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Synthesis of the Glycopeptidolipid of *Mycobacterium avium* Serovar 4: First Example of a Fully Synthetic C-Mycoside GPL

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The preparation of the glycopeptidolipid (GPL) present in the cell wall of *Mycobacterium avium* Serovar 4, namely 3,4-di-*O*-Me-α-L-Rha*p*-(1→1){*R*-$C_{21}H_{43}CH(OH)CH_2CO$-D-Phe-[4-*O*-Me-α-L-Rha*p*-(1→4)-2-*O*-Me-α-L-Fuc*p*-(1→3)-α-L-Rha*p*-(1→2)-6-deoxy-α-L-Tal*p*-(1→3)]-D-allo-Thr-D-Ala-L-Alaol} (**1**), is described. The synthesis was based on the disconnection of the final structure into four building blocks, an L-rhamnosyl pseudodipeptide, a 6-deoxy-L-talosyl dipeptide, a trisaccharide donor, and a 3-hydroxyalkanoic acid. The key steps are the creation of the glycosidic linkage between the trisaccharide donor, used as a pentenyl glycoside, and the 6-deoxy-L-talose unit of an appropriate D-Phe-*O*-(6-deoxy-L-talosyl)-D-allo-Thr derivative and the final coupling of the two glycodipeptide fragments. Pentenyl glycosides were shown to provide useful donors in several glycosylation steps. This work constitutes the first synthesis of the full structure of a so-called "polar mycoside C" GPL.

Introduction

Diseases caused by mycobacterial infections continue to constitute serious health threats. The most common species are *Mycobacterium tuberculosis* and *Mycobacterium leprae*, the pathogens responsible for tuberculosis and leprosy, respectively. Tuberculosis is the leading cause of death from a single infectious agent, and its incidence is increasing as a result of the emergence of multidrug-resistant *M. tuberculosis* strains.[1] Other representative mycobacteria such as *Mycobacterium intracellulare* and different variants of the *Mycobacterium avium* complex have been found to cause disseminated infections in many AIDS victims. Up to 50% of the AIDS patients are reported to be infected with these intracellular parasites.[2] The highly impermeable cell wall of mycobacteria[3] contains numerous immunogenic glycolipids of great structural diversity.[4] The polar glycopeptidolipids (GPL) of the *M. avium* complex are of particular interest because of their high antigenicity and their species' specificity:[5] GPLs are the chemical markers of the 31 distinct serovars known for the *M. avium* group. Several studies dealing with the structural analysis and the biological properties of these compounds as well as with partial syntheses have been published and are summarized in recent reviews.[4a,5] The core structure of glycopeptidolipids of the 'polar mycosides C' family, to which the *M. avium* GPLs belong, consists of a pseudotetrapeptide containing L-alaninol as C-terminal unit, D-Ala, D-allo-Thr, and D-Phe, *N*-acylated at the N-terminal position with a fatty acid residue, and glycosylated at both hydroxyl groups: conserved sugar units are a 3,4-di-*O*-methyl-α-L-rhamnopyranosyl group (at L-alaninol) and an *O*-(α-L-rhamnopyranosyl)−(1→2)-6-deoxy-α-L-talopyranose disaccharide *O*-linked to D-allo-Thr.[4a,6] Remarkably, very few synthetic studies have been dedicated to complete GPL structures. While numerous syntheses of antigenic oligosaccharide fragments of mycoside GPLs have been reported,[7,8] the preparation of the core pseudotetrapeptide has been achieved by Gurjar et al.,[9] and the only example of a mycoside-type glycopeptide (from *M. fortuitum*) carrying sugar residues at both hydroxylated sites has been described by this group.[10] We wish to report in this paper the first synthesis of a complete *N*-acylated, fully glycosylated mycoside-type GPL, the GPL of *Mycobacterium avium* serovar 4 (**1**);[4b] this structure is of particular interest because it is the

(1) Dye, C.; Scheele, S.; Dolin, P.; Pathania, V.; Raviglione, M. C. *JAMA* **1999**, *282*, 677−686.
(2) Collins, F. M. *Microbiol. Rev.* **1989**, *2*, 360−370.
(3) Brennan, P. J.; Nikaido, H. *Annu. Rev. Biochem.* **1995**, *64*, 29−63.
(4) (a) Aspinall, G. O. *Adv. Carbohydr. Chem. Biochem.* **1995**, *51*, 169−242 and references cited therein. In particular, see: (b) McNeil, M.; Tsang, A. Y.; Brennan, P. J. *J. Biol. Chem.* **1987**, *262*, 2630−2635. The native GPL of *M. avium* Serovar 4 is apparently di-*O*-acetylated, but the position of the acetyl groups is not known, and these groups are not necessary for antigenicity of the GPL.
(5) Chatterjee, D.; Khoo, K. H. *Cell Mol. Life Sci.* **2001**, *58*, 2018−2042.
(6) Laneelle, G.; Asselineau, J. *Eur. J. Biochem.* **1968**, *5*, 487−491.
(7) Liptak, A.; Borbas, A.; Bajza, I. *Med. Res. Rev.* **1994**, *14*, 307−352 and references cited therein.
(8) See, for example: (a) Gurjar, M. K.; Viswanadham, G. *J. Carbohydr. Chem.* **1991**, *10*, 481−485. (b) Ziegler, T. *Carbohydr. Res.* **1994**, *253*, 151−166. (c) Zegelaar-Jaarsveld, K.; van der Plas, S. C.; van der Marel, G. A.; van Boom, J. H. *J. Carbohydr. Chem.* **1996**, *15*, 561−610. (d) Varga, Z.; Bajza, I.; Batta, G.; Liptak, A. *Tetrahedron Lett.* **2001**, *42*, 5283−5286. (e) Varga, Z.; Bajza, I.; Batta, G.; Liptak, A. *Tetrahedron Lett.* **2002**, *43*, 3145−3148.
(9) Gurjar, M. K.; Saha, U. K. *Tetrahedron Lett.* **1991**, *32*, 6621−6624.
(10) Gurjar, M. K.; Saha, U. K. *Bioorg. Med. Chem. Lett.* **1993**, *3*, 697−702.

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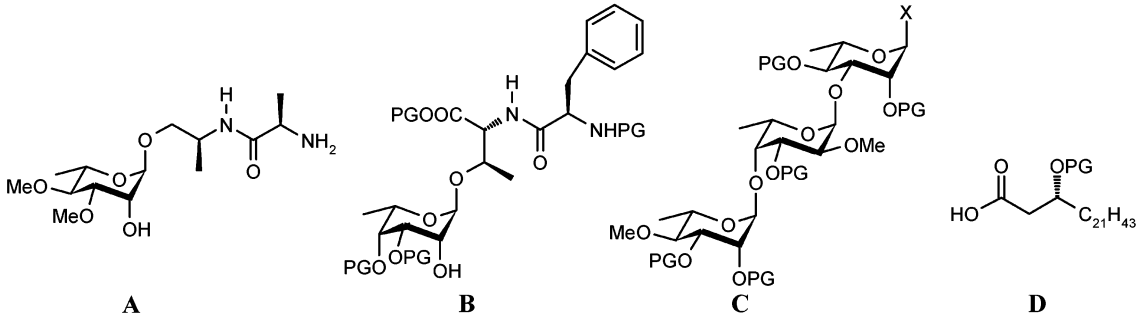
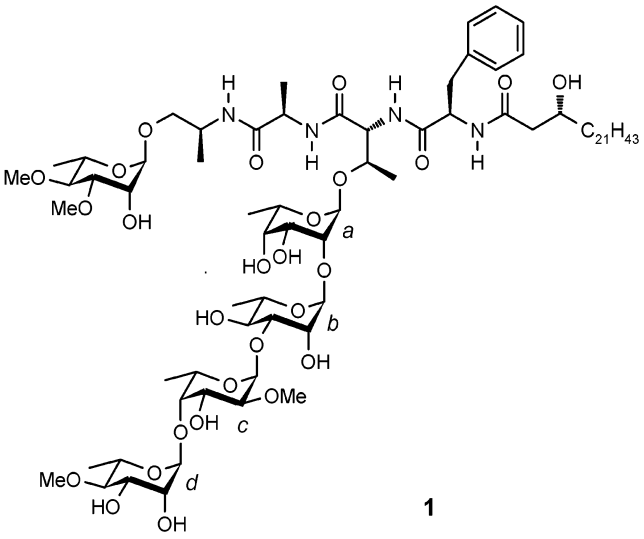
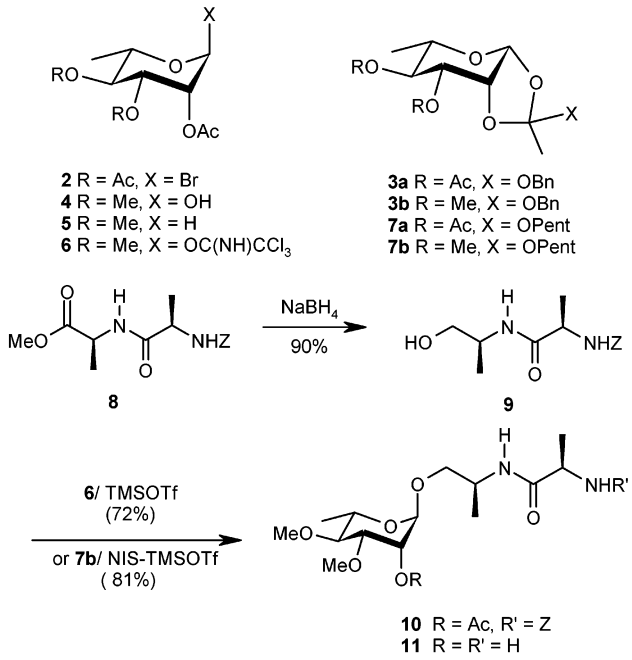


FIGURE 1. Buiding blocks for the synthesis of **1** (PG = protecting group).

variant most frequently found in AIDS patients with disseminated mycobacterial infections.[4]



SCHEME 1



Discussion

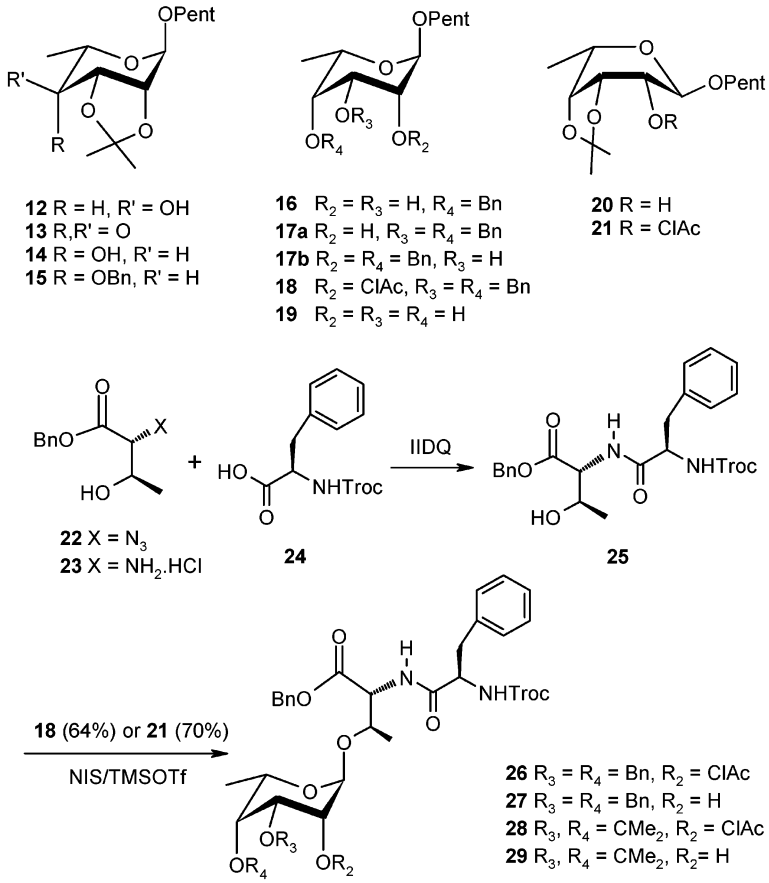
After extensive preliminary investigations, and on the basis of the previous work of Gurjar[9] on the core pseudopeptide and of van Boom et al.[11] on the tetrasaccharide component, we determined that the best strategy for the total synthesis of **1** consisted in assembling the building blocks described in Figure 1, namely a rhamnosylated pseudodipeptide (**A**), a 6-deoxytalosylated dipeptide (**B**), a trisaccharide corresponding to sugar units *b*, *c*, and *d* of **1** (**C**), and a 3-hydroxyalkanoic acid (**D**). A more complex building block was to be achieved by linking **B** to **C**, followed by *N*-acylation with **D**, before the final, crucial peptide coupling between the resulting glycolipodipeptide and **A**. The disconnection of the trisaccharide *b*−*c*−*d* from the talosylated D-allo-threonine fragment proved to be essential for the success of the synthesis.

Building Block A (Scheme 1). A synthesis of compound **10**, the precursor of glycopeptide building block **A** (**11**), has been reported by Gurjar.[9] The preparation of **10** was simplified as follows. First, the trichloroacetimidate of 2-*O*-acetyl-3,4-di-*O*-methyl-L-rhamnopyranose (compound **6**[12]) was prepared in four steps from acetobromo-L-rhamnose **2**[13] (instead of eight steps from methyl α-L-rhamnopyranoside[12]) by way of the *O-benzyl* ortho ester **3b**: compound **3b** was obtained from **2** by a standard protocol for ortho ester formation,[14] thus giving **3a** followed by a one-pot acetyl to methyl group exchange. Hydrogenolysis of **3b** in aqueous dioxane gave hemiacetal **4** in one step, and **4** was then converted into glycosyl donor **6**. Interestingly, a different result was obtained if the hydrogenation was carried out in anhydrous ethyl acetate: under these conditions, the reaction of **3b** led predominantely to anhydrorhamnitol **5** instead of **4**. The mechanism for this transformation remains uncertain. The synthesis of **10** was completed by glycosylating the preformed pseudodipeptide **9** with trichloroacetimidate **6**. Compound **9** can be prepared either by coupling Z-L-Ala with commercial L-alaninol using a standard peptide protocol or, in a much less expensive way, by the sodium borohydride-mediated reduction[15] of Z-D-Ala-L-Ala-OMe **8**. The glycosylation was performed in the presence of TMSOTf and gave glycodipeptide **10** in 72% yield. The

(11) Zuurmond, H. M.; Veenemann, G. H.; van der Marel, G. A.; van Boom, J. H. *Carbohydr. Res.* **1993**, *241*, 153−164.

(12) Gurjar, M. K.; Saha, U. K. *Tetrahedron* **1992**, *48*, 4039−4044.
(13) Fischer, E.; Bergmann, M.; Rabe, A. *Ber.* **1920**, *53*, 2362−2388.
(14) Mazurek, M.; Perlin, A. S. *Can. J. Chem.* **1965**, *43*, 1918−1923.
(15) (a) Kubota, M.; Nagase, O.; Yajima, H. *Chem. Pharm. Bull.* **1981**, *29*, 1169−1171. (b) Sohai, M.; Oyamada, H.; Takase, M. *Bull. Chem. Soc. Jpn.* **1984**, *57*, 2327−2328. (c) Kokotos, G. *Synthesis* **1990**, 299−301.

SCHEME 2



synthetic sequence was further shortened by replacing the *O*-benzyl ortho ester intermediate **3b** by the corresponding *O*-4-pentenyl ortho ester **7b**: according to Fraser-Reid et al.,[16] *O*-4-pentenyl ortho esters can indeed be used directly as glycosyl donors in the presence of NIS and TMSOTf.

Compound **7b** was prepared via **7a** under the same conditions as **3b** and was used directly as the acceptor in the glycosylation of pseudodipeptide **9**. The reaction was performed using NIS and TMSOTf as promoters and gave **10** in 81% yield; by this sequence, compound **10** is accessible in only three steps from **2** and **9**. Glycodipeptide **10** was then deprotected in two steps to afford free amine **11**.

Building Block B (Scheme 2). The preparation of the core 6-deoxy-L-talosyl dipeptide is displayed in Scheme 2. The formation of the talosyl donors followed studies previously reported by several authors. However, instead of the more commonly used methyl[17] and benzyl rhamnosides,[18] we based our synthesis on 4-pentenyl glycosides, which are readily available and can be used directly as glycosyl donors, thus shortening the synthesis. 4-Pentenyl α-L-rhamnopyranoside precursor **12** was prepared in 94% yield from L-rhamnose by reaction with 4-penten-1-ol under acidic conditions followed by acetonation of the pair of cis OH groups. Oxidation at C-4 of rhamnoside **12** followed by sodium borohydride reduction of the resulting hexos-4-uloside **13** provided access to the L-*talo* series (compound **14**). With respect to the double bond present in the pentenyl group, oxidation could only be performed using Swern conditions or a Cr(VI) oxidant while Ru(VIII)-based reagents could not be used. To perform the selective glycosylation at position 2 of the 6-deoxy-L-talose unit later in the synthesis, the selective protection of positions 3 and 4, and of position 2, was required. This could be achieved either by acetonation or by benzylation. In the first method, deacetonation of **14** followed by reacetonation[11] of triol **19** gave **20** in reasonable yield (50% overall yield from L-rhamnose) in addition to a minor amount of regenerated isomer **14** (13%). The acid-catalyzed rearrangement of **14** could be achieved as well, but provided **20** in lower yield. An important change of conformation of the taloside was observed after formation of the 3,4-*O*-linked bicyclic acetal. The coupling constant between H-1 and H-2 indicated an almost diaxial orientation of these protons, consistent with a boat or twist-boat conformation of the ring instead of the more common chair form of the precursors.

For the benzyl protection scheme, compound **14** was benzylated at position O-4, to give **15**, and compound **15** was deacetonated. The glycoside **16** thus obtained was then submitted to regioselective benzylation by way of a

(16) (a) Fraser-Reid, B.; Udodong, U. E.; Wu, Z.; Ottosson, H.; Merritt, J. R.; Rao, C. S.; Roberts, C.; Madsen, R. *Synlett* **1992**, 927−942. (b) Fraser-Reid, B.; Madsen, R. In *Preparative Carbohydrate Chemistry*; Hanessian, S., Ed.; Marcel Dekker: New York, 1996; pp 339−358.

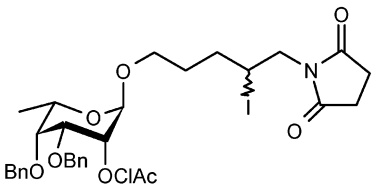
(17) (a) Gan, Z.; Kong, F. *Carbohydr. Res.* **1995**, *270*, 211−216. (b) Gurjar, M. K.; Viswanadham, G. *Tetrahedron Lett.* **1991**, *32*, 6191−6194.

(18) Aspinall, G. O.; Takeo, K. *Carbohydr. Res.* **1983**, *121*, 61−78.

2,3-*O*-stannylidene intermediate.[17a,18] The selectivity of this reaction, however, was low, and provided only a small excess of the desired isomer **17a** (ratio **17a**/**17b** ≈ 12:11). Compound **17a** could be separated by flash chromatography and isolated in 41% yield. Finally, both **17a** and **20** were chloroacetylated at the remaining free 2-OH group to give the donors **18** and **21**. The availability of two precursors carrying different protecting groups in the 6-deoxy-L-talose unit turned out to be critical in later stages of the synthesis.

The D-allothreonine precursor **22** was prepared from benzyl crotonate by the efficient asymmetric synthesis developed by Shao and Goodman;[19] the azido group of **22** could be hydrogenolyzed selectively in the presence of Pt on charcoal to form D-allothreonine benzyl ester hydrochloride **23**. The choice of the solvent (dioxane) was critical for this reaction. IIDQ-mediated coupling of **23** with D-phenylalanine derivative **24**[20] furnished the desired peptide **25** in good yield (79%).

The glycosylation of **25** with both pentenyl glycosides **18** and **21** was then investigated using NIS and TMSOTf as promoters. Both reactions gave the expected glycodipeptide **26** and **28** in good yield and with complete α-stereoselectivity as a result of the presence of an ester at position 2 of the donors. Like pentenyl ortho ester **7b**, both **18** and **21** required more than 1 equiv of Lewis acid in addition to NIS to promote the glycosylation. Immediate purification of **28** was required to avoid the decomposition of the product, probably as a result of the sensitivity of the isopropylidene group toward traces of iodine[21] formed in the course of the reaction. While **26** did not show a similar sensitivity, we isolated a minor side product (9%) in the glycosylation with **18**, compound **30**, which resulted from the addition of NIS to the pentenyl group. Such behavior of pentenyl glycosides is quite rare. Dechloroacetylation of **26** and **28** using hydrazinodithiocarbonate or thiourea furnished the acceptors **27** and **29** ready for the coupling with trisaccharide donors.

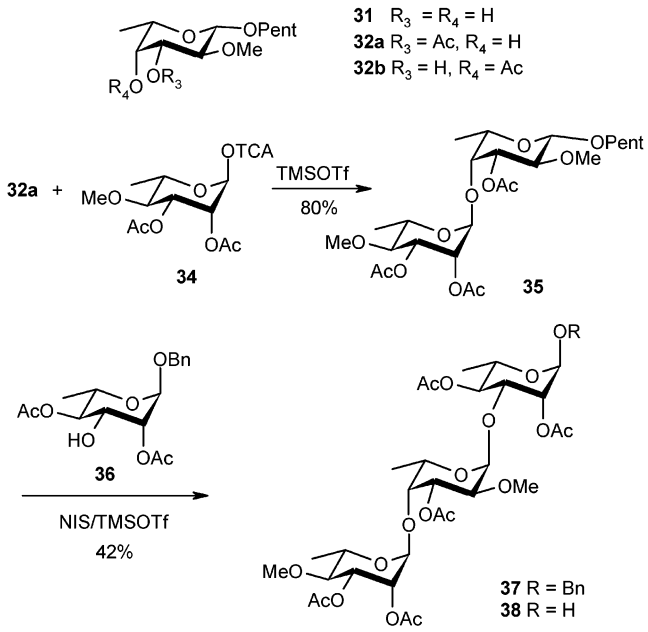


30

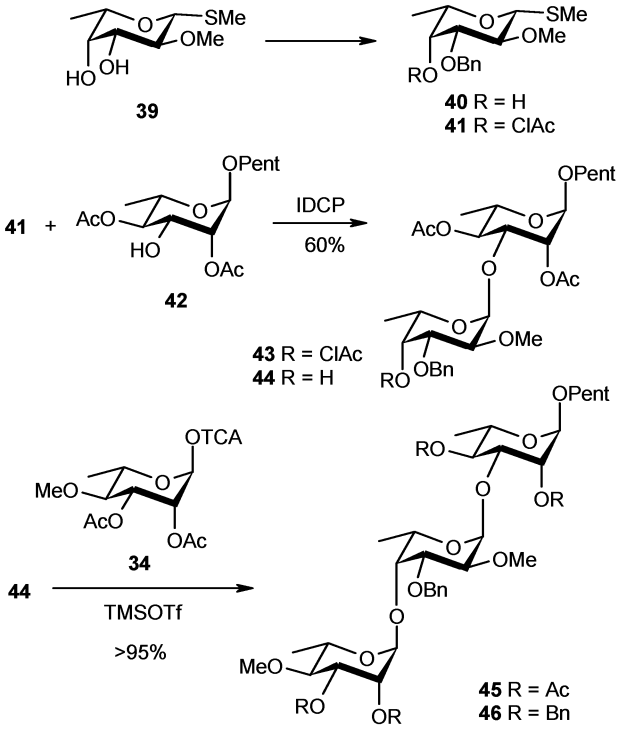
Building Block C (Schemes 3 and 4). For the synthesis of the trisaccharide donor, two different strategies were investigated, differing in the order of glycosylation. In the first approach (Scheme 3), a disaccharide donor, corresponding to residues *d*−*c*, was coupled to a monoglycoside acceptor (*b*), whereas in the second (Scheme 4), more common, approach, a monosaccharidyl donor (*d*) was attached to a disaccharide acceptor (*c*−*b*). The second approach proved more efficient.

Stannylidene-mediated regioselective acetylation of pentenyl fucoside **31**[22] gave monoacetates **32a** and **32b**,

SCHEME 3



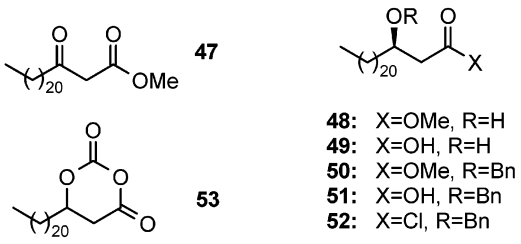
SCHEME 4



which could be separated chromatographically and isolated in 63% and 26% yield, respectively. Glycosylation of **32a** with the trichloroacetimidate **34**[23] provided the disaccharide **35** as the α-anomer exclusively. This compound was then coupled to benzyl rhamnoside **36** to give trisaccharide **37** in modest overall yield (42%).

(19) Shao, H.; Goodman, M. *J. Org. Chem.* **1996**, *61*, 2582−2583.
(20) Carson, J. F. *Synthesis* **1981**, 268−270 (L-analogue).
(21) Szarek, W. A.; Zamojski, A.; Tiwari, K. N.; Ison, E. R. *Tetrahedron Lett.* **1986**, *27*, 3827−3830.
(22) (a) Jain, R. K.; Locke, R. D.; Matta, K. L. *Carbohydr. Res.* **1991**, *212*, C1−C3. (b) Debenham, J. S.; Rodebaugh, R.; Fraser-Reid, B. *J. Org. Chem.* **1997**, *62*, 4591−4600.
(23) Aspinall, G. O.; Crane, A. M.; Gammon, D. W.; Ibrahim, I. H.; Khare, N. K.; Chatterjee, D.; Rivaire, B.; Brennan, P. J. *Carbohydr. Res.* **1991**, *216*, 337−355.

CHART 1



Although **37** could not be purified to homogeneity, it was hydrogenolyzed and gave pure reducing trisaccharide **38** after chromatography. However, the conversion of **38** into the corresponding trichloroacetimidate failed, and this approach was therefore abandoned.

Another type of trisaccharide donor was sought. With respect to our favorable experience in glycosylations with 4-pentenyl glycosides, we focused our efforts on the synthesis of a 1-*O*-pentenyl trisaccharide. Thus, it was envisaged to create the linkage between sugar units *b* and *c* by way of a thioglycoside-mediated reaction, unit *b* carrying a disarmed pentenyl glycoside, and the linkage between units *c* and *d* using a trichloroacetimidate. A high α-selectivity of the critical coupling with the 2-OMe fucose derivative was expected on the basis of previous work by Van Boom.[11] 2-O-methyl thiofucoside **39**[24] was regioselectively benzylated[11] and subsequently chloroacetylated to give donor **41**. Unlike previous acetylations, the benzylation was highly selective. Glycosylation of 4-pentenyl rhamnoside **42** with **41** using biscollidine iodonium perchlorate (IDCP) as promoter gave disaccharide **43** (60%), as α-anomer only, which was then dechloroacetylated to give **44**, and glycosylated with trichloroacetimidate **34** (∼100%). By this approach, the pentenyl trisaccharide **45** was obtained in good overall yield. To rearm the donor, compound **45** was deacetylated and subsequently benzylated at the four free OH positions to give **46** in 66% yield.

Building Block D (Chart 1). The lipidic component of mycoside C-type GPLs is an acyl group of widely diverse chain length (C_{28} is typical), saturated or monounsaturated, and carrying a 3-hydroxy or a 3-methoxy group.[4,25] The configuration at C-3 is commonly *R*, as in *β*-hydroxyacyl groups of lipid A glycolipids.[26] On the basis of starting material availability and desire to develop a synthesis applicable to a wide range of fatty acids, we chose to attach to the glycopeptide an (*R*)-3-hydroxytetracosanoyl group. The precursor of this acyl group was prepared from C_{24} *β*-ketoester **47**.[27] Enantioselective reduction[28] of the keto group led to (*R*)-*β*-hydroxy ester **48** in high yield. The racemic compound had been prepared previously by a similar approach.[29] Compound **48** was saponified to provide the fatty acid building block, (*R*)-3-hydroxylignoceric acid **49**. However, this compound proved to be very poorly soluble in organic solvents, requiring elevated temperature for dissolution. To improve its solubility, the amphiphilicity was reduced by protecting the hydroxyl group. The alcohol function of **49** was benzylated by the method of Nishizawa[30] to give **50** and the ester was saponified. Although the resulting acid **51** could be coupled to amines using a coupling reagent like EEDQ, its solubility in organic solvents remained very poor. Furthermore, the chemoselectivity of the reaction with EEDQ was not good as it led to the desired fatty acyl amides contaminated by the corresponding ethyl carbamate and was only moderately improved using the isobutyl homologue IIDQ.

A better solubility for the lipid building block was achieved by converting the acid **51** into its acyl chloride **52**. Since the preparation of **52** was rather long, we looked for a shorter alternative. In particular, we attempted to combine the necessary protection of the 3-hydroxyl group with the activation of the acid. Phosgenation of **49** led to the well-soluble, intramolecular mixed anhydride **53**, which appeared to be a suitable reagent for our purpose. The reaction of **53** with a glycopeptide amine furnished a single product in high yield, but the analysis of this product revealed that it was an urea-type dimer of the amine, R-NHCONH-R. Thus, instead of acting as an acylating agent, **53** appears to behave as a phosgene substitute. Acylation reactions will therefore be performed with the acyl chloride **52**.

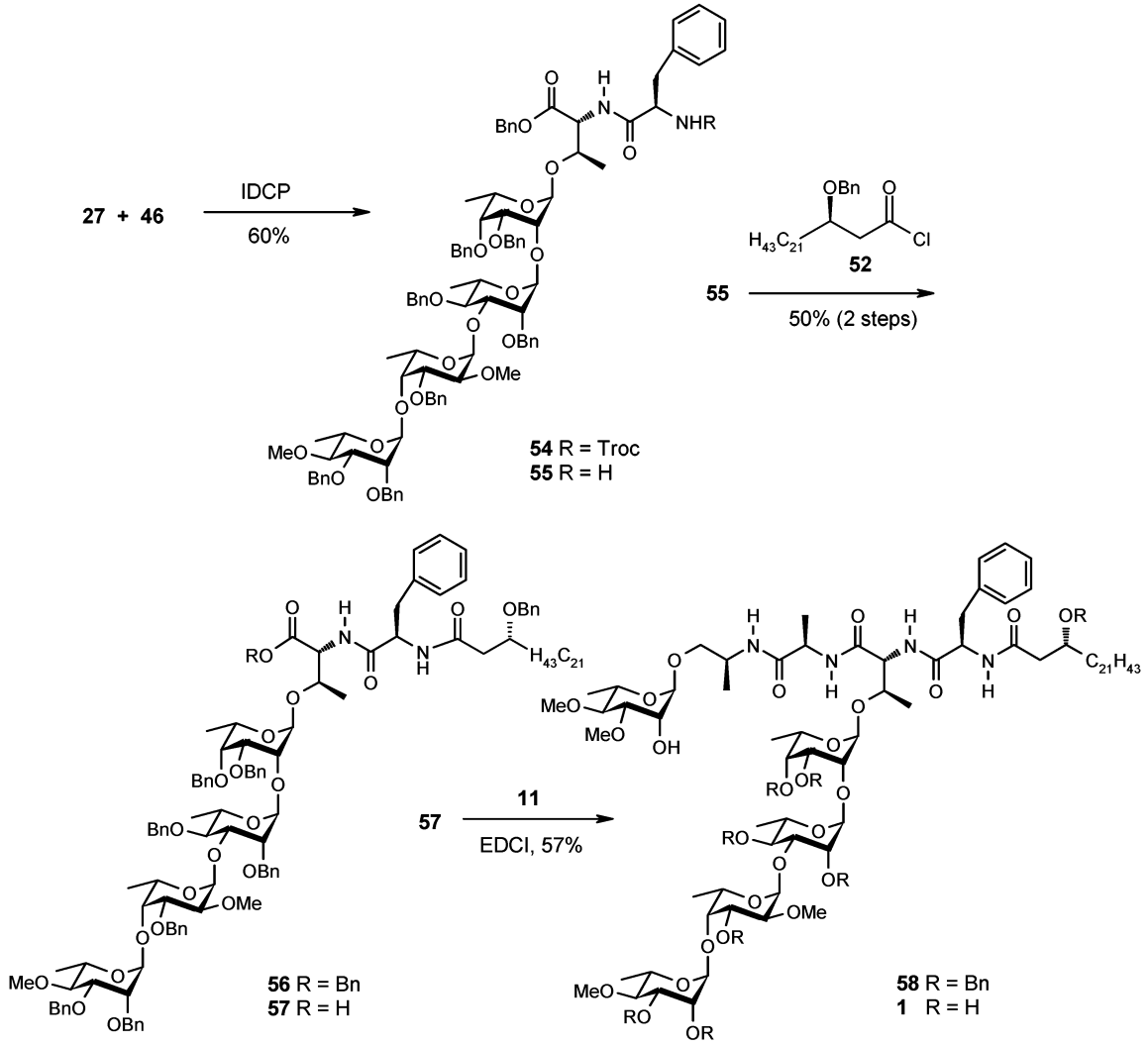
Final Assembly (Scheme 5). For the final assembly of the GPL, the first step was the glycosylation of the talosylated allothreonine-containing glycopeptide (building block **B**) with the trisaccharide donor (building block **C**). Initially, we investigated the glycosylation of glycopeptide **29** with trisaccharide donor **45** in the presence of NIS/TMSOTf. The reaction required an excess Lewis acid and led to a complex mixture, from which an unexpected product having the constitution of the original dipeptide carrying a disaccharide was isolated in 30% yield. This product was not further investigated. The same product was also obtained using the less sensitive benzylated glycopeptide **27** as the acceptor. The coupling process could not be improved by changing the temperature or using solutions of both coupling reagents.[11]

To use milder conditions for the key glycosylation step, we used the "armed" donor **46** instead of **45**. With IDCP as the promoter, compound **27** could be successfully glycosylated, and the tetrasaccharidyl dipeptide **54** was isolated in 60% yield (200 mg scale) (Scheme 5). The reaction, however, was not quite complete and some starting material was recovered (**27** in 19% yield). It should be noted that with NIS/Lewis acid as coupling reagents, the reaction provided only the unidentified product mentioned above. The α-configuration of the newly formed glycosidic bond was confirmed by a C−H-coupling constant of about 170 Hz at the anomeric center.

To link the lipidic residue (building block **D**), the N-terminal position of the glycopeptide **54** was deprotected using zinc in a buffered solution[20] and the resulting amine **55** was acylated with acyl chloride **52** to give glycopeptidolipid **56** (50% for the two steps). Selective

(24) Kerekgyarto, J.; Szurmai, Z.; Liptak, A. *Carbohydr. Res.* **1993**, *245*, 65−80.
(25) Asselineau, J. *Fortschr. Chem. Org. Naturst.* **1991**, *56*, 1−85.
(26) Zaehringer, U.; Lindner, B.; Rietschel, T. *Adv. Carbohydr. Chem. Biochem.* **1994**, *50*, 211−276.
(27) (a) Ställberg-Stenhagen, S.; Stenhagen, E. *Ark. Kemi, Mineral. Geol.* **1945**, *19A*[1], 5−13; *Chem. Abstr.* **1947**, *41*, 3047b. (b) Ställberg-Stenhagen, S. *Ark. Kemi, Mineral. Geol.* **1946**, *20A*[19], 5−22; *Chem. Abstr.* **1947**, *41*, 4105d.
(28) Capozzi, G.; Roelens, S.; Talami, S. *J. Org. Chem.* **1993**, *58*, 7932−7936.
(29) Skogh, M. *Acta Chem. Scand.* **1952**, *6*, 809−817.
(30) Hatakeyama, S.; Mori, H.; Kitano, K.; Yamada, H.; Nishizawa, M. *Tetrahedron Lett.* **1994**, *35*, 4367−4370.

SCHEME 5



debenzylation of the C-terminal benzyl ester of **56** without affecting the benzyl ethers was achieved by hydrogenolysis with palladium on charcoal in slightly amine alkaline medium. For the final coupling of the resulting glycopeptidolipid **57** with glycopeptide **11**, the carbodiimide EDCI was used together with an excess hydroxybenzotriazole (HOBt). The coupling reaction afforded the protected GPL **58** in 57% yield. Quinoline-derived coupling reagents such as IIDQ were less satisfactory as they led predominantely to carbamates instead of the desired amide. Finally, debenzylation of **58** in slightly acidic methanol furnished the target compound, the complete GPL specific of *M. avium* serovar 4 (**1**).[4b]

Conclusion

Starting from L-fucose, L-rhamnose, D-alanine, L-alanine, D-phenylalanine, behenic acid (C_{22}), and crotonic acid, the specific GPL of *M. avium* serovar 4 was synthesized in 62 steps by a convergent synthesis involving 18 steps in the longest sequence. This constitues the first total synthesis of a complete "polar mycoside C" GPL.

Experimental Section

3,4-Di-*O*-acetyl-1,2-*O*-[(*S*)-1-(4-pentenyloxy)ethylidene]-*β*-L-rhamnopyranose (7a). A solution of **2**[13] (crude product from 1.0 g of L-rhamnose monohydrate, 5.5 mmol) in absolute $CHCl_3$ (10 mL) was treated with 4-pentenol (1.15 mL, 11 mmol) and 2,6-lutidine (1.3 mL, 11 mmol). The solution was stirred at rt for 2 d, diluted with $CHCl_3$ (20 mL), and washed with water, 2 N aq HCl, and satd aq $NaHCO_3$. Drying over $MgSO_4$ was followed by coevaporation with toluene and $CHCl_3$. Chromatography using Hex/EtOAc 3:1 led to **7a** as a colorless crystallizing syrup (1.72 g, 87%). Recrystallization could be promoted by solubilization in ether followed by addition of hexane and cooling. Purification by simple crystallization without prior chromatography led to lower yields. Compound **7a**: mp 61−62 °C, recryst mp 64 °C; $[\alpha]^{25}_D$ +17 (*c* 2.0, $CHCl_3$); ^{1}H NMR (360 MHz, $CDCl_3$) δ 5.72 (m_c, 1 H), 5.33 (d, 1H, *J* 2.1 Hz), 5.15−4.85 (m, 4 H), 4.61 (dd, 1 H, *J* 2.1, 3.8 Hz), 3.50−3.35 (m, 3 H), 2.04, 1.99 (2s, 2 × 3 H), 2.01, 1.68 (2 m_c, 2 × 2 H), 1.66 (s, 3 H), 1.16 (d, 3 H); ^{13}C NMR (90 MHz, $CDCl_3$) δ 170.0, 169.7, 137.9, 124.1, 114.8, 97.1, 76.5, 70.7, 70.4, 69.1, 61.8, 30.0, 28.6, 24.7, 24.5, 20.7, 17.5.

1,2-*O*-[(*S*)-1-(4-Pentenyloxy)ethylidene]-3,4-di-*O*-methyl-*β*-L-rhamnopyranose (7b). A solution of **7a** (950 mg, 2.65 mmol) in 1,4-dioxane (25 mL) was treated with powdered NaOH (1.15 g, 29 mmol) and stirred for 2 h at rt. MeI (830 μL, 13.7 mmol) was added, and the mixture was stirred overnight. The excess methylating reagent was destroyed by addition of MeOH (1 mL). After 2 h, the solvent was evaporated and the residue taken up in CH_2Cl_2 and water. The aqueous phase was extracted twice with CH_2Cl_2, and the combined organic layers were washed with water and aq $Na_2S_2O_3$. Drying over $MgSO_4$, evaporation of the solvent, and

chromatography of the residue using Hex/EtOAc 3:1 gave pure **7b** as a colorless syrup (650 mg, 81%). The chromatographic purification may be avoided by using Me_2SO_4 (1.15 mL in two additions, 12 mmol) instead of MeI as methylating agent to give **7b** (1.67 g from 2.15 g **7a** (92%)): $[\alpha]^{25}_D$ +15 (*c* 1.9, $CHCl_3$); ^{1}H NMR (360 MHz, $CDCl_3$) δ 5.80 (m_c,1 H), 5.31 (bs, 1 H), 5.01, 4.95, 4.53 (3 m_c, 3 H), 3.56, 3.54 (2s, 2 × 3 H), 3.53 (m_c, 2 H), 3.37 (dd, 1 H, *J* 4.1, 9.1 Hz), 3.25 (dq, *J* 9.2, 3 × 6.1 Hz, H-5), 3.10 (t, 1 H), 2.11 (m_c, 2 H), 1.70 (s, 3 H), 1.65 (m_c, 2 H), 1.30 (d, 3 H); ^{13}C NMR (90 MHz, $CDCl_3$) δ 138.1, 123.6, 114.8, 97.3, 81.3, 81.2, 76.1, 70.3, 61.8, 61.0, 57.7, 30.2, 28.8, 24.5, 17.8.

***N*-Benzyloxycarbonyl-D-alaninyl-L-alaninol (9).** A solution of **8** (5.0 g, 16 mmol) in MeOH (17 mL) and THF (17 mL) was dropped into a freshly prepared solution of $NaBH_4$ (3.4 g, 90 mmol) in aq MeOH (50 mL, 80%) at 0 °C during 20 min. The reaction was stirred at rt overnight and then neutralized with 2 N aq HCl. The salts were removed by filtration and extracted with MeOH. The filtrate was evaporated to dryness, and the residue was dried by coevaporation with $CHCl_3$ before taking up in $CHCl_3$ and filtration. After concentration, the crude product was crystallized from toluene leading to compound **9** (4.1 g, 90%): mp 134 °C; $[\alpha]^{21}_D$ +2 (*c* 2.0 $CHCl_3$); ^{1}H NMR (360 MHz, $CDCl_3$) δ 7.37−7.28 (m, 5 H), 6.57 (bs, 1 H), 5.72 (d, 1 H, *J* 7.0 Hz), 5.08, 5.06 (2 d, 2 H, *J* 12.3 Hz), 4.21 (dq, 1 H, *J* 6.4, 7.0 Hz), 4.04 (m_c 1 H), 3.63 (dd, 1 H, *J* 3.0, 11.1 Hz), 3.43 (dd, 1 H, *J* 6.0, 11.1 Hz), 3.22 (bs, 1 H), 1.36 (d, 3 H), 1.12 (d, 3 H, *J* 6.4 Hz); ^{13}C NMR (90 MHz, $CDCl_3$) δ 128.4, 128.0, 127.8, 66.9, 65.4, 50.5, 47.2, 18.3, 16.4. Anal. Calcd for $C_{14}H_{18}N_2O_4$: C, 59.99; H, 7.19; N, 9.99. Found: C, 59.46; H, 7.07; N, 9.96.

(2*S*)-2-(*N*-Benzyloxycarbonyl-D-alaninylamino)propyl 2-*O*-Acetyl-3,4-di-*O*-methyl-α-L-rhamnopyranoside (10). Compounds **7b** (350 mg, 1.2 mmol) and **9** (400 mg, 1.4 mmol) were dissolved in anhyd CH_2Cl_2 (25 mL). NIS (300 mg, 1.3 mmol) followed by TMS triflate (500 μL) were added under a nitrogen atmosphere, and the reaction was stirred for about 30 min at rt. The mixture was diluted with CH_2Cl_2 and washed with aq $Na_2S_2O_3$ and aq $NaHCO_3$. After having been dried with $MgSO_4$, the organic solution was concentrated and the residue purified by chromatography using CH_2Cl_2/acetone/MeOH 100:5:1−2 to give **10** (465 mg, 81%) as a glass-forming syrup: $[\alpha]^{21}_D$ −38 (*c* 1.0, $CHCl_3$); ^{1}H NMR (360 MHz, $CDCl_3$) δ 7.38−7.29 (m, 5 H), 6.18 (d, 1 H, *J* 7.0 Hz), 5.54 (bs, 1 H), 5.22 (dd, 1 H, *J* 1.6, 3.4 Hz), 5.13 (m_c, 2 H), 4.68 (d, 1 H, *J* 1.6 Hz), 4.22, 4.18 (2 m_c, 2 H), 3.63 (dd, 1 H, *J* 4.5, 10.0 Hz), 3.54 (s, 3 H), 3.52 (dq, 1 H, *J* 9.3, 4 × 6.2 Hz), 3.51 (dd, 1 H, *J* 3.4, 9.3 Hz), 3.35 (s, 3 H), 3.33 (dd, 1 H, *J* 4.3, 10.0 Hz), 3.06 (t, 1 H, *J* 9.3 Hz), 2.11 (s, 3 H), 1.38 (d, 3 H, *J* 7.0 Hz), 1.29 (d, 3 H, *J* 6.2 Hz), 1.18 (d, 3 H, *J* 6.1 Hz); ^{13}C NMR (90 MHz, $CDCl_3$) δ 171.5 (C), 170.5 (C), 156.4 (C), 136.2 (C), 128.6, 128.2, 128.1, 97.7 ($^1J_{CH}$ 172 Hz, Rha-C_1), 81.9, 79.6, 70.2 (CH_2), 68.4, 67.8, 67.1 (CH_2), 60.9, 57.5, 50.7, 44.8, 21.0, 18.3, 17.9, 17.6. Anal. Calcd for $C_{24}H_{36}N_2O_9$: C, 58.05; H, 7.31; N, 5.64. Found: C, 57.77; H, 7.30; N, 5.60.

(2*S*)-2-(D-Alaninylamino)propyl 3,4-Di-*O*-methyl-α-L-rhamnopyranoside (11). Compound **10** (375 mg, 76 mmol) was dissolved in anhyd MeOH (20 mL) and treated with methanolic NaOMe (2 mL, 50 mM). The reaction was stirred for several hours at rt until TLC indicated complete conversion. Neutralization with Amberlite IR 120(H^+) ion-exchange resin was followed by filtration and concentration to dryness. The obtained **(2*S*)-2-(*N*-benzyloxycarbonyl-D-alaninylamino)-propyl 3,4-Di-*O*-methyl-α-L-rhamnopyranoside** was homogeneous by NMR spectroscopy. It may be purified by chromatography using CH_2Cl_2/acetone/MeOH 100:5:3−3.5. The intermediate was dissolved in MeOH (70 mL), treated with $Pd(OH)_2$/C (20%, 50 mg) and hydrogenolyzed under 100 psi hydrogen overnight. The catalyst was removed by microfiltration and the solution concentrated. After drying under vacuum, compound **11** (235 mg, 97%) was obtained as a spectroscopically pure colorless syrup: ^{1}H NMR (360 MHz, $CDCl_3$) δ 7.42 (d, 1 H, *J* 6.0 Hz), 4.79 (≈s, 1 H), 4.16, 4.02 (2 m_c, 2 H), 3.64−3.37 (m, 5 H), 3.53, 3.49 (2 s, 2 × 3 H), 3.07 (t, 1 H, *J* 9.5 Hz), 1.34 (d, 3 H, *J* 6.8 Hz), 1.29 (d, 3 H, *J* 6.2 Hz), 1.19 (d, 3 H, *J* 6.7 Hz); ^{13}C NMR (90 MHz, $CDCl_3$) δ 99.4, 81.8, 81.3, 70.6, 67.8, 67.5, 60.8, 57.4, 50.7, 44.3, 21.6, 17.7.

4-Pentenyl 2,3-*O*-isopropylidene-α-L-rhamnopyranoside (12). A mixture of L-rhamnose monohydrate (1.5 g, 8.2 mmol) and *p*-toluenesulfonic acid monohydrate (20 mg, 105 μmol) was treated with 4-pentenol (12 mL) under nitrogen. The mixture was heated to 95 °C for 1.5 d, and the solvent was then removed under vacuum. The crude pentenyl rhamnoside was dissolved in CH_2Cl_2 (50 mL), and 2,2-dimethoxypropane (5 mL) was added. The solution was stirred at rt for 1 d (2 h are sufficient) and then washed with aq $NaHCO_3$ and dried over $MgSO_4$. The solvent was evaporated, and residual 4-pentenol removed by coevaporation with toluene. Drying under vacuum yielded almost pure **12** (2.1 g, 94%) as a yellow syrup. Further purification by chromatography using Hex/EtOAc 3−4:1 proved to be unnecessary: $[\alpha]^{23}_D$ −29 (*c* 2.3, $CHCl_3$); ^{1}H NMR (360 MHz, $CDCl_3$) δ 5.81, 5.03, 4.98 (3 m_c, 3 H), 4.94 (∼s, 1 H, H-1), 4.14 (∼d, 1 H, *J* 5.8 Hz), 4.09 (m_c, 1 H), 3.75−3.63, 3.48−3.37 (2 m, 2 × 2 H), 2.13, 1.69 (2 m_c, 2 × CH_2), 1.53, 1.36 (2 s, 2 × 3 H), 1.29 (d, 3 H, *J* 6.3 Hz); ^{13}C NMR (90 MHz, $CDCl_3$) δ 137.9, 115.0, 109.5, 97.2, 78.3, 75. 9, 74.5, 67.0, 66.0, 30.3, 28.6, 27.9, 26.1, 17.5.

4-Pentenyl 6-Deoxy-2,3-*O*-isopropylidene-α-L-*arabino*-hexos-4-ulopyranoside (13). To a solution of **12** (2.1 g, 7.7 mmol) in anhyd CH_2Cl_2 (90 mL) were added 4 Å molecular sieves (5.0 g) and PCC (5.0 g, 23 mmol), and the mixture was stirred at rt overnight. About 50 mL of CH_2Cl_2 was evaporated, the residue was poured into ether (800 mL), and the chromium salts were removed by filtration through a short column of silica. Concentration of the filtrate led to **13** (1.85 g, 88%) as a slightly yellow syrup: ^{1}H NMR (360 MHz, $CDCl_3$) δ 5.80, 5.03, 4.99 (3 m_c, 3 H), 4.93 (s, 1 H), 4.43 (m_c, 2 H), 4.25 (q, 1 H, *J* 6.8 Hz), 3.76, 3.53 (2 m_c, 2 H), 2.13, 1.71 (2 m_c, 2 × 2 H), 1.49, 1.37 (s, 2 × 3 H), 1.40 (d, 3 H, *J* 6.8 Hz); ^{13}C NMR (90 MHz, $CDCl_3$) δ 137.7, 115.2, 111.4, 97.0, 78.8, 76.0, 70.1, 67.9, 30.1, 28.4, 26.7, 25.5, 16.1.

4-Pentenyl 6-Deoxy-2,3-*O*-isopropylidene-α-L-talopyranoside (14). Compound **13** (2.45 g, 9.1 mmol) was dissolved in ice-cold aq EtOH (95%, 40 mL) and treated with $NaBH_4$ (170 mg, 4.5 mmol). After 30 min, the mixture was allowed to warm to rt and stirred for a further 2 h. The salts were removed by filtration, and the solution was concentrated to dryness. The residue was dissolved in CH_2Cl_2 and washed with a small amount of water. Drying over $MgSO_4$ and concentration furnished **14** (2.3 g, 93%/74% based on L-rhamnose) as a clear colorless syrup: $[\alpha]^{23}_D$ −41 (*c* 2.1, $CHCl_3$); ^{1}H NMR (360 MHz, $CDCl_3$) δ 5.81, 5.03, 4.98 (3 m_c, 3 H), 5.01 (∼s, 1 H), 4.21 (dd, 1 H, *J* 6.4, 5.4 Hz), 4.03 (∼d, 1 H), 3.84 (∼q, 1 H, *J* 6.6 Hz), 3.72, 3.45 (2 m_c, 2 H), 3.54 (∼dd, 1 H, *J* 5.4, 5.8 Hz), 2.31, 1.69 (2 m_c, 2 × 2 H), 1.58, 1.38 (2 s, 2 × 3 H), 1.31 (d, 3 H, *J* 6.6 Hz); ^{13}C NMR (90 MHz, $CDCl_3$) δ 138.0, 114.9, 109.3, 97.5, 73.5, 73.1, 67.1, 67.0, 64.4, 30.3, 28.7, 25.9, 25.3, 16.7.

4-Pentenyl 4-*O*-benzyl-6-deoxy-α-L-talopyranoside (16). To a solution of **14** (5.35 g, 20 mmol) in 1,4-dioxane (50 mL) were added powdered NaOH (2 g, 50 mmol) and BnBr (2.5 mL, 21 mmol), and the reaction was heated to 80 °C overnight. More BnBr (0.5 mL, 4 mmol) was then added, and heating was continued for 2 d. The solvent was then evaporated and the residue taken up in CH_2Cl_2 and water. The organic layer was separated, washed with brine, and dried over $MgSO_4$. Concentration afforded crude **15**: ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.45−7.23 (m, 5 H), 5.80, 5.01, 4.96 (3 m_c, 3 H), 4.90 (d, 1 H, *J* 1.6 Hz), 4.85, 4.56 (2 d, 2 H, *J* 12.1 Hz), 4.41 (dd, 1 H, *J* 6.8, 4.6 Hz), 4.04 (dd, 1 H, *J* 1.6, 6.8 Hz), 3.88 (dq, 1 H, *J* 3.7, 3 × 6.6 Hz), 3.70 (m_c, 1 H), 3.61 (dd, 1 H, *J* 3.7, 4.6 Hz), 3.45 (m_c, 1 H), 2.09, 1.66 (2 m_c, 2 × 2 H), 1.57, 1.38 (2 s, 2 × 3 H), 1.21 (d, 3 H, *J* 6.6 Hz); ^{13}C NMR (63 MHz, $CDCl_3$) δ 138.0, 137.99, 128.5−127.6 (m), 114.8, 109.6, 97.6, 74.4, 74.0, 72.7, 72.1, 67.6, 67.0, 30.2, 28.7, 26.2, 25.4, 16.8; $C_{21}H_{30}O_5$. Compound **15** was

dissolved in 80% aq AcOH (50 mL), and the solution was heated to 50 °C for about 1 h and then concentrated. Coevaporation with toluene followed by chromatography using Hex/EtOAc 5:1 gave pure **16** (3.5 g, 55%) and slightly contaminated **16** (750 mg, 12%, 67% in total): mp 53−55 °C; $[\alpha]^{20}_D$ −86 (*c* 1.2, $CDCl_3$); ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.45−7.28 (m, 5 H), 5.80, 5.01, 4.97 (3 m_c, 3 H), 4.84 (bs, 1 H), 4.78, 4.71 (2 d, 2 H, *J* 11.0 Hz), 3.89 (bq, 1 H, *J* 3 × 6.6 Hz), 3.84 (≈dd, 1 H, *J* 3.4, 10.3 Hz), 3.71−3.60 (m, 3 H), 3.41 (m_c, 1 H), 3.36 (d, 1 H, *J* 11.7 Hz, 3-OH), 2.78 (d, 1 H, *J* 10.3 Hz, 2-OH), 2.11, 1.66 (2 m_c, 2 × 2 H), 1.26 (d, 3 H, *J* 6.6 Hz, H-6); ^{13}C NMR (63 MHz, $CDCl_3$) δ 138.0, 137.5, 128.6, 128.2, 128.1, 114.9, 100.9, 81.4, 76.7, 70.9, 67.1, 66.8, 65.8, 30.3, 28.6, 16.9.

4-Pentenyl 3,4-Di-*O*-benzyl-6-deoxy-α-L-talopyranoside (17a). A mixture of **16** (2.2 g, 6.8 mmol) and Bu_2SnO (1.7 g, 6.8 mmol) was treated with benzene (150 mL) and heated to reflux with continuous removal of water (Dean Stark) for 1 d. The resulting cloudy solution was concentrated to about 100 mL, and Bu_4NBr (2.2 g, 6.8 mmol) and BnBr (1.8 mL, 15 mmol) were added. Reflux was continued for 1 d, and the solvent was then evaporated. Residual BnBr was removed by coevaporation with water, and the residue was taken up in CH_2Cl_2 and washed with water. After drying with $MgSO_4$, the solvent was evaporated and the crude mixture was separated by chromatography using Hex/EtOAc 10:1 to afford **17a** (1.15 g, 41%), **17b** (1.06 g, 38%), and a mixture of both isomers (300 mg, 10%). Compound **17a**: $[\alpha]^{20}_D$ −49 (*c* 2.0, $CDCl_3$); ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.53−7.21 (m, 10 H), 5.79 (m_c, 1 H), 5.06−4.92 (m, 2 H), 5.00, 4.84, 4.63, 4.56 (4 d, 4 H), 4.87 (d, 1 H, *J* 1.5 Hz), 4.23 (d, 1 H, *J* 10.3 Hz, 2-OH), 3.97 (ddt, 1 H, ^3J 10.3, 3.0, 1.5 Hz, ^4J 1.5 Hz), 3.84 (bq, 1 H, *J* 3 × 6.6 Hz), 3.75 (∼t, 1 H, *J* 3.0 Hz), 3.66 (m_c, 1 H, H-4), 3.63, 3.42 (2 m_c, 2 H), 2.08, 1.64 (2 m_c, 2 × 2 H), 1.21 (d, 3 H, *J* 6.6 Hz); ^{13}C NMR (63 MHz, $CDCl_3$) δ 138.2, 138.0, 137.7, 128.5, 128.4, 128. 3, 127. 9, 127.6, 127.6, 114.9, 101.5, 78.8, 75.5, 74.4, 69. 8, 68.1, 67.1, 66.4, 30.3, 28.6, 16.8.

4-Pentenyl 3,4-Di-*O*-benzyl-2-*O*-chloroacetyl-6-deoxy-α-L-talopyranoside (18). A solution of chloroacetic anhydride (790 mg, 4.6 mmol) in anhyd CH_2Cl_2 (5 mL) was added dropwise to an ice-cold solution of **17a** (1.2 g, 2.9 mmol) and pyridine (1.8 mL, 22 mmol) in anhyd CH_2Cl_2 (15 mL). Stirring was continued and the reaction was allowed to warm to rt overnight. The diluted mixture was washed with 2 N aq HCl and aq $NaHCO_3$, dried over $MgSO_4$, and concentrated, and the crude product was purified by chromatography using Hex/EtOAc 9:1 to give **18** (1.3 g, 91%): $[\alpha]^{18}_D$ −35 (*c* 1.25, $CDCl_3$); ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.45−7.23 (m, 10 H), 5.79 (m_c, 1 H), 5.36 (∼dt, 1 H, ^3J 1.5, 3.0 Hz, ^4J 1.5 Hz), 5.01, 4.96 (2 m_c, 2 H), 4.85 (∼bs, 1 H), 4.87, 4.66 (2 d, 2 H, *J* 11.5 Hz), 4.77, 4.52 (2 d, 2 H, *J* 11.7 Hz), 4.07, 3.95 (AB, 2 H, *J* 15.4 Hz), 3.88 (dq, 1 H, *J* 1, 3 × 6.6 Hz), 3.81 (∼t, 1 H, *J* 3.3 Hz), 3.64 (m_c, 1 H), 3.55 (m_c, 1 H), 3.41 (m_c, 1 H), 2.09, 1.66 (2 m_c, 2 × 2 H), 1.26 (d, 3 H, *J* 6.6 Hz); ^{13}C NMR (63 MHz, $CDCl_3$) δ 167.4, 138.8, 137.9, 137. 9, 128.4, 128.3, 128.1, 127.7, 127.6, 127.55, 115.0, 98.2, 75.9, 75.0, 74. 5, 71.1, 68. 9, 67.1, 66.9, 41.1, 30.2, 28.5, 16.7.

4-Pentenyl 6-Deoxy-3,4-*O*-isopropylidene-α-L-talopyranoside (20). Compound **14** (crude product from 1.5 g, 8.2 mmol, L-rhamnose monohydrate) was dissolved in aq HOAc (50 mL, 90%), and the mixture was kept at 50 °C for 2 h. After evaporation of the solvent and coevaporation of traces of AcOH with toluene, pure **19** was obtained: ^{1}H NMR (360 MHz, $CDCl_3$) δ 5.81, 5.01, 4.97 (3 m_c, 3 H), 4.85 (∼s, 1 H), 3.91 (∼q, 1 H, *J* 3 × 6.4 Hz), 3.78 (m_c, 2 H), 3.67, 3.67, 3.44 (3 m_c, 3 H), 2.99 (bs, 3 H, OH), 2.11, 1.67 (2 m_c, 2 × 2 H), 1.29 (d, 3 H, *J* 6.4 Hz); ^{13}C NMR (90 MHz, $CDCl_3$) δ 137.9, 114.4 (CH_2), 100.4, 72.9, 70.6, 67.2 (CH_2), 66.6, 65.9, 30.3 (CH_2), 28.7 (CH_2), 16.5; $C_{11}H_{20}O_5$. A solution of the sample of **19** thus obtained and HOTs·H_2O (20 mg, 0.1 mmol) in CH_2Cl_2 (50 mL) was treated with 2,2-dimethoxypropane (5 mL). The solution was stirred at rt for about 1 h and then washed with satd aq $NaHCO_3$. Drying with $MgSO_4$ followed by concentration and flash chromatography afforded **20** (1.35 g, 50% based on rhamnose monohydrate) and isomer **14** (290 mg, 13% based on rhamnose monohydrate). Compound **20**: $[\alpha]^{25}_D$ −77 (*c* 1.7, $CDCl_3$); ^{1}H NMR (360 MHz, $CDCl_3$) δ 5.81, 5.01, 4.95 (3 m_c, 3 H), 4.73 (d, 1 H, *J* 5.4 Hz), 4.49 (dd, 1 H, *J* 3.4, 7.4 Hz), 4.09 (dd, 1 H, *J* 7.4, 2.0 Hz), 3.81 (dq, 1 H, *J* 2.0, 3 × 6.5 Hz), 3.77, 3.46 (2 m_c, 2 H), 3.68 (dd, 1 H, *J* 5.4, 3.4 Hz), 2.31 (bs, 1 H, OH), 2.11, 1.69 (2 m_c, 2 × 2 H), 1.51, 1.35 (2 s, 2 × 3 H), 1.24 (d, 3 H, *J* 6.5 Hz); ^{13}C NMR (90 MHz, $CDCl_3$) δ 138.2, 114.8, 109.9, 100.5, 76.2, 73.5, 68.8, 67.4, 65.0, 30.3, 28.9, 26.0, 25.2, 15.9.

4-Pentenyl 2-*O*-Chloroacetyl-6-deoxy-3,4-*O*-isopropylidene-α-L-talopyranoside (21). A solution of chloroacetic anhydride (1.0 g, 5.8 mmol) in anhyd CH_2Cl_2 (25 mL) was added dropwise to an ice-cold solution of **20** (1.1 g, 4.0 mmol) and NEt_3 (800 μL, 5.7 mmol) in anhyd CH_2Cl_2 (30 mL). Stirring was continued overnight, allowing the mixture to warm to rt. After dilution with CH_2Cl_2 the reaction mixture was washed with 1 N aq HCl and satd aq $NaHCO_3$. Drying with $MgSO_4$, concentration of the solution, and chromatography of the crude product using Hex/EtOAc 10:1 gave **21** (1.2 g, 85%) as a colorless syrup: $[\alpha]^{23}_D$ −100 (*c* 1.1, $CDCl_3$); ^{1}H NMR (250 MHz, $CDCl_3$) δ 5.80 (m_c, 1 H), 5.06−4.92 (m, 2 H), 5.00 (dd, 1 H, *J* 6.4, 2.9 Hz), 4.85 (d, 1 H, *J* 6.4 Hz), 4.60 (dd, 1 H, *J* 2.9, 7.6 Hz), 4.19, 4.15 (2 d, 2 H, *J* 15.3 Hz), 4.15 (dd, 1 H, *J* 7.6, 1.7 Hz), 3.86 (dq, 1 H, *J* 1.7, 3 × 6.4 Hz), 3.75, 3.44 (2 m_c, 2 H), 2.09, 1.65 (2 m_c, 2 × 2 H), 1.51, 1.33 (2 s, 2 × 3 H), 1.23 (d, 3 H, *J* 6.4 Hz); ^{13}C NMR (63 MHz, $CDCl_3$) δ 167.2, 138.4, 115.2, 111.0, 97.7, 76.9, 73.2, 72.5, 67.6, 66.3, 41.3, 30.5, 29.1, 26.5, 25.7, 15.9. Anal. Calcd for $C_{16}H_{25}ClO_6$: C, 55.09; H, 7.22; Cl, 10.16. Found: C, 53.91; H, 7.08; Cl, 11.24; these results are consistent with the presence of 0.1 equiv of CH_2Cl_2 in the product.

D-Allothreonine Benzyl Ester Hydrochloride (23). A solution of **22**[19] (1.78 g, 7.6 mmol) in 1,4-dioxane (150 mL) was treated with 0.5 N aq HCl (15 mL, 7.5 mmol) and Pt/C (180 mg, 5−10%). The mixture was hydrogenolyzed at normal pressure until TLC indicated total conversion (2−7 d); the atmosphere was replaced with fresh hydrogen several times. After removal of the catalyst by membrane filtration, the solution was concentrated to dryness and the residue was dried under vacuum leaving crude **23**. For purification the compound was dissolved in MeOH (5 mL) and precipitated by addition of ether (100 mL). After filtration and drying under vacuum, pure **23** (1.5 g, 81%) was obtained: mp 145−147 °C; $[\alpha]^{21}_D$ ∼0 (*c* 2.0, MeOH); ^{1}H NMR (250 MHz, CD_3OD) δ 7.45−7.36 (m, 5 H), 5.33, 5.28 (AB, 2 H, *J* 12.1 Hz), 4.26 (dq, 1 H, *J* 3.5, 3 × 6.6 Hz), 4.11 (d, 1 H, *J* 3.5 Hz), 1.20 (d, 3 H, *J* 6.6 Hz); ^{13}C NMR (63 MHz, CD_3OD) δ 168.3, 136.3, 129.8, 129.8, 129.7, 69.1, 66.5, 59.4, 18.5.

***N*-2,2,2-Trichloroethoxycarbonyl-D-phenylalaninyl-D-allothreonine Benzyl Ester (25).** A solution of **24**[20] (1.0 g, 2.9 mmol) and IIDQ (0.91 g, 3.0 mmol) in anhyd CH_2Cl_2 (50 mL) was stirred for a few minutes and then treated with **23** (700 mg, 2.85 mmol). After stirring overnight, the solution was washed with aq HCl and then with aq $NaHCO_3$, dried over $MgSO_4$, and concentrated. Chromatography of the residue using Hex/EtOAc 2:1 gave **25** (1.2 g, 79%) as a syrup. Alternatively, the product may be purified by crystallization from toluene leading to solid **25** in 64% yield: mp 108−109 °C; $[\alpha]^{23}_D$ −15 (*c* 1.1, $CHCl_3$); ^{1}H NMR (360 MHz, $CDCl_3$) δ 7.39−7.17 (m, 10 H), 6.59 (d, 1 H, *J* 7.0 Hz, NH), 5.56 (d, 1 H, *J* 7.3 Hz, NH), 5.17 (s, 2 H), 4.70 (m_c, 2 H), 4.59 (dd, 1 H, *J* 3.2, 7.0 Hz), 4.47 (∼q, 1 H, *J* 7.3 Hz), 4.13 (m_c, aThr-3), 3.09 (m_c, 2 H), 1.05 (d, 3 H, *J* 7.5 Hz); ^{13}C NMR (90 MHz, $CDCl_3$) δ 129.2−128.4, 127.3, 74.7 (CH_2), 68.9 (CH_2), 67.6, 58.5, 56.5, 38.4, 18.6. Anal. Calcd for $C_{23}H_{25}Cl_3N_2O_6$: C, 51.94; H, 4.74; N, 5.27; Cl, 20.00. Found: C, 52.21; H, 4.77; N, 5.21; Cl, 20.34.

***N*-(2,2,2-Trichloroethoxycarbonyl)-D-phenylalaninyl-[*O*-(3,4-di-*O*-benzyl-2-*O*-chloroacetyl-α-L-talopyranosyl)-D-allothreonine benzyl ester] (26).** A solution of **18** (800 mg, 1.6 mmol) and **25** (850 mg, 1.6 mmol) in anhyd CH_2Cl_2 (50 mL) was treated with NIS (412 mg, 1.8 mmol). TMS triflate

(0.8 mL, 4.4 mmol) was added dropwise under an inert atmosphere, and the reaction mixture was stirred for 15 min at rt. The diluted reaction mixture was washed with aq $NaHCO_3$, aq $Na_2S_2O_3$ and again aq $NaHCO_3$, dried over $MgSO_4$, and concentrated. Final purification by chromatography using Hex/EtOAc 3:1 to 3:2 led to **26** (950 mg, 64%). Besides **26**, slightly impure **25** (300 mg, ~30%) and **30** (180 mg, 9%) were also isolated. Compound **26**: $[\alpha]^{20}_D$ −21 (*c* 1.1, $CDCl_3$); ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.42−7.13 (m, 20 H), 6.71 (d, 1 H, *J* 7.8 Hz, NH), 5.50 (d, 1 H, *J* 6.8 Hz, NH), 5.17 (m_c, 1 H), 5.12 (m_c, 2 H, *J* 12.2 Hz), 4.85 (bs, 1 H), 4.81 (d, 1 H), 4.75−4.57 (m, 5 H), 4.41 (d, 1 H), 4.36 (m_c, 1 H), 4.05, 3.91 (AB, 2 H, *J* 15.4 Hz), 3.97 (dq, 1 H, *J* 3.2, 3 × 6.6 Hz), 3.71 (dq, 1 H, *J* 1, 3 × 6.6 Hz), 3.57 (t, 1 H, *J* 3.3 Hz), 3.42 (m_c, 1 H), 3.08 (d, 2 H, *J* 7.1 Hz), 1.23, 1.16 (2 d, 2 × 3 H, *J* 6.6 Hz); ^{13}C NMR (63 MHz, $CDCl_3$) δ 169.9, 168.7, 167.3, 151.5, 138.6, 137.8, 135.8, 135.0, 129.3−127.2 (m), 97.1, 95.2, 75.5, 75.4, 74.60, 74.6, 74.3, 71.1, 69.2, 68.1, 67.4, 56.7, 56.5, 41.0, 38.3, 16.7, 16.6.

***N*-(2,2,2-Trichloroethoxycarbonyl)-D-phenylalaninyl-[*O*-(3,4-di-*O*-benzyl-α-L-talopyranosyl)-D-allothreonine benzyl ester] (27).** Compound **26** (900 mg, 0.95 mmol) and thiourea (250 mg, 3.3 mmol) were dissolved in a mixture of pyridine (5 mL) and EtOH (5 mL), and the mixture was heated to 60 °C for 3 h (TLC monitoring). After evaporation of the solvents, the crude product was dissolved in CH_2Cl_2 and the solution was washed with dilute aq HCl and aq $NaHCO_3$. The organic solution was dried with $MgSO_4$ and concentrated, and the residual product was purified by chromatography using Hex/EtOAc 3:1 to 2:1 to give **27** (780 mg, 94%): mp 50−58 °C; $[\alpha]^{17}_D$ −27 (*c* 1.0, $CDCl_3$); ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.44−7.14 (m, 20 H), 6.76 (d, 1 H, *J* 8.6 Hz, NH), 5.50 (d, 1 H, *J* 7.8 Hz, NH), 5.11 (AB, 2 H, *J* 12.8 Hz), 4.95 (d, 1 H, *J* 12.0 Hz), 4.84 (bs, 1 H), 4.73 (d, 1 H, *J* 11.7 Hz), 4.74−4.56 (m, 4 H), 4.45 (d, 1 H, *J* 11.7 Hz), 4.39 (m_c, 1 H), 4.26 (d, 1 H, *J* 10.3 Hz, 2-OH), 3.95 (dq, 1 H, *J* 3.2, 3 × 6.5 Hz), 3.80 (dddd, 1 H, ^3J 1, 2.9, 10.3 Hz, ^4J 1−1.5 Hz), 3.66 (bq, 1 H, *J* 3 × 6.6 Hz), 3.52 (~bs, 1 H), 3.47 (t, 1 H, *J* 2.9 Hz), 3.11, 3.05 (ABX, 2 H, *J* 13.9, 6.6, 6.4 Hz), 1.21, 1.09 (2 d, 2 × 3 H, *J* 6.4 and 6.6 Hz); ^{13}C NMR (63 MHz, $CDCl_3$) δ 169.8, 168.9, 154.0, 138.1, 137.4, 135.8, 135.0, 129.3−127.2, 100.6, 95.2, 78.3, 75.5, 75.4, 74.5, 73.9, 69.7, 68.4, 67.4, 67.3, 56.8, 56.4, 38.3, 16.9, 16.8. Anal. Calcd for $C_{43}H_{47}Cl_3N_2O_{10}$: C, 60.18; H, 5.52; N, 3.26; Cl, 12.39. Found: C, 59.67; H, 5.38; N, 3.26; Cl, 12.06.

***N*-(2,2,2-Trichloroethoxycarbonyl)-D-phenylalaninyl-[*O*-(2-*O*-chloroacetyl-3,4-*O*-isopropylidene-α-L-talopyranosyl)-D-allothreonine benzyl ester] (28).** A solution of **21** (100 mg, 0.29 mmol) and **25** (120 mg, 0.23 mmol) in anhyd CH_2Cl_2 (9 mL) was treated with NIS (70 mg, 0.31 mmol) and TMS triflate (140 μL, 0.77 mmol, dropwise) under inert atmosphere. After 30 min, TLC (Hex/EtOAc 3:2) indicated complete conversion. NEt_3 (several drops) was added to neutralize the acid, and the solution was diluted and washed with aq $Na_2S_2O_3$ and aq $NaHCO_3$. Drying over $MgSO_4$ was followed by concentration and immediate chromatography using Hex/EtOAc 4:1 to give pure **28** (125 mg, 70%) as a solidifying syrup: mp 60−75 °C; $[\alpha]^{23}_D$ −41 (*c* 0.8, $CDCl_3$); ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.46−7.14 (m, 10 H), 6.97 (d, 1 H, *J* 9.0 Hz, NH), 5.57 (d, 1 H, *J* 7.3 Hz, NH), 5.19, 5.15 (2 d, 2 H, *J* 12.5 Hz), 4.82 (dd, 1 H, *J* 6.7, 2.6 Hz), 4.74, 4.62 (2 d, 2 H, *J* 12.0 Hz), 4.70 (d, 1 H, *J* 6.7 Hz), 4.69 (dd, 1 H, *J* 2.8, 9.0 Hz), 4.51 (dd, 1 H, *J* 2.6, 7.6 Hz), 4.44 (m_c, 1 H), 4.14, 4.10 (2 d, 2 H, *J* 15.0 Hz), 4.01 (dd, 1 H, *J* 7.6, 1.6 Hz), 3.85 (m_c, 1 H), 3.37 (dq, 1 H, *J* 1.6, 3 × 6.6 Hz), 3.13 (dd, 1 H, *J* 13.9, 6.1 Hz), 3.06 (dd, 1 H, *J* 13.9, 6.9 Hz), 1.47, 1.30 (2 s, 2 × 3 H), 1.24 (d, 3 H, *J* 6.6 Hz), 1.14 (d, 3 H, *J* 6.2 Hz); ^{13}C NMR (63 MHz, $CDCl_3$) δ 169.7, 168.6, 166.7, 153.9, 135.9, 135.3, 129.4, 128.7, 128.6. 127.1, 110.8, 97.4, 95.3, 77.2, 74.5, 72.5, 72.0, 67.2, 66.8, 56.6, 56.4, 40.7, 38.8, 26.1, 25.2, 18.1, 15.4. Anal. Calcd for $C_{34}H_{40}Cl_4N_2O_{11}$: C, 51.40; H, 5.07; N, 3.53; Cl, 17.85. Found: C, 51.13; H, 5.27; N, 3.35; Cl, 17.88.

***N*-(2,2,2-Trichloroethoxycarbonyl)-D-phenylalaninyl-[*O*-(3,4-*O*-isopropylidene-α-L-talopyranosyl)-D-allothreonine benzyl ester] (29).** A solution of **28** (365 mg, 0.45 mmol) in lutidine (3.6 mL) and HOAc (1.2 mL) was treated with hydrazinodithiocarbonate (HDTC, 4 mL of ethanolic solution, ~80 mmol)[31] and stirred at rt for 10 min. The reaction was diluted with CH_2Cl_2 (15 mL), and 2 N aq HCl was added. The mixture was stirred for a few minutes at rt before separating the layers. The aqueous phase was extracted twice with CH_2Cl_2, and the combined organic phases were washed with aq HCl and aq $NaHCO_3$. After drying with $MgSO_4$, the crude product was purified by chromatography using Hex/EtOAc 3:2. Compound **29** (235 mg, 71%) was obtained as a solidifying syrup: mp 56−67 °C; $[\alpha]^{19}_D$ −21 (*c* 1.3, $CDCl_3$); ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.43−7.10 (m, 10 H), 7.01 (d, 1 H, *J* 8.6 Hz, NH), 5.60 (d, 1 H, *J* 7.8 Hz, NH), 5.18 (s, 2 H), 4.73, 4.63 (2 d, 2 H, *J* 12.0 Hz), 4.71 (dd, 1 H, *J* 8.6, 2.9 Hz), 4.63 (d, 1 H, *J* 6.6 Hz), 4.45 (dd, 1 H, *J* 3.0, 7.8 Hz), 4.44 (dt, 1 H, *J* 7.8, 2 × 6.6 Hz), 3.99 (dd, 1 H, *J* 7.8, 1.7 Hz), 3.92 (dq, 1 H, *J* 2.9, 3 × 6.5 Hz), 3,44 (m_c, 2 H), 3.13 (dd, 1 H, *J* 13.9, 6.6 Hz), 3.06 (dd, 1 H, *J* 13,9, 6.6 Hz), 1.47, 1.33 (2 s, 2 × 3 H), 1.29 (d, 3 H, *J* 6.6 Hz), 1.16 (d, 3 H, *J* 6.5 Hz); ^{13}C NMR (63 MHz, $CDCl_3$) δ 169.8 (C), 168.8 (C), 153.9 (C), 135.9 (C), 135.4 (C), 129.5, 128.7, 128.6, 128.5, 127.1, 110.2 (C), 100.0, 95.3 (C), 76.4, 75.9, 74.6 (CH_2), 73.6, 68.9, 67.1 (CH_2), 66.2, 56.7, 56.3, 38.8 (CH_2), 26.1, 25.0, 17.9, 15.8. Anal. Calcd for $C_{32}H_{39}Cl_3N_2O_{10}$: C, 53.53; H, 5.47; N, 3.90; Cl, 14.81. Found: C, 53.31; H, 5.65; N, 3.77; Cl, 14.78.

Methyl 3-*O*-Benzyl-2-*O*-methyl-1-thio-β-L-fucopyranoside (40). To a solution of **39**[24] (2.37 g, 11 mmol) in benzene (80 mL) was added Bu_2SnO (3.61 g, 14.5 mmol), and the mixture was refluxed with continuous removal of water (Dean Stark) for 1 d. The solvent was then removed and the residue dried under vacuum. DMF (60 mL) was added, and the resulting suspension was treated with anhyd CsF (2.2 g, 14.5 mmol) and BnBr (2 mL, 17 mmol). The reaction mixture was stirred at rt for 2 d, and the DMF was then evaporated. The residue was distributed between EtOAc (100 mL) and 1 N aq KF (60 mL). The aqueous phase was extracted with EtOAc (50 mL), and the combined organic layers were washed with water (60 mL) and dried over $MgSO_4$. Chromatography of the crude product using Hex/EtOAc 1:0 − 3:1 led to pure **40** (2.2 g, 65%) as a slightly cloudy syrup: $[\alpha]^{23}_D$ +13 (*c* 1.2, $CHCl_3$); ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.45−7.28 (m, 5 H), 4.73 (m_c, 2 H), 4.18 (d, 1 H, *J* 9.5 Hz), 3.79 (~bt, 1 H, *J* 3.4, 2.7 Hz), 3.63 (s, 3 H), 3.53 (~bq, 1 H, *J* 6.4 Hz), 3.46 (dd, 1 H, *J* 9.0, 3.4 Hz), 3.33 (~t, 1 H, *J* 9 Hz), 2.29 (d, 1 H, *J* 2.7 Hz, OH), 2.22 (s, 3 H), 1.33 (d, 3 H, *J* 6.4 Hz); ^{13}C NMR (63 MHz, $CDCl_3$) δ 137.9, 128.5, 128.0, 127.8, 85.1, 82.6, 79.0, 74.1, 72.2, 69.6, 61.2, 16.6, 12.7. Anal. Calcd for $C_{15}H_{22}O_4S$: C, 60.38; H, 7.43. Found: C, 60.27; H, 7.30.

Methyl 3-*O*-Benzyl-4-*O*-chloroacetyl-2-*O*-methyl-1-thio-β-L-fucopyranoside (41). To a solution of **35** (2.24 g, 7.5 mmol) and pyridine (6 mL, 74 mmol) in anhyd CH_2Cl_2 (50 mL) was added dropwise a solution of chloroacetic anhydride (2.59 g, 15 mmol) in anhyd CH_2Cl_2 at −15 °C. Stirring was continued below 0 °C for 1 h, and the reaction was then worked up as described for the preparation of **18** to give **41** (2.57 g, 91%): $[\alpha]^{27}_D$ −2.5 (*c* 1.2, $CDCl_3$); ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.40−7.28 (m, 5 H), 5.39 (bd, 1 H, *J* 3.5 Hz), 4.72, 4.55 (2 d, 2 H, *J* 11.4 Hz), 4.24 (d, 1 H, *J* 9.5 Hz), 4.19 (s, 2 H), 3.68 (dq, 1 H, *J* 0.7, 3 × 6.4 Hz), 3.60 (s, 3 H), 3.54 (dd, 1 H, *J* 9.0, 3.5 Hz), 3.27 (t, 1 H, *J* 9 Hz), 2.24 (s, 3 H), 1.23 (d, 3 H, *J* 6.4 Hz); ^{13}C NMR (63 MHz, $CDCl_3$) δ 137.5, 128.4, 127.9, 127.8, 85.3, 80.5, 78.8, 72.6, 72.1, 71.9, 61.2, 40.8, 16.5, 12.9.

4-Pentenyl 2,4-Di-*O*-acetyl-α-L-rhamnopyranoside (42). 4-Pentenyl α-L-rhamnopyranoside (crude product from 1.0 g L-rhamnose monohydrate, 5.5 mmol, see **12**) and $TsOH\cdot H_2O$ (20 mg, 0.1 mmol) were dissolved in DMF (23 mL), and

(31) van Boeckel, C. A. A.; Beetz, T. *Tetrahedron Lett.* **1983**, *24*, 3775−3778.

trimethyl orthoacetate (1.5 mL, 12 mmol) was added. The mixture was heated to 50 °C for 2 h and then cooled to rt. NEt_3 (2 mL) was added, and the solvent was evaporated. The residue was taken up in pyridine (6 mL), and Ac_2O (2.5 mL) was added. After being stirred for 2 d at rt, MeOH (2.5 mL) was added to destroy the excess anhydride. After 2 h, the mixture was poured into 2 N aq HCl (70 mL), and the product was extracted with CH_2Cl_2. After washing with aq HCl and aq $NaHCO_3$, the solution was dried over $MgSO_4$ and concentrated and the crude **42** purified by chromatography using Hex/EtOAc 3:1: yield 985 mg, 57% based on rhamnose monohydrate; $[\alpha]^{23}_D$ −38 (*c* 1.5, $CHCl_3$); ^{1}H NMR (250 MHz, $CDCl_3$) δ 5.80 (m_c, 1 H), 5.09−4.96 (m, 3 H), 4.84 (∼t, 1 H, *J* 9.7 Hz), 4.77 (d, 1 H, *J* 1.2 Hz), 4.03 (ddd, 1 H, *J* 3.6, 9.0, 9.7 Hz), 3.81 (dq, 1 H, *J* 9.8, 3 × 6.4 Hz), 3.67, 3.43 (2 m_c, 2 H), 2.20−2.08 (m, 2 H), 2.16, 2.13 (2 s, 2 × 3 H), 2.06 (d, 1 H, *J* 9.0 Hz, OH), 1.69 (m_c, 2 H), 1.21 (d, 3 H, *J* 6.4 Hz); ^{13}C NMR (63 MHz, $CDCl_3$) δ 171.5, 170.6, 137.9, 115.1, 97.1, 74.8, 72.9, 68.6, 67.3, 65.9, 30.2, 28.6, 21.1, 17.4. Anal. Calcd for $C_{15}H_{24}O_7$: C, 56.95; H, 7.65. Found: C, 56.75; H, 7.69.

4-Pentenyl 2,4-Di-*O*-acetyl-3-*O*-(3-*O*-benzyl-4-*O*-chloroacetyl-2-*O*-methyl-α-L-fucopyranosyl)-α-L-rhamnopyranoside (43). Compounds **41** (300 mg, 0.8 mmol) and **42** (235 mg, 0.74 mmol) were dissolved in anhyd CH_2Cl_2/Et_2O (18 mL, 1:5), and 4 Å MS were added. The suspension was stirred at rt under argon for a few minutes before the addition of IDCP (iodonium biscollidine perchlorate, 800 mg, 1.7 mmol; smaller amount led to incomplete reaction). After 30 min, TLC (CH_2Cl_2/acetone 20:1) showed complete conversion. The solids were filtered and washed with CH_2Cl_2 (50 mL). The organic solution was washed successively with aq $Na_2S_2O_3$, 2 N aq HCl, and aq $NaHCO_3$ and then dried with $MgSO_4$. The crude product obtained after evaporation of the solvent was purified by chromatography using Hex/EtOAc 5:1 to give **43** (290 mg, 60%): $[\alpha]^{23}_D$ −96 (*c* 1.1 $CDCl_3$); ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.38−7.27 (m, 5 H), 5.81 (m_c, 1 H), 5.37 (bd, 1 H, *J* 3.3 Hz), 5.21−4.94 (m, 2 H), 5.14 (dd, 1 H, *J* 1.2, 3.4 Hz), 5.08 (dd≈t, 1 H, *J* 9.8, 10.0 Hz), 5.02 (d, 1 H, *J* 3.5 Hz), 4.70 (d, 1 H, *J* 1.2 Hz), 4.65, 4.50 (2 d, 2 H, *J* 11.3 Hz), 4.11 (bq, 1 H, *J* 3 × 6.6 Hz), 4.02 (dd, 1 H, *J* 3.4, 9.8 Hz), 3.82 (dd, 1 H, *J* 3.3, 10.0 Hz), 3.79, 3.67 (2 m_c, 2 H), 3.47 (dd, 1 H, *J* 3.5, 10.0), 3.46 (s, 3 H), 3.42 (dq, 1 H, *J* 10.0, 3 × 6.4 Hz), 2.21−2.04 (m, 2 H), 1.69 (m_c, 2 H), 1.20 (d, 3 H, *J* 6.4 Hz), 1.10 (d, 3 H, *J* 6.6 Hz); ^{13}C NMR (63 MHz, $CDCl_3$) δ 170.5, 169.9, 167.2, 137.9, 128.3, 127.9, 127.6, 115.1, 99.7, 97.2, 77.2, 75.8, 75.6, 72.9, 72.3, 71.9, 71.8, 67.4, 66.5, 65.2, 59.5, 40.8, 30.2, 28.5, 21.1, 20.9, 17.4, 16.0. Anal. Calcd for $C_{31}H_{43}ClO_{12}$: C, 57.89; H, 6.74; Cl, 5.51. Found: C, 57.81; H, 6.67; Cl, 5.39.

4-Pentenyl 2,4-di-*O*-acetyl-3-*O*-(3-*O*-benzyl-2-*O*-methyl-α-L-fucopyranosyl)-α-L-rhamnopyranoside (44). A mixture of **43** (266 mg, 0.41 mmol) and thiourea (103 mg, 1.35 mmol) was treated with pyridine (1.5 mL) and anhyd EtOH (1.5 mL) and heated to 60 °C for 1.5 h until TLC (Hex/EtOAc 3:2) indicated complete conversion. The solvents were evaporated, and the residue was distributed between CH_2Cl_2 and dilute aq HCl. The aqueous layer was extracted with CH_2Cl_2, and the combined organic phases were washed with 2 N aq HCl and sat aq $NaHCO_3$. Drying over $MgSO_4$ was followed by evaporation of the solvent. Chromatography of the crude product using Hex/EtOAc 3:1 gave **44** (205 mg, 87%): $[\alpha]^{24}_D$ −69 (*c* 1.2 $CDCl_3$); ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.42−7.28 (m, 5 H), 5.81 (m_c, 1 H), 5.15 (dd, 1 H, *J* 1.7, 3.4 Hz), 5.08 (dd≈t, 1 H, *J* 9.8, 10.0 Hz), 5.00−4.95 (m, 2 H), 4.99 (d, 1 H, *J* 3.7 Hz), 4.71 (d, 1 H, *J* 1.7 Hz), 4.71, 4.63 (2 d, 2 H, *J* 11.8 Hz), 4.02 (dd, 1 H, *J* 3.4, 9.8 Hz), 3.94 (∼bq, 1 H, J ≈ 6 Hz), 3.86−3.61 (m, 3 H), 3.69, 3.45 (2 m_c, 2 H), 3.58 (dd, 1 H, *J* 3.7, 9.8 Hz), 3.46 (s, 3 H), 2.34 (bs, 1 H, OH), 2.14 (m_c, 2 H), 2.12, 2.08 (2 s, 2 × 3 H), 1.70 (m_c, 2 H), 1.22, 1.19 (2 d, 2 × 3 H, *J* 6.4, 6.0 Hz); ^{13}C NMR (63 MHz, $CDCl_3$) δ 170.5 (C), 170.0 (C), 138.2 (C), 137.9, 128.5, 127.8, 127.8, 115.1 (CH_2), 99.5, 97.2, 77.4, 77.2, 75.5, 72.4, 72.3 (CH_2), 71.9, 70.0, 67.4 (CH_2), 66.4, 66.1, 59.2, 30.2 (CH_2), 28.5 (CH_2), 21.1, 20.9, 17.4, 16.0.

4-Pentenyl 2,4-Di-*O*-acetyl-3-*O*-[3-*O*-benzyl-2-*O*-methyl-4-*O*-(2,3-di-*O*-acetyl-4-*O*-methyl-α-L-rhamnopyranosyl)-α-L-fucopyranosyl]-α-L-rhamnopyranoside (45). To a solution of **34**[23] (159 mg, 0.39 mmol) and **44** (180 mg, 0.32 mmol) in anhyd CH_2Cl_2 (10 mL) was added powdered activated 4 Å MS, and the mixture was stirred for a few minutes at rt under argon. After the mixture was cooled in an acetone−dry ice bath, TMSOTf (5 μL) was added, and the mixture was allowed to warm inside the cooling bath overnight. The acid was neutralized with NEt_3 (50 μL), and the solids were filtered. After concentration, the crude product was purified by chromatography using Hex/EtOAc 3:1 to give **45** (260 mg, quant): $[\alpha]^{26}_D$ −100 (*c* 1.0, $CHCl_3$); ^{13}C NMR (63 MHz, $CDCl_3$) δ 170.5 (C), 170.1 (C), 170.0 (C), 169.9 (C), 138.9 (C), 137.9, 128.2, 127.3, 127.2, 115.0 (CH_2), 99.5 (J_{CH} 169 Hz), 98.9 (J_{CH} 165 Hz), 97.3 (J_{CH} 175 Hz), 80.4, 78.5, 77.7, 77.2, 74.9, 72.5, 72.3 (CH_2), 71.9, 70.8, 70.6, 67.8, 67.4 (CH_2), 67.0, 66.5, 60.1, 59.2, 30.2 (CH_2), 28.5 (CH_2), 21.1, 21.0, 21.0, 20.9, 17.6, 17.4, 16.4; LRMS (MALDI-TOF) 833.5 (M + Na), 849.5 (M + K).

4-Pentenyl 2,4-Di-*O*-benzyl-3-*O*-[3-*O*-benzyl-2-*O*-methyl-4-*O*-(2,3-di-*O*-benzyl-4-*O*-methyl-α-L-rhamnopyranosyl)-α-L-fucopyranosyl]-α-L-rhamnopyranoside (46). A solution of **45** (500 mg, 0.62 mmol) in anhyd dioxane (5 mL) was treated with powdered KOH (200 mg, 3.6 mmol) and heated to 40 °C for 15 min. BnBr (0.32 mL, 2.7 mmol) was added, and the reaction was heated to 80 °C overnight. TLC indicated that saponification was complete but no benzylation occurred. More dioxane (5 mL), powdered NaOH (1 g, 25 mmol), and BnBr (1 mL, 8.4 mmol) were then added, and the mixture was stirred vigorously at 80 °C for 2 d. The solvent was evaporated and excess BnBr removed by coevaporation with water. The crude product was taken up in CH_2Cl_2, and the solution was washed with water. After drying over $MgSO_4$ and concentration, the crude product was purified by chromatography using Hex/EtOAc 5:1 to give **46** (410 mg, 66%) as an amorphous solid: $[\alpha]^{24}_D$ −97 (*c* 5.0, $CDCl_3$); ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.48−7.16 (m, 25 H), 5.80 (m_c, 1 H), 5.14 (d, 1 H, *J* 4.4 Hz), 5.13 (d, 1 H, *J* 10.3 Hz), 5.01, 4.97 (2 m_c, 2 H), 4.86−4.58 (m, 9 H), 4.54 (d, 1 H, *J* 11.0 Hz), 4.47 (d, 1 H, *J* 12.5 Hz), 4.09 (m_c, 1 H), 3.98 (dd, 1 H, *J* 9.4, 2.8 Hz), 3.86 (∼bs, 1 H), 3.77−3.33 (m, 13 H), 3.55, 3.37 (2 s, 2 × 3 H), 3.30 (dd∼t, 1 H, *J* 9.5, 9.7 Hz), 2.08, 1.63 (2 m_c, 2 × 2 H), 1.28 (d, 3 H, *J* 6.0 Hz), 1.07 (d, 3 H, *J* 6.0 Hz), 0.70 (d, 3 H, *J* 6.3 Hz); ^{13}C NMR (63 MHz, $CDCl_3$) δ 139.1, 138.8, 138.7, 138.3, 138.2, 138.1, 128.3, 128.3, 128.1, 127.7, 127.5, 127.5, 127.4, 127.3, 127.2, 127.1, 114.8, 100.3, 99.6, 96.7, 82.5, 80.0, 79.5, 79.1, 78.1, 78.0, 77.9, 76.2, 74.7, 74.0, 72.8, 72.2, 71.7, 71.6, 68.4, 68.2, 66.9, 66.3, 60.8, 59.7, 30.3, 28.6, 17.9, 17.8, 16.4.

Methyl (*R*)-3-Hydroxytetracosanoate (48). A solution of **47**[27] (4.1 g, 10 mmol) in hot anhyd MeOH (55 mL) under nitrogen was transferred into a nitrogen flushed Parr apparatus and treated with (*R*)-BINAP-ruthenium(*p*-cymene) chloride (60 mg). The mixture was heated to 90 °C and hydrogenated at 400 psi H_2 pressure for 1 d. After being cooled to rt, the suspension was treated with active charcoal and heated to reflux for 5 min. The suspension was filtered hot and slowly cooled to avoid rapid crystallization. Compound **48** (3.2 g, 78% not optimized) was obtained as a nearly colorless solid: mp 73 °C; $[\alpha]^{25}_D$ −10 (*c* 2.7, $CHCl_3$); ^{1}H NMR (360 MHz, $CDCl_3$) δ 3.97 (m_c, 1 H), 3.70 (s, 3 H), 2.48 (dd, 1 H, *J* 3.3, 16.3 Hz), 2.38 (dd, 1 H, *J* 8.9, 16.3 Hz), 1.60−1.35 (m, 2 H), 1.22 (m, 38 H), 0.85 (t, 3 H); ^{13}C NMR (90 MHz, $CDCl_3$) 173, 68.1, 50.6, 41.2, 36.6, 31.9, 29.7−29.0 (m), 25.5, 22.3, 14.1. Anal. Calcd for $C_{25}H_{50}O_3$: C, 75.32; H, 12.64. Found: C, 74.84; H, 12.23.

Methyl (*R*)-3-Benzyloxytetracosanoate (50). To a solution of **48** (1.25 g, 3.1 mmol) in anhyd CH_2Cl_2 (25 mL) was added NEt_3 (1 mL, 7.2 mmol) followed by TMSCl (0.8 mL, 6.3 mmol). The solution was stirred at rt under inert atmosphere for a few hours until TLC (Hex/EtOAc 10:1) showed complete conversion. After cooling to 0 °C, the mixture was washed with ice-cold aq $NaHCO_3$ and water. The solution was dried over

$MgSO_4$ and concentrated to give the O-TMS derivative of **48** (1.40 g, 95%): ^{1}H NMR (250 MHz, $CDCl_3$) δ 4.11 (m_c, 1 H), 3.68 (s, 3 H), 2.44 (d, 2 H, *J* 6.4 Hz), 1.52−1.39 (m, 2 H), 1.25 (m_c, 38 H), 0.88 (t, 3 H, *J* 6.7 Hz), 0.10 (s, 9 H); $C_{28}H_{58}O_3Si$. This compound and benzaldehyde (370 μL, 3.6 mmol) were dissolved in anhyd CH_2Cl_2 (30 mL) and the solution was cooled to 0 °C. TMS triflate (54 μL, 0.3 mmol) was added and the mixture was stirred at 0 °C for 1 h before the addition of triethylsilane (0.5 mL, 3 mmol). The reaction mixture was stirred at rt for 2−4 h and then diluted with ether (50 mL) and washed with satd aq $NaHCO_3$ (100 mL) and water (50 mL). After being dried over $MgSO_4$, the organic solution was concentrated. Crystallization of the crude product from MeOH led to pure **50** (1.02 g, 70%): $[\alpha]^{20}_D$ −3 (*c* 1.1, $CDCl_3$); ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.33−7.20 (m, 5 H), 4.54 (s, 2 H), 3.88 (m_c, 1 H), 3.67 (s, 3 H), 2.61 (dd, 1 H, *J* 14.7, 7.2 Hz), 2.47 (dd, 1 H, *J* 14.7, 5.1 Hz), 1.70−1.52 (m, 2 H), 1.25 (m_c, 38 H), 0.88 (t, 3 H); ^{13}C NMR (63 MHz, $CDCl_3$) δ 172.7, 138.9, 128.7, 128.2, 127.9, 76.5, 71.9, 52.0, 40.2, 34.8, 32.3, 30.1−29.8 (m), 25.6, 23.1, 14.5; LRMS (IS) 489.5 (M + H).

(*R*)-3-Benzyloxytetracosanoic Acid (51). Compound **50** (1.0 g, 2.0 mmol) was dissolved in hot EtOH (50 mL) and treated with 2 N aq NaOH (2.2 mL, 2.2 mmol). The reaction was stirred for 2−4 h and occasionally warmed to dissolve the precipitating solid. When TLC (Hex/EtOAc 5:1) showed complete conversion, the solvent was evaporated and the residue distributed between CH_2Cl_2 (70 mL) and 2 N aq HCl (10 mL). Concentration of the dried organic solution ($MgSO_4$) was followed by crystallization of the product from anhyd EtOH (10 mL) to give pure **51** (277 mg) and slightly contaminated **51** (120 mg, total yield 41%): $[\alpha]^{24}_D$ −5 (*c* 1.6, $CDCl_3$); ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.77 (m_c, 5 H), 4.57 (s, 2 H), 3.87 (dddd≈p, 1 H, *J* 6.8, 5.4, 2 × 6 Hz), 2.63 (dd, 1 H, *J* 15.7, 6.8 Hz), 2.55 (dd, 1 H, *J* 15.7, 5.4), 1.75−1.47 (m, 2 H), 1.26 (m_c, 38 H), 0.88 (t, 3 H, *J* 6.6 Hz); ^{13}C NMR (63 MHz, $CDCl_3$) δ 175.9, 137.9, 128.3, 127.8, 127.7, 75.7, 71.5, 39.2, 33.8, 31.8, 29.6−29.3 (m), 25.0, 22.6, 14.0.

(*R*)-3-Benzyloxytetracosanoyl Chloride (52). Compound **51** (52 mg, 110 μmol) was dissolved in benzene (2 mL) by warming to 40 °C, and oxalyl chloride (70 μL, 0.84 mmol) was added. The reaction was stirred at 40 °C overnight. After evaporation of the solvent and excess reagent, the product was dried under vacuum to give nearly NMR pure **52** (54 mg): $[\alpha]^{24}_D$ −5 (*c* 1, CH_2Cl_2); ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.33 (m_c, 5 H), 4.56 (s, 2 H), 3.96 (m_c, 1 H), 3.12 (dd, 1 H, *J* 16.1, 7.8 Hz), 3.01 (dd, 1 H, *J* 16.1, 4.6 Hz), 1.71−1.45 (m, 2 H), 1.41−1.21 (m, 38 H), 0.89 (t, 3 H, *J* 6.5 Hz).

***N*-2,2,2-Trichloroethoxycarbonyl-D-phenylalaninyl-*O*-{3,4-di-*O*-benzyl-2-*O*-(2,4-di-*O*-benzyl-3-*O*-[3-*O*-benzyl-2-*O*-methyl-4-*O*-(2,3-di-*O*-benzyl-4-*O*-methyl-α-L-rhamnopyranosyl)-α-L-fucopyranosyl]-α-L-rhamnopyranosyl)-α-L-talopyranosyl}-D-allothreonine Benzyl Ester (54).** A solution of **46** (80 mg, 80 μmol/228 mg, 227 μmol) and **27** (65 mg, 76 μmol/186 mg, 217 μmol) in anhyd CH_2Cl_2/Et_2O (1:5, 6 mL/15 mL) was stirred with activated 4 Å MS (400 mg/1.0 g). IDCP (200 mg, 0.43 mmol/558 mg, 1.2 mmol) was added, and the reaction mixture was stirred at rt and with protection from light under argon overnight. The solids were removed by filtration, and the filtrate was diluted with CH_2Cl_2 and washed with aq $Na_2S_2O_3$, dilute aq HCl, and satd aq $NaHCO_3$. After being dried over $MgSO_4$, the solution was concentrated and the crude product purified by chromatography using Hex/EtOAc 3:1 to give **54** (74 mg, 55%/230 mg, 60%). Beside contaminated **46**, a sample of pure **27** could be recovered (second reaction: 35 mg, 19%). Compound **54**: $[\alpha]^{23}_D$ −68 (*c* 1.0,$CHCl_3$); ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.53−7.05 (m, 45 H), 6.68 (d, 1 H, *J* 8.3 Hz, NH), 5.64 (d, 1 H, *J* 7.8 Hz, NH), 5.20 (d≈bs, 1 H, H-1), 5.18−5.04 (m, 3 H), 5.00 (d, 1 H, *J* 3.7 Hz), 4.84 (d, 1 H, *J* 1.7 Hz), 4.80−4.40 (m, ≤ 19 H), 4.23 (d, 1 H, *J* 12.5 Hz), 4.12−3.89 (m, 3 H), 3.85−3.21 (m, ≤ 13 H), 3.56, 3.32 (2 s, 2 × 3 H), 1.29 (d, 3 H, *J* 6.8 Hz), 1.23 (d, 3 H, *J* 6.9 Hz), 1.19 (d, 3 H, *J* 6.6 Hz), 1.08 (d, 3 H, *J* 6.4 Hz), 0.55 (d, 3 H, *J* 6.4 Hz); ^{13}C NMR (63 MHz, $CDCl_3$) δ 169.9 (C), 168.8 (C), 154.0 (C), 139.0 (2×, C), 138.9 (C), 138.6 (C), 138.4 (C), 138.2 (C), 138.1 (C), 135.9 (C), 135.0 (C), 129.3−127.1 (m), 100.2 ($^1J_{CH}$ 170 Hz), 98.9 ($^1J_{CH}$ 169 Hz), 98.2 ($^1J_{CH}$ 168 Hz), 97.4 ($^1J_{CH}$ 175 Hz), 95.2 (C), 82.5, 80.0, 79.5, 78.3, 77.9, 77.8 (2×), 77.1, 76.0, 74.6 (CH_2), 74.5 (CH_2), 74.1, 73.0 (CH_2), 72.8 (CH_2), 72.2 (CH_2), 71.8, 71.6 (CH_2), 71.5 (CH_2), 71.4 (CH_2), 68.4, 68.3, 68.3, 67.2 (CH_2), 66.3, 60.8, 59.4, 56.8, 56.4, 38.5 (CH_2), 18.0, 17.8, 16.7, 16.6, 16.3; LRMS (IS) 1798 (M + Na), 1776 (M + H), 1526, 1280, 1185, 917, 882, 859, 623, 533; LRMS (MALDI-TOF) 1796, 1798 (M + Na).

***N*-(3*R*)-3-Benzyloxytetracosanoyl-D-phenylalaninyl-*O*-{3,4-di-*O*-benzyl-2-*O*-(2,4-di-*O*-benzyl-3-*O*-[3-*O*-benzyl-2-*O*-methyl-4-*O*-(2,3-di-*O*-benzyl-4-*O*-methyl-α-L-rhamnopyranosyl)-α-L-fucopyranosyl]-α-L-rhamnopyranosyl)-α-L-talopyranosyl}-D-allothreonine Benzyl Ester (56).** Compound **54** (72 mg, 41 μmol) was dissolved in THF (2 mL), and activated zinc powder (100 mg) was added followed by 1 M aq KH_2PO_4 (170 μL). The reaction was stirred for 5 h at rt. Because the reaction appeared to be still incomplete, more zinc and dihydrogenophosphate (same amounts as before) were added, and stirring was continued overnight. The solids were then removed by filtration and washed with THF and EtOH. The combined filtrates were concentrated, and the residual product was dissolved in CH_2Cl_2. The solution was washed with aq $NaHCO_3$, dried over $MgSO_4$, and concentrated to give the intermediate amine **55** (55 mg, 85%). This amine was dissolved in anhyd CH_2Cl_2 (2 mL), and NEt_3 (10 μL, 72 μmol) and a solution of **52** (25 mg, 49 μmol) in anhyd CH_2Cl_2 (2.5 mL) were added. The reaction mixture was stirred at rt for 2 d and then concentrated and the residue purified by chromatography using Hex/EtOAc 5:2 to give pure **56** (42 mg, 50%): $[\alpha]^{22}_D$ −60 (*c* 1.0, $CHCl_3$); ^{13}C NMR (63 MHz, $CDCl_3$) δ 171.3, 170.8, 169.2, 139.2, 139.1, 138.9, 138.6, 138.4, 138.2 (2×), 137.9, 136.5, 135.2, 129.2−126.9, 100.2, 98.8, 97.6, 97.4, 82.5, 80.0, 79.4, 78.3, 77.9, 77.8, 77.2, 76.1, 76.0, 74.7, 74.6, 74.1, 73.1, 72.9, 72.7, 72.2, 71.8, 71.6, 71.4, 71.3, 71.1, 68.4, 68.2, 68.0, 66.2 (2 C), 60.8, 59.3, 56.9, 54.8, 40.7, 37.8, 33.3, 31.9, 29.7, 29.3, 25.2, 22.7, 18.0, 17.8, 16.8, 16.3, 15.9, 14.1; LRMS (IS) 2094.5 (M + K), 2079.5 (M + Na), 2057 (M + H); LRMS (MALDI-TOF) 2080.8, 2079.8, 2078.8 (M + Na).

(2*S*)-2-[*N*-(3*R*)-3-Benzyloxytetracosanoyl-D-phenylalaninyl-*O*-{3,4-di-*O*-benzyl-2-*O*-(2,4-di-*O*-benzyl-3-*O*-[3-*O*-benzyl-2-*O*-methyl-4-*O*-(2,3-di-*O*-benzyl-4-*O*-methyl-α-L-rhamnopyranosyl)-α-L-fucopyranosyl]-α-L-rhamnopyranosyl)-α-L-talopyranosyl}-D-allothreoninyl-D-alaninylamino]propyl 3,4-di-*O*-methyl-α-L-rhamnopyranoside (58). Compound **56** (41 mg, 20 μmol) was dissolved in MeOH/EtOAc (10 mL, 1:1), and NEt_3 (500 μL) and $Pd(OH)_2$/C (20%, 23 mg) were added. The mixture was hydrogenated at rt and 1 atm for about 5 h. Removal of the catalyst followed by concentration led to **57** (41 mg, quant.). This compound was dissolved in anhyd CH_2Cl_2 (2.5 mL). Compound **11** (10 mg, 31 μmol), hydroxybenzotriazole hydrate (12 mg, 89 μmol), and after a few minutes, EDCI (10 mg, 52 μmol) were added. The reaction was stirred for 2 d at rt, diluted with CH_2Cl_2, and washed with dilute aq HCl and satd aq $NaHCO_3$. After drying over $MgSO_4$ and concentration of the solution, the crude product was purified by chromatography using CH_2Cl_2/acetone/MeOH 40:2:1 to give **58** (26 mg, 57%): $[\alpha]^{22}_D$ −70 (*c* 1.0, $CHCl_3$); ^{13}C NMR (63 MHz, $CDCl_3$) δ 172.7, 171.9, 171.2, 168.6, 139.0, 138.9, 138.8, 138.7, 138.5, 138.3, 138.3, 138.3, 137.7, 129.0−127.1, 100.2, 99.9, 99.0, 97.2 96.3, 82.5, 81.9, 80.9, 79.9, 79.5, 78.4, 77.9 (2×), 77.8, 77.0, 76.0, 75.95, 74.9, 74.6, 74.1, 73.2, 72.8, 72.6, 72.3, 71.7, 71.5, 71.2, 70.7, 69.1, 68.5, 68.3, 67.7, 67.5, 66.3, 60.9, 60.8, 59.4, 57.3 (CH_3), 57.3, 55.8, 49.1, 45.2, 40.5, 37.2, 33.0, 31.9, 29.7, 29.3, 25.3, 22.7, 18.0, 17.8 (2×), 17.5, 17.4, 16.40, 16.36, 15.5, 14.1; LRMS (IS) 2269.5 multiplet (M + H); LRMS (MALDI-TOF) 2292 multiplet (M + Na); HRMS (FAB) calcd for $C_{133}H_{182}N_4O_{27}Na$ 2290.2895, found 2290.2938.

(2*S*)-2-[*N*-(3*R*)-3-Hydroxytetracosanoyl-D-phenylalaninyl-*O*-{2-*O*-(3-*O*-[2-*O*-methyl-4-*O*-(4-*O*-methyl-α-L-rham-

nopyranosyl)-α-L-fucopyranosyl]-α-L-rhamnopyranosyl)-α-L-talopyranosyl}-D-allothreoninyl-D-alaninylamino]-propyl 3,4-Di-*O*-methyl-α-L-rhamnopyranoside (1). A solution of **58** (25 mg, 11 μmol) in methanol (15 mL) was treated with concentrated acetic acid (150 μL) and $Pd(OH)_2/C$ (20%, 20 mg) and hydrogenolyzed at rt under normal pressure H_2 for 1 d. The catalyst was removed by membrane filtration and washed with methanol, and the solution was concentrated, coevaporated with methanol, and dried under vacuum to give **1** (17 mg, quant): $[\alpha]^{24}_D$ −81 (*c* 1.0, MeOH); ^{13}C NMR (63 MHz, CD_3OD, DEPT) δ 138.4, 130.2, 129.5, 127.8, 104.3, 103.9, 101.8, 99.6, 97.7, 84.2, 83.1, 82.8, 82.3, 80.1, 79.4, 79.3, 74.0, 72.9, 72.4, 72.3, 71.8, 71.3, 71.0, 70.0, 69.7, 69.5, 69.0, 68.7, 68.3, 68.0, 67.2, 61.1, 61.0, 58.5, 57.3, 59.1, 56.4, 50.6, 46.5, 44.6, 38.3, 38.2, 33.1, 30.8, 30.5, 26.6, 23.7, 18.9, 18.2, 18.0 (2×), 17.6, 17.0 (2×), 15.4, 14.5; LRMS (IS) 1570.0, 1571.0, 1572.0 (M + Na), 1565.0, 1566.0, 1567.0 (M + NH_4), 1548.0, 1549.0, 1550.0 (M + H); HRMS (FAB) calcd for $C_{77}H_{134}N_4O_{27}Na$ 1569.9133, found 1569.9145.

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Supporting Information Available: Experimental procedures and analytical data for compounds **3a**,**b**, **4**−**6**, **8**, **9**, **10** (alternative synthesis), deacetylated **10**, **13** (alternative synthesis), **17b**, **20** (alternative synthesis), **24**, **30**−**38**, **49**, and **53**. This material is available free of charge via the Internet at http://pubs.acs.org.

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