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C-Galactosylceramide diastereomers via Sharpless asymmetric epoxidation chemistry☆

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Dedicated to the memory of Professor Giuseppe Capozzi (1941–2008), Dipartimento di Chimica Organica, Universita di Firenze, a friend and a colleague

ABSTRACT

C-Glycoside analogs of α-galactosylceramide (KRN7000) were synthesized in 19 linear steps with Sharpless asymmetric epoxidation as a key reaction. Opening of a hydroxy epoxide with sodium azide provided an *anti* vicinal azido diol with inversion of configuration at the azide-bearing carbon while opening with $Ti(O\text{-}i\text{-}Pr)_2(N_3)_2$ gave *syn* vicinal azido diol with retention. The latter, unusual outcome could be rationalized either by invoking Ti-catalyzed intramolecular double S_N2 inversion or by epoxide opening/intramolecular delivery of azide from the Ti complex.

1. Introduction

In the early 1990's, researchers at Kirin Pharma reported the results of their studies on glycolipid extracts of *Agelas Mauritianus*, an Okinawan sponge. An optimized synthetic material, α-galactosylceramide **1** (Fig. 1, also known as KRN7000 and α-Galcer), a slightly simplified version of the active materials found in the sponge extracts, displayed potent *anti*-tumor activity in a whole animal murine assay.[1]

An intensive series of biological experiments in the ensuing decade unveiled the activity of the α-Galcer as stemming from its immunostimulant activity.[2] Thus, α-Galcer is *not* cytotoxic and high-throughput cell-based assays would not have revealed its activity. The molecular basis for α-Galcer stimulation of the immune system is its initial binding to a protein receptor, named CD1d, found on the surface of antigen-presenting cells. The complex between the receptor and the α-Galcer has been crystallized and analyzed by X-ray diffraction and shows that two lipid chains of the ceramide are buried in two hydrophobic channels of the protein and that the 2,3 hydroxyls of galactose and the 3 hydroxyl of the phytosphingosine side chain participate in hydrogen bonds with the protein.[3] This binding motif leaves the 4 and 6 hydroxyls of the α-Galcer available to be recognized by receptors on natural killer T cells. In a very recent disclosure, the crystal structure of the triple complex of CD1d/ α-Galcer/NKT receptor shows the binding of the gal-4-OH to the NKT, but the 6-OH seems to be free.[4] The effect of the second protein molecule's recognition of the initial complex is to produce a powerful surge of cytokines interferon-γ, (IFNγ), interleukin-4 (IL-4), and interleukin-12 (IL-12), which then signal for the eventual cytotoxic immune response. Extensive analog studies in the O-glycoside series revealed the importance of the galactose configuration and the free hydroxyls. The only allowed substitution of the galactose OH's is *N*-acyl at the 6-position of galactose. Variation of lipid chain length and degrees of unsaturation in both the phytosphingosine and the *N*-acyl side chains is permissible.[5] In most cases, small changes in cytokine levels are the

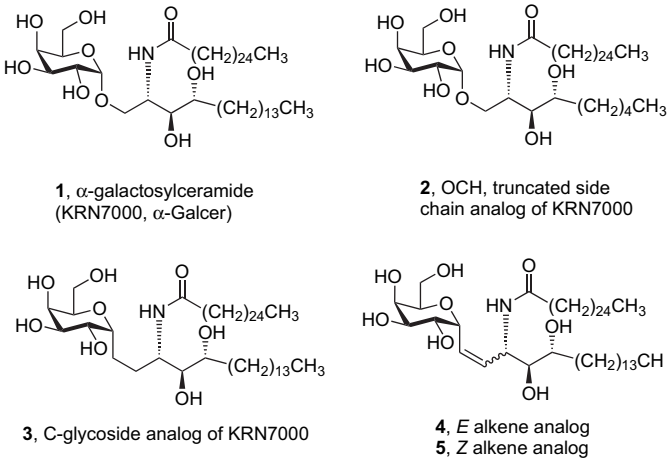

Figure 1. α-Galactosylceramide **1** (KRN7000) and its analogs.

☆ Taken from the doctoral dissertation of J.P. submitted to the City University of New York, 2006.

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result; but in one striking example, shortening the lipid of the phytosphingosine from 14 to 5 carbons (Fig. 1, compound **2**, named as *OCH*) stimulates almost exclusive production of IL-4 with a great diminution of IFNγ and IL-12. In immunology terms, this change is said to favor a TH2 immune response whereas the reverse, a decrease in IL-4 and an increase in the other cytokines, is called a TH1 response. In the mouse, the TH2 effect offers protection against autoimmune diseases while the TH1 pathway protects against 'foreign' pathogens.

The investigation of α-Galcer in our laboratory began with the concept that the C-glycoside **3** might provide a more deep-seated change in the structure–activity profile. Aside from the obvious stability to enzymatic hydrolysis provided by replacement of anomeric O by CH_2, the important changes are (i) the loss of one hydrogen-bond acceptor and (ii) the destabilization of the galactose chair through replacement of axial O-anomeric stabilization with axial CH_2 steric repulsion. In the event, the C-glycoside **3** was prepared and we were rewarded with striking enhancement of in vivo activity in blocking malaria and melanoma in mice. Assay for cytokines revealed that IFNγ and IL-12 levels were about the same as for the O-glycoside while the IL-4 titer was dramatically reduced. We also studied the *E* and *Z* alkene analogs **4** and **5** and found that the *E* material **4** was active whereas the *Z* analog **5** was essentially inert in our assays (Fig. 1).[6]

Since stereochemistry in both the galactose and the linker region had been found to be a critical element for activity, we deemed it worthwhile to examine the effects of stereoisomers in the phytosphingosine chain. There had been an early report on a study in the O-series where the four possible stereoisomers **6** bearing the 4-deoxyphytosphingosine chain were studied.[7] Interestingly, the only isomer other than the natural 2*S*,3*R* to show tumor growth inhibitory effects was **7** with the phytosphingosine in the unnatural, enantiomeric 2*R*,3*S* form. Also, there has been a recent evaluation of the natural 4-deoxy series with the exact analogs of both α-Galcer and OCH. The activities **6** and **8** in the 4-deoxy series were similar to those of the parent materials (Fig. 2).[8]

Since our earlier preparations of C-glycoside **3** had been convergent and involved coupling of intact phytosphingosines with galactose, they would not be suitable for our proposed stereoisomerism study. Thus, we embarked on a scheme where the phytosphingosine was elaborated from a pre-formed C-glycoside, which we now describe.[9]

The known aldehyde **10** was obtained in five steps from commercially available β-D-galactose pentaacetate **9** according to a literature procedure (Scheme 1).[10] Homologation of **10** via Horner–Wadsworth–Emmons reaction afforded (*E*)-α,β-unsaturated ester **11**. DIBAL-H reduction gave the (*E*)-allylic alcohol **12** in 92% yield. Sharpless asymmetric epoxidation (SAE)[11] using substoichiometric

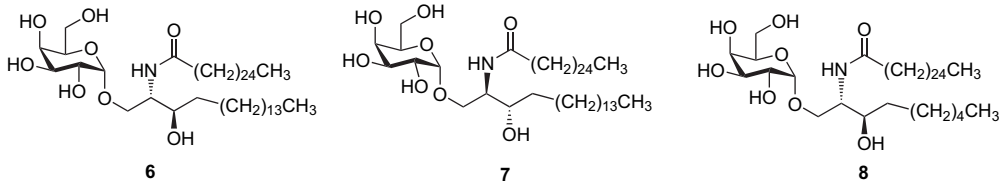
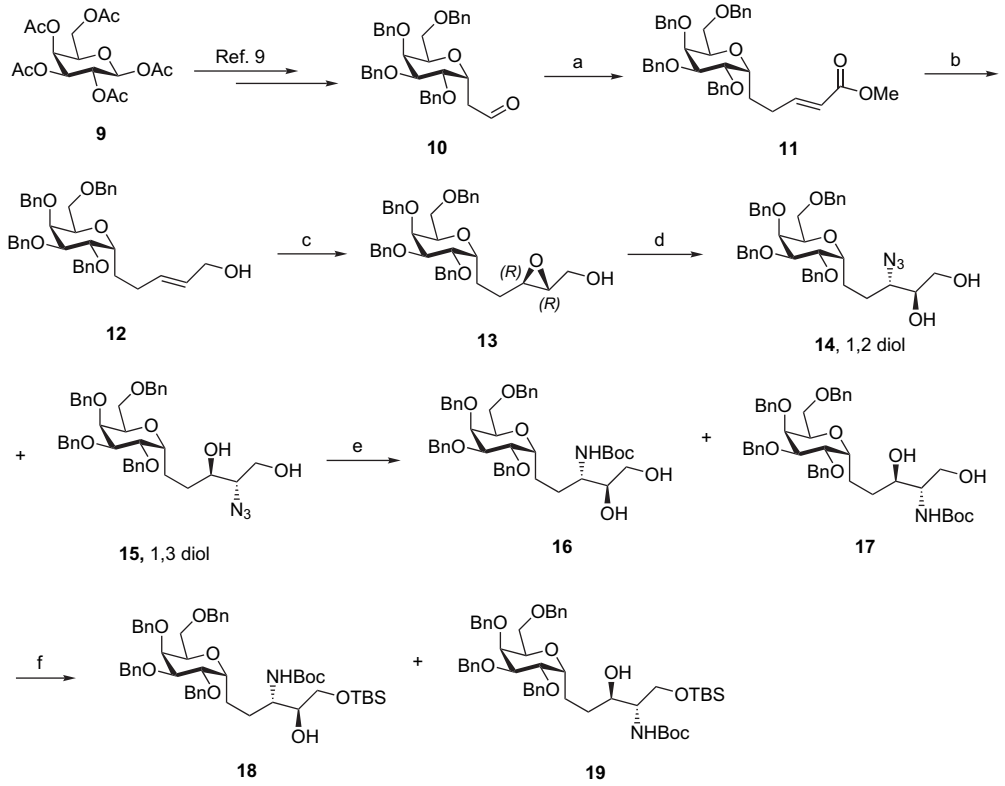


Figure 2. 4-Deoxy analogs **6**–**8** of α-Galcer and OCH.



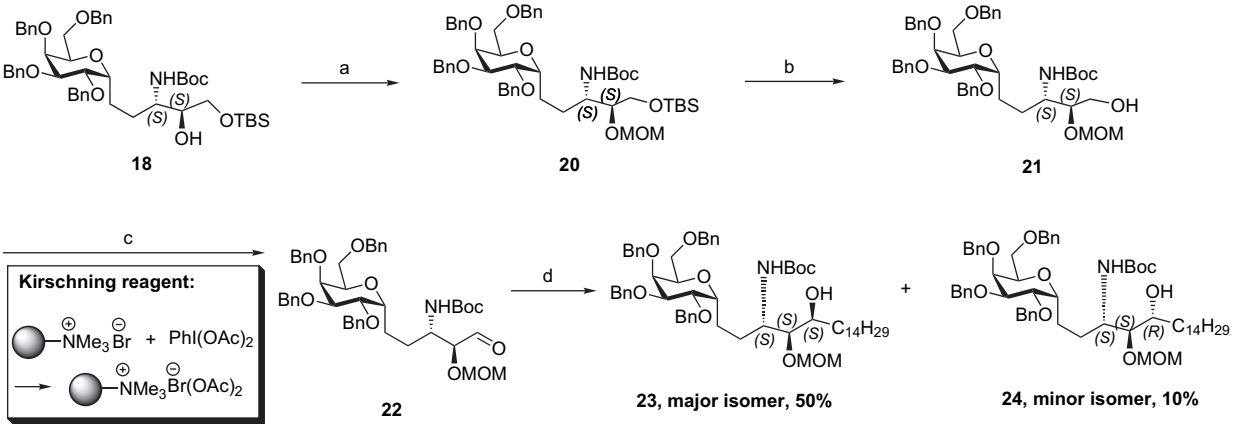
Scheme 1. Regents and conditions: (a) $(MeO)_2POCHCO_2Me$, MeCN, rt, overnight, 89%. (b) DIBAL-H, CH_2Cl_2, −78 °C, 2 h, 90%. (c) TTIP, D-(−)-DIPT, TBHP, 4 Å MS, CH_2Cl_2, −20 °C, 18 h, 70%. (d) NaN_3/NH_4Cl, $MeOH/H_2O$ (8:1), 80 °C, overnight, 93%. (e) (i) $P(Me)_3$, THF, overnight; (ii) 1 N NaOH, 2 h; (iii) $(t\text{-Boc})_2O$, satd $NaHCO_3$, THF/1,4-dioxane(1:1), rt, overnight, 78% for three steps. (f) TBSCl, imidazole, CH_2Cl_2, rt, 88%.

amount of catalysts (50 mol % TTIP, 60 mol % D-(−)-DIPT) ensured conversion of **12** to (2*R*,3*R*) epoxy alcohol **13** in high enantiomeric excess (ee>95%). Opening the (2*R*,3*R*) epoxy alcohol **13** using NaN_3/NH_4Cl in a simple S_N2 conversion provided an inseparable mixture of the desired 3-azido-1,2 vicinal diol **14** and by-product 1,3 diol **15** in 90% yield.[12] The 8:1 ratio of **14**/**15** was determined at a later stage. Thus, the mixture of azides was reduced with $P(Me)_3$ to provide amine intermediate,[13] which was then protected with $(t\text{-}Boc)_2O$ to afford an inseparable mixture of regioisomers **16** and **17**. To our delight, selective protection of the primary hydroxyl group as its TBS ether gave a separable mixture of **18** and **19** in a ratio of 8:1 in 90% yield. To assign their structures, **18** and **19** were deprotected with TBAF and the products were treated with $NaIO_4$. Only a compound derived from 1,2 diol could be cleaved by $NaIO_4$ to give the corresponding aldehyde while the 1,3 diol could not be cleaved by $NaIO_4$. In this way, **18** was confirmed to be the 1,2 vicinal diol.

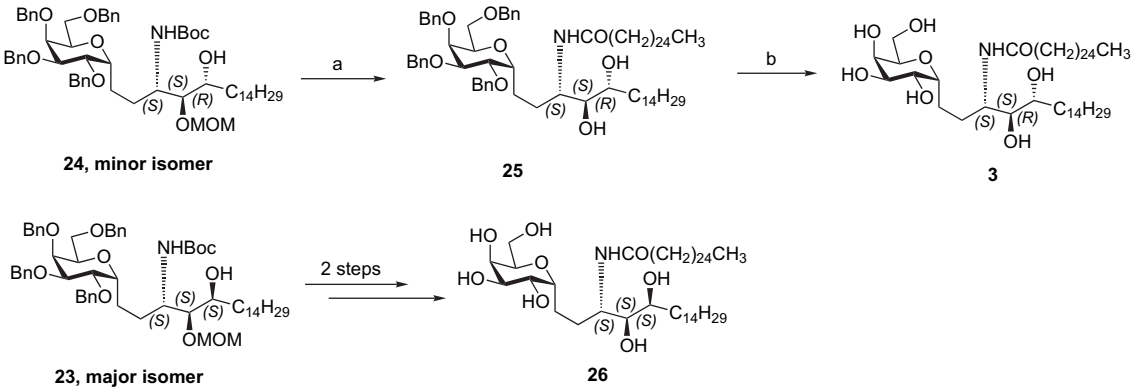
Protection of the secondary hydroxyl of compound **18** with MOM and removal of the TBS group gave primary alcohol **21** in high yield. Oxidation of alcohol to aldehyde **22** proceeded without epimerization at the neighboring α stereocenter using either Dess–Martin periodinane or a novel Kirschning solid phase oxidant,[14] both procedures taking place in high yield without causing epimerization at the α position. Inverse addition of the crude aldehyde **22** to freshly prepared tetradecyl magnesium bromide ($C_{14}H_{29}MgBr$) provided a separable mixture of **23** and **24** in a ratio of 5:1 and in 60% combined yield for two steps. Based on the 'Cram-chelation control rule',[15] the stereochemistry of **23** and **24** was tentatively assigned as (3*S*,4*S*,5*S*) and (3*S*,4*S*,5*R*), respectively, with the minor isomer **24** proposed as the desired or natural (3*S*,4*S*,5*R*) configuration at the three contiguous stereocenters. The structural assignment was confirmed later by correlation with the corresponding final products (Scheme 2).

Acidic hydrolysis of **24** removed MOM and Boc groups in one step and the resulting amine was converted to amide **25** in 80% yield. Hydrogenation of amide **25** using Pearlman's catalyst ($Pd(OH)_2/C$) in THF/EtOH solution afforded the fully deprotected C-glycoside analog of KRN7000 **3**. Its NMR spectra matched with those of the previously synthesized C-glycoside analog of KRN7000 (see Supplementary data). Similarly, the major isomer **23** was converted to the corresponding C-glycoside analog **26**, which is a 5-OH epimer of the target C-glycoside analog of the KRN7000 (Scheme 3).

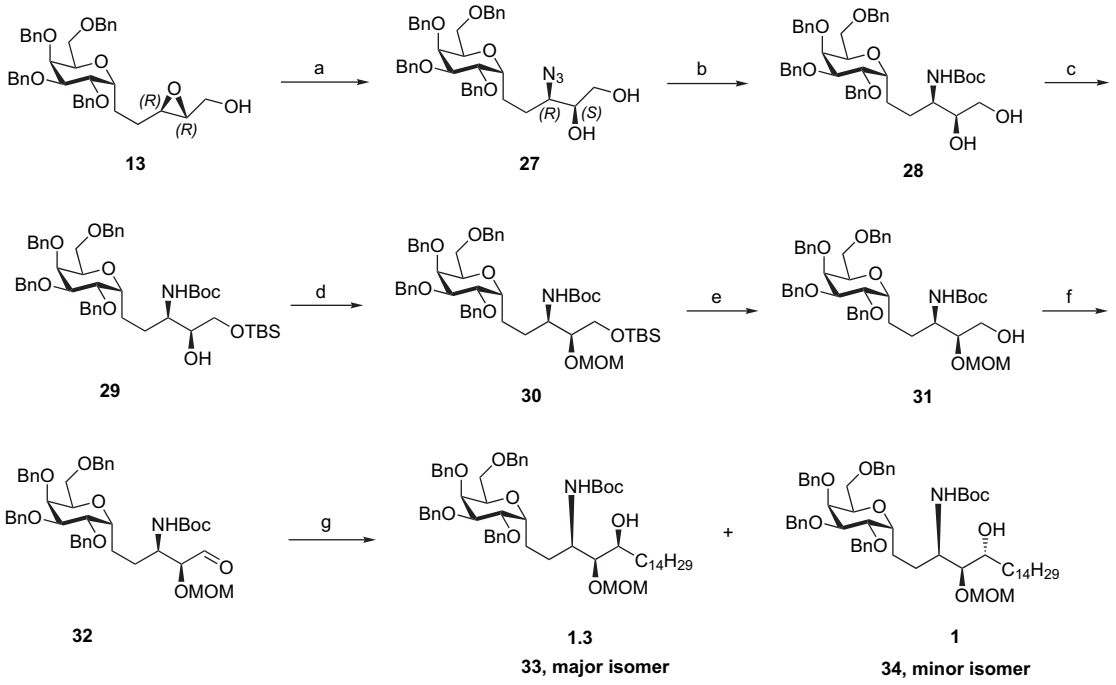
As described above, the key step of opening of epoxide **13** by sodium azide was not a very clean reaction, requiring extended reaction time in refluxing MeOH. Furthermore, about 10% of the regioisomeric azide (at C-4), which was obtained required separation via careful chromatography at a later stage. Therefore, we adopted the $Ti(O\text{-}i\text{-}Pr)_2(N_3)_2$ conditions described by Sharpless.[16] In our case, treatment of the (2*R*,3*R*) epoxy alcohol **13** with $Ti(O\text{-}i\text{-}Pr)_2(N_3)_2$ gave a single product, which we assigned as the desired *anti*-3-azido-2-OH **14** on the basis of the hypothesis that ring opening of the oxirane was a single S_N2 reactionas in the sodium azide experiment. Spectral comparison with the authentic **14** was not definitive because the batch obtained in the sodium azide experiment was a mixture. In actual fact, the $Ti(O\text{-}i\text{-}Pr)_2(N_3)_2$ single product was ultimately revealed to be 3-azido-1,2 vicinal diol **27**. As our synthesis proceeded via duplication of the sequence described above, detailed comparison of the final products derived from the



Scheme 2. Reagents and conditions: (a) MOMCl, DIPEA, CH_2Cl_2, 0 °C to rt, 12 h, 95%. (b) TBAF, THF, rt, 2 h, 100%. (c) Kischning reagent, TEMPO (cat.), CH_2Cl_2, rt, 2 h, or Dess–Martin oxidation, CH_2Cl_2, rt, 1 h, quantitative. (d) $C_{14}H_{29}MgBr$, THF, 0 °C to rt, 2 h, 58% for two steps.



Scheme 3. Reagents and conditions: (a) (i) HCl, THF/MeOH/1,4-dioxane (1:1:1), rt, overnight; (ii) $CH_3(CH_2)_{24}COOPhNO_2$, DMAP, THF, rt, 24 h, 72% for two steps. (b) H_2, $Pd(OH)_2/C$, THF/EtOH (1:1), 24 h, 42%. For compound **26**, 35% for three steps.



Scheme 4. Reagents and conditions: (a) Ti(*i*-OPr)$_2$(N$_3$)$_2$, benzene, 70 °C,10 min, 64%. (b) (i) P(Me)$_3$, THF, rt, 18 h; (ii) 1 N NaOH, 2 h; (iii) (*t*-Boc)$_2$O, THF/1,4-dioxane(1:1), satd NaHCO$_3$, rt,12 h; 91% for three steps. (c) TBSCl, imidazole, CH$_2$Cl$_2$, rt, 2 h, 99%. (d) MOMCl, DIPEA, CH$_2$Cl$_2$, 0 °C to rt, 24 h, 99%. (e) TBAF, THF, 0 °C to rt, 2 h, 92%. (f) Dess–Martin oxidation, CH$_2$Cl$_2$, rt, 2 h. (g) C$_{14}$H$_{29}$MgBr, THF, 0 °C to rt, 2 h, 50% combined yield for two steps.

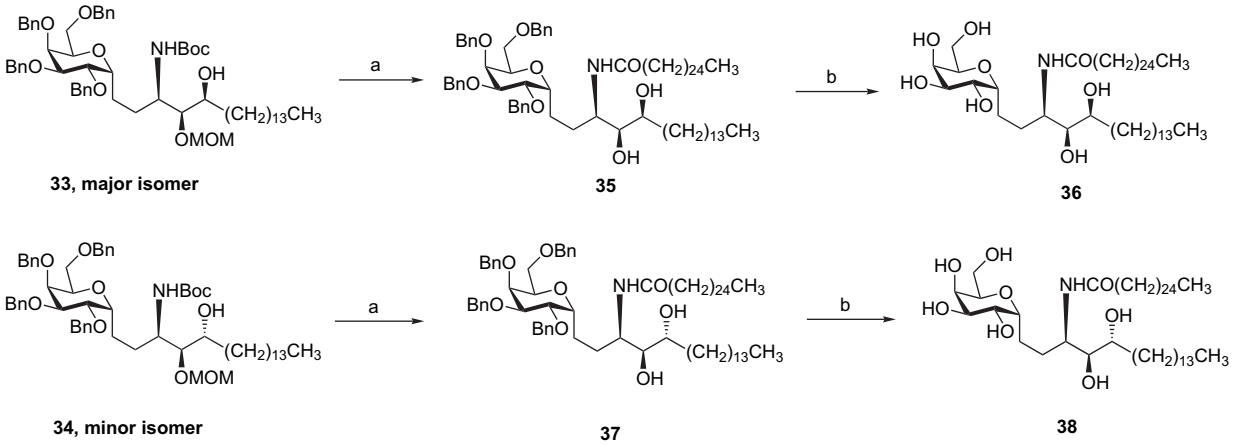
Ti(O-*i*-Pr)$_2$(N$_3$)$_2$ opening of the epoxy alcohol **13** did not match with those compounds derived from NaN$_3$ opening. The correct structural assignment in this section (Scheme 4) reveals a series that are diastereomeric to those obtained from the sodium azide opening. The (2*S*,3*R*) epoxy alcohol **27** was converted to aldehyde **32** in an identical manipulation sequence as described in the previous section. Grignard reaction between the aldehyde **32** and C$_{14}$H$_{29}$MgBr gave a separable mixture, and the ratio of the major isomer **33** and minor isomer **34** was 1.3:1. The stereochemical assignment was based on the 'Cram-chelation control' model as was shown to be operative in the epimeric series (Scheme 4).

Both major isomer **33** and minor isomer **34** were converted to the corresponding C-glycoside analogs **36** and **38**, respectively (Scheme 5). The revelation that neither of the NMR spectra of these two final products (see Supplementary data) matched with those of the α-*C*-Galcers from the sodium azide sequence forced us to assign their stereochemistries and to account for a divergence from the expected stereochemical outcome.

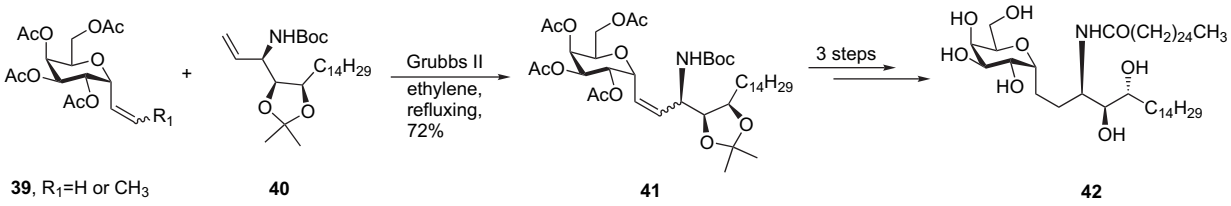
In fact, the C-glycoside analog **38**, the minor isomer derived from the Ti-catalyzed sequence, was identical to the C-3 epimer **42**, which had been obtained in earlier work from our group. This material arose from the linking of a phytosphingosine derivative **40**, epimeric at C-3, to a galactose **39** via cross-metathesis. The epimeric configuration of the amino group was unambiguous because it was derived from natural phytosphingosine in which the primary alcohol had been oxidized to an aldehyde, which had then been treated to form an epimeric mixture at the N-bearing carbon (Scheme 6).[17]

The NMR spectrum of epimer **38** also closely matched with the spectrum of the C-glycoside **48**, a material of the same configuration prepared by Annoura, differing only in carbon chain length (Scheme 7).[18]

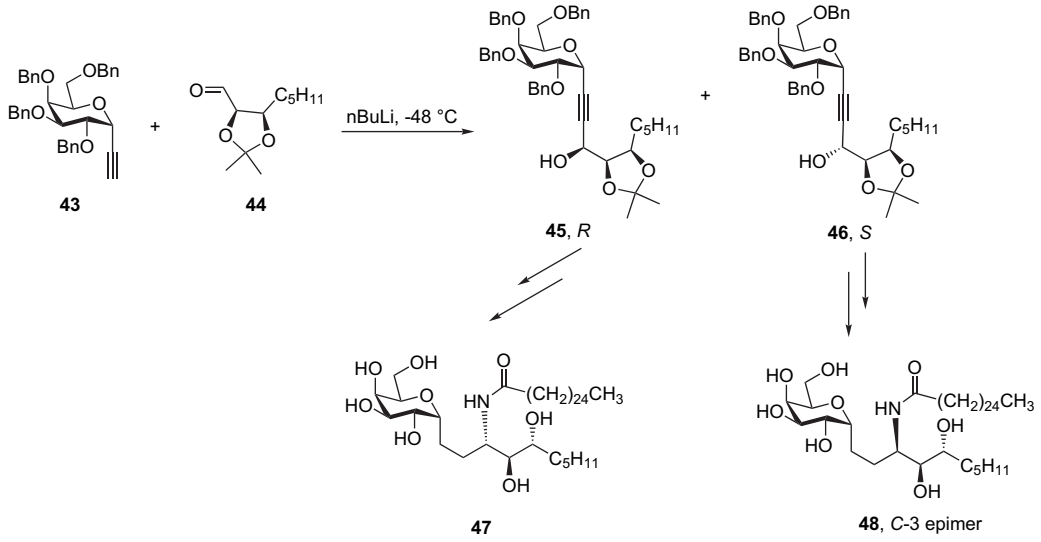
Therefore, it must have been the case that the Ti-aided azide opening of epoxide **13** had occurred with retention of the 3-N stereocenter. To obtain diagnostic NMR confirmation of stereochemistry, the *trans*-amino alcohol **18** and *cis*-amino alcohol **29**,



Scheme 5. Reagents and conditions: (a) (i) 6 N HCl, THF/MeOH (1:1) overnight; (ii) CH$_3$(CH$_2$)$_{24}$COOPhNO$_2$, DMAP, THF, 24 h. (b) Pd(OH)$_2$/C, THF/EtOH (1:1), H$_2$, 24 h; 54% for **36**, three steps from **33**; 55% for **38**, three steps from **34**.



Scheme 6. Alternative synthesis of *C*-3 epimer **42** (Guangwu Chen, Hunter College).



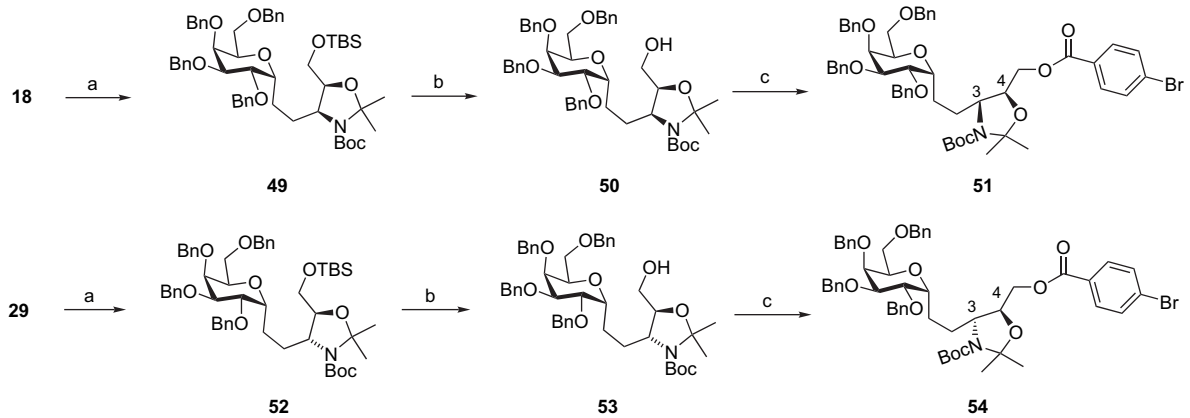
Scheme 7. Annoura et al.'s synthesis of C-glycoside analog of OCH and its *C*-3 epimer.

derived from opening of epoxide **13** with NaN_3 and Ti-aided azide, respectively, were transformed to the corresponding *cis* five-membered oxazolidine benzoyl ester **51** and *trans*-benzoyl ester **54** (Scheme 8).

In its NOESY spectrum, strong correlation between H_2, H_2' and H_5, H_5' of the *p*-bromo benzoyl ester **51** clearly demonstrated the cis relationship of these groups, therefore, the corollary cis relationship of H_3 and H_4, thus establishes the *anti* relationship of the corresponding H_3 and H_4 in the 1,2 diol **14** before the heterocycle is formed (Fig. 3).

For the *p*-bromo benzoyl ester **54**, which was derived from Ti(*O*-*i*-Pr)$_2$(N$_3$)$_2$ opening of epoxide **13**, no correlation in the NOESY between H_3 and H_4 was detected. Significantly, two sets of correlation were observed: between H_3 and H_5, H_5' protons and H_4 and H_2, H_2' protons. This correlation is that which is anticipated for a trans five-membered cyclic ring system (Fig. 4). In this way, the stereochemical relationship between the 3-azide and 2-hydroxy of 1,2 diol **27** was proved to be *syn*, thus, the 3-*C* stereocenter was proved unambiguously to be retained during Ti(O-*i*-Pr)$_2$(N$_3$)$_2$ opening of epoxide **13**.

This epoxide opening with retention can be rationalized by invoking Ti-catalyzed intramolecular participation by the pyranosidic O or 2-BnO to form an intermediate oxonium ion (Scheme 9, path A or B, respectively), inverting the epoxide center, reminiscent of earlier work of Fraser-Reid and Mootoo.[19] This would be followed by an intermolecular azide opening with a second inversion, i.e., net retention, to afford azido alcohol **27**. It is also possible to rationalize the stereochemcial result by invoking a Ti-catalyzed epoxide opening/intramolecular delivery of azide from the Ti complex as suggested by Tan et al. (path C) (Scheme 9).[20] There is no simple experiment that will distinguish between these two retention pathways.



Scheme 8. Reagents and conditions: (a) 2,2-dimethoxy-propane, *p*-TsOH, CH_2Cl_2, 0 °C to rt; 75% for **49**, 91% for **52**. (b) TBAF, THF, 0 °C to rt; 95% for **50**, 90% for **53**. (c) 4-BrPhCOCl, pyridine, CH_2Cl_2, rt; 82% for **51**, 90% for **54**.

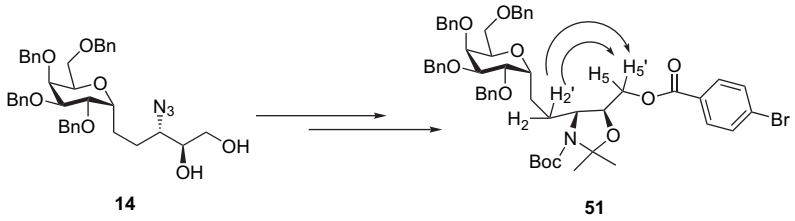


Figure 3. NOESY effect of **51**, derived from NaN_3 opening of epoxide **13**.

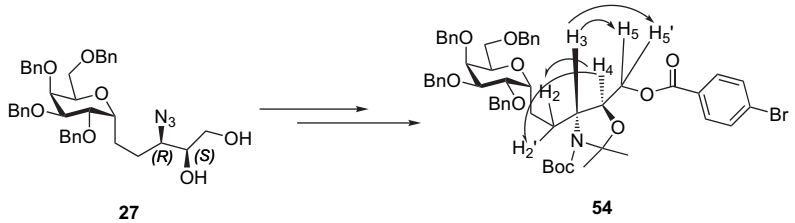
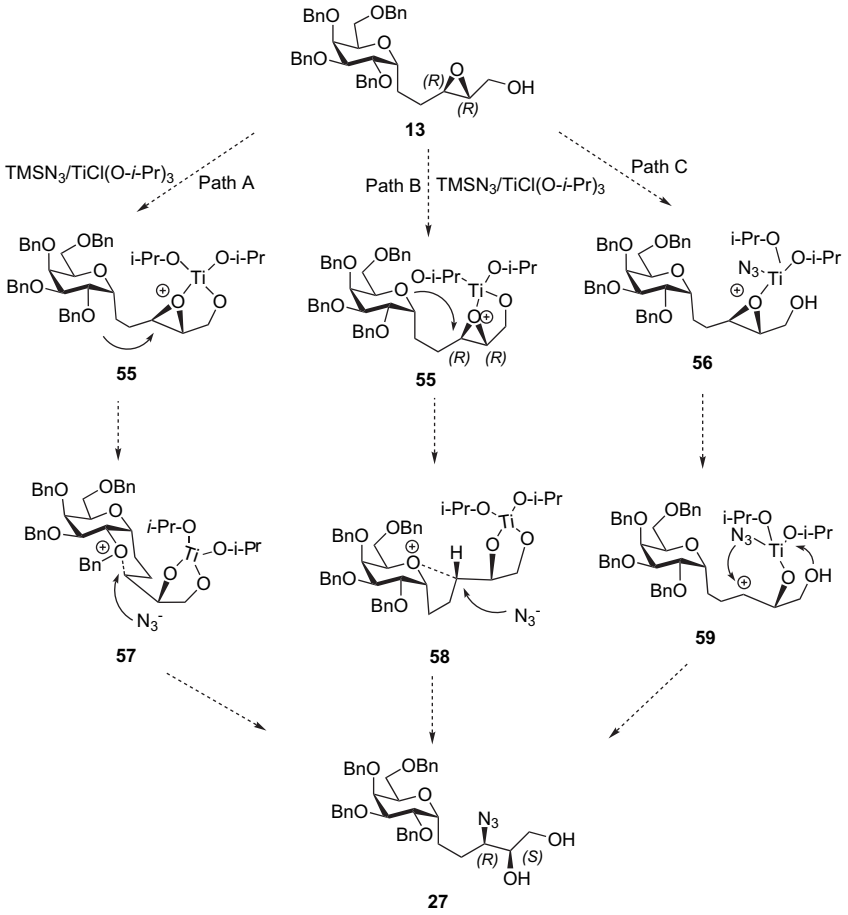


Figure 4. NOESY effect of **54**, derived from $Ti(O\text{-}i\text{-}Pr)_2(N_3)_2$ opening of epoxide **13**.



Scheme 9. Mechanism for the retention of configuration of 3-*N* stereocenter.

1.1. Immunostimulant activity

Our collaborating immunology group conducted in vitro assays for cytokine production using a system three separate NKT cell hybridomas paired with a CD1d antigen-presenting HeLa cell. With NKT line 829, the stereoisomers described (compounds **26**, **36**, and **38**) produced 40-fold less IFNγ than the positive control of α-Galcer. With NKT 912, our stereoisomers were seven fold less productive and with NKT 926, they were 50-fold less productive. Further, there was no significant difference among these unnatural stereoisomers.[21] Our observations may be compared with those recently reported for *O*-galcer stereoisomers where a range of bioactivity was detected.[22,23]

In summary, the C-glycoside analog **3** of α-galactosylceramide **1** (KRN7000) was synthesized in 19 linear steps in 3.3% overall yield through the Sharpless asymmetric epoxidation method as the controller of stereochemistry. Sodium azide opening of epoxide **13** gave *anti* vicinal azido diol **14** with inverted stereocenter at C-3 but $Ti(O\text{-}i\text{-}Pr)_2(N_3)_2$ opening of epoxide **13** provided *syn* vicinal azido diol **27** with retention of the C-3 configuration. This unusual

phenomenon could be rationalized by related pathways, which find literature precedent, and therefore this result should serve as a cautionary note for researchers planning to use Ti catalysis for epoxide opening.

2. Experimental

2.1. Instruments and materials

NMR spectra were recorded with a QE 300 MHz (^{1}H) and 75 MHz (^{13}C) with a TECMAG data system or Bruker 500 MHz (^{1}H) and 125 MHz (^{13}C) in deuterated solvents. The assignment of proton and carbon NMR peaks was supported by routine COSY and HSQC spectra and for some cases by NOESY spectra. Melting points were determined on a Fisher–Johns apparatus and were uncorrected. Electrospray ionization (ESI) mass spectral experiments were performed at the Hunter College Mass Spectrometry Facility on an Agilent Technologies 1100 LC/MSD. *Typical ESI method*: solvent: 1:1 acetonitrile/water+0.1% HOAc+50 μL NH_4Ac, flow: 0.5 mL/min, positive ion mode, fragmentor voltage: 30–200 V, drying gas at 175 °C. All air and moisture sensitive reactions were performed under a positive pressure of dry N_2 gas. All solvents and reagents were purified prior to use according to standard laboratory procedures. Low temperatures were recorded as bath temperatures. Thin layer chromatographic analysis was carried out on precoated aluminum sheets of silica gel 60 F_{254}. UV light, vanillin, phosphomolybdic acid spray or DNP spray was used to visualize the components on the TLC plates. Flash column chromatography was carried out with silica gel 60 (230–400 mesh) purchased from ChemAbsorb, using ACS reagent grade petroleum ether, hexane, ethyl acetate, methylene chloride, chloroform, and methanol as eluents.

2.1.1. 5-(3,4,5-Tris-benzyloxy-6-benzyloxymethyl-tetrahydro-pyran-2-yl)-pent-2-enoic acid methyl ester (**11**)

To a solution of crude 3-(3,4,5-tris-benzyloxy-6-benzyloxymethyl-tetrahydro-pyran-2-yl)-propionaldehyde (**10**) (1.3 g, 2.3 mmol) in anhydrous MeCN (30 mL) was added methyl(triphenylphosphoronylidene)acetate (1.5 g, 4.5 mmol) in one portion at room temperature under N_2. The solution was stirred overnight at room temperature. The mixture was diluted with CH_2Cl_2 (50 mL), washed with H_2O (20 mL), extracted with CH_2Cl_2 (3×50 mL), dried over Na_2SO_4 (anhydrous), filtered, and concentrated in vacuo. Purification by flash chromatography eluting with 30% ethyl acetate/petroleum ether provided α,β unsaturated ester **11** (1.27 g, 89% yield) as yellow oil. MS: m/z 654 (M^++NH_4^+). HRMS calcd for $C_{40}H_{44}O_7$ 636.3087, found 636.3085. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.45–7.20 (m, 20H, Ph), 7.0–6.9 (d, t, J=15.6, 6.9 Hz, 1H, CH=), 5.80 (d, J=15.5 Hz, 1H, =CH), 4.76–4.78 (m, 8H, CH_2Ph), 4.05–3.90 (m, 4H), 3.85–3.75 (m, 5H), 3.70–3.65 (m, 1H), 2.40–2.30 (m, 1H), 2.25–2.10 (m, 1H), 1.90–1.80 (m, 1H), and 1.65–1.55 (m, 1H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 167.2, 149.1, 138.7, 138.6, 138.5, 138.4, 128.6, 128.6, 128.5, 128.6, 128.5, 128.5, 128.4, 128.3, 128.1, 128.0, 128.0, 127.9, 127.9, 127.8, 127.7, 121.4, 77.4, 77.1, 76.8, 74.5, 73.4, 73.3, 73.2, 72.4, 67.8, 51.5, and 28.7.

2.1.2. 5-(3,4,5-Tris-benzyloxy-6-benzyloxymethyl-tetrahydro-pyran-2-yl)-pent-2-en-1-ol (**12**)

α,β Unsaturated ester **11** (1.20 g, 1.89 mmol) was dissolved in anhydrous CH_2Cl_2 (10 mL) and was cooled to −78 °C under N_2. DIBAL-H (5.7 mL, 5.7 mmol, 1 M in hexane) was added dropwise over 10 min. After completion of addition, the reaction mixture was slowly warmed up to room temperature and was stirred for 2 h at room temperature. The solution was cooled to 0 °C and MeOH (10 mL) was added dropwise followed by addition of satd potassium sodium tartrate solution (30 mL). The solution was stirred vigorously until two clear phases appeared. The mixture was extracted with ethyl acetate (3×50 mL). The combined organic layer was dried over Na_2SO_4, filtered, and concentrated in vacuo. Purification by flash chromatography eluting with 30–50% ethyl acetate/petroleum ether afforded the allylic alcohol **12** (1.03 g, 90% yield) as pale yellow oil. MS: m/z 626 (M^++NH_4^+). HRMS calcd for $C_{39}H_{44}O_6$ 608.3138, found 608.3134. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.35–7.20 (m, 20H, Ph), 5.71–5.65 (m, 2H, –CH=CH–), 4.75–4.52 (m, 8H, CH_2Ph), 4.05 (m, 2H, –CH_2OH), 3.99–3.90 (m, 3H), 3.85–3.75 (m, 2H), 3.73–3.67 (m, 1H), 3.65–3.3.0 (dd, J=10.3, 4.5 Hz, 1H), 2.20 (m, 1H), 2.05–1.99 (m, 1H), 1.74–1.70 (m, 1H), and 1.60–1.50 (br, 1H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 138.8, 138.7, 138.5, 138.5, 132.7, 129.6, 128.6, 128.6, 128.6, 128.5, 128.4, 128.2, 128.0, 127.9, 127.9, 127.8, 127.8, 127.8, 127.7, 127.6, 77.0, 76.9, 74.7, 73.5, 73.4, 73.4, 73.3, 73.1, 72.3, 68.0, 63.8, and 28.7.

2.1.3. (3′*R*,4′*R*)-1-(3′,4′-Oxiran-5′-hydroxy-pentanyl)-(2,3,4,6-tetra-O-benzyl)-α-C-D-galactopyranoside (**13**)

A 100 mL round bottom flask containing powdered 4 Å molecular sieves (4 g) was heated with a heating gun in vacuo for 10 min and was cooled down to room temperature under N_2. The flask was then filled with dry CH_2Cl_2 (10 mL) and was cooled to −20 °C. Titanium(IV) isopropoxide (0.4 mL, 1.35 mmol) and diisopropyl D-(−)-tartrate (0.28 mL, 1.62 mmol) were then added. The solution was stirred for 30 min at −20 °C. *tert*-Butyl hydroperoxide (0.54 mL, 2.7 mmol, 5 M in toluene) was added dropwise over a period of 10 min. The solution was stirred for another 30 min at −20 °C. Allylic alcohol **12** (0.82 g, 1.35 mmol, pre-dried with 4 Å MS for 30 min) in dry CH_2Cl_2 (5 mL) was added dropwise. The solution was stirred at −20 °C for 18 h (stored in freezer overnight) and was cooled to 0° C. H_2O (10 mL) was added and the mixture was stirred for 30 min at 0 °C, then 30% NaOH solution saturated by NaCl (10 mL) was added, and the solution was stirred for 30 min at 0 °C. The mixture was filtered through a pad of Celite and the Celite was washed with CH_2Cl_2 (50 mL). The organic phase was separated and the aqueous layer was extracted with CH_2Cl_2 (3×30 mL). The organic phase was combined and washed with brine (20 mL), dried over Na_2SO_4, filtered, and concentrated in vacuo. The crude mixture was purified by flash chromatography eluting with 50% ethyl acetate/petroleum ether to provide epoxide **13** (0.50 g, 70% yield) as pale yellow oil. MS: m/z 642 (M^++NH_4^+). HRMS calcd for $C_{39}H_{44}O_7$ 624.3087, found 624.3082. ^{1}H NMR (300 MHz, C_6D_6): δ 7.0 (m, 20H, Ph), 4.45–4.10 (m, 8H, CH_2Ph), 3.95–3.85 (m, 2H), 3.83–3.80 (m, 1H), 3.80–3.75 (m, 1H, –CH_2OH), 3.70–3.60 (m, 1H, –CH_2OH), 3.50–3.45 (m, 1H), 3.35–3.3.14 (m, 3H), 2.70 (m, 1H), 2.55–2.45 (m, 1H), 1.80–1.46 (m, 3H), and 1.40–1.11 (m, 2H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 138.7, 138.5, 138.4, 138.2, 128.5, 128.4, 128.4, 128.3, 128.2, 128.1, 128.0, 127.9, 127.8, 127.8, 127.8, 127.7, 76.9, 74.6, 73.7, 73.5, 73.4, 73.3, 73.2, 72.4, 68.0, 61.8, 58.5, 55.6, 28.2, and 23.4.

2.1.4. 3-Azido-1,2 diol **14** and 2-azido-1,3 diol (**15**)

The (2*R*,3*R*) epoxide **13** (23.8 g, 38 mmol) was dissolved in a mixed solution of MeOH/H_2O (400 mL/50 mL, 8:1). NaN_3 (12.4 g, 190 mmol) and NH_4Cl (4.5 g, 84 mmol) were added in one portion. The solution was refluxed at 80 °C under N_2 for 16 h. The solution was cooled down to room temperature and the solvent was removed under reduced pressure. The mixture was diluted with ethyl acetate (200 mL) and washed with H_2O (200 mL). The aqueous layer was separated from organic layer and was extracted with ethyl acetate (3×150 mL). The combined organic layers were dried over Na_2SO_4 (anhydrous), filtered, and concentrated in vacuo. The crude mixture was purified by flash chromatography eluting with 30–50% ethyl acetate/petroleum ether to afford a mixture of 1,2 diol **14** and 1,3 diol **15** (23.6 g, 93% yield) as yellow oil. MS: m/z 685 (M^++NH_4^+). HRMS calcd for $C_{39}H_{45}N_3O_7$, 667.3258, found 667.3256. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.34–7.24 (m, 20H, Ph), 4.74–4.49 (m,

8H, CH_2Ph), 4.03–3.86 (m, 4H), 3.82–3.71 (m, 2H), 3.66–3.61 (m, 1H), 3.58–3.53 (m, 3H), 3.52–3.48 (m, 1H), 2.71 (br s, 1H, –OH), 1.96 (br s, 1H, –OH), 1.85–1.78 (m, 1H), 1.74–1.68 (m, 2H), and 1.51–1.42 (m, 1H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 138.5, 138.4, 138.2, 138.1, 128.5, 128.5, 128.4, 128.4, 128.1, 128.1, 128.0, 128.0, 127.9, 127.8, 127.7, 127.7, 127.6, 127.6, 74.4, 73.8, 73.3, 73.3, 73.2, 72.4, 67.7, 64.4, 63.2, and 27.1.

*2.1.5. 1,2 Diol **16** and 1,3 diol (**17**)*

The mixture of 1,2 diol **14** and 1,3 diol **15** (24.6 g, 37 mmol) was dissolved in anhydrous THF (400 mL). A solution of $P(Me)_3$ (220 mL, 221 mmol, 1 M in THF) was added dropwise at 0 °C under N_2 over 30 min. The solution was then stirred at room temperature overnight. A solution of NaOH (200 mL, 0.4 mol, 2 M) was added and the solution was stirred for 2 h. The mixture was extracted with ethyl acetate (3×200 mL). The combined organic layers were dried over Na_2SO_4 (anhydrous), filtered, and concentrated in vacuo. The crude amine was dissolved in a solution of THF/1,4-dioxane (100 mL/100 mL, 1:1). A satd solution of $NaHCO_3$ (50 mL) was added followed by addition of $(t\text{-Boc})_2O$ (11.1 mL, 48.1 mmol). The solution was stirred for 24 h at room temperature. The mixture was concentrated to a total volume of 50 mL under reduced pressure. The solution was extracted with ethyl acetate (3×200 mL). The combined organic layers were dried over Na_2SO_4 (anhydrous), filtered, and concentrated in vacuo. The crude mixture was purified by flash chromatography eluting with 30–50% ethyl acetate/petroleum ether to afford a mixture of 1,2 diol **16** and 1,3 diol **17** (21.3 g, 78% combined yield) as yellow oil. MS: m/z 759 (M^++NH_4^+). HRMS calcd for $C_{44}H_{55}NO_9$ 741.3877, found 741.3874. ^1H NMR (500 MHz, $CDCl_3$): δ 7.32–7.25 (m, 20H, Ph), 4.921 (d, J=8.4 Hz, 1H, NH), 4.71–4.44 (m, 8H, CH_2Ph), 4.05 (br s, 1H), 3.97–3.93 (m, 3H), 3.74–3.73 (br s, 1H), 3.69 (br s, 1H), 3.59 (dd, J=10.4, 3.52 Hz, 1H), 3.54–3.42 (m, 3H), 3.21–3.19 (br s, 1H), 3.12 (br s, 1H), 2.66 (br peak, OH), 2.41 (br peak, OH), 1.87–1.86 (m, 1H), 1.71–1.69 (m, 1H), 1.58–1.55 (m, 1H), 1.43 (s, 9H, $(CH_3)_3$), and 1.36–1.28 (m, 1H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 157.5, 138.7, 138.5, 138.4, 138.4, 128.6, 128.6, 128.5, 128.5, 128.3, 128.2, 128.1, 128.1, 128.0, 127.9, 127.8, 127.7, 127.7, 127.7, 80.1, 76.5, 74.6, 74.5, 73.4, 73.3, 73.2, 73.2, 72.4, 67.5, 63.1, 53.9 (NHCO), 53.1 (NHCO), 29.1, 28.5, 27.0, 24.6, and 20.9.

*2.1.6. (3′S,4′S)-1-{3′-N-tert-Butylcarbamate-4′-hydroxy-5′-(tert-butyl-dimethyl-silanyloxy)-pentanyl}-(2,3,4,6-tetra-O-benzyl)-α-C-D-galactopyranoside (**18**)*

The mixture of compounds **16** and **17** (11.8 g, 15.9 mmol) was dissolved in anhydrous CH_2Cl_2 (200 mL) at room temperature under N_2. Imidazole (3.3 g, 48.0 mmol) and *tert*-butyl-dimethylsilyl chloride (3.2 g, 20.7 mmol) were added in one portion. The solution was stirred for 1 h at room temperature. The mixture was washed with satd NH_4Cl solution (200 mL) and extracted with CH_2Cl_2 (3×150 mL). The combined organic layers were dried over Na_2SO_4 (anhydrous), filtered, and concentrated in vacuo. The crude mixture was purified by flash chromatography eluting with 10–20% ethyl acetate/petroleum ether to get the first fraction **19** (1.3 g, 10% yield) and the second fraction **18** (10.6 g, 78% yield), which is the desired product as yellow oil. MS: m/z 873 (M^++NH_4^+). HRMS calcd for $C_{50}H_{69}NO_9Si$ 855.4742, found 855.4738. ^1H NMR (500 MHz, $CDCl_3$): δ 7.33–7.20 (m, 20H, Ph), 4.99–4.97 (d, J=8.9 Hz, 1H, NH), 4.67–4.44 (m, 8H, CH_2), 4.02–3.95 (br s, 1H), 3.92–3.91 (m, 1H), 3.87–3.86 (m, 1H), 3.81–3.77 (m, 1H), 3.72 (br s, 1H), 3.68–3.66 (m, 1H), 3.61–3.53 (m, 4H), 3.49–3.39 (m, 1H), 1.74–1.64 (m, 4H), 1.38 (s, 9H, $(CH_3)_3$), 0.89–0.70 (s, 9H, CH_3), and 0.02 (s, 6H, CH_3). ^{13}C NMR (125 MHz, $CDCl_3$): δ 156.4, 138.8, 138.7, 138.6, 138.5, 128.6, 128.5, 128.5, 128.5, 128.4, 128.2, 128.1, 128.1, 128.0, 127.9, 127.8, 127.8, 127.7, 127.6, 79.3, 77.1, 74.7, 73.4, 73.4, 73.3, 72.3, 67.9, 64.7, 53.9, 28.6, 27.9, 26.1, 18.4, −5.2, and −5.3.

*2.1.7. (3′S,4′S)-1-{3′-N-tert-Butyl carbamate-4′-methoxymethoxy-5′-(tert-butyl-dimethyl-silanyloxy)-pentanyl}-(2,3,4,6-tetra-O-benzyl)-α-C-D-galactopyranoside (**20**)*

The TBS protected ether **18** (5.8 g, 6.8 mmol) was dissolved in anhydrous CH_2Cl_2 (200 mL). Freshly distilled diisopropylethylamine (11.8 mL, 67.9 mmol) was added at 0 °C under N_2. Methoxymethyl chloride (2.1 mL, 27.2 mmol) was then added dropwise over 10 min. The solution was stirred at room temperature for 18 h. The reaction was quenched by addition of satd NH_4Cl solution (100 mL) and extracted with CH_2Cl_2 (3×100 mL). The combined organic layers were dried over Na_2SO_4 (anhydrous), filtered, and concentrated in vacuo. The crude mixture was purified by flash chromatography eluting with 10–20% ethyl acetate/petroleum ether to get the fully protected compound **20** (5.79 g, 95%) as yellow oil. MS: m/z 917 (M^++NH_4^+). HRMS calcd for $C_{52}H_{73}NO_{10}Si$ 899.5004, found 899.5007. ^1H NMR (500 MHz, $CDCl_3$): δ 7.31–7.26 (m, 20H, Ph), 5.52–5.23 (d, J=8.5 Hz, 1H, NH), 4.69–4.47 (m, 10H, CH_2Ph and OCH_2O), 3.97 (br s, 2H), 3.89 (br s, 1H), 3.77–3.76 (m, 3H), 3.73–3.70 (m, 2H), 3.67–3.64 (m, 2H), 3.57–3.56 (m, 1H), 3.35 (s, 3H, OCH_3), 1.68 (br s, 3H), 1.53 (s, 1H), 1.42 (s, 9H, $(CH_3)_3$), 0.89 (s, 9H, CH_3), 0.05 (s, 3H, CH_3), and 0.04 (s, 3H, CH_3). ^{13}C NMR (125 MHz, $CDCl_3$): δ 156.0, 138.7, 138.6, 138.5, 138.4, 128.3, 128.2, 128.1, 128.0, 128.0, 128.0, 127.9, 127.7, 127.6, 127.5, 127.5, 127.2, 96.5, 79.4, 78.8, 77.4, 77.1, 74.8, 73.6, 73.4, 73.3, 73.2, 72.2, 68.0, 64.2, 55.8, 52.2, 28.7, 27.9, 18.4, and −5.9.

*2.1.8. (3′S,4′S)-1-{3′-N-tert-Butyl carbamate-4′-methoxymethoxy-5′-hydroxy-pentanyl}-(2,3,4,6-tetra-O-benzyl)-α-C-D-galactopyranoside (**21**)*

The fully protected compound **20** (4.6 g, 5.2 mmol) was dissolved in anhydrous THF (100 mL) and the solution was cooled to 0 °C under N_2. A solution of tetrabutylammonium fluoride (10.3 mL, 10.3 mmol, 1 M THF solution) was added. The mixture was stirred for 2.5 h at room temperature. The solution was washed with satd NH_4Cl solution (100 mL) and extracted with ethyl acetate (3×100 mL). The combined organic layers were dried over Na_2SO_4 (anhydrous), filtered, and concentrated in vacuo. The crude mixture was purified by flash chromatography eluting with 20–60% ethyl acetate/petroleum ether to get the primary alcohol **21** (4.0 g, 100% yield) as white solid. MS: m/z 803 (M^++NH_4^+). HRMS calcd for $C_{46}H_{59}NO_{10}$ 785.4139, found 785.4135. ^1H NMR (500 MHz, $CDCl_3$): δ 7.33–7.26 (m, 20H, Ph), 4.88 (d, J=8.9 Hz, 1H, NH), 4.71–4.47 (m, 10H, CH_2Ph and OCH_2O), 4.02 (br s, 1H), 3.96 (br s, 1H), 3.95–3.3.85 (m, 2H), 3.72 (br s, 2H), 3.69–3.62 (m, 1H), 3.61–3.54 (m, 2H), 3.54–3.48 (m, 1H), 3.36 (s, 3H, OCH_3), 3.35 (br peak, 1H), 3.28 (m, 1H), 1.78 (br s, 1H), 1.71–1.69 (br s, 1H), 1.61–1.55 (br s, 1H), 1.43 (s, 9H, $(CH_3)_3$), and 1.29–1.26 (br s, 1H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 156.6, 138.8, 138.7, 138.5, 128.6, 128.5, 128.5, 128.4, 128.4, 128.3, 128.2, 128.1, 127.9, 127.8, 127.8, 127.8, 127.7, 96.9, 82.7, 79.7, 77.4, 77.1, 76.7, 74.7, 73.3, 73.3, 72.2, 67.8, 62.3, 55.9, 51.6, 28.6, and 26.9.

*2.1.9. (3′S,4′S,5′S)-1-{3′-N-tert-Butylcarbamate-4′-methoxy-methoxy-5′-hydroxy-nonadecanyl}-(2,3,4,6-tetra-O-benzyl)-α-C-D-galactopyranoside (**23**)*

The primary alcohol **21** (0.6 g, 0.77 mmol) was dissolved in anhydrous CH_2Cl_2 (10 mL) under N_2. Dess–Martin periodinane (0.42 g, 1 mmol) was added in one portion at room temperature. The solution was stirred for 45 min at room temperature and was diluted with CH_2Cl_2 (20 mL) followed by addition of satd $NaHCO_3$ solution (10 mL) and satd $Na_2S_2O_3$ solution (10 mL). The mixture was stirred until two clear phases appeared. The solution was extracted with CH_2Cl_2 (3×60 mL). The combined organic layers were dried over Na_2SO_4 (anhydrous), filtered, and concentrated in vacuo. The crude product was coevaporated with anhydrous toluene (3×10 mL) and was then put under high vacuum to afford the crude aldehyde **22** (0.55 g), which was used in the next step without further purification.

2.1.9.1. Kirschning oxidation[14]. A mixture of the primary alcohol **21** (0.8 g, 0.8 mmol) and a polymer bound resin prepared according to the literature procedure[14] (1.4 g, 4.9 mmol) in dry CH_2Cl_2 (10 mL) with catalytic amount of 2,2,6,6-tetramethyl-1-piperidinyloxyl (TEMPO) under nitrogen was stirred at room temperature for 2 h. After disappearance of starting material, the resin was washed with CH_2Cl_2 (3×30 mL) and the combined organic washings and filtrate were concentrated under reduced pressure to afford the crude aldehyde **22** (0.97 g), which was used in the next step without further purification.

The aldehyde **22** was dissolved in anhydrous THF (5 mL) and the solution was added dropwise to a solution of freshly prepared tetradecyl magnesium bromide ($C_{14}H_{29}MgBr$, 2.3 mmol) in anhydrous THF (5 mL) at 0 °C under N_2 over 10 min. The mixture was stirred at 0 °C for 30 min and was then stirred for 2 h at room temperature. The reaction was quenched by addition of satd NH_4Cl solution (20 mL) and the mixture was stirred for 10 min. The mixture was extracted with ethyl ether (3×50 mL). The combined organic layers were dried over Na_2SO_4 (anhydrous), filtered, and concentrated in vacuo. The crude mixture was purified by flash chromatography eluting with ethyl acetate/petroleum ether (polarity increased from 5% to 20%) to get the major isomer **23** (0.36 g, 48% yield) as the first fraction and the minor isomer **24** (72 mg, 10% yield) as the second fraction.

*2.1.9.2. The major isomer **23**.* MS: *m*/*z* 999 (M^++NH_4^+). HRMS calcd for $C_{60}H_{87}NO_{10}$ 981.6330, found 981.6322. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.35–7.29 (m, 20H, Ph), 5.26 (d, *J*=9.1 Hz, 1H, NH), 4.76–4.48 (m, 10H, CH_2Ph and OCH_2O), 3.99 (br s, 2H), 3.96 (m, 1H), 3.86–3.74 (m, 4H), 3.65–3.63 (m, 2H), 3.41 (s, 3H, OCH_3), 3.31 (m, 1H), 2.76 (d, *J*=5.2 Hz, 1H), 1.71–1.66 (m, 4H), 1.57–1.54 (m, 2H), 1.45 (s, 9H, $(CH_3)_3$), 1.33–1.19 (br s, 24H, CH_2), and 0.91 (t, *J*=6.9 Hz, 3H, CH_3). ^{13}C NMR (125 MHz, $CDCl_3$): δ 156.4, 138.8, 138.7, 138.6, 128.5, 128.5, 128.4, 128.3, 128.1, 128.1, 128.0, 127.9, 127.9, 127.8, 127.8, 127.7, 97.9, 83.9, 79.3, 77.4, 77.3, 76.8, 76.8, 74.8, 73.5, 73.5, 73.3, 72.2, 67.9, 56.3, 52.1, 34.0, 32.1, 30.0, 29.9, 29.8, 29.6, 28.6, 27.4, 25.8, 22.9, and 14.3.

*2.1.10. (3′S,4′S,5′R)-1-{3′-N-tert-Butylcarbamate-4′-methoxy-methoxy-5′-hydroxy-nonadecanyl}-(2,3,4,6-tetra-O-benzyl)-α-C-D-galactopyranoside (**24**)*

MS: *m*/*z* 999 (M^++NH_4^+). HRMS calcd for $C_{60}H_{87}NO_{10}$ 981.633, found 981.6320. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.37–7.29 (m, 20H, Ph), 4.89 (d, *J*=9.4 Hz, 1H, NH), 4.75–4.48 (m, 10H, CH_2Ph and OCH_2O), 3.99–3.96 (m, 3H), 3.84–3.77 (m, 3H), 3.75 (d, *J*=5.2 Hz, 1H), 3.61–3.59 (m, 1H), 3.56 (dd, *J*=10.6, 3.8 Hz, 1H), 3.39 (s, 3H, OCH_3), 3.34 (t, *J*=5.0 Hz, 1H), 2.73 (d, *J*=6.1 Hz, 1H), 1.91 (m, 1H), 1.71 (m, 2H), 1.62–1.59 (m, 2H), 1.53 (m, 1H), 1.45 (s, 9H, $(CH_3)_3$), 1.38–1.27 (m, 24H, CH_2), and 0.91 (t, *J*=6.6 Hz, 3H, CH_3). ^{13}C NMR (125 MHz, $CDCl_3$): δ 155.9, 138.9, 138.7, 138.6, 138.5, 128.6, 128.6, 128.4, 128.3, 128.2, 128.1, 128.1, 128.0, 127.9, 127.8, 127.7, 98.6, 87.5, 79.3, 77.1, 76.9, 76.5, 74.9, 73.6, 73.4, 73.3, 71.8, 68.4, 56.2, 51.8, 33.0, 32.1, 29.9, 29.8, 29.6, 28.7, 27.1, 26.4, 22.9, and 14.3.

*2.1.11. (3′S,4′S,5′R)-3′-N-Hexacosanoyl-4′,5′-dihydroxy-nonadecacyl-α-C-D-galactopyranoside (**3**)*

To a solution of the minor isomer **24** (45 mg, 0.046 mmol) in MeOH/1,4-dioxane (1 mL/1 mL) was added HCl solution (2 mL, 12 mmol, 6 M in MeOH) and the solution was stirred at room temperature overnight. The solution was concentrated to dryness under reduced pressure. The mixture was dissolved in THF (5 mL) and was neutralized with satd ammonium hydroxide solution (5 mL). The mixture was extracted with $CHCl_3$ (3×20 mL). The combined organic layers were dried over Na_2SO_4 (anhydrous), filtered, and concentrated in vacuo. The crude compound was coevaporated with anhydrous toluene (3×10 mL) and was then put under high vacuum pump for 1 h to afford crude amine (40 mg) as yellow oil.

The amine was dissolved in anhydrous THF (2 mL). The activated ester $C_{25}H_{51}COOPhNO_2$ (55 mg, 0.091 mmol) and DMAP (3 mg) were added at room temperature under N_2. The mixture was stirred at room temperature overnight. Celite 545 (0.5 g) was added and the solvent was removed in vacuo to get powder. Flash chromatographic purification eluting with 10% ethyl acetate/petroleum ether to remove the excess amount of ester and using 20–30% ethyl acetate/petroleum ether to give the amide **25** (0.04 g, 72% yield).

The amide **25** (0.04 g, 0.033 mmol) was dissolved in a solvent of THF/EtOH (3 mL/3 mL, 1:1). $Pd(OH)_2$/C (0.10 g, 20% by weight) was added in one portion. The solution was degassed three times and was stirred under H_2 balloon (1 atm) for 24 h. At the end of the reaction, a white precipitate formed. The solution was filtered through a pad of Celite, which was washed with 50% $CHCl_3$/MeOH solution (30 mL) followed by pyridine (20 mL). The solvent was removed in vacuo and the solid was dissolved in pyridine (2 mL). Celite 545 (0.5 g) was added and the solvent was removed in vacuo. The powder was put to the top of the column. Flash chromatographic separation eluting with $CHCl_3$ and 5%, 10%, and 20% MeOH/$CHCl_3$ afforded the target C-glycoside **3** (0.016 g, 42% and 30% yield for three steps) as a white solid. Mp 176–179 °C. HRMS calcd for $C_{51}H_{101}N_1O_8$ 855.7527, found 855.7514. ^{1}H NMR (500 MHz, C_5D_5N): δ 8.49 (d, *J*=8.9 Hz, 1H, NH), 4.73 (dd, *J*=8.8, 5.5 Hz, 1H), 4.52 (m, 3H), 4.37 (dd, *J*=11.2, 4.5 Hz, 1H), 4.25 (m, 4H), 3.97 (s, 1H, impurity), 2.72 (m, 1H), 2.55 (m, 1H), 2.48 (m, 3H), 2.33 (m, 2H), 2.20 (m, 1H), 2.05 (m, 5H, impurity), 1.96 (m, 2H), 1.86 (m, 3H), 1.69 (m, 1H), 1.57 (m, 5H), 1.31 (m, 56H), 1.03 (m, 3H), and 0.89 (t, *J*=6.9 Hz, 6H, CH_3). ^{13}C NMR (125 MHz, C_5D_5N): δ 173.9, 78.9, 77.5, 74.3, 73.2, 72.7, 71.1, 70.9, 63.2, 53.2, 37.3, 34.8, 32.4, 30.7, 30.5, 30.3, 30.3, 30.2, 30.2, 30.2, 30.1, 29.9, 29.9, 26.8, 26.7, 23.2, 23.0, and 14.6.

*2.1.12. (3′S,4′S,5′S)-3′-N-Hexacosanoyl-4′,5′-dihydroxy-nonadecacyl-α-C-D-galactopyranoside (**26**)*

This material was obtained from major isomer **23** (35% overall yield for three steps) following the same procedures as described for processing isomer **24**. Mp 170–175 °C. HRMS calcd for $C_{51}H_{101}N_1O_8$ 855.7527, found 855.7515. ^{1}H NMR (500 MHz, C_5D_5N): δ 6.80 (br peak, OH), 6.51 (br peak, OH), 6.33 (br peak, OH), 6.09 (br peak, OH), 5.72 (br peak, OH), 4.77–4.73 (m, 2H), 4.66 (s, 1H), 4.53 (s, 2H), 4.48 (s, 1H), 4.31–4.29 (m, 2H), 4.20 (s, 1H), 3.79 (s, 1H), 2.89 (br s, 1H), 2.63 (br s, 1H), 2.48 (t, *J*=7.2 Hz, 2H), 2.31–2.24 (m, 3H), 2.22–2.14 (m, 1H), 2.09–1.97 (m, 1H), 1.91–1.73 (m, 7H), 1.71–1.59 (m, 2H), 1.39–1.26 (m, 58H), and 0.92–0.87 (m, 6H). ^{13}C NMR (125 MHz, C_5D_5N): δ 175.5, 77.3, 74.3, 72.6, 71.4, 70.7, 62.7, 53.4, 37.1, 34.6, 32.4, 37.1, 34.6, 32.4, 30.6, 30.5, 30.3, 30.2, 30.1, 30.1, 29.9, 29.9, 29.1, 27.2, 26.8, 23.3, 23.1, and 14.6.

*2.1.13. (3′R,4′S)-1-{3′-Azido-4′,5′-dihydroxy-pentanyl}-(2,3,4,6-tetra-O-benzyl)-α-C-D-galactopyranoside (**27**)*

Titanium(IV) isopropoxide (0.22 mL, 0.73 mmol) and azido trimethylsilane (0.2 mL, 1.5 mmol) were added to anhydrous benzene (10 mL), and the solution was refluxed at 80 °C under N_2 for at least 5 h. Epoxide **13** (0.30 g, 0.48 mmol) was dissolved in anhydrous benzene (10 mL) and was added to the solution in one portion. The mixture was stirred for 15–30 min at 80 °C and was cooled to room temperature. The solvent was removed under reduced pressure. Diethyl ether (20 mL) was added followed by addition of 5% H_2SO_4 (10 mL, v/v). The solution was stirred at room temperature until two clear phases appeared. The mixture was extracted with CH_2Cl_2 (3×30 mL). The organic phase was dried over Na_2SO_4, filtered, and concentrated in vacuo. Flash chromatographic purification eluting with 50% ethyl acetate/petroleum ether afforded 3-azido-1,2 diol **27** (0.21 g, 64% yield) as yellow oil. MS: *m*/*z* 685.3 (M^++NH_4^+). HRMS calcd for $C_{39}H_{45}N_3O_7$ 667.3258, found 667.3254. IR (KBr): 3435.98, 2873.99, 2100.89, 763.72 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$):

δ 7.30 (m, 20H), 4.8–4.4 (m, 8H), 4.01–3.83 (m, 4H), 3.77–3.69 (m, 2H), 3.60–3.45 (m, 4H), 3.42–3.34 (m, 1H), 2.5–2.4 (br, OH), 2.25–2.15 (br, OH), 1.90–1.75 (m, 1H), and 1.74–1.50 (m, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 138.7, 138.6, 138.5, 138.3, 128.5, 128.4, 128.3, 128.1, 128.0, 127.9, 127.8, 127.7, 127.6, 77.4, 76.9, 74.7, 74.0, 73.8, 73.5, 73.5, 73.4, 72.5, 70.5, 68.1, 64.0, 63.5, 26.9, and 23.9.

*2.1.14. (3′R,4′S)-1-{3′-N-tert-Butyl carbamate-4′,5′-dihydroxy-pentanyl}-(2,3,4,6-tetra-O-benzyl)-α-C-D-galactopyranoside (**28**)*

The following materials were obtained from azido diol **27** via the procedures used for azido diol **13**. Yield: 91% yield for two steps from **27**. MS: *m*/*z* 742.3 (M^++H^+). HRMS calcd for $C_{44}H_{55}NO_9$ 741.3877, found 741.3869. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.35–7.22 (m, 20H, Ph), 4.75–4.50 (m, 8H, CH_2Ph), 4.05–3.98 (br, 1H), 3.98–3.95 (br, 2H), 3.93–3.88 (m, 1H), 3.76–3.72 (m, 2H), 3.69–3.63 (m, 1H), 3.62–3.56 (m, 2H), 3.55–3.48 (m, 1H), 3.44–3.39 (m, 1H), 3.10–3.00 (br, 1H, –OH), 2.18–2.10 (br, 1H, –OH), 1.80–1.72 (m, 1H), 1.69–1.62 (m, 1H), 1.62–1.52 (m, 1H), 1.52–1.47 (m, 1H), and 1.46–1.42 (s, 9H, $(CH_3)_3$). ^{13}C NMR (125 MHz, $CDCl_3$): δ 157.5, 138.8, 138.6, 138.5, 138.4, 128.6, 128.6, 128.5, 128.3, 128.1, 128.1, 128.0, 127.9, 127.8, 127.7, 80.1, 77.2, 76.8, 74.7, 74.6, 73.5, 73.4, 73.4, 73.3, 72.5, 68.1, 63.6, 51.6, 28.6, and 24.1.

*2.1.15. (3′R,4′S)-1-{3′-N-tert-Butyl carbamate-4′-hydroxy-5′-(tert-butyl-dimethyl-silanyloxy)-pentanyl}-(2,3,4,6-tetra-O-benzyl)-α-C-D-galactopyranoside (**29**)*

Yield: 99%. MS: *m*/*z* 873.3 (M^++NH_4^+). HRMS calcd for $C_{50}H_{69}NO_9Si$ 855.4742, found 855.4736. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.35–7.22 (m, 20H, Ph), 4.75–4.50 (m, 8H, CH_2Ph), 4.05–3.95 (m, 3H), 3.85–3.80 (m, 1H), 3.78–3.73 (m, 1H), 3.73–3.70 (m, 1H), 3.65–3.60 (m, 3H), 3.55–3.50 (m, 1H), 3.48–3.45 (m, 1H), 2.65–2.60 (br, 1H, –OH), 1.76–1.65 (m, 2H), 1.60–1.50 (m, 2H), 1.45–1.40 (s, 9H, $(CH_3)_3$), 0.92 (s, 9H, CH_3), and 0.06 (s, 6H, CH_3). ^{13}C NMR (125 MHz, $CDCl_3$): δ 156.2, 138.8, 138.7, 138.6, 138.5, 128.5, 128.5, 128.4, 128.3, 128.2, 128.1, 128.0, 127.9, 127.9, 127.8, 127.7, 127.7, 127.7, 127.6, 127.6, 79.1, 76.9, 76.8, 74.6, 73.3, 73.2, 73.1, 73.0, 72.4, 67.8, 65.0, 50.9, 29.0, 28.5, 26.0, 18.4, −5.2, and −5.3.

*2.1.16. (3′R,4′S)-1-{3′-N-tert-Butyl carbamate-4′-methoxy-methoxy-5′-(tert-butyl-dimethyl-silanyloxy)-pentanyl}-(2,3,4,6-tetra-O-benzyl)-α-C-D-galactopyranoside (**30**)*

Yield: 99%. MS: *m*/*z* 917 (M^++NH_4^+). HRMS calcd for $C_{52}H_{73}NO_{10}Si$ 899.5004, found 855.4993. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.35–7.22 (m, 20H, Ph), 4.83 (d, *J*=9.7 Hz, 1H, NH), 4.75–4.50 (m, 10H, $4CH_2$ and OCH_2O–), 4.05–3.96 (m, 3H), 3.80–3.70 (m, 3H), 3.70–3.65 (m, 1H), 3.65–3.55 (m, 4H), 3.29 (s, 3H, OCH_3), 1.76–1.74 (m, 1H), 1.70–1.55 (m, 2H), 1.56–1.48 (m, 1H), 1.42 (s, 9H, $(CH_3)_3$, Boc), 0.85 (s, 9H, CH_3), and 0.05 (s, 6H, CH_3). ^{13}C NMR (125 MHz, $CDCl_3$): δ 155.9, 138.9, 138.8, 138.7, 138.6, 128.5, 128.5, 128.4, 128.1, 128.0, 127.9, 127.8, 127.7, 127.6, 97.9, 79.5, 78.9, 77.2, 74.7, 73.4, 73.2, 72.4, 67.9, 63.9, 55.9, 50.9, 29.1, 28.6, 26.1, 18.4, and −5.4.

*2.1.17. (3′R,4′S)-1-{3′-N-tert-Butyl carbamate-4′-methoxymethoxy-5′-hydroxy-pentanyl}-(2,3,4,6-tetra-O-benzyl)-α-C-D-galactopyranoside (**31**)*

Yield: 92%. MS: *m*/*z* 803 (M^++NH_4^+). HRMS calcd for $C_{52}H_{73}NO_{10}Si$ 785.4139, found 785.4133. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.34–7.24 (m, 20H, Ph), 4.73–4.45 (m, 10H, $-CH_2$Ph and OCH_2O), 3.97–3.93 (m, 3H), 3.85–3.79 (m, 2H), 3.74–3.3.71 (m, 2H), 3.65–3.57 (m, 3H), 3.51–3.48 (m, 1H), 3.42–3.40 (m, 1H), 3.33–3.31 (s, 3H, OCH_3), 1.76–1.71 (m, 1H), 1.68–1.66 (m, 1H), 1.56–1.53 (m, 2H), and 1.42 (s, 9H, $-C(CH_3)_3$). ^{13}C NMR (125 MHz, $CDCl_3$): δ 156.9, 138.5, 138.4, 138.3, 138.1, 128.4, 128.3, 128.2, 128.2, 128.1, 128.0, 127.9, 127.8, 127.7, 127.6, 127.5, 127.5, 127.4, 97.0, 81.0, 79.5, 77.3, 76.9, 74.4, 73.2, 73.1, 72.9, 72.8, 72.3, 70.5, 67.8, 61.8, 55.6, 50.3, 28.3, and 28.2.

*2.1.18. (3′R,4′S,5′R)-1-{3′-N-tert-Butyl carbamate-4′-methoxy-methoxy-5′-hydroxy-nonadecanyl}-(2,3,4,6-tetra-O-benzyl)-α-C-D-galactopyranoside (**33**)*

Major isomer: yield: 28% for two steps from **31**. MS: *m*/*z* 999 (M^++NH_4^+). HRMS calcd for $C_{60}H_{87}NO_{10}$ 981.6330, found 981.6322. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.35–7.21 (m, 20H, Ph), 4.74–4.49 (m, 10H, CH_2Ph and OCH_2O), 4.05–3.96 (m, 3H), 3.85–3.74 (m, 3H), 3.74–3.69 (m, 1H), 3.65–3.60 (dd, *J*=3.9, 10.3 Hz, 1H), 3.55–3.52 (br s, 1H), 3.34 (s, 3H, OCH_3), 3.21 (d, *J*=6.9 Hz, 1H), 3.05 (d, *J*=2.3 Hz, –OH), 1.76–1.51 (m, 4H), 1.42 (s, 9H, Boc), 1.35–1.22 (m, 26H), and 0.90 (t, *J*=6.7 Hz, 3H, CH_3). ^{13}C NMR (125 MHz, $CDCl_3$): δ 155.8, 138.9, 138.8, 138.7, 138.6, 128.6, 128.5, 128.2, 128.1, 128.0, 127.9, 127.9, 127.8, 127.8, 127.7, 99.2, 87.4, 79.3, 77.1, 76.6, 76.4, 76.4, 74.7, 73.5, 73.3, 73.3, 73.1, 71.6, 68.1, 56.3, 50.8, 32.9, 32.2, 30.0, 29.9, 29.9, 29.8, 29.6, 28.6, 25.8, 22.9, and 14.3.

*2.1.19. (3′R,4′S,5′S)-1-{3′-N-tert-Butyl carbamate-4′-methoxy-methoxy-5′-hydroxy-nonadecanyl}-(2,3,4,6-tetra-O-benzyl)-α-C-D-galactopyranoside (**34**)*

Minor isomer, yield: 22% for two steps from **31**. MS: *m*/*z* 999 (M^++NH_4^+). HRMS calcd for $C_{60}H_{87}NO_{10}$ 981.6330, found 981.6325. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.51–7.24 (m, 20H, Ph), 4.76–4.48 (m, 10H, $4CH_2$ and OCH_2O–), 4.05–3.90 (m, 4H), 3.90–3.85 (m, 1H), 3.85–3.74 (m, 2H), 3.74–3.70 (m, 1H), 3.65–3.60 (m, 1H), 3.31 (s, 3H, OCH_3), 3.19 (m, 1H), 1.78–1.51 (m, 4H), 1.50–1.45 (m and s, 11H), 1.45–1.21 (m, 24H), and 0.90 (*t*, 3H, CH_3). ^{13}C NMR (125 MHz, $CDCl_3$): δ 157.5, 138.9, 138.7, 138.6, 138.5, 128.7, 128.6, 128.5, 128.4, 128.4, 128.3, 128.2, 128.1, 128.0, 127.9, 127.9, 127.8, 127.8, 127.7, 98.7, 85.2, 80.0, 76.9, 76.6, 74.8, 73.6, 73.5, 73.4, 73.3, 73.2, 70.8, 68.1, 56.5, 50.8, 32.8, 32.1, 30.1, 29.9, 29.6, 29.1, 28.5, 26.1, 22.9, and 14.3.

*2.1.20. (3′R,4′S,5′S)-3′-N-Hexacosanoyl-4′,5′-dihydroxy-nonadecacyl-α-C-D-galactopyranoside (**36**)*

Yield: 54% for three steps from **33**. Mp 183–185 °C. HRMS calcd for $C_{51}H_{101}N_1O_8$ 855.7527, found 855.7522. ^{1}H NMR (500 MHz, C_5D_5N): δ 8.05 (d, *J*=9.2 Hz, 1H, NH), 6.65 (br, OH), 6.40 (br, OH), 6.20 (br, OH), 5.80 (br, OH), 4.76–4.72 (m, 1H), 4.72–4.66 (m, 2H), 4.54–4.48 (m, 1H), 4.45–4.34 (m, 2H), 4.32–4.27 (m, 1H), 4.12–4.06 (m, 1H), 4.01–3.94 (m, 1H), 2.49–2.35 (m, 5H), 2.27–2.23 (m, 1H), 2.16–2.10 (m, 1H), 1.91–1.77 (m, 5H), 1.52–1.21 (m, 66H), and 0.87 (t, 6H, CH_3). ^{13}C NMR (125 MHz, C_5D_5N): δ 173.7, 77.5, 75.8, 74.7, 73.0, 72.7, 71.0, 70.7, 62.8, 50.9, 37.3, 32.6, 32.5, 30.8, 30.7, 30.6, 30.5, 30.4, 30.4, 30.3, 30.3, 30.2, 30.0, 30.0, 27.0, 27.0, 23.4, and 14.7.

*2.1.21. (3′R,4′S,5′R)-3′-N-Hexacosanoyl-4′,5′-dihydroxy-nonadecacyl-α-C-D-galactopyranoside (**38**)*

Yield: 55% for three steps from **34**. Mp 178–182 °C. HRMS calcd for $C_{51}H_{101}N_1O_8$ 855.7527, found 855.7523. ^{1}H NMR (500 MHz, C_5D_5N): δ 8.65 (d, *J*=9.0 Hz, 1H, NH), 6.65 (br, OH), 6.40 (br, OH), 6.20 (br, OH), 5.80 (br, OH), 5.02–5.01 (m, 1H), 4.76–4.72 (m, 1H), 4.72–4.66 (br s, 1H), 4.59–4.56 (m, 1H), 4.42 (m, 1H), 4.38 (m, 1H), 4.33 (m, 1H), 4.19 (br, 1H), 3.94 (m, 1H), 3.89 (m, 1H), 3.63 (d, *J*=4.7 Hz, less than 1H), 2.49–2.35 (m, 5H), 2.27–2.23 (m, 1H), 2.16–2.10 (m, 1H), 1.91–1.769 (m, 5H), 1.52–1.21 (m, 66H), and 0.87 (m, 6H, CH_3). ^{13}C NMR (125 MHz, C_5D_5N): δ 175.2, 77.8, 76.3, 74.5, 72.8, 72.7, 71.0, 70.9, 63.1, 51.5, 37.1, 34.9, 32.7, 32.7, 30.9, 30.8, 30.8, 30.7, 30.6, 30.6, 30.5, 30.5, 30.4, 30.3, 30.2, 30.1, 29.6, 27.3, 27.2, 23.5, 23.3, and 14.8.

*2.1.22. (3′S,4′S)-1-{5′-(tert-Butyl-dimethyl-silanyloxy)-2′,2′-dimethyl-4′-propyl-oxazolidine-3′-N-tert-butylcarbamate-pentanyl}-(2,3,4,6-tetra-O-benzyl)-α-C-D-galactopyranoside (**49**)*

The TBS ether compound **18** (0.51 g, 0.6 mmol) was dissolved in anhydrous CH_2Cl_2 (10 mL). 2,2-Dimethoxy-propane (1 mL) was added followed by addition of *p*-TsOH (7 mg) at 0 °C under N_2. The solution was then stirred at room temperature for 1 h. The solution

was washed with satd $NaHCO_3$ solution (10 mL) and extracted with CH_2Cl_2 (3×50 mL). The combined organic layer was dried over Na_2SO_4 (anhydrous), filtered, and concentrated under reduced pressure. The crude mixture was purified by flash chromatography eluting with 10–30% ethyl acetate/petroleum ether to afford the cyclic compound **49** (0.41 g, 75% yield) as yellow oil. MS: *m*/*z* 913 (M^++NH_4^+) (calcd for $C_{53}H_{73}NO_9Si$, 895). ^1H NMR (500 MHz, $CDCl_3$): δ 7.32–7.25 (m, 20H, Ph), 4.79–4.37 (m, 8H, CH_2Ph), 4.09–4.05 (m, 2H), 3.97–3.94 (br s, 2H), 3.91–3.86 (m, 3H), 3.79–3.75 (m, 1H), 3.73 (d, *J*=7.5 Hz, 1H), 3.67–3.55 (m, 2H), 1.82–1.79 (m, 2H), 1.66–1.63 (m, 1H), 1.59–1.55 (br s, 4H), 1.51 (s, 3H, CH_3), 1.44 (s, 3H, CH_3), 1.39 (s, 6H, CH_3), 0.87 (s, 9H, CH_3), 0.05 (s, 3H, CH_3), and 0.03 (s, 3H, CH_3). ^{13}C NMR (125 MHz, $CDCl_3$): δ 152.7, 152.2, 138.9, 138.9, 138.8, 138.7, 138.6, 138.4, 128.8, 128.8, 128.7, 128.5, 128.4, 128.3, 128.2, 128.1, 127.9, 127.8, 127.7, 127.7, 127.6, 93.4, 92.9, 79.9, 79.7, 77.3, 77.1, 76.6, 74.9, 73.8, 73.6, 73.5, 73.4, 73.1, 71.6, 68.5, 68.2, 61.3, 58.8, 28.7, 28.6, 28.3, 27.5, 27.4, 27.0, 26.1, 25.3, 23.9, 23.7, 18.5, −5.0, and −5.1. (*Note*. Because the existence of two conformers of amide, the carbon peaks become to two series of peaks.)

*2.1.23. (3′S,4′S)-1-{2′,2′-Dimethyl-4′-propyl-oxazolidine-3′-N-tert-butylcarbamate-5′-hydroxy-pentanyl}-(2,3,4,6-tetra-O-benzyl)-α-C-D-galactopyranoside (**50**)*

To a solution of cyclic compound **49** (0.40 g, 0.45 mmol) in anhydrous THF (5 mL) was added tetrabutylammonium fluoride (1.4 mL, 1.4 mmol, 1 M in THF) dropwise at 0 °C under N_2. The solution was stirred at room temperature for 1 h. The solvent was removed under reduced pressure. The crude mixture was purified by flash chromatography eluting with 10–30% ethyl acetate/petroleum ether to afford the primary alcohol **50** (0.34 g, 95% yield) as yellow oil. MS: *m*/*z* 799 (M^++NH_4^+) (calcd for $C_{47}H_{59}NO_9$ 781). ^1H NMR (500 MHz, $CDCl_3$): δ 7.33–7.23 (m, 20H, Ph), 4.74–4.49 (m, 8H, CH_2Ph), 4.13–4.11 (br s, 1H), 3.93–3.83 (m, 5H), 3.82–3.62 (m, 4H), 3.62–3.53 (br s, 1H), 1.79 (br s, 2H), 1.67 (br s, 2H), 1.55 (br s, 6H, CH_3), and 1.41 (s, 9H, $C(CH_3)_3$). ^{13}C NMR (125 MHz, $CDCl_3$): δ 152.1, 138.9, 138.8, 138.7, 138.4, 128.6, 128.5, 128.4, 128.2, 128.1, 128.0, 127.8, 127.8, 127.7, 93.6, 93.0, 79.8, 77.9, 76.8, 76.5, 76.3, 74.9, 73.8, 73.6, 73.3, 72.3, 71.9, 69.1, 68.5, 61.1, 58.8, 28.7, 28.3, 27.6, 25.3, 24.3, and 23.9.

*2.1.24. (3′S,4′S)-1-{2′,2′-Dimethyl-4′-propyl-oxazolidine-3′-N-tert-butylcarbamate-5′-(4-bromo-benzoyloxymethyl)-pentanyl}-(2,3,4,6-tetra-O-benzyl)-α-C-D-galactopyranoside (**51**)*

To a solution of alcohol **50** (0.33 g, 0.42 mmol) was dissolved in anhydrous CH_2Cl_2 (10 mL) were added anhydrous pyridine (0.5 mL) and *para*-bromobenzoyl chloride (0.18 g, 0.84 mmol) at 0 °C under N_2. The solution was stirred at room temperature for 2 h. The solution was washed with satd NH_4Cl solution (20 mL) and extracted with CH_2Cl_2 (3×50 mL). The combined organic layer was dried over Na_2SO_4 (anhydrous), filtered, and concentrated under reduced pressure. The crude mixture was purified by flash chromatography eluting with 10–20% ethyl acetate/petroleum ether to afford benzoyl ester **51** (0.34 g, 82% yield) as yellow oil. MS: *m*/*z* 981 (M^++NH_4^+) (calcd for $C_{54}H_{62}BrNO_{10}$ 963). ^1H NMR (500 MHz, $CDCl_3$): δ 7.88–7.86 (d, *J*=8.4 Hz, 2H), 7.52–7.51 (d, *J*=8.4 Hz, 2H), 7.33–7.23 (m, 20H, Ph), 4.72–4.43 (m, 8H, –CH_2Ph), 4.31–4.30 (dd, *J*=11.2, 5.8 Hz, 2H, CH_2OCO), 4.17–4.16 (s, 1H, CHO), 4.02–3.90 (m, 4H), 3.73 (br s, 1H), 3.69–3.68 (br s, 1H), 3.65–3.62 (dd, *J*=9.9, 4.8 Hz, 1H), 1.96–1.91 (m, 1H), 1.73–1.54 (br s, 5H), 1.53–1.49 (br s, 4H), and 1.49–1.42 (m, 9H, $C(CH_3)_3$). ^{13}C NMR (125 MHz, $CDCl_3$): δ 165.6, 152.6, 152.0 (amide CO), 138.8, 138.6, 138.2, 131.9, 131.5, 128.9, 128.5, 128.4, 128.2, 128.0, 127.9, 127.8, 127.7, 126.8, 126.5, 93.9, 93.3 ($OC(CH_3)_2N$), 80.3, 80.0, 77.9, 76.6, 76.4, 74.9, 74.3, 73.8, 73.6, 73.2, 72.2, 71.9, 68.6, 68.5, 63.1, 58.8, 28.6, 28.2, 27.7, 27.6, 27.3, 25.4, 24.2, and 23.9.

*2.1.25. (3′R,4′S)-1-{5′-(tert-Butyl-dimethyl-silanyloxy)-2′,2′-dimethyl-4′-propyl-oxazolidine-3′-N-tert-butylcarbamate-pentanyl}-(2,3,4,6-tetra-O-benzyl)-α-C-D-galactopyranoside (**52**)*

Yield: 91% from TBS ether compound **29**. MS: *m*/*z* 913 (M^++NH_4^+) (calcd for $C_{53}H_{73}NO_9Si$ 895). ^1H NMR (500 MHz, $CDCl_3$): δ 7.33–7.24 (m, 20H, Ph), 4.735–4.43 (m, 8H, CH_2Ph), 3.98 (s, 1H), 3.93–3.91 (m, 2H), 3.85–3.71 (m, 4H), 3.69 (dd, *J*=7.9, 2.5 Hz, 1H), 3.65 (dd, *J*=10.0, 5.3 Hz, 1H), 3.59 (s, 2H), 1.91–1.89 (m, 1H), 1.57–1.52 (s, 6H, CH_3 and CH_2), 1.49 (s, 3H, CH_3), 1.42 (s, 9H, $(CH_3)_3$), 0.88 (s, 9H, CH_3), 0.07 (s, 3H, CH_3), and 0.04 (s, 3H, CH_3). ^{13}C NMR (125 MHz, $CDCl_3$): δ 152.1, 138.9, 138.8, 138.7, 128.5, 128.4, 128.1, 128.1, 128.0, 127.9, 127.8, 127.7, 127.7, 127.3, 94.7, 94.4, 80.9, 79.8, 79.1, 76.9, 76.6, 76.3, 74.7, 73.5, 73.2, 72.1, 68.0, 64.8, 59.6, 28.7, 27.7, 26.2, 23.7, 18.5, −5.1, and −5.2.

*2.1.26. (3′R,4′S)-1-{2′,2′-Dimethyl-4′-propyl-oxazolidine-3′-N-tert-butylcarbamate-5′-hydroxy-pentanyl}-(2,3,4,6-tetra-O-benzyl)-α-C-D-galactopyranoside (**53**)*

Yield: 90%. MS: *m*/*z* 799 (M^++NH_4^+) (calcd for $C_{47}H_{59}NO_9$ 781). ^1H NMR (500 MHz, $CDCl_3$): δ 7.33–7.24 (m, 20H, Ph), 4.74–4.45 (m, 8H, CH_2Ph), 4.05–3.81 (m, 6H), 3.73–3.69 (s, 2H), 3.66–3.55 (m, 2H), 3.47–3.42 (br s, 2H), 1.94–1.85 (m, 1H), 1.67–1.59 (m, 3H), 1.54 (s, 3H, CH_3), 1.48 (s, 3H, CH_3), and 1.42 (s, 9H, $(CH_3)_3$). ^{13}C NMR (125 MHz, $CDCl_3$): δ 152.1, 138.8, 138.6, 138.5, 128.6, 128.5, 128.4, 128.4, 128.4, 128.3, 128.2, 128.2, 128.1, 128.0, 127.9, 127.8, 127.7, 127.7, 79.9, 77.4, 77.1, 74.5, 73.7, 73.6, 73.3, 63.9, 58.4, and 28.7. (*Note*. $C(CH_3)_3$ peak at 94 ppm was too small.)

*2.1.27. (3′R,4′S)-1-{2′,2′-Dimethyl-4′-propyl-oxazolidine-3′-N-tert-butylcarbamate-5′-(4-bromo-benzoyloxymethyl)-pentanyl}-(2,3,4,6-tetra-O-benzyl)-α-C-D-galactopyranoside (**54**)*

Yield: 90%. MS: *m*/*z* 981 (M^++NH_4^+). HRMS calcd for $C_{54}H_{62}BrNO_{10}$ 963.3557, found 963.3550. ^1H NMR (500 MHz, $CDCl_3$): δ 7.92–7.90 (d, *J*=8.42 Hz, 2H), 7.57–7.55 (d, *J*=8.4 Hz, 2H), 7.37–7.29 (m, 20H, Ph), 4.76–4.47 (m, 8H, CH_2), 4.35–4.34 (m, 2H), 4.22–4.19 (m, 1H), 4.01 (m, 4H), 3.82 (br s, 2H), 3.74–3.72 (m, 1H), 3.69–3.66 (dd, *J*=10.2, 4.6 Hz, 1H), 2.00–1.98 (m, 1H), 1.62 (br s, 5H), 1.56 (br s, 4H), and 1.47 (s, 9H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 165.7, 152.1, 138.7, 138.6, 138.4, 131.9, 131.4, 128.9, 128.6, 128.5, 128.5, 128.4, 128.2, 128.1, 127.9, 127.8, 127.8, 127.7, 95.3, 94.5, 80.2, 77.4, 76.7, 76.4, 74.6, 73.5, 73.3, 59.7, and 28.7.

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Supplementary data

Supplementary data associated with this article can be found in the online version, at doi:10.1016/j.tet.2008.06.007.

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