Pergamon

Tetrahedron: *Asymmetry* 11 (2000) 151–172

TETRAHEDRON:
ASYMMETRY

A new strategy in oligosaccharide synthesis using lipophilic protecting groups: synthesis of a tetracosasaccharide

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Received 1 November 1999; accepted 1 December 1999

Abstract

The use of lipophilic, acyl-type protecting groups in the synthesis of higher-membered oligosaccharides is described by the example of oligosaccharides corresponding to the O-specific polysaccharide (O-SP) of *Shigella dysenteriae* type 1. Thus, *O*-stearoylated and *O*-lauroylated L-rhamnose and D-galactose precursors, respectively, were synthesized and were combined together with a 2-azido-2-deoxy-D-glucopyranosyl donor to form a fully protected lipidated repeating unit of the O-SP. This module was condensed with another tetrasaccharide containing conventional blocking groups. The resulting lipidated octasaccharide was isolated in a pure form by adsorption to a reverse phase adsorbent from which it could be selectively desorbed by alcoholic solvents. Subsequent chain elongation using the conventionally protected tetrasaccharide module as glycosyl donor afforded oligosaccharides up to and including a tetracosasaccharide. The proposed approach can substantially alleviate the difficulties associated with the conventional silica gel chromatographic purification of protected oligosaccharide intermediates and utilizes environmentally friendly solvents that are less expensive than the solvents used for silica gel chromatography. A new, highly efficient method is also proposed for the synthesis of carbohydrate acetals and cyclic orthoesters employing scandium trifluoromethanesulfonate as the catalyst.

1. Introduction

Complex oligosaccharides are essential reagents in glycomedicine, for example, in antibacterial vaccine research,[1–3] in purification of medically important proteins using saccharide-based affinity materials,[4] in mapping the carbohydrate binding specificity of anti-carbohydrate antibodies,[5,6] and in numerous other areas. Advances in oligosaccharide synthesis, including the development of versatile glycosidation methods and powerful protecting group schemes, have made chemical synthesis of many highly complex oligosaccharides possible.[7] Contrary to this evolution, little progress has occurred in the

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0957-4166/00/$ - see front matter
PII: S0957-4166(99)00553-4

separation and purification phase of the synthetic operations. Practitioners are well aware of the fact that product isolation requires as much attention in chemical synthesis of oligosaccharides as do protecting group manipulations and glycosyl-bond formations. Therefore, the possible methods for product isolation should already be taken into account in the planning phase of the synthetic approaches. In recent years, explorations of solid-phase techniques for oligosaccharide synthesis have received much attention.[8] While this technique has been very successful in the peptide and the oligonucleotide fields, its general advantage in oligosaccharide synthesis over liquid-phase methods has yet to be demonstrated by way of direct comparison. Additionally, chemical synthesis of oligosaccharides on solid support has so far been limited to small- to medium-sized structures.[8] As a variation on this theme, the use of soluble macromolecular carriers that can be precipitated under suitable conditions has also been proposed.[9] In another approach towards efficient product isolation a glycolipid was employed as glycosyl-acceptor in an enzymatic glycosylation.[10] After the glycosylation step, the lipid-containing product could be extracted selectively on a dimethyloctadecylsilyl-coated silica particle. This technique was adopted for glycosyltransferase assays using synthetic substrates containing the lipophilic 8-methoxycarbonyloctyl group as the aglycon.[11,12] The hydrophobic 8-*p*-methoxyphenoxyoctyl aglycon was also exploited for partial separation of glycosylation mixtures using the C-18 adsorbent technique.[13] As an interesting recent development towards efficient product isolation in oligosaccharide synthesis, Curran proposed the use of a fluoroalkyl-substituted benzyl protecting group that renders the sector to which it is attached insoluble in water and common organic solvents, and soluble in a perfluorinated solvent, thus permitting the isolation of the oligosaccharide product in a three-phase liquid–liquid extraction procedure.[14,15] Because of the large number of fluorines in the proposed protecting group, the molecular weight of the fluorine-tagged intermediates is high, that makes characterization of the fluorous derivatives a challenge even at the disaccharide level. As a new entry to facilitate product isolation in oligosaccharide synthesis, I have reported the preparation and use of a lipophilic benzyl-type *O*-protecting group that allowed the isolation of a protected disaccharide using a reverse phase adsorbent in a simple adsorption–elution process without the need of silica gel chromatography.[16]

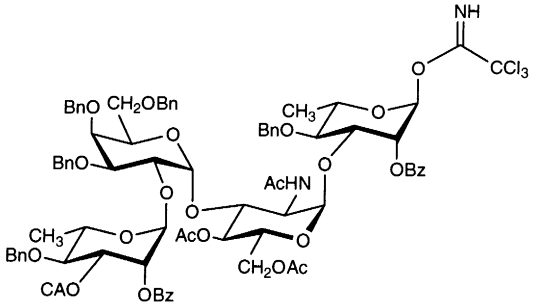
In this paper some initial results are reported towards a new strategy to higher-membered oligosaccharides that relies on lipophilic, *O*-acyl protecting groups. The proposed approach combines the advantages of solution phase glycosylations and the solid–liquid extraction methods and sidesteps many of the difficulties associated with the exclusive reliance on conventional silica gel chromatography. As will be demonstrated, purification of the lipid-tagged products is also possible by using silica gel chromatography, if necessary. The objective of the experiments described herein is to demonstrate the feasibility of the proposed approach for the synthesis of large oligosaccharides and to evaluate the optimum number of lipophilic tags that are necessary for efficient product isolation. This new method is presented by the example of synthesis of oligosaccharides corresponding to the O-specific polysaccharide of *Shigella dysenteriae* type 1 that consists of the tetrasaccharide repeating unit **1**.

3)-α-L-Rha*p*-(1→2)-α-D-Gal*p*-(1→3)-α-D-GlcNAc*p*-(1→2)-α-L-Rha*p*-(1→ **1**

2. Results and discussion

A blockwise approach to higher-membered oligosaccharides corresponding to this polysaccharide which were used as saccharide components of experimental vaccines[3] has previously been reported.[2,17] In these endeavors, a tetrasaccharide donor/acceptor module (**2**) that was first attached to a spacer moiety was assembled. Subsequent, iterative addition of unit **2** to the first module produced the targeted octa-, dodeca-, and hexadecasaccharides. Because of the identical protecting groups in the starting materials,

product, and side-products, isolation of the product was difficult at and above the dodecasaccharide level, necessitating repeated silica gel chromatographic procedures.[2] These difficulties prompted a re-design of the modular approach with the important issue of product isolation in mind. Here it is reported that tagging the initial module of the oligosaccharide chain with lipophilic protecting groups substantially alleviates the separation problem through the use of a reverse-phase adsorbent that preferentially adsorbs the lipid-tagged compounds while having no or only weak adsorption toward the untagged molecules. First, I describe the synthesis of the key lipid-tagged monosaccharide intermediates followed by their assembly to provide the lipid-labeled tetrasaccharide unit. Then the utility of this module in the synthesis of a tetracosasaccharide corresponding to six contiguous repeating units of **1** is shown.



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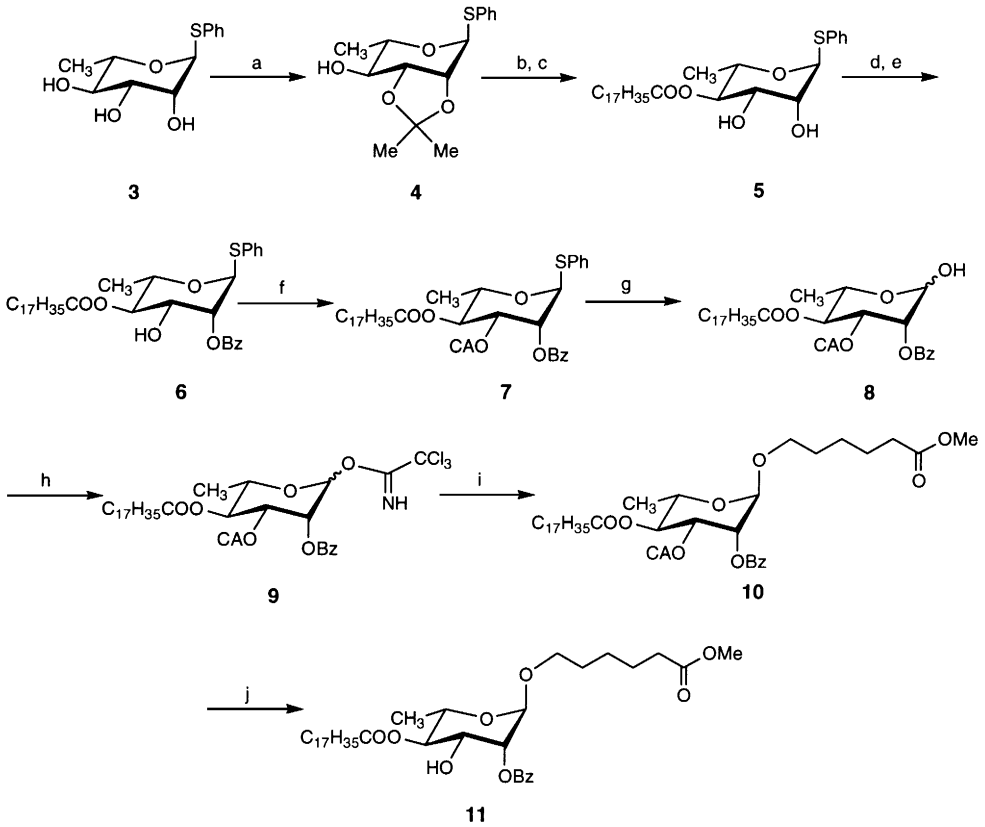
2.1. Synthesis of the lipid-tagged monosaccharides

2.1.1. The rhamnose moiety

Rhamnosyl trichloroacetimidate **9** (Scheme 1) was selected as the key intermediate for the rhamnose residues featuring a participating benzoyl group at O-2, a selectively removable monochloroacetyl group at O-3, and the stearoyl lipid label at O-4. This compound was synthesized from the thiorhamnoside **3** that was first converted to the acetal **4**.[18] In this study, the use of scandium trifluoromethanesulfonate [$Sc(OTf)_3$] as the catalyst has been investigated and it was found that $Sc(OTf)_3$ is a powerful activator in the synthesis of carbohydrate acetals and orthoesters (vide infra).[19] Thus, treatment of **3** and DMP in acetone in the presence of less than 0.1% molar equivalents of $Sc(OTf)_3$ afforded **4** in a nearly quantitative yield. It is noted that conventional approaches often require much larger amounts of the promoters, e.g. CSA or *p*-toluenesulfonic acid.[20] Treatment of **4** with stearoyl chloride in the presence of pyridine, followed by acid-catalyzed removal of the isopropylidene group, afforded the diol **5**. Conversion to the benzoylated derivative **6** was achieved in a two-step procedure. First, the diol **5** was treated with trimethyl orthobenzoate in the presence of $Sc(OTf)_3$ to give a cyclic orthoester. Next, this intermediate was treated with aqueous acetic acid to afford compound **6** in 84% overall yield. Acylation with monochloroacetic anhydride (→**7**, 94%) followed by $(CF_3CO_2)_2Hg$-assisted hydrolysis[21] gave the hemiacetal **8** in 76% yield. Subsequent reaction of **8** with trichloroacetonitrile in the presence of DBU afforded the trichloroacetimidate donor **9** that was condensed with 5-(methoxycarbonyl)pentanol[22] to yield the spacer-linked rhamnoside **10** (89%). The HO-3 group in **10** was unmasked by treatment with thiourea to provide the rhamnose acceptor **11** in 86% yield.

2.1.2. The galactose moiety

The galactosyl donor **14** was prepared (Scheme 2) from the known thiogalactoside[23] **12** which was first treated with DMP in the presence of $Sc(OTf)_3$ to afford the mixed isopropylidene acetal[20] **13** in 86%

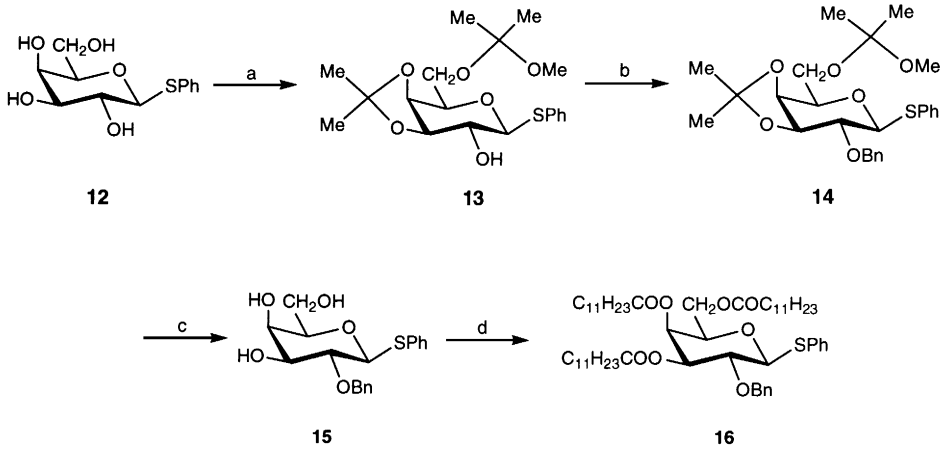


Scheme 1. Reagents and conditions: (a) CH_3COCH_3, $(CH_3)_2C(OCH_3)_2$, $Sc(OTf)_3$ (cat.), 23°C, 2 h, 96%; (b) 1.2 equiv. of $C_{17}H_{37}COCl$, C_5H_5N, CH_2Cl_2, 0°C, 15 min; (c) AcOH–H_2O, 50°C, 2 h, 79% for two steps; (d) 1.5 equiv. of $PhC(OCH_3)_3$, CH_2Cl_2, $Sc(OTf)_3$ (cat.), 23°C, 1 h; (e) MeOH–AcOH, 23°C, 8 h, 84% for two steps; (f) 1.3 equiv. of $(ClCH_2CO)_2O$, C_5H_5N, CH_2Cl_2, 0°C, 1 h, 94%; (g) 1.6 equiv. of $Hg(OCOCF_3)$, CH_2Cl_2, H_2O, 23°C, 76%; (h) 2.9 equiv. of CCl_3CN, 1,8-diazabicyclo[5.4.0]undec-7-ene (cat.), CH_2Cl_2, −10°C, 76%; (i) 1.5 equiv. of 5-(methoxycarbonyl)pentanol, CH_2Cl_2, $CF_3SO_3Si(CH_3)_3$ (cat.), 0°C, 89%; (j) 7.5 equiv. of $CS(NH_2)_2$, C_5H_5N, DMF, 23°C, 3 h, 86%

yield. Next, **13** was benzylated with benzyl bromide in the presence of sodium hydride (→**14**) followed by removal of the acetal groups in aqueous acetic acid to provide the triol **15** in 68% overall yield. Reaction of **15** with lauroyl chloride in the presence of pyridine gave the lipid-tagged galactosyl donor **16** as a crystalline material in 98% yield. It was noted that **16** separated from the reaction mixture and could be isolated in an analytically pure form by filtration followed by washing with EtOH. Unexpectedly, attempted synthesis of the corresponding *O*-stearoylated derivative failed because of solubility problems.

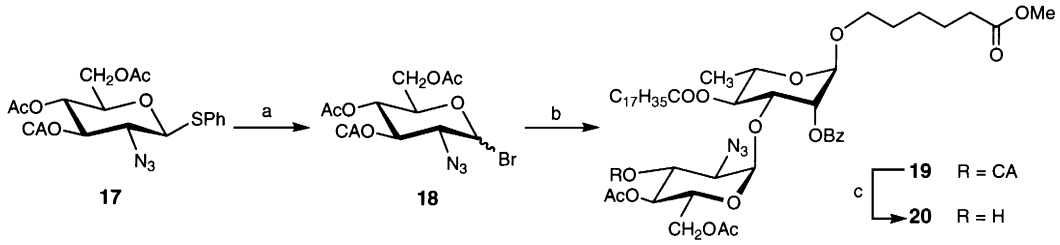
2.2. Assembly of the lipid-tagged tetrasaccharide module

The lipidated tetrasaccharide module **26** was assembled by stepwise condensation of the four monosaccharide components. Thus, glycosyl bromide **18** obtained from thioglucoside[24] **17** by treatment with bromine was condensed with rhamnosyl acceptor **11** in the presence of silver trifluoromethanesulfonate to afford the protected disaccharide **19** in 57% yield (Scheme 3). Treatment of this compound with thiourea afforded the disaccharide acceptor **20** in 85% yield. The galactosyl donor **21** was obtained from the thiogalactoside **16** by treatment with chlorine (Scheme 4) and was condensed without purification with the disaccharide **20** in the presence of silver trifluoromethanesulfonate and 2,6-di-^{t}butyl-4-methylpyridine



Scheme 2. Reagents and conditions: (a) CH_3COCH_3, $(CH_3)_2C(OCH_3)_2$, $Sc(OTf)_3$ (cat.), 23°C, 2 h, 86%; (b) approximately 2 equiv. of NaH, 1.2 equiv. of benzyl bromide, DMF, 0°C, 30 min; (c) MeOH–AcOH, 70°C, 24 h, 68% for two steps; (d) 1.3 equiv. of lauroyl chloride, CH_2Cl_2, C_5H_5N, 0°C, 3 h, 98%

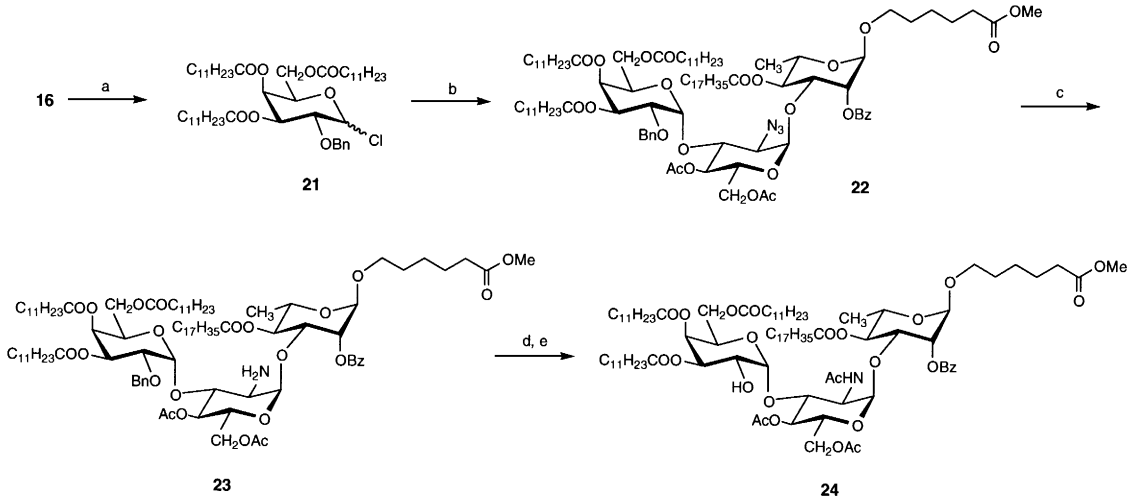
(DBMP) to give the trisaccharide **22**. At this stage, use was made of the lipophilic nature of **22** to remove impurities from **22** before further transformations. Thus, the crude reaction mixture was applied to a C-18 column containing dimethyloctadecylsilyl groups on silica particles, made in MeOH. The column was washed with MeOH that completely removed DBMP and the phenylthio moiety obtained in the chlorinolysis of **16**. Subsequent washing with MeOH–EtOH and EtOH eluted **22** together with decomposition products from **21**. Crude **22** was then subjected to a Staudinger reaction by treatment with PPh_3 followed by hydrolysis to afford the amine **23** in 78% overall yield (from **20**). Subsequent *N*-acetylation with Ac_2O in EtOH followed by hydrogenolytic removal of the benzyl group afforded the trisaccharide **24** in 93% yield. As the final step in the tetrasaccharide assembly, condensation of the rhamnosyl trichloroacetimidate **9** with the acceptor **24** (Scheme 5) in the presence of trimethylsilyl trifluoromethanesulfonate afforded tetrasaccharide **25**, which was subjected to treatment by thiourea to afford the lipidated tetrasaccharide module **26** in 85% overall yield. The assigned interglycosidic stereochemistry for **26** and the intermediates were verified by ^1H and ^{13}C NMR spectroscopic data described in the Experimental section.



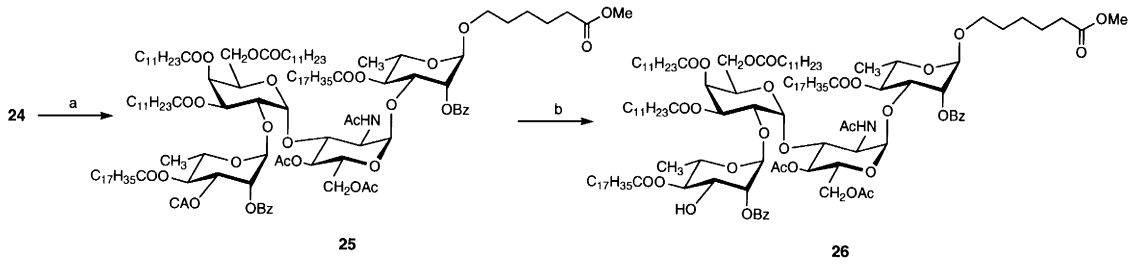
Scheme 3. Reagents and conditions: (a) 4.4 equiv. of Br_2, CH_2Cl_2, 0°C, 10 min, then hex-1-ene (excess); (b) 0.5 equiv. of **11**, 2.0 equiv. of 2,6-di-^{t}butyl-4-methylpyridine, 3 equiv. of CF_3SO_3Ag, 0°C, 20 min, 57%; (c) 6.5 equiv. of $CS(NH_2)_2$, C_5H_5N, DMF, 23°C, 8 h, 85%

2.3. Construction of the target oligosaccharides

Having prepared the lipid-tagged tetrasaccharide sector **26**, it was possible to examine the hypothesis that lipid protecting groups may, indeed, facilitate the isolation of protected oligosaccharides without



Scheme 4. Reagents and conditions: (a) Cl_2 (excess), CH_2Cl_2–CCl_4, 0°C, 10 min; (b) 0.3 equiv. of **20**, 3 equiv. of 2,6-di-^{t}butyl-4-methylpyridine, 5 equiv. of CF_3SO_3Ag, 0°C, 20 min; (c) approximately 10 equiv. of PPh_3, CH_2Cl_2, 23°C, 24 h, then H_2O, 23°C, 24 h, 78%; (d) Ac_2O, CH_2Cl_2, 0°C, 2 h; (e) H_2 Pd–C, EtOH–AcOH, 200 psi, 23°C, 24 h, 93% for two steps



Scheme 5. Reagents and conditions: (a) 2.3 equiv. of **9**, CH_2Cl_2, $CF_3SO_3Si(CH_3)_3$ (cat.), 0→23°C, 30 min; (b) approximately 13 equiv. of $CS(NH_2)_2$, DMF, 23°C, 8 h, 85% for two steps

the need of silica gel chromatography. As the first step toward higher-membered oligosaccharides, **26** was condensed with the tetrasaccharide donor **2** available from an earlier study[2] under promotion by a catalytic amount of trimethylsilyl trifluoromethanesulfonate (Scheme 6). The product mixture was applied to a C-18 column made in MeOH. Elution by a MeOH–EtOH gradient up to 40% EtOH concentration removed all the impurities and side products arising from **2**. A 1:1 mixture of MeOH–EtOH eluted unreacted acceptor **26**. Further elution with EtOH and ^{i}PrOH eluted the octasaccharide **27** in a pure form in 84% yield based on recovered **26**. The all-α-glycosidic linkages were verified by the one-bond heteronuclear coupling constants for all the anomeric proton–carbon pairs that are in the range of 167–172 Hz.[25] Next, **27** was treated with thiourea to afford the acceptor **28** in 97% yield using the C-18 column and EtOH and ^{i}PrOH for isolation. Two more cycles (Schemes 6 and 7) involving glycosylation with approximately 4 equivalents of the tetrasaccharide donor **2** under trimethylsilyl trifluoromethanesulfonate activation and deprotection by thiourea afforded the dodeca- (**29** and **30**) and hexadecasaccharides (**31** and **32**). Crucial for the structural proof of these intermediates were the NMR and mass spectroscopic data that provided evidence for the proposed structures as described in the Experimental section. All these intermediates were isolated in pure form by application of the crude reaction mixtures to a C-18 column followed by elution with MeOH, EtOH, and ^{i}PrOH. In one instance (compound **32**) MeCN and benzene were also tested as possible eluants. These had no advantages over the alcohols used in the other cases. The excellent yields in these reactions combined with the ease of

purification prompted the exploration of the limits of this new approach. Therefore, donor **2** was reacted with the hexadecasaccharide **33** in the presence of trimethylsilyl trifluoromethanesulfonate. The resulting product mixture containing eicosasaccharide **34** could be isolated by using the C-18 technique with MeOH, EtOH, and ^{i}PrOH as the eluants. However, the purity of the product was only approximately 80% as judged by HPLC, necessitating the use of silica gel chromatography to obtain **33** in pure form. Thus, it appears that the five lipid protecting groups, including two stearoyl and three lauroyl groups, can render the hexadecasaccharide **31** sufficiently lipophilic for product isolation by using solely the C-18 technique, whereas this combination of lipophilic protecting groups is not sufficient for the purification of higher-membered oligosaccharides. Dechloroacetylation of **33** with thiourea afforded the eicosasaccharide acceptor **34** in 84% yield after purification through the C-18 column. As the final glycosylation experiment in this work, alcohol **34** and tetrasaccharide **2** were condensed under trimethylsilyl trifluoromethanesulfonate activation to afford the tetracosasaccharide **35**. Again, much of the side products could be removed by using the C-18 technique and silica gel chromatography was used for the final purification. Conventional deprotection of **35** involving NaOMe-assisted methanolysis (→**36**) and hydrogenolysis afforded the spacer-linked tetracosasaccharide **37** after purification by Biogel P-6 chromatography (Fig. 1). The structure of **37** is supported by spectroscopic evidence reported in the Experimental section.

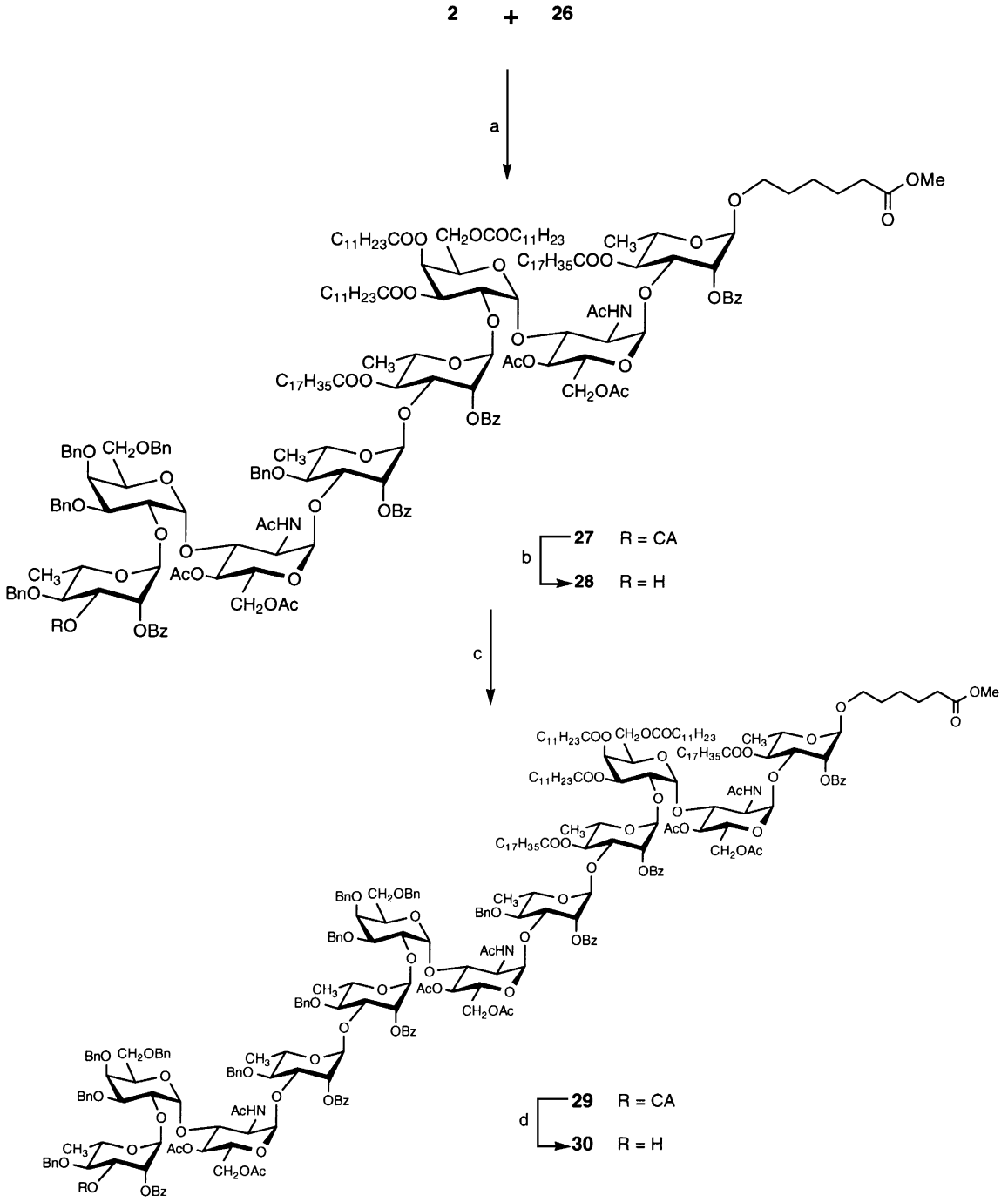
3. Conclusions

In summary, a new approach has been proposed for chemical synthesis of higher-membered oligosaccharides that involves the use of strategically positioned lipid-type protecting groups. It has been demonstrated that intermediates containing such groups may be isolated and purified by the use of a commercially available reverse-phase adsorbent that can be re-used many times. It has been shown that five lipid groups can provide sufficient hydrophobicity to an oligosaccharide up to a hexadecasaccharide to allow product isolation solely by the C-18 technique. This number may show some variance with other protecting group combinations. The proposed approach can substantially alleviate the difficulties associated with the conventional silica gel chromatographic purification of protected oligosaccharide intermediates and utilizes environmentally friendly solvents that are less expensive than the solvents conventionally used for silica gel chromatography. The technique preserves the efficiency of the solution-phase reactions. Importantly, the lipidated intermediates may also be purified by the conventional methods, that may be necessary when anomeric mixtures are present. Additionally, a new, highly efficient method has been proposed for the synthesis of carbohydrate acetals and cyclic orthoesters employing scandium trifluoromethanesulfonate as the catalyst.

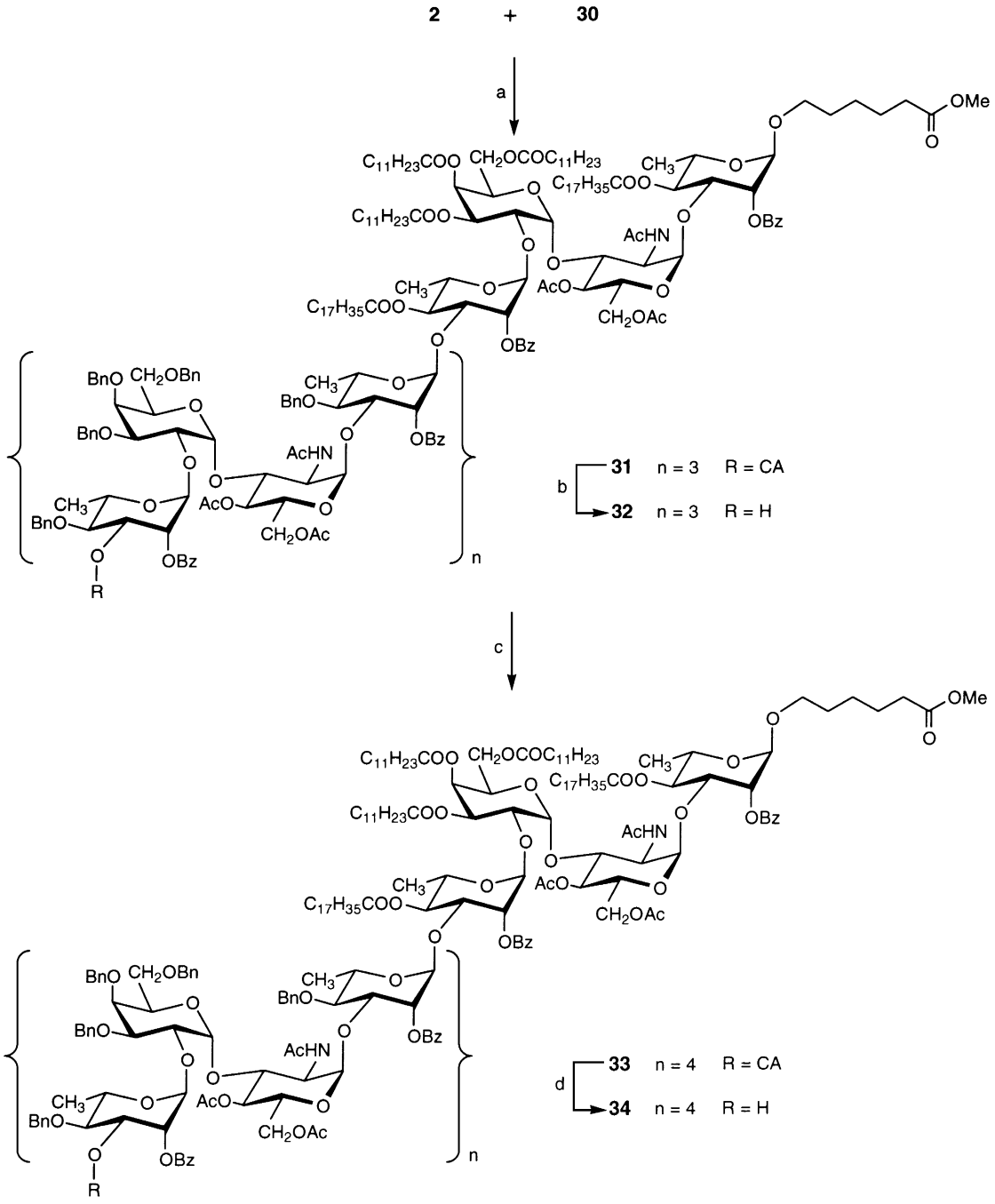
4. Experimental

4.1. General methods

All chemicals were commercial grade and used without purification. Solvents for chromatography were distilled prior to use. Anhydrous solvents were obtained from Aldrich. Column chromatography was performed on either dimethyloctadecylsilyl-bonded amorphous silica (C-18 adsorbent, 125 Å) obtained from Waters Corp., Milford, MA, or on silica gel 60 (0.040–0.063 mm). HPTLC plates were obtained from Merck. Melting points were taken on a Meltemp capillary melting point apparatus and



Scheme 6. Reagents and conditions: (a) approximately 3.6 equiv. of **2**, $CF_3SO_3Si(CH_3)_3$ (cat.), 0°C, 4 h, 84%; (b) 5 equiv. of $CS(NH_2)_2$, C_5H_5N, DMF, 23°C, 24 h, 97%; (c) 4.5 equiv. of **2**, $CF_3SO_3Si(CH_3)_3$ (cat.), 0°C, 3 h, 89%; (d) 12 equiv. of $CS(NH_2)_2$, 2,6-di-^{t}butyl-4-methylpyridine, DMF, 23°C, 24 h, 97%



Scheme 7. Reagents and conditions: (a) 4 equiv. of **2**, $CF_3SO_3Si(CH_3)_3$ (cat.), 0°C, 3 h, 77%; (b) 6.5 equiv. of $CS(NH_2)_2$, 2,6-di-^{t}butyl-4-methylpyridine, DMF, 23°C, 24 h, 92%; (c) 4 equiv. of **2**, $CF_3SO_3Si(CH_3)_3$ (cat.), 0°C, 2 h, 53%; (d) 10 equiv. of $CS(NH_2)_2$, 2,6-di-^{t}butyl-4-methylpyridine, DMF, 23°C, 24 h, 84%

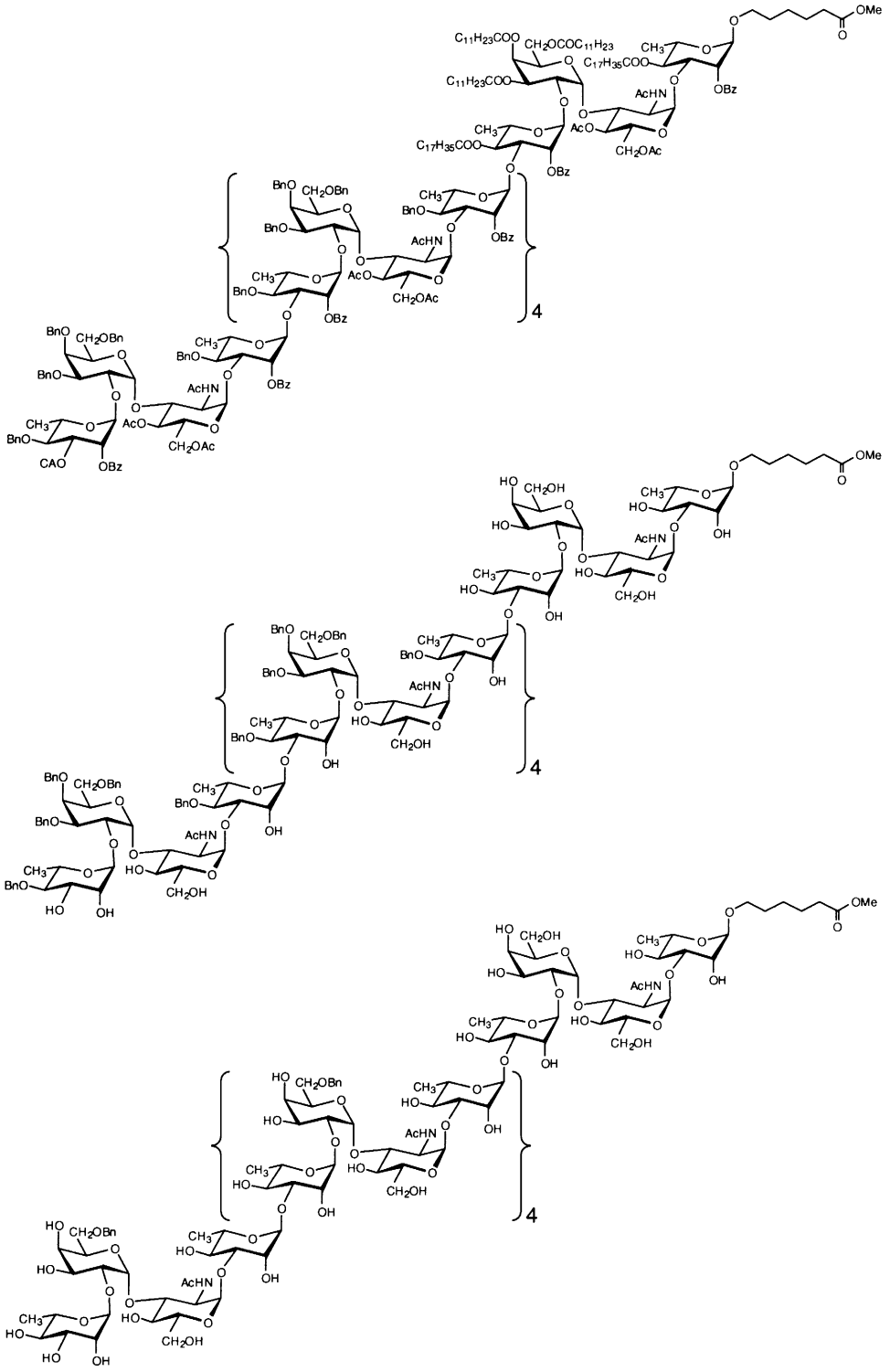


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Fig. 1.

are uncorrected. Optical rotations were measured at 23°C with a Perkin–Elmer Type 341 polarimeter. The ^{1}H and ^{13}C NMR spectra were recorded at 300 and 75.5 MHz, respectively, in $CDCl_3$, unless stated otherwise. Internal references: TMS (0.000 ppm for ^{1}H for solutions in $CDCl_3$), acetone (2.225 ppm for ^{1}H and 31.00 ppm for ^{13}C for solutions in D_2O), methanol (3.358 ppm for ^{1}H and 49.68 ppm for ^{13}C for solutions in D_2O), and $CDCl_3$ (77.00 ppm for ^{13}C for solutions in $CDCl_3$). Coupling constants are given in hertz. The mass spectra were recorded at the Laboratory of Analytical Chemistry, NIDDK, NIH, Bethesda, MD. Ammonia was used as the ionizing gas for the chemical ionization (CI) mass spectra. The fast atom bombardment (FAB) mass spectra were obtained using 6 keV Xe atoms to ionize samples from dithiothreitol/dithioerythritol, 3-nitrobenzyl alcohol or glycerol as the matrix. Elemental analyses were performed by Atlantic Microlab, Inc., Norcross, GA.

Abbreviations: Ac=acetyl, AgOTf=silver trifluoromethanesulfonate, Bz=benzoyl, Bn=benzyl, CA=chloroacetyl, CI=chemical ionization, DBMP=2,6-di-*t*butyl-4-methylpyridine, DBU=diazabicyclo[5.4.0]undec-7-ene, DMF=*N*,*N*-dimethylformamide, FAB=fast atom bombardment, Gal*p*=galactopyranosyl, Glc*p*=glucopyranosyl, GlcpNAc=2-acetamido-2-deoxy-D-glucopyranosyl, HPTLC=high performance thin layer chromatography, Ph=phenyl, Rha*p*=rhramnopyranosyl, TMSOTf=trimethylsilyl trifluoromethanesulfonate.

*4.2. Phenyl 2,3-*O*-isopropylidene-1-thio-α-*L*-rhamnopyranoside **4***

Scandium trifluoromethanesulfonate (50 mg, 0.1 mmol) was added to a solution of **3**[18] (45 g, 330 mmol) in a 1:1 mixture of acetone and 2,2-dimethoxypropane (200 mL) at room temperature. After 2 h, the solution was treated with Et_3N (2 mL) and was concentrated. Trituration of the residue in hexane afforded **4** (50.0 g, 96%) whose physical and spectral properties matched those of the authentic preparation.[18]

*4.3. Phenyl 4-*O*-stearoyl-1-thio-α-*L*-rhamnopyranoside **5***

To a stirred solution of **4** (10.0 g, 33.8 mmol) in CH_2Cl_2 (40 mL) and C_5H_5N (10 mL) was added stearoyl chloride (13.7 mL, 40.6 mmol) at 0°C. After 15 min, the reaction mixture was treated with MeOH (excess). The volatiles were removed by distillation to afford a solid {$[\alpha]_D$ −110 (*c* 0.7, $CHCl_3$); ^{1}H NMR: δ 7.25–7.50 (m, 5H), 5.77 (br s, 1H), 4.95 (dd, 1H, *J*=7.9, *J*=9.8), 4.36 (dd, 1H, *J*=1.0, *J*=5.3), 4.24 (dd, 1H, *J*=5.3, *J*=7.7), 4.21 (dq, 1H), 2.28–2.44 (m, 2H), 1.60–1.70 (m, 2H), 1.57 (s, 3H), 1.36 (s, 3H), 1.19–1.33 (m), 1.12 (d, 1H, *J*=6.3), 0.88 (m, 3H); ^{13}C NMR: δ 172.9, 131.8, 129.1, 127.7, 110.0, 83.7, 76.5, 75.6, 74.3, 65.7, 34.4, 31.9, 29.7, 29.6, 29.5, 29.4, 29.2, 29.1, 27.7, 26.6, 24.9, 22.7, 16.9, 14.1. CI-MS: *m/z* 580 ($C_{33}H_{54}O_5S+NH_4$). Anal. calcd for $C_{33}H_{54}O_5S$: C, 70.42; H, 9.67. Found: C, 70.59; H, 9.80.} Toluene was added to and removed from the residue several times. A solution of the residue in AcOH (100 mL) and H_2O (20 mL) was stirred at 50°C for 2 h. Cooling to 0°C afforded a precipitate which was isolated by filtration followed by washing with H_2O to afford **5** (14.2 g, 79%): mp 79–81°C; $[\alpha]_D$ –160 (*c* 0.6, $CHCl_3$); ^{1}H NMR: δ 7.22–7.49 (m, 5H), 5.54 (d, 1H, *J*=1.6), 4.86 (t, 1H, *J*=9.5), 4.30 (dq, 1H), 4.21 (dd, 1H, *J*=1.6, *J*=3.5), 3.90 (dd, 1H, *J*=3.5, *J*=9.5), 2.40 (dd, 1H, *J*=6.9, *J*=8.0), 1.60–1.70 (m, 1H), 1.25–1.35 (m), 1.23 (d, 1H, *J*=6.3), 0.88 (m, 3H); ^{13}C NMR: δ 175.0, 131.3, 129.1, 127.5, 87.2, 75.6, 72.3, 70.9, 66.9, 34.4, 31.9, 29.7, 29.6, 29.5, 29.4, 29.2, 29.1, 24.7, 22.7, 17.4, 14.1). CI-MS: *m/z* 540 ($C_{30}H_{50}O_5S+NH_4$). Anal. calcd for $C_{30}H_{50}O_5S$: C, 68.93; H, 9.64. Found: C, 69.07; H, 9.70.

4.4. *Phenyl 2*-O-*benzoyl-4*-O-*stearoyl-1-thio-α*-L-*rhamnopyranoside* **6**

A stirred mixture of **5** (21.0 g, 40.2 mmol), trimethyl orthobenzoate (10.3 mL, 60.3 mmol), and CH_2Cl_2 (100 mL) was treated at room temperature with scandium trifluoromethanesulfonate (50 mg). After 1 h, to the solution was added Et_3N (1 mL) followed by removal of the volatiles by distillation. To a solution of the residue in MeOH (80 mL) was added 90% acetic acid (150 mL). After 8 h, the solution was concentrated to afford a residue that was purified by column chromatography (10:1 hexane:EtOAc) to give **6** as a syrup (21.1g, 84%): $[\alpha]_D$ −61 (*c* 0.7, $CHCl_3$); ^{1}H NMR: δ 7.05–7.87 (m, 5H), 5.41 (d, 1H, *J*=1.5), 5.39 (dd, 1H, *J*=1.5, *J*=3.3), 4.88 (t, 1H, *J*=9.5), 4.19 (dq, 1H), 3.92 (ddd, 1H), 2.21 (t, 2H, *J*=7.9), 1.46 (m, 2H), 0.97–1.15 (m), 0.67 (m, 3H); ^{13}C NMR: δ 174.5, 165.7, 122.7–133.4, 85.8, 74.8, 69.6, 67.4, 34.4, 31.9, 29.7, 29.6, 29.4, 29.3, 29.2, 29.1, 24.9, 22.7, 17.4, 14.1. CI-MS: *m/z* 644 ($C_{37}H_{54}O_6S$+NH_4). Anal. calcd for $C_{37}H_{54}O_6S$: C, 70.89; H, 8.68. Found: C, 70.71; H, 8.52.

4.5. *Phenyl 2*-O-*benzoyl-3*-O-*chloroacetyl-4*-O-*stearoyl-1-thio-α*-L-*rhamnopyranoside* **7**

To a solution of **6** (8.5 g, 13.6 mmol) in CH_2Cl_2 (50 mL) were added at 0°C C_5H_5N (10 mL) and chloroacetic anhydride (3.0 g, 17.6 mmol). After 1 h, the solution was treated with MeOH (excess) and was concentrated. Column chromatographic purification of the residue (10:1 hexane:EtOAc) gave **7** as a syrup (8.9 g, 94%): $[\alpha]_D$ −33 (*c* 2.5, $CHCl_3$); ^{1}H NMR: δ 728–8.08 (m, 10H), 5.76 (dd, 1H), 5.57 (d, 1H), 5.47 (dd, 1H, *J*=3.1, *J*=9.9), 5.30 (t, 1H, *J*=3.9, *J*=9.9), 4.45 (dq, 1H), 3.98 (d, 1H, *J*=∼15), 3.92 (d, 1H, *J*=∼15), 2.33 (br t, 2H, *J*=7.4), 1.54–1.66 (m, 2H), 1.29 (d, 1H, *J*=6.3), 1.23–1.27 (m), 0.88 (m, 3H); ^{13}C NMR: δ 174.2, 166.1, 165.7, 121.9–133.0, 85.7, 71.6, 71.5, 70.7, 67.9, 40.5, 34.2, 29.7, 29.4, 29.1, 24.9, 17.5. CI-MS: *m/z* 720 ($C_{39}H_{55}ClO_7S$+NH_4). Anal. calcd for $C_{39}H_{55}ClO_7S$: C, 66.60; H, 7.88. Found: C, 66.92; H, 8.01.

4.6. *2*-O-*Benzoyl-3*-O-*chloroacetyl-4*-O-*stearoyl*-L-*rhamnopyranose* **8**

To a stirred mixture of **7** (10.0 g, 14.2 mmol), CH_2Cl_2 (90 mL), and H_2O (8.7 mL) was added $Hg(OCOCF_3)_2$ (9.1 g, 21.3 mmol) at 0°C. After 3 h, the mixture was treated with an aqueous solution of KI. The solids so obtained were removed by filtration through a layer of Celite. The organic layer was concentrated and the residue was treated with isopropyl ether. Removal of the solids followed by concentration of the solution afforded a residue that was purified by column chromatography (6:1 hexane:EtOAc) to give crystalline **8** (6.6 g, 76%): $[\alpha]_D$ +53 (*c* 0.5, $CHCl_3$); ^{1}H NMR: δ 7.46–8.09 (m, 5H), 5.58–5.53 (m, 2H), 5.35 (dd, 1H), 5.25 (t, 1H, *J*=9.8 Hz), 4.20 (dq, 1H, *J*=6.3), 3.97 and 3.91 (1 d, 2H, *J*=∼15), 2.83 (d, 1H, *J*=3.9), 2.31 (t, 2H, *J*=7.4), 1.52–1.64 (m, 2H), 1.36–1.62 (m), 0.88 (m, 3H); ^{13}C NMR: δ 172.9, 166.6, 165.7, 133.6, 130.0, 128.7, 128.6, 92.2, 70.9, 70.6, 70.4, 66.5, 40.5, 34.2, 31.9, 29.7, 29.6, 29.4, 29.3, 29.2, 29.1, 24.9, 22.7, 17.6, 14.1. Anal. calcd for $C_{31}H_{51}ClO_8$: C, 63.41; H, 8.75. Found: C, 65.05; H, 8.45.

4.7. *2*-O-*Benzoyl-3*-O-*chloroacetyl-4*-O-*stearoyl*-L-*rhamnopyranosyl trichloroacetimidate* **9**

To a stirred solution of **8** (8.15 g, 13.3 mmol) in CH_2Cl_2 (50 mL) were added at −10°C CCl_3CN (3.1 mL, 38.8 mmol) and DBU (0.2 mL). The reaction mixture was allowed to reach room temperature then was concentrated. Filtration through a column of silica gel (10:1 hexane:EtOAc) afforded **9** (7.7 g, 76%) as a syrup: (major isomer) ^{1}H NMR: δ 7.40–8.77 (m, 5H), 6.36 (d, 1H, *J*=1.5), 5.71 (dd, 1H), 5.53 (dd,

1H, *J*=3.4, *J*=10.0), 5.33 (t, 1H, *J*=10.0), 2.32 (t, 2H, *J*=7.6), 1.53–1.65 (m, 2H), 1.33 (d, 3H, *J*=6.3), 1.2–1.3 (m), 0.88 (m, 3H).

*4.8. 5-(Methoxycarbonyl)pentyl 2-*O*-benzoyl-3-*O*-chloroacetyl-4-*O*-stearoyl-α-*L*-rhamnopyranoside **10***

To a solution of **9** (1.5 g, 1.98 mmol) and 5-(methoxycarbonyl)pentanol (430 μL, 3 mmol) in CH_2Cl_2 (10 mL) was added TMSOTf (5 μL) at 0°C. After 10 min, the solution was treated with Et_3N (excess) and was concentrated. Column chromatographic purification of the residue (10:1 hexane:EtOAc) afforded **10** (1.3 g, 89%) as a syrup: $[\alpha]_D$ +20 (*c* 0.5, $CHCl_3$); ^{1}H NMR: δ 7.45–8.09 (m, 5H), 5.43–5.49 (m, 2H), 5.22 (t, 1H, *J*=9.6), 4.87 (br s, 1H), 3.96 (dq, 1H), 3.89 and 3.96 (2 d, 2H, *J*=~15), 3.72 (m, 1H), 3.68 (s, 3H), 3.46 (m, 1H), 2.35 and 2.30 (2 t, 4H), 1.60–1.73 (m, 4H), 1.47–1.38 (m, 2H), 1.22–1.33 (m), 0.87 (m, 3H); ^{13}C NMR: δ 173.0, 166.8, 165.7, 139.9, 133.5, 128.6, 97.4, 71.3, 70.7, 70.3, 68.0, 66.4, 51.5, 40.6, 34.2, 33.9, 31.9, 29.7, 29.5, 29.4, 29.3, 29.2, 29.1, 29.0, 25.6, 24.9, 24.7, 22.7, 17.5, 14.1. CI-MS: *m/z* 756 ($C_{40}H_{63}ClO_{10}$+NH_4). Anal. calcd for $C_{40}H_{63}ClO_{10}$: C, 64.98; H, 8.59. Found: C, 64.84; H, 8.44.

*4.9. 5-(Methoxycarbonyl)pentyl 2-*O*-benzoyl-4-*O*-stearoyl-α-*L*-rhamnopyranoside **11***

A solution of **10** (3.9 g, 5.27 mmol), thiourea (3 g, 39.5 mmol), C_5H_5N (2 mL), and DMF (20 mL) was kept at 23°C for 3 h followed by removal of the volatiles under vacuum. The residue was treated with $CHCl_3$ and the solids so obtained were removed by filtration. Extractive work-up ($CHCl_3$/H_2O) followed by column chromatographic purification of the residue (10:1 hexane:EtOAc) afforded **11** (3.0 g, 86%) as a syrup: $[\alpha]_D$ +14 (*c* 0.7, $CHCl_3$); ^{1}H NMR: δ 7.45–8.09 (m, 5H), 5.30 (dd, 1H, *J*=1.4, *J*=3.4), 5.00 (t, 1H, *J*=10.0), 4.90 (d, 1H), 4.14 (ddd, 1H, *J*=3.4, *J*=8.3, *J*=10.0), 3.87 (dq, 1H), 3.70 (m, 1H), 3.68 (s, 3H), 3.45 (m, 1H), 2.40 (br t, 1H), 2.33 (br t, 1H), 2.20 (d, 1H, *J*=8.2), 1.59–1.73 (m, 6H), 1.35–1.46 (m, 2H), 1.18–1.33 (m), 0.88 (m, 3H); ^{13}C NMR: δ 174.6, 165.9, 133.5, 129.9, 128.5, 97.2, 74.7, 73.4, 69.0, 67.9, 66.0, 51.5, 34.4, 33.9, 31.9, 29.7, 29.6, 29.5, 29.4, 29.3, 29.1, 25.7, 25.0, 24.7, 22.7, 17.6, 14.1. CI-MS: *m/z* 680 ($C_{38}H_{62}O_9$+NH_4). Anal. calcd for $C_{38}H_{62}O_9$: C, 68.85; H, 9.43. Found: C, 68.70; H, 9.39.

*4.10. Phenyl 3,4-*O*-isopropylidene-6-O-(2-methoxy-2-methyl-ethyl)-1-thio-β-*D*-galactopyranoside **13***

To a solution of phenyl 1-thio-β-D-galactopyranoside[23] (**12**, 15.0 g, 55.4 mmol) in acetone (200 mL) were added 2,2-dimethoxypropane (100 mL) and scandium trifluoromethanesulfonate (50 mg) at 23°C. After 30 min, the solution was treated with Et_3N (1 mL) and was concentrated. Column chromatographic purification of the residue (3:1 hexane:EtOAc containing 0.01% of Et_3N) afforded **13** (18.2 g, 86%) as a syrup: $[\alpha]_D$ –11 (*c* 0.7, $CHCl_3$); ^{1}H NMR: δ 4.48 (d, 1H, *J*=10.1), 4.20 (dd, 1H, *J*=2.0, *J*=5.4), 4.04 (br t, 1H), 3.90 (ddd, 1H), 3.76 (dd, 1H, *J*=6.9, *J*=9.9), 3.67 (dd, 1H, *J*=5.2, *J*=9.9), 3.58 (dd, 1H, *J*=6.9, *J*=10.1), 3.23 (s, 3H), 1.42 (s, 3H), 1.38 (s, 3H), 1.37 (s, 3H), 1.33 (s, 3H); ^{13}C NMR: δ 132.3, 128.9, 127.8, 110.2, 100.1, 87.8, 79.1, 76.0, 73.8, 71.5, 60.5, 48.6, 28.1, 26.3, 24.4. Anal. calcd for $C_{19}H_{28}O_6S$: C, 59.35; H, 8.34. Found: C, 59.47; H, 7.50.

*4.11. Phenyl 2-O-benzyl-1-thio-β-*D*-galactopyranoside **15***

To a stirred solution of **13** (21.3 g, 55.4 mmol) in DMF (100 mL) was added at 0°C NaH (4.0 g of a 60% suspension in mineral oil, approximately 100 mmol) in small portions over 15 min. The mixture

was stirred for another 20 min, then was treated with benzyl bromide (7.9 mL, 66.4 mmol). After 30 min, the mixture was treated with MeOH (excess). Extractive work-up ($CHCl_3/H_2O$) followed by column chromatographic purification of the residue (4:1 hexane:EtOAc) afforded phenyl 2-*O*-benzyl-3,4-*O*-isopropylidene-6-*O*-(2-methoxy-2-methyl-ethyl)-1-thio-β-D-galactopyranoside **14** as a syrup {$[\alpha]_D$ −17 (*c* 0.7, $CHCl_3$); ^{1}H NMR: δ 7.20–7.58 (m, 5H), 4.82 (d, 1H, *J*=12.2), 4.68 (d, 1H, *J*=12.2), 4.66 (d, 1H, *J*=9.6), 4.26 (dd, 1H), 4.21 (dd, 1H, *J*=1.7, *J*=5.7), 3.85 (ddd, 1H), 3.74 (dd, 1H, *J*=7.1, *J*=9.9), 3.64 (dd, 1H, *J*=5.0, *J*=9.9), 3.53 (dd, 1H, *J*=6.2, *J*=9.6), 3.13 (s, 3H), 1.41 (s, 3H), 1.35 (s, 6H), 1.34 (s, 3H); ^{13}C NMR: δ 137.8, 137.1, 131.5, 128.7, 128.3, 128.2, 128.1, 127.7, 127.1, 110.0, 100.0, 86.1, 79.8, 78.2, 75.8, 73.9, 73.4, 60.5, 48.6, 27.8, 26.3, 24.4. Anal. calcd for $C_{26}H_{34}O_6S$: C, 65.80; H, 7.22. Found: C, 65.55; H, 7.14.} To a solution of **14** in MeOH (100 mL) was added 80% aqueous acetic acid (200 mL). After 24 h at 70°C the volatiles were removed by distillation under vacuum. Trituration of the residue with ether afforded crystalline **15** (13.5 g, 68%): mp 125–126°C; $[\alpha]_D$ −18 (*c* 0.5, DMF); ^{1}H NMR (CD_3OD): δ 7.17–7.56 (m, 5H), 4.82 (d, 1H, *J*=10.9), 4.77 (d, 1H, *J*=10.9), 4.66 (d, 1H, *J*=8.8), 3.90 (br d, 1H, *J*=2.7), 3.78 (dd, 1H, *J*=6.7, *J*=11.4), 3.71 (dd, 1H, *J*=5.5, *J*=11.4), 3.65 (m, 1H), 3.62 (t, 1H, *J*=9.2), 3.54 (br t, 1H), 3.31 (m, 1H); ^{13}C NMR: δ 140.4, 136.7, 132.6, 130.5, 129.9, 129.8, 129.3, 128.6, 89.8, 81.0, 80.2, 77.0, 71.3, 63.2. CI-MS: *m/z* 380 ($C_{19}H_{22}O_5S$+NH_4). Anal. calcd for $C_{19}H_{22}O_5S$: C, 62.96; H, 6.12. Found: C, 62.83; H, 6.12.

*4.12. Phenyl 2-*O*-benzyl-3,4,6-tri-*O*-lauroyl-1-thio-β-D-galactopyranoside **16***

To a stirred solution of **15** (5.8 g, 16.0 mmol) in CH_2Cl_2 (25 mL) were added, in succession at 0°C, C_5H_5N (12 mL) and lauroyl chloride (14.0 mL, 60.5 mmol). After 3 h, the mixture was treated with cold EtOH (150 mL). Filtration afforded crystalline **16** (14.5 g, 98%): mp 83–85°C; $[\alpha]_D$ +12 (*c* 0.6, $CHCl_3$); ^{1}H NMR: δ 7.30–7.60 (m, 5H), 5.43 (br d, 1H, *J*=3.0), 5.05 (dd, 1H, *J*=3.2, *J*=9.6), 4.83 (d, 1H, *J*=10.7), 4.73 (d, 1H, *J*=9.6), 4.57 (d, 1H, *J*=10.7), 4.18 (dd, 1H), 4.08 (d, 1H), 3.92 (br t, 1H), 3.72 (t, 1H, *J*=9.6), 2.36 (t, 1H, *J*=7.3), 2.28 (t, 1H, *J*=7.5), 2.34 (m 1H), 1.45–1.68 (m), 0.98–1.40 (m), 0.88 (m, 9H); ^{13}C NMR: δ 173.2, 172.7, 172.6, 132.5, 129.0, 128.8, 128.0, 87.8, 75.4, 75.2, 74.3, 74.0, 67.4, 61.6, 34.1, 34.0, 31.9, 29.6, 29.5, 29.4, 29.35, 29.26, 29.14, 25.1, 24.8, 24.6, 22.7, 14.1. CI-MS: *m/z* 926 ($C_{55}H_{88}O_8S$+NH_4). Anal. calcd for $C_{55}H_{88}O_8S$: C, 72.64; H, 9.75. Found: C, 72.86; H, 9.42.

*4.13. 5-(Methoxycarbonyl)pentyl (4,6-di-*O*-acetyl-2-azido-3-*O*-chloroacetyl-2-deoxy-α-D-Glc*p*)-(1→3)-2-*O*-benzoyl-4-*O*-stearoyl-α-L-rhamnopyranoside **19***

A solution of compound **17**[24] (2.2 g, 5.30 mmol) in CH_2Cl_2 (10 mL) was treated at 0°C with Br_2 (1.2 mL, 23.3 mmol). After 10 min, the solution containing **18** was treated with hex-1-ene (excess), then was transferred to a stirred mixture of **11** (1.6 g, 2.41 mmol), 2,6-di-^{t}butyl-4-methylpyridine (2.0 g), and 4 Å molecular sieves (~2 g) at 23°C. After 15 min, the mixture was cooled to 0°C, then was treated with AgOTf (4.0 g, 14.7 mmol). After 20 min, the mixture was treated with aqueous $NaHCO_3$. The usual processing, followed by column chromatographic purification of the residue (3:1 hexane:EtOAc), afforded **19** (1.4 g, 57%) as a syrup: $[\alpha]_D$ +80 (*c* 0.6, $CHCl_3$); ^{1}H NMR (selected): δ 5.52 (dd, 1H), 5.13–5.24 (m, 3H), 4.97 (t, 1H, *J*=9.7), 4.82 (d, 1H, *J*=1.7), 3.78 (dq, 1H), 3.63 (m, 1H), 3.61 (s, 3H), 3.39 (m, 1H), 3.27 (dd, 1H, *J*=3.2, *J*=9.7), 2.25–2.32 (m, 2H), 2.03 (s, 3H), 1.92 (s, 3H), 1.51–1.68 (m, 2H), 1.13–1.39 (m), 0.81 (m, 3H); ^{13}C NMR: δ 173.9, 172.2, 170.4, 169.5, 169.1, 166.1, 165.9, 133.4, 129.9, 129.0, 128.4, 97.5, 93.5, 72.1, 71.5, 71.3, 68.0, 67.6, 67.5, 66.5, 61.4, 60.3, 51.5, 40.3, 34.1, 33.8, 31.8, 29.6, 29.5, 29.3, 29.0, 25.6, 24.7, 24.6, 22.6, 20.6, 20.5, 17.6, 14.1. CI-MS: *m/z* 1027 ($C_{50}H_{76}ClN_3O_{16}$+ NH_4). Anal. calcd for $C_{50}H_{76}ClN_3O_{16}$: C, 59.42; H, 7.58. Found: C, 59.17; H, 7.46.

*4.14. 5-(Methoxycarbonyl)pentyl (4,6-di-*O*-acetyl-2-azido-2-deoxy-α-*D*-Glc*p*)-(1→3)-2-*O*-benzoyl-4-*O*-stearoyl-α-*L*-rhamnopyranoside **20***

A solution of **19** (2.0 g, 1.98 mmol), thiourea (1.0 g, 13.1 mmol), C_5H_5N (0.5 mL), and DMF (10 mL) was kept at 23°C for 8 h followed by removal of the volatiles under vacuum. The residue was treated with $CHCl_3$ then the solids so obtained were removed by filtration. Extractive work-up ($CHCl_3/H_2O$) followed by column chromatographic purification of the residue (4:1 hexane:EtOAc) afforded **20** (1.55 g, 85%) as a syrup: $[\alpha]_D$ +56 (*c* 0.6, $CHCl_3$); ^{1}H NMR (selected): δ 5.58 (dd, 1H), 5.38 (t, 1H, *J*=9.8), 5.15 (d, 1H, *J*=3.4), 4.44 (d, 1H, *J*=1.7), 4.44 (t, 1H, *J*=~9.6), 4.21 (ddd, 1H), 3.69 (m, 1H), 3.67 (s, 3H), 3.45 (m, 1H), 3.22 (dd, 1H, *J*=3.4, *J*=9.7); 2.05 (s, 3H), 1.96 (s, 3H), 1.50–1.68 (m, 2H), 1.12–1.42 (m), 0.81 (m, 3H); ^{13}C NMR: δ 174.0, 172.4, 170.5, 165.9, 163.2, 162.9, 133.4, 129.9, 129.3, 128.4, 97.6, 93.8, 71.8, 71.4, 70.6, 69.8, 68.0, 67.9, 67.7, 66.4, 63.0, 61.8, 51.5, 34.2, 33.9, 31.9, 29.7, 29.5, 29.3, 29.0, 25.6, 24.8, 24.6, 22.7, 20.7, 17.6, 14.1. CI-MS: *m/z* 951 ($C_{48}H_{75}N_3O_{15}$+NH_4). Anal. calcd for $C_{48}H_{75}N_3O_{15}$: C, 61.72; H, 8.09. Found: C, 61.88; H, 8.11.

*4.15. 5-(Methoxycarbonyl)pentyl (3,4,6-tri-*O*-lauroyl-α-*D*-Gal*p*)-(1→3)-(4,6-di-*O*-acetyl-α-*D*-Glc*p*NAc)-(1→3)-2-*O*-benzoyl-4-*O*-stearoyl-α-*L*-rhamnopyranoside **24***

To a solution of **16** (860 mg, 0.945 mmol) in CH_2Cl_2 (5 mL) was added at 0°C a solution of chlorine in CCl_4 (excess). After 10 min, ^{1}H NMR indicated complete disappearance of **16**. The solution containing **21** was treated with hex-1-ene (excess), then was transferred via syringe to a stirred mixture of **20** (290 mg, 0.315 mmol), 2,6-di-^{t}butyl-4-methylpyridine (600 mg, 2.92 mmol), 4 Å molecular sieves (approximately 1 g), and CH_2Cl_2 (4 mL). The mixture was stirred at 23°C for 20 min, then was cooled to 0°C followed by treatment with AgOTf (1.3 g, 5.0 mmol). The mixture was allowed to reach room temperature then was treated with aqueous sodium hydrogen carbonate. Filtration followed by extractive work-up afforded a syrup that was purified through a C-18 column made in MeOH. Elution with MeOH–EtOH mixtures up to 25% EtOH eluted impurities. Subsequently, the column was eluted with 1:1 MeOH:EtOH, then with EtOH. The fractions containing the product were pooled and concentrated to afford impure **22** as a syrup. A stirred solution of the residue in CH_2Cl_2 (5 mL) was treated with PPh_3 (1.0 g, 3.71 mmol) for 24 h followed by addition of H_2O (0.5 mL). After an additional 24 h, the volatiles were removed by distillation to afford a residue that was purified by column chromatography (3:1 hexane:EtOAc) to give **23** (420 mg, 78%) as a homogeneous syrup. A solution of this material in CH_2Cl_2 (5 mL) was treated with Ac_2O (0.5 mL) at 0°C for 2 h, then the volatiles were removed. Intermediate so obtained was dissolved in a mixture of EtOH (5 mL) and AcOH (0.5 mL) and the solution stirred under H_2 in the presence of Pd–C (10%, ~0.2 g) at 200 psi for 24 h. The mixture was filtered and the filtrate concentrated. Filtration of the residue through a short column of silica gel (1:1 hexane:EtOAc) afforded **24** (370 mg, 93%): $[\alpha]_D$ +42 (*c* 0.5, $CHCl_3$); ^{1}H NMR: δ 7.49–8.14 (m, 5H), 6.54 (d, 1H, *J*=9.6), 5.47 (dd, 1H, *J*=1.8, *J*=3.7), 5.38 (dd, 1H, *J*=1.0, *J*=3.3), 5.10 (t, 1H, *J*=9.8), 5.08 (t, 1H, *J*=9.6), 5.01 (dd, 1H, *J*=3.4, *J*=10.7), 4.99 (d, 1H, *J*=3.7), 4.88 (d, 1H, *J*=3.9), 4.85 (d, 1H, *J*=1.8), 3.69 and 3.44 (2 m, 2H), 3.67 (s, 3H), 3.57 (t, 1H, *J*=9.9), 2.30–2.38 (m, 6H), 2.27–2.22 (m, 4H), 2.08, 1.95, 1.82 (3 s, 3×3H), 1.18–1.72 (m), 0.89 (m, 12H); ^{13}C NMR: δ 178.0, 173.1, 173.0, 172.5, 170.7, 170.2, 170.0, 166.5; 134.0, 131.0, 129.0, 128.8, 100.8 (*J*=167), 98.5 (*J*=170), 97.6 (*J*=170), 77.7, 77.2, 76.7, 76.3, 72.5, 70.0, 69.9, 69.6, 68.7, 68.0, 67.2, 66.9, 66.2, 61.0, 60.0, 52.1, 51.5, 34.5, 34.0, 33.8, 31.9, 29.7, 29.6, 29.5, 29.4, 29.3, 29.11, 29.08, 29.0, 25.6, 25.0, 24.8, 22.7, 22.6, 20.8, 20.7, 17.6, 14.1. Anal. calcd for $C_{92}H_{155}NO_{24}$: C, 66.60; H, 9.42. Found: C, 66.72; H, 9.37.

*4.16. 5-(Methoxycarbonyl)pentyl (2-*O*-benzoyl-4-*O*-stearoyl-α-*L*-Rha*p*)-(1→2)-(3,4,6-tri-*O*-lauroyl-α-*D*-Gal*p*)-(1→3)-(4,6-di-*O*-acetyl-α-*D*-Glc*pNAc*)-(1→3)-2-*O*-benzoyl-4-*O*-stearoyl-α-*L*-rhamnopyranoside **26***

To a stirred solution of **24** (3.4 g, 2.09 mmol) and **9** (3.6 g, 4.76 mmol) in CH_2Cl_2 (30 mL) was added TMSOTf (40 μL, 0.22 mmol) at 0°C, then the solution was allowed to reach ambient temperature. After 30 min, the solution was treated with Et_3N (excess) followed by concentration. Column chromatographic purification of the residue (3:1 hexane:EtOAc) afforded **25** (4.60 g): $[\alpha]_D$ +43 (*c* 0.8, $CHCl_3$); ^{1}H NMR (selected): δ 7.39–8.11 (m, 10H), 6.47 (d, 1H, *J*=9.5), 5.46 (dd, 1H, *J*=1.9, *J*=3.4), 5.33–5.41 (m, 3H), 5.25 (dd, 1H, *J*=8.9, *J*=9.9), 5.20 (dd, 1H, *J*=3.3, *J*=10.0), 5.11 (t, 1H, *J*=9.9), 5.07 (d, 1H, *J*=3.2), 5.04 (d, 1H, *J*=1.8), 4.97 (d, 1H, *J*=3.8), 4.84 (d, 1H, *J*=1.9), 4.45 (ddd, 1H, *J*=3.4, *J*=9.8), 4.35 (dd, 1H, *J*=6.1, *J*=9.2), 3.92 (d, 1H, *J*=∼15), 3.85 (d, 1H, *J*=∼15), 3.68 (s, 3H), 3.44 (m, 1H), 2.11, 2.03, 1.77 (3 s, 3×3H), 1.15–1.33 (m), 1.06 (d, 3H, *J*=5.9), 0.83–0.91 (m, 15H); ^{13}C NMR: δ 173.2, 172.9, 172.8, 172.5, 172.3, 170.8, 170.3, 168.9, 166.3, 166.0, 165.3, 133.8, 133.6, 130.1, 129.9, 129.1, 129.0, 128.6, 98.5 (170), 97.7 (168), 97.6 (170), 97.5 (172), 75.0, 74.4, 74.1, 72.1, 70.5, 70.1, 69.9, 69.7, 68.7, 68.1, 67.4, 67.1, 66.5, 66.4, 61.4, 60.0, 51.8, 51.5, 40.4, 34.5, 34.1, 34.0, 33.9, 33.8, 31.9, 29.7, 29.6, 29.5, 29.4, 29.3, 29.1, 29.0, 25.6, 25.0, 24.9, 24.8, 24.7, 24.6, 24.4, 22.6, 20.8, 20.7, 17.6, 17.5, 14.1. To a stirred solution of **25** (4.60 g) in DMF (20 mL) was added thiourea (2 g). After 8 h, the solution was concentrated under vacuum and the residue was treated with $CHCl_3$. The solids were removed by filtration. Concentration of the filtrate followed by column chromatographic purification of the residue (3:1 hexane:EtOAc) afforded amorphous **26** (3.80 g, 85% for two steps): $[\alpha]_D$ +36 (*c* 1.1, $CHCl_3$); ^{1}H NMR (selected): δ 7.42–8.12 (m, 10H), 6.32 (d, 1H, *J*=9.6), 5.48 (dd, 1H, *J*=2.0, *J*=3.6), 5.38 (dd, 1H, *J*=1.6, *J*=3.2), 5.22–5.10 (m, 3H), 5.07 (d, 1H, *J*=1.6), 5.03 (d, 1H, *J* =3.4), 4.99 (d, 1H, *J*=3.5), 4.98 (t, 1H, *J*=∼10.0), 4.85 (d, 1H, *J*=2.0), 4.43 (ddd, 1H, *J*=3.5, *J*=9.5), 4.35 (dd, 1H), 4.22 (dd, 1H, *J*=6.3, *J*=11.0), 4.15 (dd, 1H, *J*=3.2, *J*=10.0), 3.68 (s, 3H), 3.45 (m, 1H), 2.25–2.47 (m), 2.13–2.23 (m), 2.11, 2.02, 1.73 (3 s, 3×3H), 1.15–1.33 (m), 1.13 (d, 3H, *J*=5.9), 0.83–0.92 (m); ^{13}C NMR: δ 174.4, 173.3, 172.5, 170.7, 170.3, 168.8, 166.1, 165.5, 133.8, 133.4, 130.0, 129.8, 129.3, 129.1, 128.7, 128.5, 98.2, 97.6, 97.4, 96.6, 74.2, 74.0, 73.6, 72.9, 72.1, 72.0, 70.1, 69.5, 69.0, 68.6, 68.1, 67.9, 67.3, 67.0, 66.4, 61.5, 60.2, 51.6, 51.5, 34.5, 34.3, 34.0, 33.9, 33.8, 31.9, 29.7, 29.6, 29.5, 29.4, 29.3, 29.2, 29.1, 29.0, 28.9, 25.6, 25.0, 24.9, 24.8, 24.7, 24.6, 24.5, 22.7, 20.9, 20.7, 17.6, 14.1. Anal. calcd for $C_{123}H_{203}NO_{30}$: C, 67.89; H, 9.40. Found: C, 67.14; H, 9.31.

*4.17. 5-(Methoxycarbonyl)pentyl (2-*O*-benzoyl-4-*O*-benzyl-3-*O*-chloroacetyl-α-*L*-Rha*p*)-(1→2)-(3,4,6-tri-*O*-benzyl-α-*D*-Gal*p*)-(1→3)-(4,6-di-*O*-acetyl-α-*D*-Glc*pNAc*)-(1→3)-(2-*O*-benzoyl-4-*O*-benzyl-α-*L*-Rha*p*)-(1→3)-(2-*O*-benzoyl-4-*O*-stearoyl-α-*L*-Rha*p*)-(1→2)-(3,4,6-tri-*O*-lauroyl-α-*D*-Gal*p*)-(1→3)-(4,6-di-*O*-acetyl-α-*D*-Glc*pNAc*)-(1→3)-2-*O*-benzoyl-4-*O*-stearoyl-α-*L*-rhamnopyranoside **27***

To a stirred solution of the imidate[2] **2** (1.12 g, 0.68 mmol) and the alcohol **26** (618 mg, 0.27 mmol) in CH_2Cl_2 (5 mL) was added at 0°C TMSOTf (10 μL). After 3 h, more **2** (approximately 0.5 g) was added to the reaction mixture. After an additional 1 h, the mixture was treated with Et_3N then was concentrated. The reaction mixture was applied to a C-18 column made in MeOH that was subsequently eluted with 6:4 MeOH:EtOH to remove impurities. Elution with 1:1 MeOH:EtOH removed unreacted **26** (170 mg). Subsequent elution with EtOH followed by ^{i}PrOH eluted **27** (625 mg, 84% based on recovery) obtained as amorphous substance after removal of the volatiles: $[\alpha]_D$ +62 (*c* 0.5, $CHCl_3$); ^{1}H NMR (selected): δ 7.29–8.16 (m), 6.37 (d, 1H, *J*=9.7), 5.66 (d, 1H, *J*=∼10), 5.60 (dd, 1H, *J*=1.7, *J*=3.5), 5.47 (dd, 1H, *J*=1.8, *J*=3.5), 5.37–5.41 (m, 2H), 5.26 (dd, 1H, *J*=1.7, *J* =3.4), 5.05 (d, 1H, *J*=3.6), 5.02 (d, 1H, *J*=1.8),

4.97 (d, 1H, *J*=3.8), 4.82 (d, 1H, *J*=1.6), 4.80 (d, 1H, *J*=3.5), 4.75 (d, 1H, *J*=3.6), 3.81 (d, 1H, *J*=∼15), 3.73 (d, 1H, *J*=∼15), 3.67 (s, 3H), 3.22 (t, 1H, *J*=9.6), 2.29–2.42 (m), 2.01, 2.00, 1.98, 1.92, 1.72, 1.61 (6 s, 6×3H), 1.18–1.40 (m), 1.13, 1.10, 0.85 (3 d, 3×3H, *J*=∼6), 0.84–0.91 (m); ^{13}C NMR: δ 173.3, 172.8, 172.7, 172.5, 172.4, 170.8, 170.5, 170.1, 170.0, 169.3, 168.6, 166.0, 165.8, 165.5, 165.2, 138.3, 137.8, 137.7, 137.5, 133.7, 133.6, 133.5, 133.3, 130.0–126.7, 99.2 (171), 98.9 (168), 98.8 (172), 98.3 (171), 97.5 (167), 96.8 (172), 96.2 (171), 95.4 (168), 78.8, 78.7, 78.5, 76.6, 75.1, 74.7, 74.6, 74.4, 74.2, 73.8, 73.7, 73.6, 73.5, 73.3, 72.8, 72.2, 72.1, 72.0, 71.8, 71.7, 70.5, 70.1, 69.5, 69.4, 69.2, 69.1, 69.0, 68.5, 68.1, 68.0, 67.8, 67.5, 67.1, 66.8, 66.3, 65.9, 61.4, 60.9, 60.1, 51.6, 51.4, 51.2, 40.4, 34.3, 34.1, 34.0, 33.9, 33.8, 33.7, 33.6, 31.8, 28.9–30.0, 24.3–25.5, 22.8, 22.6, 22.4, 20.9, 20.8, 20.7, 20.5, 17.9, 17.6, 17.5, 17.4, 14.1. FAB-MS: *m/z* 3785.0 [($C_{204}H_{289}ClN_2O_{53}$+Cs)$^+$]. Anal. calcd for $C_{204}H_{289}ClN_2O_{53}$: C, 67.08; H, 7.97. Found: C, 67.09; H, 8.03.

*4.18. 5-(Methoxycarbonyl)pentyl (2-*O*-benzoyl-4-*O*-benzyl-α-*L*-Rha*p*)-(1→2)-(3,4,6-tri-*O*-benzyl-α-*D*-Gal*p*)-(1→3)-(4,6-di-*O*-acetyl-α-*D*-Glc*p*NAc)-(1→3)-(2-*O*-benzoyl-4-*O*-benzyl-α-*L*-Rha*p*)-(1→3)-(2-*O*-benzoyl-4-*O*-stearoyl-α-*L*-Rha*p*)-(1→2)-(3,4,6-tri-*O*-lauroyl-α-*D*-Gal*p*)-(1→3)-(4,6-di-*O*-acetyl-α-*D*-Glc*p*NAc)-(1→3)-2-*O*-benzoyl-4-*O*-stearoyl-α-*L*-rhamnopyranoside **28***

To a solution of **27** (900 mg, 0.241 mmol) in DMF (5 mL) and C_5H_5N (0.5 mL) was added thiourea (92 mg, 1.20 mmol) at 23°C. After 24, the mixture was processed as described for compound **11** followed by C-18 chromatographic purification using EOH to elute impurities followed by elution with ^{i}PrOH. Concentration of the ^{i}PrOH fractions afforded **28** (860 mg, 97%) as an amorphous substance: $[\alpha]_D$ +59 (*c* 0.4, $CHCl_3$); ^{1}H NMR (selected): δ 7.00–8.11 (m), 6.31 and 5.57 (2 d, 2H, *J*=∼10), 5.48, 5.42, 5.38 (3 dd, 3H, *J*=∼1.7, ∼3.5), 5.30 (d, 1H, *J*=1.8), 5.05 (d, 1H, *J*=∼1.7), 5.04 (d, 1H, *J*=3.4), 5.01 (d, 1H, *J*=1.8), 4.97 (d, 1H, *J*=3.5), 4.84 (d, 1H, *J*=1.8), 4.78 (d, 1H, *J*=∼10), 4.76 and 4.97 (2 d, 2H, *J*=11), 4.57 (d, 1H, *J*=2.0), 4.36 and 4.28 (2 d, 2H, *J*=∼12), 3.65 (s, 3H), 3.23 (t, 1H, *J*=9.6), 2.29–2.42 (m), 2.11–2.22 (m), 2.01, 2.00, 1.98, 1.85, 1.72, 1.54 (6 s, 6×3H), 1.08–1.40 (m), 0.83–0.93 (m); ^{13}C NMR: δ 173.9, 173.3, 172.8, 172.7, 172.5, 172.4, 170.7, 170.6, 170.0, 169.9, 169.0, 168.6, 166.1, 166.0, 165.5, 165.2, 138.4, 138.3, 137.9, 137.8, 137.7, 133.8, 133.7, 133.5, 133.2, 133.3–126.8, 99.2, 98.9, 98.4, 98.2, 97.6, 96.9, 96.5, 94.8, 81.6, 79.2, 78.9, 76.4, 75.3, 75.1, 74.7, 74.6, 74.3, 74.0, 73.4, 73.1, 73.0, 72.9, 72.3, 72.2, 72.1, 71.9, 71.8, 70.6, 70.3, 69.7, 69.4, 69.3, 69.2, 69.1, 69.0, 68.6, 68.3, 68.1, 68.0, 67.5, 67.2, 66.9, 66.4, 66.0, 61.4, 61.0, 60.2, 51.6, 51.5, 51.3, 34.4, 34.2, 34.0, 33.9, 33.8, 33.7, 31.9, 29.0–29.8, 25.6, 25.0, 24.9, 24.8, 24.7, 24.6, 24.4, 22.8, 22.7, 22.5, 20.9, 20.7, 20.6, 17.9, 17.8, 17.7, 17.6, 14.1. FAB-MS: *m/z* 3709.5 [($C_{202}H_{288}N_2O_{52}$+Cs)$^+$]. Anal. calcd for $C_{202}H_{288}N_2O_{52}$: C, 67.84; H, 8.12. Found: C, 67.71; H, 8.13.

*4.19. 5-(Methoxycarbonyl)pentyl (2-*O*-benzoyl-4-*O*-benzyl-3-*O*-chloroacetyl-α-*L*-Rha*p*)-(1→2)-(3,4,6-tri-*O*-benzyl-α-*D*-Gal*p*)-(1→3)-(4,6-di-*O*-acetyl-α-*D*-Glc*p*NAc)-(1→3)-(2-*O*-benzoyl-4-*O*-benzyl-α-*L*-Rha*p*)-(1→3)-(2-*O*-benzoyl-4-*O*-benzyl-α-*L*-Rha*p*)-(1→2)-(3,4,6-tri-*O*-benzyl-α-*D*-Gal*p*)-(1→3)-(4,6-di-*O*-acetyl-α-*D*-Glc*p*NAc)-(1→3)-(2-*O*-benzoyl-4-*O*-benzyl-α-*L*-Rha*p*)-(1→3)-(2-*O*-benzoyl-4-*O*-stearoyl-α-*L*-Rha*p*)-(1→2)-(3,4,6-tri-*O*-lauroyl-α-*D*-Gal*p*)-(1→3)-(4,6-di-*O*-acetyl-α-*D*-Glc*p*NAc)-(1→3)-2-*O*-benzoyl-4-*O*-stearoyl-α-*L*-rhamnopyranoside **29***

To a solution of **28** (500 mg, 0.137 mmol) and **2** (1.0 g, 0.61 mmol) in CH_2Cl_2 (5 mL) was added TMSOTf (8 μL) at 0°C. After 3 h, the mixture was processed as described for **27**. The syrupy residue

was applied to a C-18 column that was eluted, in succession, with MeOH, 3:1 MeOH:EtOH, 3:2 EtOH:MeOH, and EtOH. Concentration of the EtOH fraction afforded amorphous **29** (620 mg, 89%): $[\alpha]_D$+69 (*c* 0.5, $CHCl_3$); ^{1}H NMR (selected): δ 7.32–8.14 (m), 6.32 (d, 1H, *J*=10), 5.80 (d, 1H, *J*=~10), 5.68 (d, 1H, *J*=9.6), 5.60 (dd, 1H, *J*=1.7, *J*=3.4), 5.54 (dd, 1H, *J*=1.3, *J*=3.3), 5.51 (d, 1H, *J*=1.4), 5.47 (dd, 1H, *J*=1.8, *J*=3.2), 5.38 (d, 2H, *J*=~3.6), 5.35 (d, 1H, *J*=3.6), 4.86 and 4.82 (2 d, 2H, *J*=~15), 3.62 (s, 3H), 2.05, 1.95, 1.94, 1.92, 1.79, 1.73, 1.72, 1.71 1.46 (9 s, 9×3H), 1.1–1.3 (m), 0.83–0.96 (m); ^{13}C NMR: δ 173.8, 173.3, 172.8, 172.7, 172.5, 172.4, 170.7, 170.53, 170.48, 170.45, 170.0, 169.5, 169.4, 168.8, 168.5, 166.1, 165.8, 165.6, 165.4, 165.2, 165.1, 164.9, 138.4, 138.2, 138.05, 138.0, 137.9, 137.6, 137.57, 137.5, 133.7, 133.5, 133.3, 133.2, 126.5–130.8, 99.5, 99.3, 99.2, 98.9, 98.4, 97.9, 97.8, 97.6, 96.8, 96.5, 96.2, 93.9, 80.1, 79.4, 79.0, 78.9, 78.6, 78.2, 75.4, 75.3, 75.2, 75.0, 74.8, 74.6, 74.5, 74.3, 74.1, 73.9, 73.5, 73.3, 72.7, 72.2, 72.0, 71.9, 71.8, 71.7, 70.5, 70.1, 69.8, 69.6, 69.5, 69.4, 69.2, 68.8, 68.5, 68.4, 68.1, 68.0, 67.9, 67.8, 67.7, 67.6, 67.4, 67.1, 66.9, 66.3, 66.0, 61.4, 60.8, 60.6, 60.2, 51.6, 51.4, 51.3, 51.2, 40.8, 38.7, 34.5, 34.3, 33.9, 33.7, 32.0, 28.2–30.3, 25.5, 25.0, 24.8, 24.7, 24.5, 24.3, 23.7, 23.1, 22.9, 22.6, 22.5, 20.9, 20.7, 20.5, 20.4, 18.1, 17.8, 17.6, 17.5, 17.2, 17.1. FAB-MS: *m/z* 5186.1 [($C_{283}H_{374}ClN_3O_{75}$+Cs)$^+$]. Anal. calcd for $C_{283}H_{374}ClN_3O_{75}$: C, 67.26; H, 7.46. Found: C, 67.12; H, 7.48.

*4.20. 5-(Methoxycarbonyl)pentyl (2-*O*-benzoyl-4-*O*-benzyl-α-*L*-Rha*p*)-(1→2)-(3,4,6-tri-*O*-benzyl-α-*D*-Gal*p*)-(1→3)-(4,6-di-*O*-acetyl-α-*D*-Glc*pNAc*)-(1→3)-(2-*O*-benzoyl-4-*O*-benzyl-α-*L*-Rha*p*)-(1→3)-(2-*O*-benzoyl-4-*O*-benzyl-α-*L*-Rha*p*)-(1→2)-(3,4,6-tri-*O*-benzyl-α-*D*-Gal*p*)-(1→3)-(4,6-di-*O*-acetyl-α-*D*-Glc*pNAc*)-(1→3)-(2-*O*-benzoyl-4-*O*-benzyl-α-*L*-Rha*p*)-(1→3)-(2-*O*-benzoyl-4-*O*-stearoyl-α-*L*-Rha*p*)-(1→2)-(3,4,6-tri-*O*-lauroyl-α-*D*-Gal*p*)-(1→3)-(4,6-di-*O*-acetyl-α-*D*-Glc*pNAc*)-(1→3)-2-*O*-benzoyl-4-*O*-stearoyl-α-*L*-rhamnopyranoside **30***

A solution of **29** (570 mg, 0.113 mmol), 2,6-di-^{t}butyl-4-methylpyridine (300 mg), and thiourea (100 mg) in DMF (5 mL) was stirred at 23°C for 24 h. The usual processing as described for **11** afforded a syrup that was dissolved in MeOH. The resulting solution was applied to a C-18 column made in MeOH that was then sequentially eluted with MeOH, 9:1 MeOH:EtOH, 1:1 MeOH:EtOH, and *i*-PrOH. Concentration of the *i*-PrOH fraction afforded **30** (545 mg, 97%) as an amorphous substance: $[\alpha]_D$ +68 (*c* 0.6, $CHCl_3$); ^{1}H NMR (selected): δ 7.32–8.14 (m), 6.32, 5.74, 5.68 (3 d, 3H, *J*=~10), 5.53, 5.47, 5.41 (3 dd, 3H, *J*=~1.7, *J*=3.3), 5.49 (d, 1H, *J*=1.7), 5.38 (dd, 1H, *J*=1.2, *J*=3.4), 3.67 (s, 3H), 1.99 (s, 6H), 1.97, 1.84, 1.74, 1.73, 1.72, 1.71, 1.46 (7 s, 7×3H), 0.83–0.92 (m); ^{13}C NMR: δ 173.2, 172.7, 172.6, 172.4, 172.3, 170.6, 170.5, 170.3, 170.0, 169.4, 168.9, 168.8, 168.5, 166.0, 165.5, 165.4, 165.1, 164.9, 138.3, 138.2, 138.1, 138.0, 137.9, 137.8, 137.7, 137.5 137.4, 133.1–134.0, 130.0, 129.8, 139.7, 126.5–129.2, 99.25, 99.20, 98.8, 98.33, 98.28, 97.9, 97.5, 96.8, 96.4, 95.4, 93.8, 81.5, 80.1, 79.3, 79.0, 78.9, 78.8, 78.0, 76.4, 75.34, 75.29, 75.2, 75.0, 74.7, 74.6, 74.3, 74.1, 73.9, 73.8, 73.4, 73.3, 73.2, 73.1, 72.8, 72.6, 72.5, 72.1, 72.0, 71.9, 71.8, 71.7, 70.5, 70.3, 69.8, 69.6, 69.5, 69.4, 69.3, 69.1, 68.8, 68.5, 68.4, 68.1, 68.0, 67.9, 67.8, 67.5, 67.4, 67.3, 67.1, 66.9, 66.3, 65.9, 61.3, 60.9, 60.6, 60.1, 51.5, 51.4, 51.2, 51.1, 34.2, 34.1, 33.9, 33.7, 31.8, 28.9–29.6, 25.5, 25.0, 24.7, 24.6, 24.5, 24.3, 23.0, 22.6, 22.5, 20.8, 20.7, 20.5, 20.3, 17.9, 17.8, 17.6, 17.5, 14.0. FAB-MS: *m/z* 5109.5 [($C_{281}H_{373}N_3O_{74}$+Cs)$^+$]. Anal. calcd for $C_{281}H_{373}N_3O_{74}$: C, 67.81; H, 7.55. Found: C, 67.16; H, 7.45.

*4.21. 5-(Methoxycarbonyl)pentyl (2-*O*-benzoyl-4-*O*-benzyl-3-*O*-chloroacetyl-α-*L*-Rha*p*)-(1→2)-(3,4,6-tri-*O*-benzyl-α-*D*-Gal*p*)-(1→3)-(4,6-di-*O*-acetyl-α-*D*-Glc*p*NAc)-(1→3)-(2-*O*-benzoyl-4-*O*-benzyl-α-*L*-Rha*p*)-(1→3)-[(2-*O*-benzoyl-4-*O*-benzyl-α-*L*-Rha*p*)-(1→2)-(3,4,6-tri-*O*-benzyl-α-*D*-Gal*p*)-(1→3)-(4,6-di-*O*-acetyl-α-*D*-Glc*p*NAc)-(1→3)-(2-*O*-benzoyl-4-*O*-benzyl-α-*L*-Rha*p*)-(1→3)-]$_2$2-*O*-benzoyl-4-*O*-stearoyl-α-*L*-Rha*p*)-(1→2)-(3,4,6-tri-*O*-lauroyl-α-*D*-Gal*p*)-(1→3)-(4,6-di-*O*-acetyl-α-*D*-Glc*p*NAc)-(1→3)-2-*O*-benzoyl-4-*O*-stearoyl-α-*L*-rhamnopyranoside **31***

To a solution of **30** (480 mg, 0.096 mmol) and **2** (667 mg, 0.407 mmol) in CH_2Cl_2 (4 mL) was added TMSOTf (8 μL) at 0°C. After 3 h, the mixture was processed as described for **27**. The syrupy residue was applied to a C-18 column that was eluted, in succession, with 1:1 MeOH:EtOH, EtOH, 1:1 EtOH:*i*-PrOH, and *i*PrOH. Fractions containing *i*PrOH were pooled and concentrated. Repeated purification through a C-18 column, using a gradient of EtOH and *i*PrOH, afforded amorphous **31** (480 mg, 77%): $[\alpha]_D$ +75 (*c* 0.6, $CHCl_3$); ^{13}C NMR: δ 173.2, 172.7, 172.6, 172.44, 172.40, 172.3, 170.7, 170.5, 170.42, 170.38, 170.0, 169.8, 169.5, 169.4, 168.9, 168.8, 168.5, 166.0, 165.8, 165.5, 165.4, 165.3, 165.2, 165.1, 165.0, 164.8, 138.4, 138.2, 138.0, 133.7, 133.4, 133.3, 133.2, 126.4–130.1, 99.5, 99.3, 98.9, 98.4, 98.0, 97.6, 96.9, 96.6, 96.1, 94.3, 94.0, 80.1, 79.4, 79.3, 79.0, 78.6, 78.3, 77.9, 75.4, 75.2, 75.0, 74.8, 74.6, 74.4, 74.2, 74.0, 73.9, 73.5, 73.4, 73.3, 72.9, 72.7, 72.5, 72.4, 72.2, 72.0, 71.9, 71.5, 70.5, 70.1, 69.8, 69.5, 69.3, 69.0, 68.8, 68.5, 67.9, 67.7, 67.6, 67.4, 67.2, 66.9, 66.3, 66.0, 61.37, 61.32, 60.81, 60.85, 60.68, 60.63, 51.6, 51.4, 51.3, 51.2, 51.1, 40.4, 33.7–34.3, 31.8, 28.9–30.0, 24.3–25.5, 22.5–23.1, 17.5–18.0, 17.2, 14.1. FAB-MS: *m/z* 6586.9 [($C_{362}H_{459}ClN_4O_{97}$+Cs)$^+$]. Anal. calcd for $C_{362}H_{459}ClN_4O_{97}$: C, 67.37; H, 7.17. Found: C, 67.14; H, 7.22.

*4.22. 5-(Methoxycarbonyl)pentyl (2-*O*-benzoyl-4-*O*-benzyl-α-*L*-Rha*p*)-(1→2)-(3,4,6-tri-*O*-benzyl-α-*D*-Gal*p*)-(1→3)-(4,6-di-*O*-acetyl-α-*D*-Glc*p*NAc)-(1→3)-(2-*O*-benzoyl-4-*O*-benzyl-α-*L*-Rha*p*)-(1→3)-[(2-*O*-benzoyl-4-*O*-benzyl-α-*L*-Rha*p*)-(1→2)-(3,4,6-tri-*O*-benzyl-α-*D*-Gal*p*)-(1→3)-(4,6-di-*O*-acetyl-α-*D*-Glc*p*NAc)-(1→3)-(2-*O*-benzoyl-4-*O*-benzyl-α-*L*-Rha*p*)-(1→3)-]$_2$2-*O*-benzoyl-4-*O*-stearoyl-α-*L*-Rha*p*)-(1→2)-(3,4,6-tri-*O*-lauroyl-α-*D*-Gal*p*)-(1→3)-(4,6-di-*O*-acetyl-α-*D*-Glc*p*NAc)-(1→3)-2-*O*-benzoyl-4-*O*-stearoyl-α-*L*-rhamnopyranoside **32***

A solution of **31** (450 mg, 0.069 mmol), 2,6-di-^{t}butyl-4-methylpyridine (200 mg), and thiourea (0.5 g) in DMF (5 mL) was stirred at 23°C for 24 h. The usual processing as described for **11** afforded a syrup that was dissolved in MeOH. The resulting solution was applied to a C-18 column made in MeOH that was then sequentially eluted with MeOH, MeCN, and benzene. Concentration of the benzene fraction afforded a syrup that was equilibrated between $CHCl_3$ and H_2O. The organic layer was dried (Na_2SO_4) and concentrated to afford **32** (410 mg, 92%) as an amorphous substance: $[\alpha]_D$ +71 (*c* 1.1, $CHCl_3$); ^{1}H NMR: δ 7.9–8.10 (m), 6.84–7.65 (m), 6.30, 5.74, 5.73, 5.66 (4 d, 4H, *J*=~9.5–10.1), 3.62 (s, 3H), 2.26–2.46 (m), 2.10–2.22 (m), 1.98, 1.97, 1.84, 1.73, 1.72, 1.71, 1.70, 1.64, 1.60, 1.47 (10 s), 1.05–1.37 (m), 0.82–0.92 (m); ^{13}C NMR: δ 173.9, 173.3, 172.7, 172.6, 172.4, 170.6, 170.5, 170.4, 170.3, 170.0, 169.8, 169.5, 168.9, 168.8, 168.7, 168.5, 166.1, 165.4, 165.1, 165.0, 164.8, 137.5–138.4, 133.1–133.7, 126.4–131.0, 99.2, 98.9, 98.4, 98.0, 97.6, 96.9, 96.6, 95.4, 94.3, 94.0, 81.6, 80.1, 79.4, 79.3, 79.1, 79.0, 78.9, 78.2, 77.8, 77.7, 75.4, 75.2, 75.0, 74.7, 74.6, 74.4, 74.2, 74.1, 74.0, 73.9, 73.5, 73.2, 73.0, 72.8, 72.6, 72.4, 72.2, 72.0, 71.9, 71.8, 71.5, 70.4, 69.8, 69.7, 69.6, 69.3, 69.0, 68.8, 68.5, 68.1, 68.0, 67.8, 67.5, 67.4, 67.2, 66.9, 66.3, 66.0, 61.4, 60.9, 60.7, 60.2, 51.5, 51.46, 51.3, 51.2, 51.1, 33.8–34.3, 31.9, 28.9–29.6, 24.3–25.5, 22.5–23.0, 20.4–20.9, 17.6–17.9, 14.1. FAB-MS: *m/z* 6510.4 [($C_{360}H_{458}N_4O_{96}$+Cs)$^+$]. Anal. calcd for $C_{360}H_{458}N_4O_{96}$: C, 67.80; H, 7.24. Found: C, 67.36; H, 7.31.

*4.23. 5-(Methoxycarbonyl)pentyl (2-*O*-benzoyl-4-*O*-benzyl-3-*O*-chloroacetyl-α-*L*-Rha*p*)-(1→2)-(3,4,6-tri-*O*-benzyl-α-*D*-Gal*p*)-(1→3)-(4,6-di-*O*-acetyl-α-*D*-Glc*p*NAc)-(1→3)-(2-*O*-benzoyl-4-*O*-benzyl-α-*L*-Rha*p*)-(1→3)-[(2-*O*-benzoyl-4-*O*-benzyl-α-*L*-Rha*p*)-(1→2)-(3,4,6-tri-*O*-benzyl-α-*D*-Gal*p*)-(1→3)-(4,6-di-*O*-acetyl-α-*D*-Glc*p*NAc)-(1→3)-(2-*O*-benzoyl-4-*O*-benzyl-α-*L*-Rha*p*)-(1→3)-]$_3$(2-*O*-benzoyl-4-*O*-stearoyl-α-*L*-Rha*p*)-(1→2)-(3,4,6-tri-*O*-lauroyl-α-*D*-Gal*p*)-(1→3)-(4,6-di-*O*-acetyl-α-*D*-Glc*p*NAc)-(1→3)-2-*O*-benzoyl-4-*O*-stearoyl-α-*L*-rhamnopyranoside **33***

To a stirred mixture of **32** (360 mg, 0.056 mmol), **2** (390 mg, 0.238 mmol), and $CaSO_4$ (3 g) in CH_2Cl_2 (5 mL) was added TMSOTf (6 μL) at 0°C. After 2 h, the mixture was processed as described for **27**. The syrupy residue was applied to a C-18 column that was eluted, in succession, with MeOH, 1:1 MeOH:EtOH, EtOH, and *i*PrOH. The latter two fractions were pooled and and concentrated. Silica gel column chromatography of the residue (3:2 hexane:EtOAc) afforded amorphous **33** (235 mg, 53%): $[\alpha]_D$ +65 (*c* 0.5, $CHCl_3$); ^{1}H NMR (selected): δ 6.90–8.1 (m), 6.33 (d, 1H, *J*=10.1), 5.81 (d, 1H, *J*=10.5), 5.77 (d, 2H, *J*=~10.3), 5.69 (d, 1H, *J*=10.1), 3.66 (s, 3H), 2.28–2.40 (m), 2.05, 1.95, 1.94, 1.79, 1.74, 1.73, 1.70, 1.68, 1.63, 1.62 (10 s), 1.08–1.48 (m), 0.84–0.95 (m); ^{13}C NMR: δ 173.3, 172.8, 172.7, 172.45, 172.41, 170.7, 170.5, 170.44, 170.1, 170.0, 169.9, 169.6, 169.4, 168.9, 168.8, 168.7, 168.5, 167.7, 167.6, 166.0, 165.8, 165.5, 165.4, 165.3, 165.2, 165.1, 165.0, 164.9, 164.8, 137.5–138.4, 133.1–133.8, 132.4, 130.8, 126.5–131.0, 99.5, 99.3 (3C), 99.2, 98.9, 98.4, 98.2, 98.0 (5C), 97.6, 96.8, 96.4, 96.1, 94.4, 94.3, 94.0, 80.1, 79.3, 78.9, 78.6, 78.3, 77.9, 75.4, 75.3, 75.2, 75.1, 75.0, 74.8, 74.6, 74.3, 74.2, 73.9, 73.4, 73.3, 72.9, 72.7, 72.5, 72.3, 72.2, 72.0, 71.8, 71.4, 70.5, 70.1, 69.8, 69.5, 69.4, 69.2, 68.8, 68.5, 68.0, 67.8, 67.6, 67.4, 67.1, 66.9, 66.3, 65.9, 62.0, 61.4, 60.8, 60.6 (2C), 60.1, 51.6, 51.4, 51.3, 51.1 (2C), 40.4, 38.6, 36.6, 34.3, 34.1, 33.94, 33.90, 33.8, 31.8, 30.3, 28.8–29.6, 25.5, 25.0, 24.8, 24.7, 24.6, 24.5, 24.3, 23.7, 23.3, 23.1, 22.9, 22.6, 22.5, 20.9, 20.7, 20.5, 18.0, 17.9, 17.8, 17.1, 17.6, 17.5, 17.2, 14.05, 13.98. FAB-MS: *m/z* 7856.2 [$(C_{441}H_{544}ClN_5O_{119}+H)^+$]. Anal. calcd for $C_{441}H_{544}ClN_5O_{119}$: C, 67.44; H, 6.98. Found: C, 67.71; H, 6.78.

*4.24. 5-(Methoxycarbonyl)pentyl (2-*O*-benzoyl-4-*O*-benzyl-α-*L*-Rha*p*)-(1→2)-(3,4,6-tri-*O*-benzyl-α-*D*-Gal*p*)-(1→3)-(4,6-di-*O*-acetyl-α-*D*-Glc*p*NAc)-(1→3)-(2-*O*-benzoyl-4-*O*-benzyl-α-*L*-Rha*p*)-(1→3)-[(2-*O*-benzoyl-4-*O*-benzyl-α-*L*-Rha*p*)-(1→2)-(3,4,6-tri-*O*-benzyl-α-*D*-Gal*p*)-(1→3)-(4,6-di-*O*-acetyl-α-*D*-Glc*p*NAc)-(1→3)-(2-*O*-benzoyl-4-*O*-benzyl-α-*L*-Rha*p*)-(1→3)-]$_3$(2-*O*-benzoyl-4-*O*-stearoyl-α-*L*-Rha*p*)-(1→2)-(3,4,6-tri-*O*-lauroyl-α-*D*-Gal*p*)-(1→3)-(4,6-di-*O*-acetyl-α-*D*-Glc*p*NAc)-(1→3)-2-*O*-benzoyl-4-*O*-stearoyl-α-*L*-rhamnopyranoside **34***

A solution of **33** (210 mg, 0.027 mmol), 2,6-di-^{t}butyl-4-methylpyridine (100 mg), and thiourea (0.2 g) in DMF (5 mL) was stirred at 23°C for 24 h. The usual processing as described for **11** afforded a syrup that was dissolved in MeOH. The resulting solution was applied to a C-18 column made in MeOH that was then sequentially eluted with MeOH, EtOH, and 1:1 EtOH:*i*-PrOH. Concentration of the EtOH:*i*-PrOH fraction afforded **34** (175 mg, 84%) as an amorphous substance: $[\alpha]_D$ +76 (*c* 0.4, $CHCl_3$); ^{1}H NMR (selected): δ 6.90–8.12 (m), 6.28 (d, 1H, *J*=10.0), 5.74 (d, 3H, *J*=~9.5), 5.66 (d, 1H, *J*=9.0), 3.67 (s, 3H), 2.27–2.42 (m), 2.12–2.20 (m), 2.00, 1.98, 1.97, 1.84, 1.74, 1.73, 1.72, 1.64, 1.62, 1.47 (10 s), 1.04–1.42 (m), 0.84–0.90 (m); ^{13}C NMR (selected): δ 173.3, 172.8, 172.7, 172.4, 170.7, 170.1, 170.0, 169.9, 169.6, 169.5, 168.9, 168.8, 168.5, 167.8, 166.1, 165.8, 165.5, 165.4, 165.2, 165.1, 165.0, 164.8, 99.2, 98.9, 98.3, 98.2, 98.0, 97.6, 96.8, 96.5, 95.4, 94.5, 94.3, 94.0, 81.5, 80.1, 79.3, 79.0, 78.0, 77.7, 75.4, 75.0, 74.7, 74.6, 74.4, 74.0, 73.9, 73.4, 73.2, 72.8, 72.5, 72.2, 72.0, 71.9, 71.5, 70.5, 70.4, 69.6, 69.3, 68.5, 68.1, 68.0, 67.8, 67.5, 67.4, 67.2, 66.9, 66.4, 61.4, 60.9, 60.6, 60.2, 51.5, 51.45, 51.3, 51.15,

51.1, 31.9–34.3, 31.9, 28.9–29.6, 24.3–25.5, 22.5–23.1, 20.4–20.9, 17.6–17.9, 14.1. FAB-MS: *m/z* 7778 [($C_{439}H_{542}N_5O_{118}$+H)$^+$]. Calcd for $C_{439}H_{542}N_5O_{118}$: C, 67.80; H, 7.02. Found: C, 68.11; H, 6.95.

*4.25. 5-(Methoxycarbonyl)pentyl α-*L*-Rha*p*-(1→2)-α-*D*-Gal*p*-(1→3)-α-*D*-Glc*p*NAc-(1→3)-α-*L*-Rha*p*-(1→3)-[α-*L*-Rha*p*-(1→2)-α-*D*-Gal*p*-(1→3)-α-*D*-Glc*p*NAc-(1→3)-α-*L*-Rha*p*-(1→3)-]$_4$α-*L*-Rha*p*-(1→2)-α-*D*-Gal*p*-(1→3)-α-*D*-Glc*p*NAc-(1→3)-α-*L*-rhamnopyranoside **37***

To a stirred mixture of **34** (150 mg, 19.3 μM), compound **2** (260 mg, 159 μM), $CaSO_4$ (2 g), and CH_2Cl_2 was added TMSOTf (7 μL) at 0°C. After 2 h, the mixture was treated with Et_3N then filtered. The residue obtained upon concentration of the filtrate was applied to a C-18 column made in MeOH. The column was eluted successively with MeOH, EtOH, and 1:1 EtOH:*i*-PrOH. The latter two fractions were combined and concentrated. The residue so obtained was further purified by silica gel chromatography (3:2 hexane:EtOAc) to afford the intermediate **35** (45 mg) in pure form (HPTLC). An additional amount (26 mg) was also obtained that contained <10% impurities. Yield: approximately 35%. To a solution of compound **35** (35 mg) in CH_2Cl_2 (1 mL) was added MeOH followed by NaOMe in MeOH. After 4 days at 23°C, the crystalline precipitate formed was removed by filtration. The clear solution was treated with Dowex 50×8 (H^+), filtered, and concentrated. The residue was purified by silica gel chromatography (10:1 MeOH:EtOAc) to afford **36** as an amorphous material {$[\alpha]_D$ +90 (*c* 0.2, $CHCl_3$); FAB-MS *m/z* 5345.6 ($C_{338}H_{422}N_6O_{111}$+H)$^+$} which was dissolved in EtOH (4 mL) and AcOH (0.5 mL). The solution was stirred under H_2 at 200 psi in the presence of Pd–C (10%, approximately 100 mg) for 48 h. The mixture was filtered and the filtrate concentrated. The residue was purified by gel filtration through Biogel P-6 using H_2O as eluant to give, after freeze-drying, **37** (10 mg, 67%): $[\alpha]_D$ +62 (*c* 0.4, H_2O); ^{1}H NMR (selected): δ 5.60 (br s, 6H), 5.10 (br s, 5H), 5.07 (br s, 1H), 5.04 (br s, 10H), 4.99 (d, 1H, *J*=3.3), 3.57 (br t, *J*=∼10), 3.37 (s, 3H), 2.17 (br t, 2H, *J*=7.5), 2.05 (br s, 18H), 1.51–1.66 (m, 4H), 1.35–1.44 (m, 2H), 1.27–1.35 (m); ^{13}C NMR: δ 175.0, 102.7 (5C), 102.3, 102.2 (5C), 100.2, 98.4 (6C), 94.8 (6C), 78.9, 75.7, 75.6, 75.4, 75.0, 74.5, 74.4, 72.6, 72.4, 72.0, 71.9, 71.6, 71.1, 70.8, 70.6, 70.3, 70.2, 70.1, 70.0, 69.7, 69.3, 68.6, 67.4, 61.4, 61.2, 60.8, 60.7, 52.7, 38.3, 29.1, 26.4, 26.1, 22.8, 17.6, 17.4, 17.3. FAB-MS: *m/z* 4091.8 ($C_{163}H_{272}N_6O_{111}$+H)$^+$, 4113.7 ($C_{163}H_{272}N_6O_{111}$+Na)$^+$.

Acknowledgements

The author thanks Dr. Lewis Pannell and Mr. Noel Whittaker for the mass spectra.

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