alpha]_D = +0.2$ ($c = 1.5$, $CHCl_3$). FT-IR (neat): 2926, 2854, 1460, 1121, 1066, 1034, 991. ^{1}H-NMR (600 MHz, $CDCl_3$): 4.58 (t, $J = 4.0$, 1 H); 3.85–3.78 (m, 2 H); 3.49–3.42 (m, 2 H); 2.25–2.23 (m, 2 H); 2.13–2.11 (m, 2 H); 1.83–1.65 (m, 4 H); 1.59–1.54 (m, 2 H); 1.54–1.42 (m, 6 H); 1.40–1.20 (m, 18 H); 1.15–1.11 (m, 2 H); 0.86 (t, $J = 6.5$, 3 H); 0.63 (m, 2 H); 0.55 (m, 1 H); −0.28– −0.34 (m, 1 H). ^{13}C-NMR (150 MHz, $CDCl_3$): 98.8; 80.58; 79.4; 66.1; 62.1; 31.9; 30.7; 30.2; 29.7; 29.7; 29.7; 29.7; 29.4; 29.4; 29.3; 29.1; 28.7; 28.2; 25.5; 22.7; 19.5; 18.8; 15.8; 15.6; 15.6; 14.1; 10.9. HR-MS (MALDI-FT): 427.3546 ($[M+Na]^+$, $C_{27}H_{48}NaO_2^+$; calc. 427.3552).

*9-[(1*R,*2*S*)-2-Decylcyclopropyl]dec-4-yn-1-ol* (**38**). To a soln. of **37** (9.08 g, 22.45 mmol) in MeOH (300 ml) was added pyridium toluene-4-sulfonate (1.13 g, 4.49 mmol). The mixture was heated at 55° for 5 h before it was cooled and concentrated *in vacuo*. The residue was then taken up in Et_2O (250 ml) and washed with sat. aq. $NaHCO_3$ soln. (100 ml) and brine (100 ml). The org. layer was dried ($MgSO_4$) and concentrated *in vacuo*. The residue was then purified by FC (silica gel; 5% AcOEt in hexanes) to afford **38** (7.20 g, 100%). Clear oil. R_f 0.55 (silica gel; 12% AcOEt in hexanes). $[\alpha]_D = +0.5$ ($c = 2.5$, $CHCl_3$). FT-IR (neat): 3332, 2925, 2854, 1460, 1331, 1058, 930, 721. ^{1}H-NMR (600 MHz, $CDCl_3$): 3.74 (q, $J = 4.8$, 2 H); 2.28–2.25 (m, 2 H); 2.14–2.12 (m, 2 H); 1.74–1.70 (m, 2 H); 1.59–1.54 (m, 1 H); 1.51–1.42 (m, 4 H); 1.40–1.20 (m, 18 H); 1.15–1.11 (m, 2 H); 0.86 (t, $J = 6.5$, 3 H); 0.63 (m, 2 H); 0.55 (m, 1 H); −0.34 (m, 1 H). ^{13}C-NMR (500 MHz, $CDCl_3$): 81.2; 79.2; 62.1; 31.9; 31.6; 30.2; 29.7 (4 C); 29.4; 29.4; 29.0; 28.7; 28.2; 22.7; 18.8; 15.8; 15.6; 15.5; 14.1; 10.9. HR-MS (FAB): 321.3152 ($[M+H]^+$, $C_{22}H_{40}O^+$; calc. 321.3157).

*9-[(1*R,*2*S*)-2-Decylcyclopropyl]dec-4-ynal* (**39**). To a soln. of oxalyl chloride (2.56 ml, 28.82 mmol) in CH_2Cl_2 (75 ml) at −78° was added dropwise a soln. of DMSO (2.73 ml, 38.43 mmol) in CH_2Cl_2 (25 ml). The resulting mixture was stirred at −78° for 30 min, and then **38** (6.16 g, 19.22 mmol) in CH_2Cl_2 (75 ml) was added dropwise *via* cannula. The mixture was stirred at −78° for 30 min, and then Et_3N (13.39 ml, 96.08 mmol) was added dropwise, followed by stirring at that temp. for 30 min before warming to 25° over a period of 30 min. The mixture was diluted with Et_2O (250 ml) and washed with sat. aq. NH_4Cl soln. (2 × 75 ml), H_2O (75 ml), and brine (75 ml). The org. layer was dried ($MgSO_4$) and concentrated *in vacuo*. The resulting oil was then purified by FC (silica gel; 5% Et_2O in hexanes) to afford **39** (5.94 g, 97%). Clear oil. R_f 0.62 (silica gel; 17% AcOEt in hexanes). $[\alpha]_D = +0.6$ ($c = 4.0$, $CHCl_3$). FT-IR (neat): 2923, 2853, 2719, 1731, 1463, 1410, 1385, 1357, 1332, 1056, 1020, 846, 722. ^{1}H-NMR (500 MHz, $CDCl_3$): 9.78 (t, $J = 1.0$, 1 H); 2.60 (dt, $J = 1.0$, 22.5, 2 H); 2.48–2.45 (m, 2 H); 2.12–2.09 (m, 2 H); 1.48–1.43 (m, 4 H); 1.43–1.30 (m, 4 H); 1.30–1.15 (m, 14 H); 1.15–1.07 (m, 2 H); 0.86 (t, $J = 7.0$, 3 H); 0.65–0.58 (m, 2 H); 0.57–0.53 (m, 1 H); −0.34 (m, 1 H). ^{13}C-NMR (125 MHz, $CDCl_3$): 201.1; 81.6; 77.7; 43.0; 31.9; 30.2; 30.1; 29.7; 29.7; 29.6; 29.4; 29.3; 29.8; 28.7; 28.2; 22.7; 22.5; 18.7; 15.7; 15.6; 14.1; 10.9. HR-MS (FAB): ($[M+Na]^+$, $C_{22}H_{38}NaO^+$; calc. 341.2820).

*10-[1(*R,*2*S*)-2-Decylcyclopropyl]dec-1-en-5-yne* (**40**). To a supension of CH_2PPh_3Br (2.10 g, 5.88 mmol) in THF (40 ml) at 0° was added NaHMDS soln. (1.0M in THF, 5.14 ml, 5.14 mmol). The mixture was stirred at 0° for 15 min before the addition of **39** (1.17 g, 3.67 mmol) in THF (20 ml). The mixture was stirred at 0° for further 45 min before it was diluted with Et_2O (200 ml), and a sat. aq. NH_4Cl soln. (75 ml) was added. The layers were separated, and the org. layer was successively washed with sat. aq. NH_4Cl soln. (75 ml), H_2O (75 ml), brine (75 ml), and dried ($MgSO_4$), and concentrated *in vacuo*. The residue was purified by FC (silica gel; 10% AcOEt in hexanes) to afford **40** (1.15 g, 97%). Clear oil. R_f 0.73 (silica gel; 10% AcOEt in hexanes). $[\alpha]_D = +0.6$ ($c =$ 4.7, $CHCl_3$). FT-IR (neat): 3059, 2923, 2854, 1642, 1463, 1332, 1020, 993, 912, 722. ^{1}H-NMR (400 MHz, $CDCl_3$): 5.87–5.81 (m, 1 H); 5.10–4.93 (m, 2 H); 2.22 (d, $J = 3.0$, 4 H); 2.13 (t, $J = 6.5$, 2 H); 1.52–1.32 (m, 6 H); 1.28–1.25 (m, 16 H); 1.18–1.09 (m, 2 H); 0.86 (t, $J = 6.9$, 3 H); 0.64–0.63 (m, 2 H); 0.57–0.53 (m, 1 H); −0.34 (q, $J = 4.8$, 9.2, 1 H). ^{13}C-NMR (100 MHz, $CDCl_3$): 137.3; 115.3; 80.7; 79.3; 33.4; 31.9; 30.2; 29.7 (3 C); 29.4; 29.4; 29.1; 28.7; 28.2; 22.7; 18.8; 18.7; 15.8; 15.6; 15.5; 14.1; 10.9. GC/MS: 316 (M^+, $C_{23}H_{40}^+$; calc. 316).

*10-[(1*R,*2*S*)-2-Decylcyclopropyl]dec-5-yn-1-ol* (**41**). To a soln. of **40** (0.83 g, 2.63 mmol) in THF (50 ml) at 0° was added dropwise a soln. of 9-BBN (0.5M in THF, 5.50 ml, 2.75 mmol) *via* syringe. The mixture was stirred

at 0° for 30 min before it was allowed to warm to 25° and stirred for an additional 1.5 h. After the mixture was cooled to 0°, sat. aq. $NaHCO_3$ soln. (40 ml), and 30% aq. H_2O_2 (3 ml) were added. The resulting mixture was stirred for 1.5 h before a soln. of sat. aq. $Na_2S_2O_3$ (10 ml) was added at 25°. The mixture was diluted with AcOEt (100 ml) and washed with H_2O (50 ml) and brine (50 ml). The org. layer was dried ($MgSO_4$) and concentrated *in vacuo*. The crude residue was then purified by FC (silica gel; 10% AcOEt in hexanes) to afford pure **41** (0.74 g, 84%). Waxy solid. R_f 0.29 (silica gel; 17% in hexanes). $[\alpha]_D = 0.2$ ($c = 1.8$, $CHCl_3$). FT-IR (neat): 3340, 2924, 2854, 1460, 1380, 1334, 1064, 1022, 722. ^{1}H-NMR (500 MHz, $CDCl_3$): 3.66 (t, $J = 2$ H); 2.20–2.12 (m, 4 H); 1.68–1.64 (m, 2 H); 1.58–1.44 (m, 6 H); 1.42–1.18 (m, 19 H); 1.17–1.05 (m, 2 H); 0.87 (t, $J = 6.0$, 3 H); 0.65–0.60 (m, 2 H); 0.58–0.55 (m, 1 H); −0.34 (m, 1 H). ^{13}C-NMR (125 MHz, $CDCl_3$): 80.7; 79.7; 62.5; 31.9; 31.9; 30.2; 29.7 (4 C); 29.4; 29.3; 29.1; 28.7; 25.3; 22.7; 22.5; 18.8; 18.5; 15.7; 15.6; 14.1; 10.9. HR-MS (MALDI-FT): 357.3141 ($[M + Na]^+$, $C_{23}H_{42}NaO^+$; calc. 357.3133).

*10-[(1*R*,2*S*)-2-Decylcyclopropyl]dec-5-ynal* (**42**). To a soln. of oxalyl chloride (1.95 ml, 21.97 mmol) in CH_2Cl_2 (25 ml) at −78° was added dropwise a soln. of DMSO (2.08 ml, 29.29 mmol) in CH_2Cl_2 (15 ml). The resulting mixture was stirred at −78° for 30 min and then **41** (4.90 g, 14.65 mmol) in CH_2Cl_2 (15 ml) was added dropwise *via* cannula. After stirring at −78° for 30 min, Et_3N (10.21 ml, 73.23 mmol) was added dropwise, and stirring was continued at −78° for 30 min before warming to 25° over a period of 30 min. The mixture was diluted with Et_2O (150 ml) and washed with sat. aq. NH_4Cl soln. (2 × 75 ml), H_2O (75 ml), and brine (75 ml). The org. layer was dried ($MgSO_4$) and concentrated *in vacuo*. The crude residue was then purified by FC (silica gel; 5% Et_2O in hexanes) to afford **42** (4.74 g, 97%). Clear oil. R_f 0.44 (silica gel; 10% Et_2O in hexanes). $[\alpha]_D = 0.1$ ($c = 2.8$, $CHCl_3$). FT-IR (neat): 2925, 2854, 2711, 1727, 1459, 1386, 1078, 1020, 722. ^{1}H-NMR (600 MHz, $CDCl_3$): 9.77 (t, $J = 1.3$, 1 H); 2.54 (dt, $J = 1.4$, 7.3, 2 H); 2.24–2.19 (m, 2 H); 1.77 (m, 2 H); 1.49–1.42 (m, 4 H); 1.38–1.15 (m, 20 H); 1.15–1.07 (m, 2 H); 0.86 (t, $J = 6.8$, 3 H); 0.65–0.60 (m, 2 H); 0.57–0.55 (m, 1 H); −0.34 (m, 1 H). ^{13}C-NMR (150 MHz, $CDCl_3$): 202.1; 81.6; 78.6; 42.8; 31.9; 30.2; 29.7 (3 C); 29.6; 29.4; 29.3; 29.0; 28.7; 28.2; 22.7; 22.5; 18.7; 18.2; 15.7; 15.6; 14.1; 10.9. HR-MS (FAB): 355.2979 ($[M + Na]^+$, $C_{23}H_{40}NaO^+$; calc. 355.2977).

*Ethyl (*E*)-12-[(1*R*,2*S*)-2-Decylcyclopropyl]dodec-2-en-7-ynoate* (**43**). To a soln. of triethyl phosphonoacetate (4.22 ml, 16.84 mmol) in THF (75 ml) at 0° was added NaH (0.65 g, 60% in mineral oil, 16.84 mmol). The resulting mixture was stirred at 0° for 15 min and then cooled to −78° before the dropwise addition of a soln. of **42** (3.62 g, 10.86 mmol) in THF (50 ml) *via* syringe. The mixture was stirred at −78° for 30 min and then warmed up to 0° before quenching with aq. NH_4Cl soln. (5 ml). The mixture was diluted with Et_2O (250 ml) and washed with sat. aq. NH_4Cl soln. (100 ml), H_2O (75 ml), and brine (75 ml). The org. layer was dried ($MgSO_4$) and concentrated *in vacuo*. The crude residue was then purified by FC (silica gel; 5% Et_2O in hexanes) to afford the desired (*E*)-ester **43** (4.21 g, 96%) and the less-polar undesired (*Z*)-ester (0.09 g, 2%) as clear oils.

Data of **43**: R_f 0.59 (silica gel; 10% Et_2O in hexanes). $[\alpha]_D = -0.2$ ($c = 2.5$, $CHCl_3$). FT-IR (neat): 2925, 2854, 1723, 1655, 1460, 1367, 1318, 1266, 1191, 1151, 1045, 979. ^{1}H-NMR (600 MHz, $CDCl_3$): 6.93 (dt, $J = 6.9$, 15.6, 1 H); 5.82 (d, $J = 15.5$, 1 H); 4.16 (q, $J = 7.1$, 2 H); 2.29 (q, $J = 7.0$, 2 H); 2.18–2.11 (m,4 H); 1.64–1.59 (m, 2 H); 1.50–1.39 (m, 4 H); 1.39–1.15 (m, 21 H); 1.17–1.07 (m, 2 H); 0.85 (t, $J = 6.8$, 3 H); 0.65–0.60 (m, 2 H); 0.57–0.55 (m, 1 H); −0.34 (m, 1 H). ^{13}C-NMR (150 MHz, $CDCl_3$): 166.8; 148.4; 121.8; 81.2; 79.0; 60.2; 31.9; 31.1; 30.2; 29.7 (4 C); 29.4; 29.4; 29.0; 28.7; 28.2; 27.4; 22.7; 18.8; 18.2; 15.7; 15.6; 14.3; 14.1; 10.9. HR-MS (FAB): 403.3564 ($[M + H]^+$, $C_{27}H_{46}O_2^+$; calc. 403.3576).

*Ethyl (*2*S,*3*R)-12-[(1*R*,2*S*)-2-Decylcyclopropyl]-2,3-dihydroxydodec-7-ynoate* (**44**). To a mixture of ^{t}BuOH (49 ml) and H_2O (49 ml) at 25° was added AD-mix β (13.00 g). The resulting mixture was stirred to produce a biphasic system before it was cooled down to 0°. Ester **43** (3.72 g, 9.24 mmol) was added, and the mixture was stirred at 0° for 8 h. Na_2SO_3 (13.85 g) was added at 0°, and the mixture was allowed to warm to 25° and stirred further for 40 min. The mixture was diluted with AcOEt (250 ml), and the aq. layer was extracted further with AcOEt (2 × 75 ml). The combined org. layers were extracted wtih 2N aq. KOH soln. (75 ml), dried ($MgSO_4$) and concentrated *in vacuo* to give a crude solid, which was purified by FC (silica gel; 20% AcOEt in hexanes) to afford **44** (2.31 g, 98%). Waxy white solid. M.p. 57–61° (AcOEt). R_f 0.18 (silica gel; 17% AcOEt in hexanes). $[\alpha]_D = +9.8$ ($c = +1.6$, $CHCl_3$). FT-IR ($CHCl_3$ soln.): 3361, 2917, 2851, 1715, 1462, 1386, 1294, 1111, 1069, 720, 639. ^{1}H-NMR (400 MHz, $CDCl_3$): 4.27 (q, $J = 7.1$, 2 H); 4.06 (dd, $J = 2.1$, 5.1, 1 H); 3.93–3.87 (m, 1 H); 2.22–2.11 (m, 4 H); 1.90–1.83 (m, 1 H); 1.74–1.41 (m, 9 H); 1.40–1.20 (m, 21 H); 1.15–1.07 (m, 2 H); 0.86 (t, $J = 6.4$, 3 H); 0.65–0.58 (m, 2 H); 0.57–0.52 (m, 1 H); −0.34 (m, 1 H). ^{13}C-NMR (100 MHz, $CDCl_3$): 172.1; 80.9; 79.5; 73.1; 72.1; 62.2; 32.9; 31.9; 30.2; 29.7 (4 C); 29.4; 29.4; 29.1; 28.7; 28.2; 25.3; 22.7; 18.8; 18.6; 15.7; 15.6; 14.1; 14.1; 10.9. HR-MS (FAB): 459.3463 ($[M + Na]^+$, $C_{27}H_{48}NaO_4^+$; calc. 459.3450).

*Ethyl (*2*S,*3*R,*7*Z)-12-[(*2*R,*3*S)-2-Decylcyclopropyl]-2,3-dihydroxydodec-7-enoate* (**45**). A mixture of **44** (1.51 g, 3.46 mmol) and *Lindlar* catalyst (180 mg) in EtOH (75 ml) was stirred under 1 atm H_2 at 25° for 40 min.

The catalyst was filtered off through a pad of *Celite* and rinsed with AcOEt (25 ml). The filtrate was concentrated *in vacuo* to afford **45** (1.51 g, 100%). Waxy white solid. M.p. 56–60° (AcOEt). R_f 0.39 (silica gel; 10% Et_2O in hexanes). $[\alpha]_D = +6.7$ ($c = 1.2$, $CHCl_3$). FT-IR ($CHCl_3$ soln.): 3416, 2925, 2860, 1737, 1455, 1273, 1208, 1084, 1038. ^{1}H-NMR (600 MHz, $CDCl_3$): 5.40–5.32 (*m*, 2 H); 4.27 (*q*, $J = 7.2$, 2 H); 4.05 (*d*, $J = 5.0$, 1 H); 3.87 (*q*, $J = 7.6$, 1 H); 3.01 (*d*, $J = 5.1$, 1 H); 2.07 (*q*, $J = 7.3$, 2 H); 2.03–1.95 (*m*, 3 H); 1.84 (*d*, $J = 9.2$, 1 H); 1.63–1.51 (*m*, 3 H); 1.45–1.15 (*m*, 25 H); 1.15–1.07 (*m*, 2 H); 0.86 (*t*, $J = 6.8$, 3 H); 0.65–0.60 (*m*, 2 H); 0.60–0.55 (*m*, 1 H); −0.35 (*m*, 1 H). ^{13}C-NMR (150 MHz, $CDCl_3$): 173.6; 130.6; 129.0; 73.0; 72.4; 62.2; 33.4; 31.9; 30.2; 29.9; 29.7 (4 C); 29.6; 29.4; 28.7; 28.6; 27.3; 26.9; 25.8; 22.7; 15.8; 15.7; 14.2; 14.1; 10.9. HR-MS (FAB): 461.3605 ($[M + Na]^+$, $C_{27}H_{50}NaO_4^+$; calc. 461.3607).

Ethyl (2S,3R,7Z)-12-[(1R,2S)-2-Decylcyclopropyl]-3-hydroxy-2-[(4-nitrophenylsulfonyl)oxy]dodec-7-enoate (**46**). To a soln. of **45** (0.94 g, 2.14 mmol) in pyridine (45 ml) at 0° was added 4-nitrobenzenesulfonyl chloride (0.61 g, 2.46 mmol) in one portion. The resulting mixture was stirred at 0° for 6.5 h before it was quenched with icy cold H_2O (2 ml). The mixture was diluted with cold Et_2O (200 ml) and extracted with cold sat. aq. $CuSO_2$, soln. (50 ml), cold H_2O (2 × 100 ml), and cold brine (100 ml). The org. layer was dried ($MgSO_4$) and concentrated *in vacuo* (below 10°). The oily residue was purified by FC (silica gel; 12% chilled AcOEt in hexanes) to afford **46** (1.12 g, 84%) as a clear oil which solidified to a white solid upon standing. R_f 0.53 (silica gel; 25% AcOEt in hexanes). $[\alpha]_D = +2.5$ ($c = 1.7$, $CHCl_3$). FT-IR (neat): 3436, 2925, 2855, 1750, 1534, 1354, 1188, 1102, 1025, 855. ^{1}H-NMR (600 MHz, $CDCl_3$): 8.38 (*d*, $J = 8.2$, 2 H); 8.16 (*d*, $J = 8.0$, 2 H); 5.41–5.27 (*m*, 2 H); 4.97 (*d*, $J = 2.4$, 1 H); 4.15 (*q*, $J = 7.1$, 2 H); 4.10–4.07 (*m*, 1 H); 2.07–1.99 (*m*, 4 H); 1.76 (*d*, $J = 8.4$, 1 H); 1.60–1.50 (*m*, 4 H); 1.45–1.15 (*m*, 25 H); 1.15–1.07 (*m*, 1 H); 0.86 (*t*, $J = 7.0$, 3 H); 0.65–0.60 (*m*, 2 H); 0.55–0.52 (*m*, 1 H); −0.34 (*m*, 1 H). ^{13}C-NMR (150 MHz, $CDCl_3$): 166.7; 151.0; 142.0; 137.8; 131.0; 129.5; 129.5; 128.5; 124.2; 124.2; 80.9; 71.6; 62.4; 32.7; 31.9; 30.2; 29.9; 29.7 (4 C); 29.4; 28.7; 28.6; 27.4; 26.7; 25.3; 22.7; 15.8; 15.7; 14.1; 14.0; 10.9. HR-MS (FAB): 646.3402 ($[M + Na]^+$, $C_{33}H_{53}NNaO_8S^+$; calc. 646.3384).

Ethyl (2R,3R,7Z)-2-Azido-12-[(1R,2S)-2-decylcyclopropyl]-3-hydroxydodec-7-enoate (**47**). A mixture of **46** (0.88 g, 1.41 mmol) and NaN_3 (0.23 g, 3.54 mmol) in DMF (8 ml) was stirred at 25° for 36 h. The mixture was diluted with Et_2O (25 ml) and washed with H_2O (2 × 10 ml), and brine (100 ml). The org. layer was dried ($MgSO_4$) and concentrated *in vacuo*. The crude residue was purified by FC (silica gel; 20% Et_2O in hexanes) to afford **47** (0.62 g, 95%). Clear oil. R_f 0.53 (silica gel; 25% AcOEt in hexanes). $[\alpha]_D = +3.4$ ($c = 0.9$, $CHCl_3$). FT-IR (neat): 3401, 2925, 2849, 2107, 1743, 1455, 1378, 1261, 1190, 1085, 1026. ^{1}H-NMR (500 MHz, $CDCl_3$): 5.53–5.30 (*m*, 2 H); 4.32–4.23 (*m*, 2 H); 3.93–3.88 (*m*, 2 H); 2.26–2.22 (*m*, 1 H); 2.10–1.95 (*m*, 4 H); 1.60–1.45 (*m*, 3 H); 1.45–1.15 (*m*, 26 H); 1.15–1.07 (*m*, 2 H); 0.86 (*t*, $J = 7.1$, 3 H); 0.65–0.58 (*m*, 2 H); 0.55–0.50 (*m*, 1 H); −0.35 (*m*, 1 H). ^{13}C-NMR (125 MHz, $CDCl_3$): 169.0; 129.8; 128.9; 71.9; 66.2; 62.1; 32.6; 32.0; 30.2; 29.9; 29.7 (4 C); 29.6; 29.4; 28.7; 28.6; 27.3; 26.9; 25.5; 22.7; 15.8; 15.7; 14.2; 14.1; 10.9. HR-MS (MALDI-FT): 436.3810 ($[M + H - N_2]^+$, $C_{27}H_{49}NO_3^+$; calc. 436.3791). LS-MS (ESI): 486 [$M + Na^+$], $C_{27}H_{49}N_3NaO_3^+$; calc. 486).

*Ethyl (2R,3R,7Z)-2-Azido-3-[(*tert*-butyl)dimethylsilyloxy]-12-[(1R,2S)-2-decylcyclopropyl]dodec-7-enoate* (**48**). To a stirred soln. of **47** (0.63 g, 1.36 mmol) and 2,6-lutidine (0.40 ml, 3.40 mmol) in CH_2Cl_2 (15 ml) at −78° was added dropwise TBDMSOTf (0.31 ml, 1.43 mmol) *via* syringe. The mixture was allowed to warm to 25° and stirred further for 25 min before it was diluted with Et_2O (25 ml) and extracted successively with aq. $CuSO_4$ soln. (5 ml), H_2O (10 ml), and brine (5 ml). The org. layer was dried ($MgSO_4$) and concentrated *in vacuo* to afford **48** (0.79 g, 100%). Faintly yellow oil. R_f 0.68 (silica gel; 10% AcOEt in hexanes). $[\alpha]_D = -7.6$ ($c = 0.5$, $CHCl_3$). FT-IR (neat): 2927, 2860, 2108, 1725, 1455, 1378, 1255, 1184, 1108, 1026, 837. ^{1}H-NMR (500 MHz, $CDCl_3$): 5.39–5.29 (*m*, 2 H); 4.21 (*q*, $J = 7.0$, 2 H); 4.07 (*td*, $J = 1.4, 4.8$, 1 H); 3.93 (*d*, $J = 5.0$, 1 H); 2.04–1.95 (*m*, 4 H); 1.69–1.62 (*m*, 1 H); 1.52–1.48 (*m*, 1 H); 1.47–1.15 (*m*, 27 H); 1.15–1.07 (*m*, 2 H); 0.87–0.84 (*m*, 12 H); 0.65–0.58 (*m*, 2 H); 0.55–0.50 (*m*, 1 H); 0.07 (*s*, 6 H); −0.35 (*m*, 1 H). ^{13}C-NMR (125 MHz, $CDCl_3$): 169.0; 130.6; 128.9; 73.1; 66.2; 61.7; 32.7; 31.9; 30.2; 29.9; 29.7 (5 C); 29.6; 29.4; 28.7; 28.6; 27.5; 27.1; 25.7; 25.7; 25.7; 24.6; 22.7; 18.0; 15.8; 15.7; 14.1; 10.9; −4.5; −4.7. HR-MS (MALDI-FT): 550.4633 ($[M + H - N_2]^+$, $C_{33}H_{63}NO_3Si^+$; calc. 550.4655) LS-MS (ESI): 601 ($[M + Na]^+$, $C_{33}H_{63}NaN_3O_3Si^+$; calc. 601).

*(2S,3R,7Z)-2-Azido-3-[(*tert*-butyl)dimethylsilyloxy]-12-[(1R,2S)-2-decylcyclopropyl]dodec-7-en-1-ol* (**14**). To a stirred soln. of **48** (0.77 g, 1.33 mmol) in THF (25 ml) at 0° was added dropwise a soln. of $LiBH_4$ (2.0M in THF, 1.66 ml, 3.32 mmol) *via* syringe. The mixture was stirred at 0° for 10 h before it was quenched carefully with MeOH (1 ml), diluted with AcOEt (10 ml) and washed successively with H_2O (5 ml) and brine (5 ml). The org. layer was dried ($MgSO_4$) and concentrated *in vacuo*. The residue was then purified by FC (silica gel; 17% AcOEt in hexanes) to afford **14** (0.63 g, 92%). Faintly yellow oil. R_f 0.39 (silica gel; AcOEt/hexanes 1:5). $[\alpha]_D = -7.1$ ($c = 1.1$, $CHCl_3$). FT-IR (neat). 3381, 2925, 2860, 2101, 1464, 1367, 1256, 1083, 1044, 836, 777. ^{1}H-NMR (500 MHz, $CDCl_3$): 5.47–5.28 (*m*, 2 H); 3.82–3.68 (*m*, 3 H); 3.50–3.45 (*m*, 1 H); 2.26 (br. *s*, OH); 2.05–1.97 (*m*, 4 H); 1.69–1.60 (*m*, 1 H); 1.50–1.44 (*m*, 2 H); 1.39–1.18 (*m*, 23 H); 1.18–1.07 (*m*, 2 H); 0.89–

0.84 (*m*, 12 H); 0.65–0.58 (*m*, 2 H); 0.55–0.50 (*m*, 1 H); 0.10 (*s*, 3 H); 0.07 (*s*, 3 H); −0.35 (*m*, 1 H). ^{13}C-NMR (125 MHz, $CDCl_3$): 130.7; 128.9; 73.1; 66.7; 62.2; 33.4; 31.9; 31.9; 30.2; 29.7 (3 C); 29.6; 29.4; 28.7; 28.6; 27.3; 27.2; 25.8; 25.8; 25.8; 24.8; 24.9; 22.7; 18.0; 15.7; 15.7; 14.1; 10.9; −4.6; −4.7. HR-MS (MALDI-FT): 508.4558 ($[M+H-N_2]^+$, $C_{31}H_{61}NO_2Si^+$; calc. 508.4550). LR-MS (ESI): 571 ($[M+Cl]^-$, $C_{31}H_{61}ClN_3O_2Si^-$; calc. 571).

*(2*R*)-12-[(1*R,2S*)-2-Decylcyclopropyl]dodec-7-yne-1,2-diol* (**49**): To a stirred biphasic mixture of $K_3Fe(CN)_6$ (9.42 g, 28.60 mmol), K_2CO_3 (4.00 g, 28.57 mmol), $K_2Os_2(OH)_4$ (13.3 g, 0.04 mmol), and $(DHQD)_2AQN$ (9.42 mg, 0.09 mmol) in ^{t}BuOH (45 ml) and H_2O (45 ml) at 0° was added **40** (3.01 g, 9.52 mmol). The flask containing the olefin was rinsed with ^{t}BuOH (1.5 ml) and H_2O (1.5 ml), and the rinse was then added to the mixture, and stirring was continued at 0° for 8 h. The mixture was quenched by addition of Na_2SO_3 (7.62 g) at 0° before it was allowed to warm to 25° over 30 min. The two phases were separated, and the aqueous layer was further extracted with AcOEt (2 × 75 ml). The combined org. layers were successively washed with H_2O (75 ml), brine (75 ml), dried ($MgSO_4$) and concentrated *in vacuo*. The residue was purified by FC (silica gel; 10% acetone in CH_2Cl_2) to afford **49** (3.04 g, 91%). White solid. M.p. 84–85° (AcOEt). R_f 0.13 (silica gel, 20% AcOEt in hexanes). $[\alpha]_D = +3.9$ ($c = 1.0$, $CHCl_3$). FT-IR ($CHCl_3$ soln.): 3379, 2924, 2854, 1458, 1377, 1091, 1044. ^{1}H-NMR (400 MHz, $CDCl_3$): 3.89–3.84 (*m*, 1 H); 3.68–3.62 (*m*, 1 H); 3.50–3.44 (*m*, 1 H); 2.42 (*d*, *J* = 4.0, 1 H); 2.32–2.30 (*m*, 2 H); 2.14–2.11 (*m*, 2 H); 1.99 (*t*, *J* = 5.6, 1 H); 1.65–1.58 (*m*, 2 H); 1.51–1.40 (*m*, 4 H); 1.35–1.24 (*m*, 18 H); 1.15–1.10 (*m*, 2 H); 0.86 (*t*, *J* = 6.8, 3 H); 0.64–0.63 (*m*, 2 H); 0.57–0.52 (*m*, 1 H); −0.34 (*m*, 1 H). ^{13}C-NMR (100 MHz, $CDCl_3$): 81.5; 79.1; 71.5; 66.6; 32.0; 31.9; 30.2; 29.7 (3 C); 29.4; 29.4; 29.0; 28.7; 28.2; 22.7; 18.7; 18.7; 15.7; 15.6; 15.2; 14.1; 10.9. HR-MS (FAB): 351.3257 ($[M+H]^+$, $C_{23}H_{42}O_2^+$; calc. 351.3263).

*(2*R*)-10-[(1*R,2S*)-2-Decylcyclopropyl]-2-hydroxydec-5-ynyl 2,2,2-Trimethylethanoate* (**50**). To a stirred soln. of **49** (1.90 g, 5.41 mmol) in pyridine (15 ml) at 0° was added freshly distilled pivaloyl chloride (0.67 ml, 5.42 mmol). The mixture was stirred at 25° for 40 min before it was quenched by the addition of cold H_2O (0.5 ml). The mixture was diluted with Et_2O (75 ml) and successively washed with sat. aq. $NaHCO_3$ soln. (2 × 50 ml), 1N aq. HCl soln. (2 × 50 ml), H_2O (50 ml), and brine (50 ml). The org. layer was dried ($MgSO_4$) and concentrated *in vacuo*. The residue was then purified by FC (silica gel; 10% AcOEt in hexanes) to afford **47** (2.14 g, 91%). Faintly yellow oil. R_f 0.57 (silica gel; 25% AcOEt in hexanes). $[\alpha]_D = +1.4$ ($c = 2.7$, $CHCl_3$). FT-IR (neat): 3478, 3058, 2921, 2853, 1738, 1715, 1455, 1285, 1158, 1107. ^{1}H-NMR (500 MHz, $CDCl_3$): 4.11 (*dd*, *J* = 2.9, 10.6, 1 H); 4.01–3.97 (*m*, 2 H); 2.33–2.30 (*m*, 2 H); 2.14–2.11 (*m*, 2 H); 1.66–1.62 (*m*, 2 H); 1.51–1.34 (*m*, 8 H); 1.30–1.20 (*m*, 24 H); 1.16–1.07 (*m*, 2 H); 0.86 (*t*, *J* = 7.0, 3 H); 0.66–0.60 (*m*, 2 H); 0.57–0.52 (*m*, 1 H); −0.34 (*m*, 1 H). ^{13}C-NMR (125 MHz, $CDCl_3$): 178.7; 81.4; 79.0; 69.3; 68.2; 38.9; 32.5; 31.9; 30.2; 29.7; 29.7; 29.7; 29.6; 29.4; 29.4; 29.0; 28.7; 28.2; 27.2 (3 C); 22.7; 18.8; 15.8; 15.6; 15.1; 14.1; 10.9. HR-MS (FAB): 435.3844 ($[M+H]^+$, $C_{28}H_{50}O_3^+$; calc. 435.3838).

*(2*R*)-2-[(*tert*-Butyl)dimethylsilyloxy]-10-[(1*R,2S*)-2-decylcyclopropyl]dec-5-ynyl 2,2,2-Trimethylethanoate* (**51**). To a stirred soln. of **50** (1.32 g, 3.03 mmol) and 2,6-lutidine (0.88 ml, 7.57 mmol) in CH_2Cl_2 (15 ml) at −78° was added dropwise TBDMSOTf (0.65 ml, 3.06 mmol) *via* syringe. The mixture was allowed to warm to 25° and stirred further for 15 min before it was diluted with Et_2O (50 ml) and successively extracted with aq. $CuSO_4$ soln. (15 ml), H_2O (20 ml), and brine (15 ml). The org. layer was dried ($MgSO_4$) and concentrated *in vacuo* to afford **51** (1.67 g, 100%). Faintly yellow oil. R_f 0.85 (silica gel; 17% Et_2O in hexanes). $[\alpha]_D = +5.2$ ($c = 1.6$, $CHCl_3$). FT-IR (neat): 2926, 2855, 1738, 1734, 1462, 1283, 1354, 1154, 1121, 1018, 837, 777. ^{1}H-NMR (500 MHz, $CDCl_3$): 3.99–3.93 (*m*, 3 H); 2.23–2.20 (*m*, 2 H); 2.13–2.11 (*m*, 2 H); 1.65–1.63 (*m*, 2 H); 1.51–1.30 (*m*, 8 H); 1.30–1.20 (*m*, 14 H); 1.18 (*s*, 9 H); 1.16–1.07 (*m*, 2 H); 0.90–0.86 (*m*, 12 H); 0.66–0.60 (*m*, 2 H); 0.57–0.53 (*m*, 1 H); 0.08 (*s*, 3 H); 0.07 (*s*, 3 H); −0.34 (*m*, 1 H). ^{13}C-NMR (125 MHz, $CDCl_3$): 178.3; 80.8; 79.4; 68.7; 67.8; 38.8; 33.9; 31.9; 30.2; 29.7; 29.7; 29.7; 29.7; 29.4; 29.3; 29.0; 28.7; 28.2; 27.2 (3 C); 25.7 (3 C); 22.7; 18.8; 18.1; 15.7; 15.6; 14.7; 14.1; 10.9; −4.6; −4.8. HR-MS (FAB): 571.4509 ($[M+Na]^+$, $C_{34}H_{64}NaO_3Si^+$; calc. 571.4522).

*(2*R*)-2-[(*tert*-Butyl)dimethylsilyloxy]-10-[(1*R,2S*)-2-decylcyclopropyl]dec-5-yn-1-ol* (**52**). To a stirred soln. of **51** (1.65 g, 3.01 mmol) in CH_2Cl_2 (20 ml) at −78° was added dropwise a soln. of DIBAL (1.0M in CH_2Cl_2, 0.68 ml, 3.19 mmol). The mixture was stirred at −78° for 20 min before it was quenched with MeOH (0.1 ml) and allowed to warm to 25°. AcOEt (25 ml) and sat. aq. soln. of *Rochelle*'s salt (5 ml) were added, and the resulting cloudy mixture was stirred further at 25° until it became clear (30 min). The org. layer was further washed with H_2O (2 ml), brine (2 ml), dried ($MgSO_4$), and concentrated *in vacuo* to give the crude product as a viscous oil. The crude product was then purified by FC (silica gel; 10% AcOEt in hexanes) to afford **52** (1.40 g, 100%). Clear oil. R_f 0.47 (silica gel; 17% AcOEt in hexanes). $[\alpha]_D = +0.1$ ($c = 1.0$, $CHCl_3$). FT-IR (neat): 3384, 2925, 2855, 1463, 1386, 1254, 1113, 1048, 837, 777. ^{1}H-NMR (500 MHz, $CDCl_3$): 3.93–3.88 (*m*, 1 H); 3.60 (*d*, *J* = 11, 1 H); 3.49–3.45 (*m*, 1 H); 2.20–2.16 (*m*, 4 H); 1.86 (br. *s*, 1 H); 1.72–1.62 (*m*, 2 H); 1.51–1.32 (*m*, 8 H);

1.31–1.20 (*m*, 14 H); 1.16–1.07 (*m*, 2 H); 0.90–0.86 (*m*, 12 H); 0.66–0.60 (*m*, 2 H); 0.57–0.53 (*m*, 1 H); 0.10 (*s*, 3 H); 0.09 (*s*, 3 H); −0.34 (*m*, 1 H). ^{13}C-NMR (125MHz, $CDCl_3$): 80.9; 79.3; 71.4; 66.1; 33.8; 31.9; 30.2; 29.7; 29.7; 29.7; 29.7; 29.4; 29.3; 29.0; 28.7; 28.2; 25.8 (3 C); 22.7; 18.8; 18.1; 15.7; 15.6; 14.8; 14.1; 10.9; −4.6; −4.6. HR-MS (FAB): 465.4115 ($[M+H]^+$, $C_{29}H_{56}O_2Si^+$; calc. 465.4128).

*(2*R*,5*Z*)-2-[(*tert*-Butyl)dimethylsilyloxy]-10-[(1*R*,2*S*)-2-decylcyclopropyl]dec-5-en-1-ol* (**53**). A mixture of **52** (1.40 g, 3.01 mmol) and *Lindlar* catalyst (150 mg) in EtOH (75 ml) under 1 atm H_2 at 25° was stirred for 30 min. The catalyst was removed by filtering through a pad of *Celite* and rinsing with AcOEt (25 ml). The filtrate was concentrated *in vacuo* to give pure **53** (1.40 g, 100%). Viscous oil. R_f 0.47 (silica gel; 12% AcOEt in hexanes). $[\alpha]_D = +0.1$ ($c = 1.7$, $CHCl_3$). FT-IR (neat): 3421, 2926, 2855, 1463, 1383, 1254, 1107, 1046, 836, 777. ^{1}H-NMR (600 MHz, $CDCl_3$): 5.39–5.31 (*m*, 2 H); 3.75–3.71 (*m*, 1 H); 3.57–3.53 (*m*, 1 H); 3.45 (*dd*, $J = 5.4$, 11.1, 1 H); 2.10–1.96 (*m*, 4 H); 1.85 (br. *s*, 1 H); 1.58–1.50 (*m*, 2 H); 1.36–1.30 (*m*, 8 H); 1.31–1.18 (*m*, 14 H); 1.16–1.07 (*m*, 2 H); 0.90–0.86 (*m*, 12 H); 0.66–0.60 (*m*, 2 H); 0.57–0.53 (*m*, 1 H); 0.07 (*s*, 3 H); 0.07 (*s*, 3 H); −0.35 (*m*, 1 H). ^{13}C-NMR (150 MHz, $CDCl_3$): 130.5; 128.8; 72.5; 66.1; 34.0; 31.9; 30.2; 29.9; 29.7; 29.7; 29.7; 29.7; 29.7; 29.4; 28.7; 28.6; 27.3; 25.8 (3 C); 23.2; 22.7; 18.1; 15.8; 15.7; 14.1; 10.9; −4.5; −4.6. HR-MS (FAB): 457.4299 ($[M+H]^+$, $C_{29}H_{58}O_2Si^+$; calc. 467.4287).

*(2*R*,5*Z*)-2-[(*tert*-Butyl)dimethylsilyloxy]-10-[(1*R*,2*S*)-2-decylcyclopropyl]dec-5-enal* (**54**). To a soln. of **53** (1.40 g, 3.01 mmol) in CH_2Cl_2 (25 ml) at 0° was added *Dess-Martin* periodinane reagent (1.50 g, 3.61 mmol). The mixture was allowed to warm to 25° and stirred further for 40 min. A soln. of $Na_2S_2O_3$ (20% in sat. $NaHCO_3$, 5 ml) was added, and the resulting cloudy mixture was stirred at 25° until it became clear (30 min). The layers were separated, and the org. layer was washed with H_2O (10 ml), brine (10 ml), dried ($MgSO_4$), and concentrated *in vacuo*. The crude product was then purified by FC (silica gel; 10% Et_2O in hexanes) to give **54** (1.34 g, 96%). Clear oil. R_f 0.59 (silica gel; 10% Et_2O in hexanes). $[\alpha]_D = +7.1$ ($c = 0.9$, $CHCl_3$). FT-IR (neat): 2925, 2854, 1738, 1464, 1376, 1255, 1112, 1020, 837, 779. ^{1}H-NMR (600 MHz, $CDCl_3$): 9.58 (*d*, $J = 1.6$, 1 H); 5.43–5.28 (*m*, 2 H); 3.98–3.96 (*m*, 1 H); 2.20–2.14 (*m*, 1 H); 2.10–2.00 (*m*, 3 H); 1.72–1.62 (*m*, 2 H); 1.36–1.30 (*m*, 8 H); 1.31–1.18 (*m*, 14 H); 1.16–1.07 (*m*, 2 H); 0.91 (*s*, 9 H); 0.86 (*t*, $J = 7.1$, 3 H); 0.66–0.60 (*m*, 2 H); 0.56–0.53 (*m*, 1 H); 0.07 (*s*, 3 H); 0.06 (*s*, 3 H); −0.35 (*m*, 1 H). ^{13}C-NMR (150 MHz, $CDCl_3$): 204.3; 131.4; 128.2; 77.3; 33.0; 31.9; 30.2; 30.0; 29.7; 29.7; 29.7; 29.7; 29.6; 29.4; 28.7; 28.6; 27.3; 25.7 (3 C); 23.2; 22.7; 18.2; 15.8; 15.7; 14.1; 10.9; −4.6; −4.9. HR-MS (FAB): ($[M+Na]^+$, $C_{29}H_{56}NaO_2Si^+$; calc. 487.3947).

*(2*R*,5*Z*)-2-[(*tert*-Butyl)dimethylsilyloxy]-10-[(1*R*,2*S*)-2-decylcyclopropyl]dec-5-enoic Acid* (**12**). To a mixture of **54** (0.80 g, 1.73 mmol) and 2-methylbut-2-ene (2.0M in THF, 17.29 ml, 34.8 mmol) in ^{t}BuOH (68 ml) and H_2O (14 ml) at 0° was added NaH_2PO_4 (3.60 g, 20.70 mmol), followed by $NaClO_2$ (0.39 g, 4.32 mmol) in small portions. The slightly yellowish mixture was stirred at 0° for 30 min before a sat. soln. of $Na_2S_2O_3$ in pH 7 phosphate buffer (3 ml) was added to the mixture. The mixture was extracted with AcOEt (3 × 75 ml), and the combined org. layers were washed with sat. aq. NH_4Cl soln. (20 ml), H_2O (20 ml), brine (20 ml), dried ($MgSO_4$), and concentrated *in vacuo* to afford **12** (> 95%) as a waxy solid, which was used in the following step without further purification. For characterization purposes, a small amount of crude product was purified by FC (silica gel; 50% AcOEt in hexanes to 50% AcOEt in CH_2Cl_2) to give pure **12** and a small amount of α-(*tert*-Butyl)dimethylsilyloxy acid **12a**.

Data of **12**: HR-MS (FAB): 411.2846 ($[M+H+2\,Na]^+$, $C_{23}H_{42}Na_2O_3^+$; calc. 411.2851).

Data of **12a**: R_f 0.12 (silica gel; 25% AcOEt in hexanes). $[\alpha]_D = +0.8$ ($c = 0.8$, $CHCl_3$). FT-IR (neat): 3383, 2924, 2854, 1730, 1459, 1279, 1088, 742. ^{1}H-NMR (500 MHz, $CDCl_3$): 9.50 (br. *s*, OH); 5.41–5.29 (*m*, 2 H); 4.28 (*t*, $J = 5.5$, 1 H); 2.18–1.95 (*m*, 4 H); 1.87–1.72 (*m*, 2 H); 1.36–1.30 (*m*, 8 H); 1.31–1.18 (*m*, 14 H); 1.16–1.07 (*m*, 2 H); 0.92 (*s*, 9 H); 0.86 (*t*, $J = 7.5$, 3 H); 0.66–0.60 (*m*, 2 H); 0.56–0.53 (*m*, 1 H); 0.12 (*s*, 3 H); 0.12 (*s*, 3 H); −0.35 (*m*, 1 H). ^{13}C-NMR (125 MHz, $CDCl_3$): 174.2; 131.4; 127.6; 71.8; 34.7; 31.9; 30.2; 29.9; 29.7; 29.7; 29.7; 29.7; 29.7; 29.4; 28.7; 28.6; 27.3; 25.6 (3 C); 22.7; 22.1; 18.1; 15.8; 15.7; 14.1; 10.9; −4.9; −5.3. HR-MS (FAB): 503.3878 ($[M+Na]^+$, $C_{29}H_{56}NaO_3Si^+$); calc. 503.3896).

*(2*S*,3*R*)-2-Azido-3-[(*tert*-Butyl)dimethylsilyloxy]-1-{6-O-[(*tert*-butyl)diphenylsilyl]-3,4-O-isopropylidene-2-O-(trimethylacetyl)-β-*D*-galactopyranosyloxy}-10-[(1*R*,2*S*)-2-decylcyclopropyl]decane* (**55**). The following protocol was followed prior to the glycosidation reaction. The mixture of glycosyl acceptor and donor was azeotroped with dry benzene (3 × 5 ml) in a dried flask and placed under vacuum for 1 h before the reaction. The glycosidation catalysts (AgOTf and $SnCl_2$) were added to a dried flask with a magnetic stirring bar. The mixture in the flask wrapped in Al foil was azeotroped with dry benzene (2 × 5 ml) in the dark. Activated 4-Å molecular sieves were added to the flask, and the mixture was azeotroped with benzene once more (5 ml) before placed under vacuum for 1 h.

To a stirred mixture of AgOTf (83 mg, 323 μmol), $SnCl_2$ (61 mg, 323 μmol), and 4-Å molecular sieves (200 mg) in dry CH_2Cl_2 (3 ml) under Ar at 0° was added a soln. of **13** (65 mg, 129 μmol) and **11** (106 mg,

194 μmol) in dry CH_2Cl_2 (3 ml) *via* syringe. To the mixture was then added 2,6-di(*tert*-butyl)-4-methylpyridine (32 mg, 155 μmol) in one portion. The mixture was then stirred at 0° in the dark for 3 h before it was allowed to warm to 25° and stirred further for 3.5 h. The mixture was diluted with AcOEt (12 ml), filtered through a pad of *Celite*, and rinsed with AcOEt (10 ml). The org. filtrate was washed with sat. aq. $NaHCO_3$ soln. (2 × 5 ml), H_2O (7 ml), and brine (7 ml). The org. extract was dried ($MgSO_4$) and concentrated *in vacuo* to a crude oil, which was then purified by FC (silica gel; 5% AcOEt in hexanes) to afford **55** (125 mg, 93%). Clear oil. R_f 0.52 (silica gel; 10% AcOEt in hexanes). $[\alpha]_D = +3.7$ ($c = 2.6$, $CHCl_3$). FT-IR (neat): 2929, 2855, 2099, 1741, 1464, 1377, 1255, 1137, 1112, 1080, 833, 704. ^{1}H-NMR (600 MHz, $CDCl_3$): 7.70–7.66 (*m*, 4 arom. H); 7.43–7.34 (*m*, 6 arom. H); 4.94 (*t*, *J* = 6.0, H–C(2′)); 4.33 (*d*, *J* = 8.1, H–C(1′)); 4.29 (*dd*, *J* = 1.9, 5.3, H–C(4′)); 4.14 (*dd*, *J* = 5.4, 7.2, H–C(3′)); 3.97 (*dd*, *J* = 7.5, 9.7, 1 H–C(6′)); 3.91 (*dd*, *J* = 6.0, 9.7, 1 H–C(6′)); 3.87–3.85 (*m*, H–C(5′)); 3.78 (*dd*, *J* = 8.3, 11.7, 1 H–C(1)); 3.73–3.70 (*m*, H–C(3)); 3.54–3.51 (*m*, 1 H–C(1), H–C(2)); 1.56–1.50 (*m*, 4 H); 1.35–1.18 (*m*, 41 H); 1.15–1.05 (*m*, 2 H); 1.04 (*s*, 9 H); 0.87–0.85 (*m*, 12 H); 0.65–0.63 (*m*, 2 H); 0.57–0.53 (*m*, 1 H); 0.02 (*s*, 6 H); −0.35 (*m*, 1 H). ^{13}C-NMR (150 MHz, $CDCl_3$): 176.8; 135.6; 135.6; 135.5; 135.5; 133.3; 133.2; 129.8; 129.7; 127.7; 127.7; 127.6; 127.6; 110.3; 100.0; 73.4; 73.2; 72.7; 72.1; 67.9; 65.3; 62.5; 32.8; 31.9; 30.2; 29.8; 29.7; 29.7; 29.7; 29.7; 29.7; 29.6; 29.6; 29.4; 28.7; 28.7; 28.7; 28.7; 27.7; 27.1; 27.1; 26.7; 26.7; 26.7; 26.4; 25.8; 25.8; 25.8; 24.8; 24.7; 22.7; 19.2; 18.0; 15.7; 15.7; 14.1; 10.9; −4.6; −4.6; HR-MS (MALDI-FT): 1056.6874 ($[M + Na]^+$, $C_{59}H_{99}N_3NaO_8Si_2^+$; calc. 1056.6868).

*(2*S*,3*R*)-2-Azido-3-[(*tert*-butyl)dimethylsilyloxy]-1-[6-O-(*tert*-butyl)diphenylsilyl]-3,4-O-isopropylidene-β-*D*-galactopyranosyloxy]-10-[(1*R*,2*S*)-2-decylcyclopropyl]decane* (**56**). To a soln. of **55** (69 mg, 67 μmol) in dry CH_2Cl_2 (1.5 ml) at −78° was added dropwise a soln. of DIBAL (1.0M in CH_2Cl_2, 133 μl, 133 μmol). The mixture was stirred at −78° for 15 min before it was quenched by the addition of MeOH (100 μl), diluted with AcOEt (5 ml) and allowed to warm to 25°. Sat. aq. soln. of *Rochelle*'s salt (1.5 ml) was added, and the resulting cloudy mixture was stirred further until it became clear (30 min). The org. layer was further washed with H_2O (2 ml), brine (2 ml), dried ($MgSO_4$), and concentrated *in vacuo*. The crude product was purified by FC (silica gel; 12% AcOEt in hexanes) to afford **56** (62 mg, 98%). Clear oil. R_f 0.18 (silica gel; 10% AcOEt in hexanes). $[\alpha]_D = +1.3$ ($c = 3.0$, $CHCl_3$). FT-IR (neat): 3424, 2927, 2855, 2099, 1462, 1380, 1253, 1110, 834, 703. ^{1}H-NMR (600 MHz, $CDCl_3$): 7.70–7.66 (*m*, 4 arom. H); 7.44–7.32 (*m*, 6 arom. H); 4.28 (*dd*, *J* = 1.4, 5.3, H–C(4′)); 4.15 (*d*, *J* = 8.2, H–C(1′)); 4.06 (*t*, *J* = 6.9, H–C(3′)); 3.97 (*dd*, *J* = 7.7, 9.5, H–C(6′)); 3.92–3.87 (*m*, 1 H–C(1), H–C(5′), 1 H–C(6′)); 3.85 (*t*, *J* = 7.3, H–C(5′)); 3.73 (*dd*, *J* = 4.7, 9.3, H–C(3)); 3.65 (*dd*, *J* = 3.9, 10.7, 1 H–C(1)); 3.58–3.53 (*m*, H–C(2), H–C(2′)); 2.40 (*d*, *J* = 2.0, 1 H); 1.60–1.56 (*m*, 1 H); 1.50 (*s*, 3 H); 1.41–1.21 (32 H); 1.15–1.09 (*m*, 2 H); 1.04 (*s*, 9 H); 0.87 (*t*, *J* = 6.7, 3 H); 0.84 (*s*, 9 H); 0.65–0.60 (*m*, 2 H); 0.57–0.53 (*m*, 1 H); 0.03 (*s*, 3 H); 0.02 (*s*, 3 H); −0.34 (*m*, 1 H). ^{13}C-NMR (100 MHz, $CDCl_3$): 135.6; 135.6; 135.5; 135.5; 133.3; 133.2; 129.7; 129.7; 127.7; 127.7; 127.6; 127.6; 110.0; 102.2 (C(1′)); 78.5 (C(3′)); 73.8 (C(2′)); 73.6 (C(5′)); 73.1 (C(4′)); 72.0 (C(3)); 68.8 (C(1)); 64.8 (C(2)); 62.4 (C(6′)); 33.3; 31.9; 30.2; 30.2; 29.8; 29.7; 29.7; 29.7; 29.7; 29.6; 29.6; 29.6; 29.4; 28.7; 28.2; 26.7; 26.7; 26.7; 26.3; 25.8; 25.8; 25.8; 22.7; 19.2; 18.0; 15.7; 15.7; 14.1; 10.9; 1.0; −4.5; −4.6. HR-MS (MALDI-FT): 972.6281 ($[M + Na]^+$, $C_{54}H_{91}N_3NaO_7Si_2^+$; calc. 972.6293).

*(2*S*,3*R*)-2-Azido-3-[(*tert*-butyl)dimethylsilyloxy]-1-[6-O-(*tert*-butyl)diphenylsilyl]-3,4-O-isopropylidene-2-O-(3-methylbut-2-enyl)-β-*D*-galactopyranosyloxy]-10-[(1*R*,2*S*)-2-decylcyclopropyl]decane* (**57**). To a soln. of **56** (46 mg, 48 μmol) in dry DMF (1 ml) at 0° was added NaH (60% in mineral oil, 3 mg, 58 μmol) in one portion. The mixture was stirred for 5 min followed by the addition of prenyl bromide (11 μl, 97 μmol). The resulting mixture was then stirred at 0° for 5 h before it was diluted with AcOEt (7 ml) and washed with H_2O (2 ml) and brine (2 ml). The org. layer was dried ($MgSO_4$) and concentrated to give the crude product as a viscous oil, which was then purified by FC (silica gel; 10% AcOEt in hexanes) to afford **57** (42 mg, 85%). Clear oil. R_f 0.71 (silica gel; 17% AcOEt in hexanes). $[\alpha]_D = +5.5$ ($c = 2.8$, $CHCl_3$). FT-IR (neat): 2928, 2856, 2110, 1462, 1377, 1251, 1106, 833, 702, 608. ^{1}H-NMR (600 MHz, $CDCl_3$): 7.70–7.66 (*m*, 4 arom. H); 7.43–7.34 (*m*, 6 arom. H); 5.37 (*t*, *J* = 7.1, Me_2CCHCH_2); 4.23 (*m*, H–C(4′), Me_2CCHCH_2); 4.20 (*d*, *J* = 8.1, H–C(1′)); 4.05 (*dd*, *J* = 5.8, 6.9, H–C(3′); 3.94 (*dd*, *J* = 7.5, 9.9, H–C(6′)); 3.90–3.84 (*m*, 1 H–C(6′), 1 H–C(1)); 3.79–3.73 (*m*, H–C(3), H–C(5′)); 3.64 (*td*, *J* = 4.5, 7.8, H–C(2)); 3.55 (*dd*, *J* = 4.6, 10.3, 1 H–C(1)); 3.29 (*t*, *J* = 7.4, H–C(2′)); 1.72 (*s*, 3 H); 1.67 (*s*, 3 H); 1.61–1.55 (*m*, 1 H); 1.48 (*s*, 3 H); 1.40–1.20 (*m*, 32 H); 1.12–1.09 (*m*, 2 H); 1.03 (*s*, 9 H); 0.87–0.83 (*m*, 12 H); 0.65–0.63 (*m*, 2 H); 0.57–0.53 (*m*, 1 H); 0.02 (*s*, 6 H); −0.35 (*m*, 1 H). ^{13}C-NMR (150 MHz, $CDCl_3$): 137.2; 135.6; 135.6; 135.5; 135.5; 133.4; 133.2; 129.7; 129.7; 127.7; 127.7; 127.6; 127.6; 121.4; 109.6; 102.9 (C(1′)); 79.3 (C(2′)); 79.1 (C(3′)); 73.2 (C(5′)); 73.2 (C(4′)); 72.3 (C(3′)); 68.6 (C(1)); 68.4 (Me_2CCHCH_2); 65.5 (C(2)); 62.5 (C(6′)); 32.5; 31.9; 30.2; 29.9; 29.7 (5 C); 29.4, 28.7; 28.6; 28.0; 27.3; 27.3; 26.7; 26.3; 25.8; 25.8; 25.8; 25.0; 24.5; 22.7; 19.2; 18.0; 18.0; 15.7; 15.7; 14.1; 10.9; −4.5; −4.6. HR-MS (MALDI-FT): 1040.6917 ($[M + Na]^+$, $C_{59}H_{99}N_3NaO_7Si_2^+$; calc. 1040.6919).

*(2*S*,3*R*)-2-Amino-3-[(*tert*-butyl)dimethylsilyloxy]-1-{6-*O*-[(*tert*-Butyl)diphenylsilyl]-3,4-*O*-isopropylidene-2-*O*-(3-methylbut-2-enyl)-β-*D*-galactopyranosyloxy}-10-[(1*R*,2*S*)-2-decylcyclopropyl]decane* (**58**). A soln. of **57** (40 mg, 39 μmol) and Ph_3P (21 mg, 79 μmol) in benzene (1.0 ml) was heated at 45° before addition of H_2O (2 μl), followed by heating at 45° for 7.5 h. Dilution with AcOEt (5 ml) and washing with sat. aq. NH_4Cl soln. (3 ml) and brine (3 ml) was followed by drying ($MgSO_4$). Concentration *in vacuo* gave the crude product as a viscous oil, which was then purified by FC (silica gel; 12% AcOEt in hexanes) to afford pure **58** (35 mg, 90%). Clear oil. R_f 0.17 (silica gel; 17% AcOEt in hexanes). $[\alpha]_D = +2.2$ ($c = 3.0$, $CHCl_3$). FT-IR (neat): 3385, 2927, 1464, 1380, 1247, 1082, 1044, 833, 704. ^{1}H-NMR (600 MHz, $CDCl_3$): 7.70–7.65 (*m*, 4 arom. H); 7.43–7.33 (*m*, 6 arom. H); 5.36 (*t*, *J* = 6.7, Me_2CCHCH_2); 4.27–4.19 (*m*, H–C(4′), Me_2CCHCH_2); 4.20 (*d*, *J* = 8.0, H–C(1′)); 4.05 (*t*, *J* = 6.4, 1 H–C(3′)); 3.94–3.85 (*m*, CH_2(6′)); 3.77 (*t*, *J* = 6.4, H–C(5′)); 3.68–3.64 (*m*, 1 H–C(1), H–C(8)); 3.60 (*dd*, *J* = 4.1, 9.7, 1 H–C(1)); 3.28 (*t*, *J* = 7.6, H–C(2′)); 3.00 (*td*, *J* = 4.1, 8.2, H–C(2)); 1.71 (*s*, 3 H); 1.69–1.54 (*m*, 5 H); 1.52–1.48 (*m*, 4 H); 1.45–1.18 (*m*, 32 H); 1.18–1.05 (*m*, 2 H); 1.03 (*s*, 9 H); 0.86 (*t*, *J* = 6.8, 3 H); 0.82 (*s*, 9 H); 0.65–0.60 (*m*, 2 H); 0.57–0.52 (*m*, 1 H); 0.01 (*s*, 3 H); 0.00 (*s*, 3 H); −0.35 (*m*, 1 H). ^{13}C-NMR (150 MHz, $CDCl_3$): 137.2; 135.6; 135.6; 135.5; 135.5; 133.4; 133.2; 129.7; 129.7; 127.7; 127.7; 127.6; 127.6; 121.4; 109.6; 102.9 (C(1′)); 79.3 (C(2′)); 79.1 (C(3′)); 73.9 (C(3)); 73.2 (C(4′)); 73.0 (C(5′)); 71.7 (C(1)); 68.3 (Me_2CCHCH_2); 62.4 (C(6′)); 54.5 (C(2)); 32.7; 31.9; 30.2; 30.2; 29.9; 29.7; 29.7; 29.7; 29.6; 29.6; 29.6; 29.4; 28.7; 28.7; 28.0; 26.7; 26.7; 26.7; 26.3; 25.8; 25.8; 25.8; 25.8; 25.2; 22.7; 19.2; 18.1; 18.0; 15.7; 15.7; 14.1; 10.9; −4.3; −4.6. HR-MS (MALDI-FT): 1014.6968 ($[M + Na]^+$, $C_{59}H_{101}NNaO_7Si_2^+$; calc. 1014.7014).

*(2*R*,5*Z*)-*N*-[(1*S*,2*R*)-2-[(*tert*-Butyl)dimethylsilyloxy]-1-({6-*O*-[(*tert*-butyl)diphenylsilyl]-3,4-*O*-isopropylidene-2-*O*-(3-methylbut-2-enyl)-β-*D*-galactopyranosyloxy}methyl)-9-[(1*R*,2*S*)-2-decylcyclopropyl]nonyl]-2-hydroxydec-5-enamide* (**59**). A mixture of **58** (30 mg, 30 μmol) and **12** (17 mg, 45 μmol) were azeotroped with benzene (3 × 3 ml) and dried further under vacuum for 2 h prior reaction. The mixture was cooled to 0° under Ar and dry THF (4 ml) was added. HOAt (12 mg, 91 μmol) was added, followed by EDC (17 mg, 88 μmol). The mixture was stirred at 0° for 5 h, before it was diluted with AcOEt (5 ml) and washed with sat. aq. $NaHCO_3$ soln. (3 ml), H_2O (3 ml) and brine (3 ml). The org. layer was dried ($MgSO_4$) and concentrated *in vacuo* to give the crude product, which was purified by FC (silica gel; 17% AcOEt in hexanes) to afford **59** (35 mg, 86%) and its diastereoisomer (5 mg, 12%) as colorless oils.

Data of **59**: R_f 0.47 (silica gel; 30% AcOEt in hexanes). $[\alpha]_D = +9.9$ ($c = 3.0$, $CHCl_3$): FT-IR (neat): 3401, 2926, 2855, 1654, 1521, 1463, 1380, 1248, 1081, 833, 703. ^{1}H-NMR (600 MHz, C_5D_5N, 300 K): 7.98 (*d*, *J* = 9.5, NH); 7.90–7.86 (*m*, 4 arom. H); 7.74 (br. *s*, OH); 7.50–7.44 (*m*, 6 arom. H); 5.66–5.60 (*m*, Me_2CCHCH_2, H–C(5)); 5.56–5.50 (*m*, H–C(6)); 4.74–4.72 (*m*, H–C(1′)); 4.62 (*d*, *J* = 8.0, H–C(1″)); 4.60–4.56 (*m*, Me_2CCHCH_2, H–C(2)); 4.48–4.45 (*m*, H–C(4″), 1 H of CH_2–C(1′)); 4.36 (*t*, *J* = 6.8, H–C(3″)); 4.26 (*dd*, *J* = 7.3, 9.7, 1 H–C(6″)); 4.22–4.13 (*m*, H–C(5″), 1 H–C(6″), H–C(2′)); 3.92 (*dd*, *J* = 4.0, 10.2, 1 H of CH_2–C(1′)); 3.66 (*t*, *J* = 7.6, H–C(2″)); 2.60–2.58 (*m*, 2 H); 2.33–2.30 (*m*, 1 H); 2.19–2.09 (*m*, 3 H); 1.80–1.73 (*m*, 2 H); 1.70 (*s*, 3 H); 1.68 (*s*, 3 H); 1.65–1.52 (*m*, 5 H); 1.50–1.18 (*m*, 53 H); 1.15 (*s*, 9 H); 0.97 (*s*, 9 H); 0.87 (*t*, *J* = 6.8, 6 H); 0.76–0.64 (*m*, 6 H); 0.27 (*s*, 3 H); 0.20 (*s*, 3 H); −0.19–−0.25 (*m*, 2 H). ^{13}C-NMR (150 MHz, C_5D_5N, 300 K): 174.6 (C(1)); 136.0 (arom. C); 136.0 (arom. C); 136.0 (arom. C); 136.0 (arom. C); 135.9 (Me_2CCHCH_2); 133.9 (arom. C); 133.8 (arom. C); 130.9 (C(6)); 130.3 (Me_2CCHCH_2); 130.3 (arom. C); 129.7 (C(5)); 128.3 (arom. C); 128.3 (arom. C); 128.2 (arom. C); 128.2 (arom. C); 122.9 (C(8′)); 109.7 (Me_2CO_2); 104.0 (C(1″)); 79.8 (C(2″)); 79.7 (C(3″)); 74.0 (C(4″)); 73.7 (C(1′)); 73.0 (C(5″)); 71.8 (C(2′)); 69.3 (CH_2–C(1′)); 68.4 (Me_2CCHCH_2); 63.5 (C(6″)); 52.2 (C(2)); 35.9; 34.3; 32.1; 32.1; 30.8; 30.6; 30.6; 30.6; 30.3, 30.2; 30.1; 30.1; 30.1; 30.0 (7 C); 29.9; 29.6; 29.6; 29.1; 29.0; 29.0; 29.0; 28.3; 27.7; 26.9; 26.9; 26.9; 26.6; 26.2; 26.2; 25.8; 25.0; 23.9; 23.0; 22.9; 19.4; 18.4; 18.3; 16.2; 16.2; 16.1; 14.3; 14.3; 11.4; 11.4; −4.0; −4.3. HR-MS (MALDI-FT): 1362.9943 ($[M + Na]^+$, $C_{82}H_{141}NNaO_9Si_2^+$; calc. 1363.0042).

*(2*R*,5*Z*)-10-[(1*R*,2*S*)-2-Decylcyclopropyl]-*N*-((1*S*,2*R*)-9-[(1*R*,2*S*)-2-decylcyclopropyl]-2-hydroxy-1-{[3,4-*O*-isopropylidene-2-*O*-(3-methylbut-2-enyl)-β-*D*-galactopyranosyloxy]methyl}nonyl)-2-hydroxydec-5-enamide* (**60**). To a soln. of **59** (30 mg, 22 μmol) in dry THF (1.5 ml) at 0° was added a soln. of TBAF (1.0M in THF, 62 μl). The mixture was allowed to warm to 25° and then stirred further for 8 h. The mixture was diluted with AcOEt (5 ml), and washed with sat. aq. NH_4Cl soln. (2 ml), H_2O (2 ml), and brine (2 ml). The org. layer was dried ($MgSO_4$) and concentrated *in vacuo* to give the crude product as a viscous oil, which was then purified by FC (silica gel; 7% MeOH in CH_2Cl_2) to afford **60** (21.5 mg, 97%). Colorless oil. R_f 0.56 (silica gel; 7% MeOH in CH_2Cl_2). $[\alpha]_D = +11.2$ ($c = 2.1$, $CHCl_3$). FT-IR (neat): 3392, 2925, 2854, 1651, 1529, 1462, 1379, 1231, 1080, 1044, 873. ^{1}H-NMR (600 MHz, C_5D_5N, 300 K): 8.23 (*d*, *J* = 9.1, NH); 5.80 (br. *s*, OH); 5.62–5.57 (*m*, H–C(5), Me_2CCHCH_2); 5.53–5.49 (*m*, H–C(6)); 4.71–4.70 (*m*, 1 H of CH_2–C(1′), H–C(1′)); 4.63–4.57 (*m*, H–C(1″), H–C(2), 1 H of Me_2CCHCH_2); 4.54 (*dd*, *J* = 6.3, 1 H of Me_2CCHCH_2); 4.43 (*dd*, *J* = 2.0, 5.5, H–C(4″)); 4.33–4.30 (*m*, H–C(3″), H–C(5″)); 4.24 (*dd*, *J* = 5.3, 11.2, H–C(6″)); 4.16–4.12 (*m*, 1 H–C(6″),

H–C(2′)); 4.04 (*d*, *J* = 6.5, 1 H of CH_2–C(1′)); 3.69 (*t*, *J* = 7.5, H–C(2″)); 3.00 (br. *s*, OH); 2.60–2.56 (*m*, 2 H); 2.33–2.30 (*m*, 1 H); 2.20–2.11 (*m*, 3 H); 1.96–1.82 (*m*, 3 H); 1.75–1.66 (*m*, 1 H); 1.64 (*s*, 3 H); 1.63 (*s*, 3 H); 1.62–1.50 (*m*, 5 H); 1.50–1.17 (*m*, 54 H); 0.85 (*t*, *J* = 6.7, 6 H); 0.75–0.60 (*m*, 6 H); −0.22–−0.26 (*m*, 2 H). ^{13}C-NMR (150 MHz, C_5D_5N, 300 K): 174.9; 136.0; 130.9; 129.7; 123.1; 109.7; 104.3; 79.9; 79.6; 75.0; 74.6; 71.9; 71.2; 70.0; 68.3; 61.9; 54.2; 35.8; 34.9; 32.1; 32.1; 30.6; 30.6; 30.6; 30.2; 30.2; 30.1; 30.0 (8 C); 29.9; 29.9; 29.6; 29.6; 29.0; 29.0; 29.0; 28.9; 28.3; 27.7; 26.6; 26.6; 23.8; 22.9; 22.9; 20.4; 18.1; 16.2; 16.2; 16.2; 16.1; 14.3; 14.3; 11.4; 11.4. HR-MS (MALDI-FT): 1010.8004 ($[M+Na]^+$, $C_{60}H_{109}NaNO_9^+$; calc. 1010.8000).

*(2*R*,5*Z*)-10-[(1*R*,2*S*)-2-Decylcyclopropyl]*-N-*((1*S*,2*R*)-9-[(1*R*,2*S*)-2-decylcyclopropyl]-2-hydroxy-1-[[2-O-(3-methylbut-2-enyl)-β-*D*-galactopyranosyloxy]methyl]nonyl)-2-hydroxydec-5-enamide* (*Plakoside A*; **1**). To a soln. of **60** (20 mg, 21 μmol) in MeOH (1.0 ml) at 25° was added 1.0N aq. HCl soln. (20 μl). The mixture was then heated at 37° for 5 h. The mixture was allowed to cool and diluted with AcOEt (5 ml). The org. layer was washed with sat. aq. $NaHCO_3$ soln. (2 ml), H_2O (2 ml), H_2O (2 ml), and brine (2 ml), dried ($MgSO_4$), and concentrated *in vacuo*. The crude product was purified by FC (silica gel; 7% MeOH in CH_2Cl_2) to afford **1** (18.4 mg, 96%). Amorphous solid. R_f 0.27 (silica gel; 7% MeOH in CH_2Cl_2). $[\alpha]_D = +10.4$ (*c* = 1.6, MeOH). FT-IR ($CHCl_3$ soln.): 3401, 2925, 2857, 1658, 1528, 1465, 1380, 1082. ^{1}H-NMR (600 MHz, C_5D_5N, 300 K): 8.24 (*d*, *J* = 9.4, NH); 5.67 (*t*, *J* = 6.8, Me_2CCHCH_2); 5.61–5.57 (*m*, H–C(5)); 5.53–5.48 (*m*, H–C(6)); 4.79 (*dd*, *J* = 4.8, 10.0, 1 H of CH_2–C(1′)); 4.73–4.70 (*m*, H–C(1′), H–C(1″), 1 H of Me_2CCHCH_2); 4.60 (*dd*, *J* = 3.7, 7.9, H–C(2)); 4.56 (*dd*, *J* = 7.2, 11.7, 1 H of Me_2CCHCH_2); 4.46 (*d*, *J* = 3.0, H–C(4″)); 4.41–4.34 (*m*, CH_2(6″)); 4.20–4.18 (*m*, H–C(2′)); 4.07–4.01 (*m*, 1 H of CH_2–C(1′), H–C(2″), H–C(3″)); 3.92 (*t*, *J* = 6.0, H–C(5″)); 2.62–2.59 (*m*, CH_2(4)); 2.33–2.28 (*m*, 1 H–C(3)); 2.16–2.12 (*m*, 1 H–C(3), Me_2CCHCH_2); 1.98–1.84 (*m*, CH_2(4), 1 H–C(5′)); 1.68–1.56 (*m*, 1 H–C(5′), Me_2CCHCH_2); 1.44–1.15 (*m*, 56 H); 0.85 (*t*, *J* = 6.8, 2 Me); 0.75–0.66 (*m*, 4 H, H–C(1) and H–C(2) of cyclopropyls); 0.66–0.62 (*m*, 1 H of CH_2 of cyclopropyls); −0.21–−0.25 (*m*, 1 H of CH_2 of cyclopropyls). ^{13}C-NMR (150 MHz, C_5D_5N, 300 K): 174.9 (C(1)); 134.9 (Me_2CCHCH_2); 130.8 (C(6)); 129.7 (C(5)); 123.1 (Me_2CCHCH_2); 105.5 (C(1″)); 79.8 (C(2″)); 77.0 (C(5″)); 74.5 (C(3″)); 71.9 (C(2)); 71.2 (C(2′)); 70.3 (C(4″)); 69.9 (CH_2–C(1′)); 69.6 (Me_2CCHCH_2); 62.2 (C(6″)); 54.4 (C(1′)); 35.8 (C(3)); 34.9 (C(3′)); 32.1 (2 $MeCH_2CH_2$); 30.6 (3 C); 30.3 (3 C); 30.1–29.9 (10 C); 29.6 (2 C); 29.0 (C(9′), C(10), C(10)CHCHCH_2, C(9′)CHCHCH_2); 27.7 (Me_2CCHCH_2); 26.8 (C(4′)); 25.7 (1 $MeCHCH_2$); 23.8 (C(4)); 22.9 (2 $MeCH_2$); 18.1 (1 *Me*CCHC_2); 16.2 (4 CH of cyclopropyls); 14.3 (2 Me); 11.4 (2 CH_2 of cyclopropyl). HR-MS (MALDI-FT: 970.7656 ($[M+Na]^+$, $C_{57}H_{105}NNaO_9^+$; calc. 970.7687).

*(2*S*,3*R*,7*Z*)-2-Azido-3-[(*tert*-butyl)dimethylsilyloxy]-1-[6-*O*-[(*tert*-butyl)diphenylsilyl]-3,4-*O*-isopropylidene-2-*O*-(trimethylacetyl)-β-*D*-galactopyranosyloxy]-12-[(1*R*,2*S*)-2-decylcyclopropyl]dodec-7-ene* (**61**). The protocol was followed as for **55** prior to the glycosidation reaction. To a stirred mixture of AgOTf (219 mg, 851 μmol), $SnCl_2$ (161 mg, 851 μmol), and activated 4-Å molecular sieves (500 mg) in dry CH_2Cl_2 (5 ml) under Ar at 0°, was added a soln. of **14** (148 mg, 284 μmol) and glycosyl fluoride **11** (309 mg, 567 μmol) in dry CH_2Cl_2 (5 ml) *via* syringe. To this mixture was added 2,6-di(*tert*-butyl)-4-methylpyridine (70 mg, 340 μmol) in one portion. The mixture was stirred at 0° in the dark for 3 h before it was allowed to warm to 25° and stirred further for 3.5 h. The mixture was diluted with AcOEt (15 ml) and filtered through a pad of *Celite* and rinsed with AcOEt (10 ml). The org. filtrate was washed with sat. aq. $NaHCO_3$ soln. (2 × 5 ml), H_2O (7 ml), and brine (7 ml). The org. extract was dried ($MgSO_4$) and concentrated *in vacuo* to a crude oil, which was then purified by FC (silica gel; 5% AcOEt in hexanes) to afford **61** (292 mg, 98%). Colorless oil. R_f 0.38 (silica gel; 10% AcOEt in hexanes). $[\alpha]_D = +3.2$ (*c* = 2.0, $CHCl_3$). FT-IR (neat): 3054, 2928, 2856, 2099, 1740, 1462, 1428, 1379, 1256, 1222, 1112, 830, 778, 704, 504. ^{1}H-NMR (500 MHz, $CDCl_3$): 7.70–7.66 (*m*, 4 arom. H); 7.43–7.34 (*m*, 6 arom. H); 5.58–5.27 (*m*, H–C(7), H–C(8)); 4.95 (*t*, *J* = 7.7, H–C(2′)); 4.34 (*d*, *J* = 8.1, H–C(1′)); 4.29 (*dd*, *J* = 1.8, 5.5, H–C(4′)); 4.14 (*dd*, *J* = 5.4, 7.3, H–C(3′)); 3.97 (*dd*, *J* = 9.5, 12.3, 1 H–C(6′)); 3.91 (*dd*, *J* = 9.5, 12.3, 1 H–C(6′)); 3.88–3.85 (*m*, H–C(5′)); 3.78 (*dd*, *J* = 8.5, 11.7, 1 H–C(1)); 3.73–3.70 (*m*, H–C(3)); 3.54–3.51 (*m*, 1 H–C(1), H–C(2)); 2.01–1.97 (*dd*, *J* = 6.6, 13.6, CH_2(6), CH_2(9)); 1.56–1.54 (*m*, 1 H–C(4), 1 Me of Me_2CCHCH_2); 1.42–1.12 (*m*, 39 H); 1.04 (*s*, *t*-Bu); 0.87 (*t*, *J* = 7.0, *Me*CH_2); 0.84 (*s*, *t*-Bu); 0.63 (*m*, 2 CH of cyclopropyl); 0.57–0.53 (*m*, 1 H of cyclopropyl); 0.02 (*s*, Me_2Si), −0.34 (*m*, 1 H of CH_2 of cyclopropyl). ^{13}C-NMR (125 MHz, $CDCl_3$): 176.8; 135.6; 135.6; 135.5; 135.5; 133.3; 133.2; 129.7; 129.7; 129.1; 127.7; 127.7; 127.6; 110.3; 100.4; 77.2; 73.4; 73.2; 72.7; 71.9; 67.8; 65.2; 62.4; 38.7; 32.4; 31.9; 30.2; 29.9; 29.7; 29.7; 29.7; 29.7; 29.7; 29.7; 29.4; 28.7; 28.6; 27.7; 27.3; 27.3; 27.1 (4 C); 26.7; 26.7; 26.7; 26.3; 25.8; 25.8; 25.8; 24.8; 22.7; 19.2; 18.0; 15.8; 15.7; 14.1; 10.9; 1.0; −4.6; −4.6. HR-MS (MALDI-FT): 1082.7000 ($[M+Na]^+$, $C_{61}H_{101}N_3NaO_8Si_2^+$; calc. 1082.7025).

*(2*S*,3*R*,7*Z*)-2-Azido-3-[(*tert*-butyl)dimethylsilyloxy]-1-[6-*O*-[(*tert*-butyl)diphenylsilyl]-3,4-*O*-isopropylidene-β-*D*-galactopyranosyloxy]-12-[(1*R*,2*S*)-2-decylcyclopropyl]dodec-7-ene* (**62**). To a soln. of **61** (80 mg, 75 μmol) in dry CH_2Cl_2 (1.5 ml) at −78° was dropwise added a soln. of DIBAL (1.0M in CH_2Cl_2, 113 μl, 113 μmol). The mixture was stirred at −78° for 15 min before it was quenched by the addition of MeOH (300 μl). The mixture

was diluted with AcOEt (5 ml) and allowed to warm to 25°. Sat. aq. soln. of *Rochelle*'s salt (1.5 ml) was added, and the resulting cloudy mixture was stirred further until it became clear (30 min). The org. layer was further washed with H_2O (2 ml), brine (2 ml), dried ($MgSO_4$), and concentrated *in vacuo*. The crude product was purified by FC (silica gel; 12% AcOEt in hexanes) to afford pure **62** (73 mg, 99%). Colorless oil. R_f 0.16 (silica gel; 10% AcOEt in hexanes. $[\alpha]_D = +2.1$ ($c = 1.3$, $CHCl_3$). FT-IR (neat): 3416, 2928, 2856, 2099, 1464, 1379, 1252, 1108, 1032, 832, 778, 704. ^{1}H-NMR (400 MHz, $CDCl_3$): 7.70–7.66 (*m*, 4 arom. H); 7.44–7.32 (*m*, 6 arom. H); 5.40–5.27 (*m*, H–C(7), H–C(8)); 4.29 (*dd*, $J = 1.7$, 7.1, H–C(4′)); 4.15 (*d*, $J = 8.2$, H–C(1′)); 4.07 (*dd*, $J = 5.5$, 7.3, H–C(3′)); 3.97 (*dd*, $J = 9.2$, 12.3, H–C(6)); 3.92–3.83 (*m*, H–C(5′), 1 H–C(6′), 1 H–C(1)); 3.77–3.73 (*m*, H–C(3)); 3.66 (*dd*, $J = 7.3$, 10.6, H–C(2′)); 3.58–3.53 (*m*, 1 H–C(1), H–C(2)); 2.42 (br. *s*, OH); 2.03–1.99 (*m*, CH_2(6), CH_2(9)); 1.60–1.56 (*m*, 1 H–C(4)); 1.42–1.21 (*m*, 31 H); 1.12–1.09 (*m*, 1 H–C(12), 1 H of CH_2-cyclopropyl); 1.04 (*s*, *t*-Bu); 0.87 (*t*, $J = 7.0$, $MeCH_2$); 0.84 (*s*, *t*-Bu); 0.63 (*m*, 2 CH of cyclopropyl); 0.57–0.53 (*m*, 1 H of CH_2 of cyclopropyl); 0.02 (*d*, $J = 2.8$, Me_2Si); −0.34 (*m*, 1 H of CH_2 of cyclopropyl). ^{13}C-NMR (100 MHz, $CDCl_3$): 135.6; 135.6; 135.5; 135.5; 133.3; 133.2; 130.6; 129.7; 129.7; 129.0; 127.7; 127.7; 127.5; 127.5; 110.0; 102.2 (C(1′)); 78.5 (C(3′)); 73.8 (C(5′)); 73.6 (C(4′)); 73.1 (C(2′)); 71.8 (C(3)); 67.8 (C(1)); 65.8 (C(2)); 62.4 (C(6′)); 32.8; 31.9; 30.2; 29.9; 29.7 (4 C); 29.4; 28.7; 28.6; 28.2; 27.3; 27.2; 26.7; 26.7; 26.7; 26.3; 25.9; 25.9; 25.9; 24.6; 22.7; 19.2; 18.0; 15.7; 15.7; 14.1; 10.9; 1.0; −4.5, −4.6. HR-MS (MALDI-FT): 998.6411 ($[M + Na]^+$, $C_{56}H_{93}N_3NaO_7Si_2^+$; calc. 998.6449).

*(2S,3R,7Z)-2-Azido-3-[(*tert*-butyl)dimethylsilyoxy]-1-[6-*O*-[(*tert*-butyl)diphenylsilyl]-3,4-*O*-isopropylidene-2-*O*-(3-methylbut-2-enyl)-β-*D*-galactopyranosyloxy}-12-[(1R,2S)-2-decylcyclopropyl]dec-7-ene* (**63**). To a soln. of **62** (70 mg, 72 μmol) in dry DMF (1 ml) at 0° was added NaH (60% in mineral oil, 3.7 mg, 84 μmol) in one portion. The mixture was stirred for 5 min followed by the addition of prenyl bromide (12 μl, 108 μmol). The mixture was then stirred at 0° for 5 h before it was diluted with AcOEt (7 ml) and washed with H_2O (2 ml) and brine (2 ml). The org. layer was dried ($MgSO_4$) and concentrated *in vacuo* to give the crude product as a viscous oil, which was then purified by FC (silica gel; 12% AcOEt in hexanes) to afford **63** (64 mg, 85%). Colorless oil. R_f 0.16 (silica gel; 17% AcOEt in hexanes). $[\alpha]_D = +5.7$ ($c = 3.5$, $CHCl_3$). FT-IR (neat): 2928, 2855, 2099, 1463, 1378, 1254, 1110, 1044, 833, 704. ^{1}H-NMR (500 MHz, $CDCl_3$): 7.70–7.66 (*m*, 4 arom. H); 7.43–7.34 (*m*, 6 arom. H); 5.39–5.28 (*m*, H–C(7), H–C(8), Me_2CCHCH_2); 4.25–4.24 (*m*, H–C(4′), Me_2CCHCH_2); 4.20 (*d*, $J = 8.1$, H–C(1′)); 4.06 (*t*, $J = 6.9$, H–C(3′)); 3.94 (*dd*, $J = 7.7$, 9.8, 1 H–C(6′)); 3.90–3.84 (*m*, 1 H–C(1), 1 H–C(6′)); 3.79–3.73 (*m*, H–C(3), H–C(5′)); 3.66–3.62 (*m*, H–C(2)); 3.55 (*dd*, $J = 4.6$, 10.3, 1 H–C(1)); 3.30 (*t*, $J = 7.4$, H–C(2′)); 2.00–1.96 (*m*, CH_2(6), CH_2(9)); 1.72 (*s*, 1 Me_2CCHCH_2); 1.67 (*s*, 1 Me_2CCHCH_2); 1.61–1.55 (*m*, 1 H–C(4)); 1.48–1.25 (*m*, 31 H); 1.12–1.09 (*m*, H–C(12), 1 H of CH_2-cyclopropyl); 1.04 (*s*, *t*-Bu); 0.87 (*t*, $J = 7.0$, $MeCH_2$); 0.85 (*s*, *t*-Bu)); 0.63 (*m*, 2 CH of cyclopropyl); 0.57–0.54 (*m*, 1 H of CH_2 of cyclopropyl); 0.03 (*s*, Me_2Si); −0.34 (*m*, 1 H of CH_2 cyclopropyl). ^{13}C-NMR (100 MHz, $CDCl_3$): 137.2; 135.6; 135.6; 135.5; 135.5; 133.3; 133.2; 130.5; 129.7; 129.7; 129.1; 127.7; 127.7; 127.7; 127.6; 121.4; 110.0; 109.7; 102.6 (C(1′)); 79.3 (C(2′)); 79.1 (C(3′)); 73.2 (C(5′)); 73.2 (C(4′)); 72.3 (C(3)); 68.6 (C(1)); 68.4 (Me_2CCHCH_2); 65.5 (C(2)); 62.5 (C(6′)); 32.5; 31.9; 30.2; 29.9; 29.7 (4 C); 29.4; 28.7; 28.6; 28.0; 27.3; 27.3; 26.7; 26.7; 26.7; 26.3; 25.8; 25.8; 25.8; 25.0; 24.6; 22.7; 19.2; 18.1; 18.0; 15.7; 15.7; 14.1; 10.9; −4.5; −4.6. HR-MS (MALDI-FT): 1066.7048 ($[M + Na]^+$, $C_{61}H_{101}N_3NaO_7Si_2^+$; calc. 1066.7075).

*(2S,3R,7Z)-2-Amino-3-[(*tert*-butyl)dimethylsilyloxy]-1-[6-*O*-[(*tert*-butyl)diphenylsilyl]-3,4-*O*-isopropylidene-2-*O*-(3-methylbut-2-enyl)-β-*D*-galactopyranosyloxy}-12-[(1R,2S)-2-decylcyclopropyl]dec-7-ene* (**64**). A soln. of **63** (56 mg, 54 μmol) and Ph_3P (28 mg, 107 μmol) in benzene (1 ml) was heated at 45° for 1 h before H_2O (2 μl) was added. The mixture was then heated at 45° for 7.5 h before it was cooled and diluted with AcOEt (5 ml), and washed with sat. aq. NH_4Cl soln. (3 ml) and brine (3 ml). The org. layer was dried ($MgSO_4$) and concentrated *in vacuo* to give the crude product as a viscous oil, which was then purified by FC (silica gel; 12% AcOEt in hexanes) to afford **64** (47 mg, 86%). Colorless oil. R_f 0.15 (silica gel; 12% AcOEt in hexanes). $[\alpha]_D = +1.8$ ($c = 3.0$, $CHCl_3$). FT-IR (neat): 3389, 2927, 2856, 1461, 1376, 1248, 1083, 1038, 931, 704. ^{1}H-NMR (500 MHz, $CDCl_3$): 7.70–7.65 (*m*, 4 arom. H); 7.43–7.33 (*m*, 6 arom. H); 5.36–5.30 (*m*, H–C(7), H–C(8), Me_2CCHCH_2); 4.27–4.24 (*m*, H–C(4′), Me_2CCHCH_2); 4.20 (*d*, $J = 8.1$, H–C(1′)); 4.06 (*dd*, $J = 5.6$, 7.0, H–C(3′)); 3.93 (*dd*, $J = 7.7$, 9.8, 1 H–C(6′)); 3.87 (*dd*, $J = 9.7$, 15.6, 1 H–C(6′)); 3.78 (*m*, H–C(5′)); 3.68–3.64 (*m*, 1 H–C(1), H–C(3)); 3.60 (*dd*, $J = 4.2$, 5.5, 1 H–C(1)); 3.29 (*t*, $J = 7.4$, H–C(2′)); 3.00 (*m*, H–C(2)); 2.02–1.95 (*m*, CH_2(6), CH_2(9)); 1.71 (*s*, 1 Me_2CCHCH_2); 1.65 (*s*, 1 Me_2CCHCH_2); 1.61–1.55 (*m*, 1 H–C(4)); 1.48–1.25 (*m*, 33 H); 1.12–1.09 (*m*, H–C(12), 1 H of CH_2-cyclopropyl); 1.03 (*s*, *t*-Bu); 0.87 (*t*, $J = 7.0$, $MeCH_2$); 0.85 (*s*, *t*-Bu); 0.63 (*m*, 2 CH of cyclopropyl); 0.57–0.53 (*m*, 1 H of CH_2 of cyclopropyl); 0.03 (*dd*, $J = 3.6$, Me_2Si); −0.35 (*m*, 1 H of CH_2 of cyclopropyl). ^{13}C-NMR (125 MHz, $CDCl_3$): 137.2; 135.6; 135.6; 135.5; 135.5; 133.4; 133.2; 130.3; 129.7; 129.6; 129.3; 127.7; 127.7; 127.6; 127.6; 121.4; 109.6; 109.7; 102.9 (C(1′)); 79.3 (C(2′)); 79.1 (C(3′)); 73.8 (C(3)); 73.2 (C(4′)); 73.0 (C(5′)); 71.7 (C(1)); 68.3 (Me_2CCHCH_2); 62.4 (C(6′)); 54.5 (C(2)); 32.3; 31.9; 30.2; 29.9; 29.7 (4 C);

29.3; 28.7; 28.6; 28.0; 27.3; 27.3; 26.7; 26.7; 26.7; 26.3; 25.8; 25.8; 25.8; 25.8; 25.2; 22.7; 19.2; 18.1; 18.0; 15.7; 15.7; 14.1; 10.9; −4.3; −4.6. HR-MS (MALDI-FT): 1040.7172 ($[M+Na]^+$, $C_{61}H_{103}NNaO_7Si_2^+$; calc. 1040.7170).

*(2*R*,5*Z*)*-N-*[(1*S*,2*R*,6*Z*)-2-[(*tert-*Butyl)dimethylsilyloxy]-1-({6*-O-*[(*tert-*butyl)diphenylsilyl]-3,4*-O-*isopropylidene-2*-O-*(3-methylbut-2-enyl)-β-*D*-galactopyranosyloxy}methyl)-11-[(1*R*,2*S*)-2-decylcyclopropyl]undec-6-enyl]-10-[(1*R*,2*S*)-2-decylcyclopropyl]-2-hydroxydec-5-enamide* (**65**). A mixture of **64** (42 mg, 41 μmol) and **12** (23 mg, 62 μmol) were azeotroped with benzene (3 × 3 ml) and dried further under vacuum for 2 h. The mixture was cooled to 0° under Ar, and dry THF (4 ml) was added. HOAt (17 mg, 128 μmol) was added, followed by EDC (24 mg, 124 μmol). The mixture was stirred at 0° for 5 h, and then diluted with AcOEt (5 ml) and washed with sat. aq. $NaHCO_3$ soln. (3 ml), H_2O (3 ml), and brine (3 ml). The org. layer was dried ($MgSO_4$) and concentrated *in vacuo* to give the crude product as a viscous oil, which was then purified by FC (silica gel; 7% AcOEt in hexanes) to afford **65** (48 mg, 86%). Colorless oil. R_f 0.47 (silica gel; 30% AcOEt in hexanes). $[\alpha]_D = +9.4$ ($c = 2.5$, $CHCl_3$). FT-IR (neat): 3401, 2926, 2855, 1654, 1520, 1463, 1379, 1248, 1155, 1083, 1038, 833, 703, 507. ^{1}H-NMR (600 MHz, C_5D_5N, 300 K): 7.98 (*d*, *J* = 9.4, NH); 7.90–7.86 (*m*, 4 arom. H); 7.50–7.44 (*m*, 6 arom. H); 5.64–5.60 (*m*, H−C(5), Me_2CCHCH_2); 5.56–5.53 (*m*, H−C(6), H−C(6′), H−C(7′)); 4.74–4.72 (*m*, H−C(1′)); 4.62–4.56 (*m*, H−C(2), H−C(1″), Me_2CCHCH_2); 4.48–4.45 (*m*, H−C(4″), 1 H of CH_2−C(1′)); 4.36 (*t*, *J* = 6.8, H−C(3″)); 4.26 (*t*, *J* = 9.4, 1 H−C(6″)); 4.22–4.13 (*m*, H−C(2′), H−C(5″), 1 H−C(6″)); 3.90 (*dd*, *J* = 3.7, 10.2, 1 H of CH_2−C(1′)); 3.65 (*t*, *J* = 7.8, H−C(2″)); 2.59 (*m*, CH_2(4)); 2.33–2.31 (*m*, 1 H−C(3)); 2.19–2.09 (*m*, 1 H−C(3), CH_2(5′), CH_2(8′)); 1.85–1.75 (*m*, 3 H); 1.75–1.71 (*s*, Me); 1.69 (*s*, Me); 1.57–1.18 (*m*, 58 H); 1.15 (*s*, *t*-Bu); 0.98 (*s*, *t*-Bu)); 0.87 (*t*, *J* = 7.0, 2 *Me*CH_2); 0.74–0.64 (*m*, 4 CH of cyclopropyls, 1 H of CH_2 of cyclopropyls); 0.24 (*dd*, *J* = 40.1, Me_2Si); −0.18–−0.24 (*m*, 1 H of CH_2 cyclopropyls). ^{13}C-NMR (150 MHz, C_5D_5N, 300 K): 174.6 (C(1)); 136.0 (arom. C); 136.0 (arom. C); 136.0 (arom. C); 136.0 (arom. C); 135.8 (Me_2CCHCH_2); 133.9 (arom. C); 133.8 (arom. C); 130.9 (C(6)); 130.6 (C(7′)); 130.3 (arom. C); 130.3 (arom. C); 130.0 (Me_2CCHCH_2); 129.7 (C(5)); 128.3 (arom. C); 128.3 (arom. C); 128.2 (arom. C); 128.2 (arom. C); 123.1 (Me_2CCHCH_2); 109.7 (Me_2CO_2); 104.0 (C(1″)); 79.8 (C(2″)); 79.7 (C(3″)); 74.0 (C(4″)); 73.7 (C(5″)); 72.8 (C(2′)); 71.8 (C(2)); 69.3 (CH_2−C(1′)); 68.4 (Me_2CCHCH_2); 63.5 (C(6″)); 52.2 (C(1′)); 35.9, 33.8; 32.2; 32.2; 30.8; 30.6; 30.3; 30.3; 30.2; 30.1; 29.9 (10 C); 29.7; 29.7; 29.1; 29.0; 29.0; 28.9; 28.3; 27.8; 27.7; 27.0; 27.0; 27.0; 26.6; 26.2; 26.2; 26.2; 25.8; 25.0; 24.0; 23.0; 23.0; 19.4; 18.4; 18.3; 16.2; 16.2; 16.2; 14.3; 14.3; 11.4; 11.4; −4.0; −4.3. HR-MS (MALDI-FT): 1389.0269 ($[M+Na]^+$, $C_{84}H_{143}NNaO_9Si_2^+$; calc. 1389.0199).

*(2*R*,5*Z*)-10-[(1*R*,2*S*)-2-Decylcyclopropyl]*-N-*((1*S*,2*R*,6*Z*)-11-[(1*R*,2*S*)-2-decylcyclopropyl]-2-hydroxy-1-{[3,4-isopropylidene-2*-O-*(3-methylbut-2-enyl)-β-*D*-galactopyranosyloxy]methyl}undec-6-enyl)-2-hydroxydec-5-enamide* (**66**). To a soln. of **65** (25 mg, 11 μmol) in dry THF (0.5 ml) at 0° was added a soln. of TBAF (1.0M in THF, 55 μl, 55 μmol). The mixture was allowed to warm to 25° and then stirred further for 5 h before it was diluted with AcOEt (5 ml) and washed with sat. aq. NH_4Cl soln. (2 ml), H_2O (2 ml), and brine (2 ml). The org. layer was dried ($MgSO_4$) and concentrated *in vacuo* to give the crude product as a viscous oil, which was then purified by FC (silica gel; 7% MeOH in CH_2Cl_2) to afford **66** (18 mg, 97%). Colorless oil. R_f 0.45 (silica gel; 7% MeOH in CH_2Cl_2). $[\alpha]_D = +13.0$ ($c = 2.7$, $CHCl_3$). FT-IR (neat): 3389, 2924, 2854, 1652, 1519, 1458, 1378, 1079. ^{1}H-NMR (600 MHz, C_5D_5N, 300 K): 8.21 (*d*, *J* = 9.2, NH); 7.70 (br. *s*, OH); 6.65 (br. *s*, OH); 6.43 (br. *s*, OH); 5.61–5.58 (*m*, H−C(5), Me_2CCHCH_2); 5.52–5.46 (*m*, H−C(6), H−C(6′), H−C(7′)); 4.71–4.69 (*m*, H−C(1′), 1 H of CH_2−C(1′)); 4.60–4.57 (*m*, H−C(2), H−C(1″), 1 H of Me_2CCHCH_2); 4.54–4.51 (*m*, 1 H of Me_2CCHCH_2); 4.43 (*dd*, *J* = 2.0, 5.5, H−C(4″)); 4.33–4.30 (*m*, H−C(3″), H−C(5″)); 4.24 (*dd*, *J* = 5.3, 11.2, 1 H−C(6″)); 4.16–4.14 (*m*, H−C(2′), 1 H−C(6″)); 4.03–4.02 (*m*, 1 H of CH_2−C(1′)); 3.68 (*t*, *J* = 12.0, H−C(2″)); 2.60–2.59 (*m*, CH_2(4)); 2.31–2.30 (*m*, 1 H−C(3)); 2.20–2.10 (*m*, 1 H−C(3), CH_2(7), CH_2(5′), CH_2(8′)); 1.96–1.84 (*m*, CH_2(3′), 1 H−C(4′)); 1.67 (*m*, 1 H−C(4′), Me_2C); 1.56 (*s*, Me); 1.44–1.17 (*m*, 51 H); 0.85 (*t*, *J* = 7.0, 2 *Me*CH_2); 0.71 (*m*, 4 CH of cyclopropyls); 0.67–0.62 (*m*, 1 H of CH_2 of cyclopropyls); −0.21–−0.25 (*m*, 1 H of CH_2 of cyclopropyls). ^{13}C-NMR (150 MHz, C_5D_5N, 300 K): 174.9 (C(1)); 136.0 (Me_2CCHCH_2); 130.9 (C(6)); 130.3 (C(7′)); 130.2 (C(6′)); 129.7 (C(5)); 123.1 (Me_2CCHCH_2); 109.7 (Me_2CO_2); 104.3 (C(1″)); 79.9; 79.6; 75.0; 74.6; 71.9; 71.1; 69.9; 68.3; 65.8; 61.9; 54.1; 35.8; 34.5; 32.1; 32.1; 30.6; 30.3; 30.2; 30.1; 30.1; 30.0; 29.9 (8 C); 29.6; 29.6; 29.0; 29.0; 29.0; 28.9; 28.3, 27.8; 27.7; 26.8; 26.6; 25.7; 23.9; 22.9; 18.2; 16.2; 16.2; 16.2; 16.1; 14.3; 14.3; 11.4; 11.4. HR-MS (MALDI-FT): 1036.8195 ($[M+Na]^+$, $C_{62}H_{111}NNaO_9^+$; calc. 1036.8156).

*(2*R*,5*Z*)-10-[(1*R*,2*S*)-2-Decylcyclopropyl]*-N-*((1*S*,2*R*,6*Z*)-11-[(1*R*,2*S*)-2-decylcyclopropyl]-2-hydroxy-1-{[2-O-(3-methylbut-2-enyl)-β-*D*-galactopyranosyloxy]methyl}undec-6-enyl)-2-hydroxydec-5-enamide* (*Plakoside B*, **2**). To a soln. of **66** (17 mg, 18 μmol) in MeOH (1 ml) at 25° was added aq. HCl soln. (1.0N, 20 μl), and the mixture was heated at 37° for 5 h. The mixture was cooled and diluted with AcOEt (5 ml), and washed with sat. aq. $NaHCO_3$ soln. (2 ml), H_2O (2 ml), and brine (2 ml). The org. layer was dried ($MgSO_4$) and concentrated *in*

vacuo to give the crude product as a viscous oil, which was then purified by FC (silica gel; 7% MeOH in CH_2Cl_2) to afford **2** (16 mg, 98%). Amorphous solid. R_f 0.43 (silica gel; 7% MeOH in CH_2Cl_2). $[\alpha]_D = +9.6$ ($c = 1.4$, MeOH). FT-IR ($CHCl_3$ soln.): 3382, 2922, 2852, 1644, 1520, 1454, 1373, 1079. ^{1}H-NMR (600 MHz, C_5D_5N, 300 K): 8.23 (*d*, *J* = 9.3, NH); 5.67 (*m*, Me_2CCHCH_2); 5.59 (*m*, H–C(5)); 5.53–5.46 (*m*, H–C(6), H–C(6′), H–C(7′)); 4.79 (*dd*, *J* = 4.8, 10.0, 1 H of CH_2–C(1′)); 4.73–4.70 (*m*, H–C(1′), H–C(1″), 1 H of Me_2CCHCH_2); 4.60–4.55 (*m*, H–C(2), 1 H of Me_2CCHCH_2); 4.46 (*d*, *J* = 2.4, H–C(4″)); 4.41–4.34 (*m*, CH_2(6″)); 4.19 (*t*, *J* = 7.1, H–C(2′)); 4.07–4.01 (*m*, H–C(2″), H–C(3″), 1 H of CH_2–C(1′)); 3.92 (*t*, *J* = 5.8, H–C(5″)); 2.60–2.59 (*m*, CH_2(4)); 2.33–2.31 (*m*, 1 H–C(3)); 2.21–2.11 (*m*, 1 H–C(3), CH_2(7), CH_2(5′), CH_2(8′)); 1.98–1.87 (*m*, CH_2(3′), 1 H–C(4′)); 1.67 (*m*, 1 H–C(4′)); 1.58 (*s*, Me_2CCHCH_2); 1.44–1.23 (*m*, 55 H); 0.85 (*t*, *J* = 7.0, 2 $MeCH_2$); 0.71 (*m*, 4 CH of cyclopropyls); 0.67–0.62 (*m*, 2 H, 1 H of CH_2 of cyclopropyls); −0.21– −0.25 (*m*, 1 H of CH_2 of cyclopropyls). ^{13}C-NMR (150 MHz, C_5D_5N, 300 K): 174.9 (C(1′)); 135.0 (Me_2CCHCH_2); 130.9 (C(6)); 130.3 (C(7′)); 130.2 (C(6′)); 129.7 (C(5)); 123.1 (Me_2CCHCH_2); 105.5 (C(1″)); 79.8 (C(2″)); 77.0 (C(5″)); 74.5 (C(3″)); 71.9 (C(2)); 71.1 (C(2′)); 70.3 (C(4″)); 69.9 (CH_2–C(1′)); 69.6 (Me_2CCHCH_2); 62.2 (C(6″)); 54.3 (C(1′)); 35.9 (C(3)); 34.5 (C(3′)); 32.1 (2 $MeCH_2CH_2$); 30.6; 30.6; 30.3; 30.2; 30.1; 30.1; 30.0; 29.9 (7 C); 29.6; 29.6; 29.0 (C(10), C(13), C(11′), CH_2 of cyclopropyl); 27.8 (C(7), C(5′), C(8′)); 26.8 (C(4′)); 25.7 (1 Me_2CCHCH_2); 23.9 (C(4)); 22.9 (2 $MeCH_2CH_2$); 18.1 (1 Me_2CCHCH_2); 16.2 (4 CH of cyclopropyls): 14.3 (2 $MeCH_2$); 11.4 (2 CH_2 of cyclopropyl). HR-MS (MALDI-FT): 996.7850 ($[M+Na]^+$, $C_{59}H_{107}NNaO_9^+$; calc. 996.7843).

*(2*R*,5*Z*)-10-[(1*R*,2*S*)-2-Decylcyclopropyl]*-N*-((1*S*,2*R*)-9-[(1*R*,2*S*)-2-decylcyclopropyl]-2-hydroxy-1-{[2-O-(prop-2-enyl)-β-*D*-galactopyranosyloxy]methyl}nonyl)-2-hydroxydec-5-enamide* (**3**). Amorphous solid. R_f 0.39 (silica gel; 7% MeOH in CH_2Cl_2).^{1}H-NMR (600 MHz, C_5D_5N, 300 K): 8.24 (*d*, *J* = 10.8, NH); 6.25–6.17 (*m*, 1 H); 5.63–5.59 (*m*, 1 H); 5.51–5.42 (*m*, 2 H); 5.51 (*d*, *J* = 12.4, 1 H); 4.76–4.71 (*m*, 4 H); 4.66–4.64 (*m*, 1 H); 4.57–4.50 (*m*, 2 H); 4.26–4.21 (*m*, 2 H); 4.11–4.03 (*m*, 3 H); 3.92 (*t*, *J* = 7.9, 1 H); 2.63–2.59 (*m*, 2 H); 2.33–2.28 (*m*, 1 H); 2.16–2.12 (*m*, 3 H); 1.98–1.84 (*m*, 3 H); 1.68–1.56 (*m*, 7 H); 1.44–1.15 (*m*, 52 H); 0.85 (*t*, *J* = 6.9, 6 H); 0.75–0.66 (*m*, 4 H); 0.66–0.62 (*m*, 2 H); −0.21– −0.26 (*m*, 2 H). HR-MS (MALDI-FT): 942.7372 ($[M+Na]^+$, $C_{55}H_{101}NNaO_9^+$; calc. 942.7374).

*(2*R*,5*Z*)-10-[(1*R*,2*S*)-2-Decylcyclopropyl]*-N*-[(1*S*,2*R*)-9-[(1*R*,2*S*)-2-decylcyclopropyl]-1-({2-O-[(2*E*,6*E*)-3,7-dimethylocta-2,6-dienyl]-β-*D*-galactopyranosyloxy}methyl)-2-hydroxynonyl]-2-hydroxydec-5-enamide* (**4**). Amorphous solid. R_f 0.43 (silica gel; 7% MeOH in CH_2Cl_2). ^{1}H-NMR (500 MHz, $CDCl_3$): 293 K): 7.48 (*d*, *J* = 7.4, NH); 5.43–5.38 (*m*, 3 H); 5.11 (*t*, *J* = 6.2, 1 H); 4.41–4.37 (*dd*, *J* = 7, 11.8, 1 H); 4.33–4.23 (*m*, 4 H); 4.16–4.12 (*m*, 2 H); 4.08–3.92 (*m*, 4 H); 3.89 (br. *s*, 2 H); 3.69 (br. *s*, 1 H); 3.56–3.55 (*m*, 1 H); 3.50–3.48 (*m*, 2 H); 3.40 (*t*, *J* = 8.1, 1 H); 3.01 (br. *s*, 1 H); 2.23–2.22 (*m*, 2 H); 2.11–2.03 (*m*, 6 H); 1.98–1.94 (*m*, 1 H); 1.85–1.82 (*m*, 6 H); 1.75–1.65 (*m*, 6 H); 1.62 (*s*, 3 H); 1.44–1.15 (*m*, 51 H); 0.85 (*t*, *J* = 6.6, 6 H); 0.65–0.60 (*m*, 4 H); 0.55–0.53 (*m*, 2 H); −0.25– −0.27 (*m*, 2 H). HR-MS (MALDI-FT): 1038.8317 ($[M+Na]^+$, $C_{62}H_{113}NaNO_9^+$; calc. 1038.8313).

*(2*R*,5*Z*)-N-{(1*S*,2*R*)-1-[(2-O-Benzyl)-β-*D*-galactopyranosyloxy)methyl]-9-[(1*R*,2*S*)-2-decylcyclopropyl]-2-hydroxynonyl}-10-[(1*R*,2*S*)-2-decylcyclopropyl]-2-hydroxydec-5-enamide* (**5**). Amorphous solid. R_f 0.40 (silica gel; 7% MeOH in CH_2Cl_2). ^{1}H-NMR (600 MHz, C_5D_5N, 300 K): 8.30 (*d*, *J* = 10.5, NH); 7.68 (*d*, *J* = 9.16, 2 H); 7.28 (*t*, *J* = 8.8, 2 H); 7.22 (*t*, *J* = 7.2, 1 H); 5.57–5.55 (*m*, 1 H); 5.52–5.47 (*m*, 1 H); 5.37 (*d*, *J* = 14.8, 1 H); 4.99 (*d*, *J* = 14.2, 1 H); 4.82 (*d*, *J* = 9.2, 1 H); 4.77–4.72 (*m*, 2 H); 4.61–4.60 (*m*, 1 H); 4.49–4.48 (*m*, 1 H); 4.44–4.36 (*m*, 2 H); 4.20–4.10 (*m*, 3 H); 3.95 (*t*, *J* = 5.8, 1 H); 2.60–2.58 (*m*, 2 H); 2.32–2.29 (*m*, 1 H); 2.16–2.12 (*m*, 3 H); 1.94–1.84 (*m*, 3 H); 1.68–1.56 (*m*, 7 H); 1.44–1.15 (*m*, 52 H); 0.85 (*t*, *J* = 6.9, 6 H); 0.75–0.66 (*m*, 4 H); 0.66–0.62 (*m*, 2 H); −0.21– −0.26 (*m*, 2 H). HR-MS (MALDI-FT): 992.77 ($[M+Na]^+$, $C_{59}H_{103}NaNO_9^+$; calc. 992.7530).

*(2*R*,5*Z*)-10-[(1*R*,2*S*)-2-Decylcyclopropyl]*-N*-{(1*S*,2*R*)-9-[(1*R*,2*S*)-2-decylcyclopropyl]-1-[(β-*D*-galacto-pyranosyloxy)methyl]-2-[(prop-2-enyl)oxy]nonyl}-2-hydroxydec-5-enamide* (**6**). Amorphous solid. R_f 0.39 (silica gel; 7% MeOH in CH_2Cl_2). ^{1}H-NMR (500 MHz, $CDCl_3$, 293 K): 7.32 (*d*, *J* = 9.2, NH); 5.37–5.28 (*m*, 3 H); 4.90 (br. *s*, 1 H); 4.76 (br. *s*, 1 H); 4.39 (br. *s*, 2 H); 4.23 (*d*, *J* = 6.6, 1 H); 4.17–4.10 (*m*, 2 H); 4.02–3.89 (*m*, 5 H); 3.84–3.82 (*m*, 3 H); 3.58 (*m*, 2 H); 3.48 (*t*, *J* = 6.2, 1 H); 3.40–3.39 (*m*, 1 H); 2.96 (*t*, *J* = 8.1, 1 H); 2.16 (*m*, 2 H); 2.03–1.94 (*m*, 5 H); 1.77–1.72 (*m*, 5 H); 1.64–1.61 (*m*, 5 H); 1.47–1.11 (*m*, 49 H); 1.11–1.01 (*m*, 4 H); 0.86 (*t*, *J* = 7.0, 3 H); 0.63–0.61 (*m*, 4 H); 0.56–0.52 (*m*, 2 H); −0.26– −0.29 (*m*, 2 H). HR-MS (MALDI-FT): 970.7658 ($[M+Na]^+$, $C_{57}H_{105}NaNO_9^+$; calc. 970.7687).

*(2*R*,5*Z*)-10-[(1*R*,2*S*)-2-Decylcyclopropyl]*-N*-((1*S*,2*R*,6*Z*)-11-[(1*R*,2*S*)-2-decylcyclopropyl]-2-hydroxy-1-{[2-O-(prop-2-enyl)-β-*D*-galactopyranosyloxy]methyl}undec-6-enyl)-2-hydroxydec-5-enamide* (**7**). Amorphous solid. R_f 0.43 (silica gel; 7% MeOH in CH_2Cl_2). ^{1}H-NMR (600 MHz, C_5D_5N, 300 K): 8.25 (*d*, *J* = 9.2, NH); 6.19–6.12 (*m*, 1 H); 5.62–5.58 (*m*, 1 H); 5.52–5.45 (*m*, 3 H); 5.32 (*dd*, *J* = 1.7, 11.7, 1 H); 4.98 (*d*, *J* = 10.7, 1 H);

4.73–4.71 (*d*, 4 H); 4.61–4.59 (*m*, 1 H); 4.51–4.48 (*m*, 1 H); 4.46–4.45 (*m*, 1 H); 4.40–4.33 (*m*, 2 H); 4.16 (*t*, *J* = 6.8, 1 H); 4.09–4.02 (*m*, 3 H); 3.92 (*t*, *J* = 5.6, 1 H); 2.60–2.56 (*m*, 2 H); 2.33–2.30 (*m*, 1 H); 2.20–2.10 (*m*, 7 H); 1.96–1.92 (*m*, 3 H); 1.64–1.58 (*m*, 1 H); 1.45–1.15 (*m*, 53 H); 0.85 (*t*, *J* = 7.0, 6 H); 0.71 (*m*, 4 H); 0.67–0.62 (*m*, 2 H); −0.21– −0.26 (*m*, 2 H). ^{13}C-NMR (150 MHz, C_5D_5N, 300 K): 174.9; 136.8; 130.8; 130.3; 130.2; 129.7; 116.2; 105.4; 80.3; 77.0; 74.3; 73.9; 71.9; 71.1; 70.3; 69.8; 62.2; 54.2; 35.9; 34.5; 32.1; 32.1; 30.6; 30.6; 30.2; 30.2; 30.1; 30.0 (8 C); 29.9; 29.6; 29.6; 29.0; 29.0; 28.9; 28.9; 27.8; 27.7; 27.7; 26.7; 23.9; 22.9; 22.9; 16.2; 16.2; 16.2; 16.1; 14.3; 14.3; 11.4; 11.4. HR-MS (MALDI-FT): 968.7561 ($[M+Na]^+$, $C_{57}H_{103}NaNO_9^+$; calc. 968.7530).

*(2*R*,5*Z*)-10-[(1*R*,2*S*)-2-Decylcyclopropyl]*-N-*[(1*S*,2*R*,6*Z*)-11-[(1*R*,2*S*)-2-decylcyclopropyl]-1-({2-*O*-[(2*E*,6*E*)-3,7-dimethylocta-2,6-dienyl]-β-*D*-galactopyranosyloxy}methyl)-2-hydroxydec-5-enamide* (**8**). Amorphous solid. R_f 0.44 (silica gel; 7% MeOH in CH_2Cl_2). ^{1}H-NMR (600 MHz, C_5D_5N, 300 K): 8.25 (*d*, *J* = 9.3, NH); 5.73 (*t*, *J* = 6.2, 1 H); 5.62–5.59 (*m*, 1 H); 5.52–5.46 (*m*, 3 H); 5.14 (*t*, *J* = 6.8, 1 H); 4.78–4.72 (*m*, 4 H); 4.62–4.59 (*m*, 1 H); 4.46 (*d*, *J* = 2.8, 1 H); 4.40–4.33 (*m*, 2 H); 4.20 (*t*, *J* = 6.8, 1 H); 4.09–4.01 (*m*, 3 H); 3.92 (*t*, *J* = 5.6, 1 H); 2.60–2.58 (*m*, 2 H); 2.33–2.31 (*m*, 1 H); 2.20–1.80 (*m*, 15 H); 1.70–1.64 (*m*, 7 H); 1.54 (*s*, 3 H); 1.45–1.15 (*m*, 53 H); 0.85 (*t*, *J* = 7.0, 6 H); 0.71 (*m*, 4 H); 0.67–0.62 (*m*, 2 H); −0.21– −0.25 (*m*, 2 H). ^{13}C-NMR (150 MHz, C_5D_5N, 300 K): 174.9; 138.6; 131.3; 130.8; 130.3; 130.2, 129.7; 124.8; 122.6; 105.6; 79.9; 77.0; 74.4; 71.9; 71.2; 70.3; 69.9; 69.7; 62.2; 54.3; 39.9; 35.9; 34.5; 32.1; 32.1; 30.6; 30.6; 30.3; 30.2; 30.2; 30.1; 30.0 (8 C); 29.9; 29.6; 29.6; 29.0; 29.0; 29.0; 28.9; 28.9; 27.8; 27.7; 27.7; 26.9; 26.8; 25.7; 23.9; 22.9; 22.9; 17.7; 16.7; 16.2; 16.2; 16.2; 16.1; 14.3; 14.3; 11.4; 11.4. HR-MS (MALDI-FT): 1064.8511 ($[M+Na]^+$, $C_{64}H_{115}NNaO_9^+$; calc. 1064.8469).

*(2*R*,5*Z*)-*N*-[(1*S*,2*R*,6*Z*)-1-[(2-*O*-benzyl-β-*D*-galactopyranosyloxy)methyl]-11-[(1*R*,2*S*)-2-decylcyclopropyl]-2-hydroxyundec-6-enyl]-10-[(1*R*,2*S*)-2-decylcyclopropyl]-2-hydroxydec-5-enamide* (**9**). Amorphous solid. R_f 0.44 (silica gel; 7% MeOH in CH_2Cl_2). ^{1}H-NMR (600 MHz, C_5D_5N, 300 K): 8.25 (*d*, *J* = 9.0, NH); 7.72 (*d*, *J* = 7.6, 2 H); 7.28 (*t*, *J* = 7.8, 2 H); 7.21 (*t*, *J* = 6.9, 1 H); 5.61–5.60 (*m*, 1 H); 5.52–5.45 (*m*, 3 H); 5.32 (*d*, *J* = 11.7, 1 H); 4.98 (*d*, *J* = 11.7, 1 H); 4.80 (*d*, *J* = 7.8, 1 H); 4.75–4.71 (*m*, 2 H); 4.59–4.58 (*m*, 1 H); 4.47 (*d*, *J* = 2.8, 1 H); 4.41–4.34 (*m*, 2 H); 4.18–4.15 (*m*, 3 H); 4.10–4.08 (*m*, 1 H); 3.95 (*t*, *J* = 5.6, 1 H); 3.64–3.61 (*m*, 2 H); 2.59–2.56 (*m*, 2 H); 2.31–2.30 (*m*, 1 H); 2.16–2.09 (*m*, 6 H); 1.94–1.92 (*m*, 2 H); 1.64–1.58 (*m*, 1 H); 1.45–1.15 (*m*, 53 H); 0.85 (*t*, *J* = 6.9, 6 H); 0.71 (*m*, 4 H); 0.67–0.62 (*m*, 2 H); −0.21– −0.25 (*m*, 2 H). ^{13}C-NMR (150 MHz, C_5D_5N, 300 K): 174.9; 140.2; 130.8; 130.3; 130.2; 129.7; 128.5; 128.5; 128.4; 128.4; 127.5; 105.4; 80.9; 77.0; 74.9; 74.4; 71.9; 71.2; 70.4; 69.8; 67.8; 62.2; 54.3; 35.9; 34.5; 32.1; 32.1; 30.6; 30.6; 30.2; 30.2; 30.1; 30.0 (6 C); 29.9; 29.9; 29.6; 29.6; 29.0; 29.0; 28.9; 28.9; 27.8; 27.7; 27.7; 26.7; 23.9; 22.9; 22.9; 16.2; 16.2; 16.2; 16.1; 14.3; 14.3; 11.4; 11.4. HR-MS (MALDI-FT): 1018.7735 ($[M+Na]^+$, $C_{61}H_{105}NNaO_9^+$; calc. 1018.7687).

*(2*R*,5*Z*)-10-[(1*R*,2*S*)-2-Decylcyclopropyl]*-N-*((1*S*,2*R*,6*Z*)-11-[(1*R*,2*S*)-2-decylcyclopropyl]-2-hydroxy-1-{[3-*O*-(prop-2-enyl)-β-*D*-galactopyranosyloxy]methyl}undec-6-enyl)-2-hydroxydec-5-enamide* (**10**). Amorphous solid. R_f 0.41 (silica gel; 7% MeOH in CH_2Cl_2). ^{1}H-NMR (500 MHz, $CDCl_3$, 293 K): 7.32 (*d*, *J* = 7.7, NH); 5.42–5.29 (*m*, 5 H); 4.26 (*d*, *J* = 7.7, 1 H); 4.20–4.17 (*m*, 1 H); 4.14–4.11 (*m*, 2 H); 4.05–3.85 (*m*, 5 H); 3.81–3.79 (*m*, 1 H); 3.69–3.65 (*m*, 2 H); 3.48 (*m*, 1 H); 3.37 (br. *s*, 1 H); 3.28 (*dd*, *J* = 3.3, 9.6, 1 H); 3.17 (br. *s*, 2 H); 2.94 (br. *s*, 1 H); 2.19–2.16 (*m*, 2 H); 2.04–1.98 (*m*, 4 H); 1.86–1.83 (*m*, 1 H); 1.74 (*s*, 3 H); 1.66 (*s*, 3 H); 1.56–1.45 (*m*, 3 H); 1.40–1.11 (*m*, 49 H); 1.11–1.01 (*m*, 4 H); 0.86 (*t*, *J* = 7.0, 6 H); 0.63–0.61 (*m*, 4 H); 0.56–0.52 (*m*, 2 H); −0.26– −0.29 (*m*, 2 H). HR-MS (FAB): 1106.7045 ($[M+Cs]^+$, $C_{59}H_{107}CsNO_9^+$; calc. 1106.7000).

Preparation of Stock Solutions of Test Compounds. For all biological experiments, stock solns. of the plakosides were prepared in DMSO at 10 mM concentration. The highest concentration tested was 50 μM. The reference compounds cyclosporine A (CsA) and azathioprine were dissolved in EtOH and DMSO at 1 mM and 2 mM, resp.

Allogeneic Mixed Lymphocyte Reaction (MLR). The two-way MLR was performed according to standard procedures [27][29] and has been described in [29]. Briefly, spleen cells from CBA and BALB/c mice (1.6×10^5 cells from each strain per well in flat bottom tissue culture microtiter plates, 3.2×10^5 in total) were incubated in RPMI medium containing 10% FCS, 100 U/ml penicillin, 100 μg/ml streptomycin (*Gibco BRL*, Basel, Switzerland), 50 μM 2-mercaptoethanol (*Fluka*, Buchs, Switzerland), and serially diluted compounds. Seven fivefold dilution steps in duplicates per test compound were performed. After 4 days of incubation 1 μCi [^{3}H]thymidine was added. Cells were harvested after an additional 5-h incubation period, and incorporated [^{3}H]thymidine was determined according to standard procedures. Background values (low control) of the MLR were the proliferation of BALB/c cells alone.

Concanavalin A (Con A) Response. The Con A response with mouse spleen cells was performed according to standard procedures [30]. Briefly, spleen cells from CBA mice (2×10^5 cells per well) were incubated for 2 days in RPMI medium as described above. Cells were stimulated with 2 μg/ml Con A (*Boehringer*, Mannheim, Germany). Compounds were tested and proliferation was assessed as described for the MLR. Background values were the proliferation of cells in the absence of Con A.

Murine Bone Marrow Cell Proliferation Assay. Bone marrow cells from CBA mice (2.5×10^4 cells per well) were incubated for 4 days in 100 µl RPMI medium. WEHI-3-Conditioned medium (7.5% (*v*/*v*)) and L929-conditioned medium (3% (*v*/*v*)) were added as a source of growth factors. Compounds were tested and proliferation was assessed as described above. Conditioned media were prepared as follows. WEHI-3 Cells (ATCC TIB68) and L929 cells (ATCC CCL 1) were grown in RPMI medium until confluence for 4 days and one week, resp. Cells were harvested, resuspended in the same culture flasks in medium C containing 1% FCS [31], and incubated for 2 days (WEHI-3) or one week (L929). The supernatant was collected, filtered through 0.2 µm and stored in aliquots at $-80°$. Cultures without test compounds and without WEHI-3 and L929 supernatants were used as low controls.

Data Analysis. Low controls were subtracted from all values. High controls without any sample were taken as 100% proliferation. Percent inhibition by the samples was calculated, and the concentrations required for 50% inhibition (IC_{50} values) were determined using a four parameter logistic function.

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