Synthesis of a Hexadecasaccharide Fragment of the *O*-Polysaccharide of *Shigella dysenteriae* Type 1

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Abstract: A synthetic route is described to a hexadecasaccharide fragment of the *O*-polysaccharide portion of the lipopolysaccharide of *Shigella dysenteriae* type 1, a Gram-negative human pathogen. The key intermediate was a trichloroacetimidate derivative of the tetrasaccharide Rhaα1→2Galα1→3GlcNAcα1→3Rhaα1→3 (**23**) which corresponds to a complete repeating unit of this polysaccharide, Important stages involved the stereoselective construction of a GlcNAcα1→3Rha synthon (**7**) which was transformed into a glycosyl acceptor (**13**) that was α-galactosylated in a stereocontrolled reaction with a thiogalactoside donor (**14**). Conversion of the Galα1→3GlcNAcα1→3Rha intermediate **15** into the glycosyl acceptor **17** followed by stereoselective α-rhamnosylation afforded the fully protected tetrasaccharide glycoside from which the tetrasaccharide donor **23** was prepared that contains a selectively removable, benzyl protecting group at the site of the chain extension. The donor was first coupled with 1-decanol to give the tetrasaccharide glycoside **24**. One-step conversion provided the tetrasaccharide acceptor **25**, Subsequent, iterative glycosylations with the donor **23**, used in excess, afforded the fully protected octa-, dodeca-, and hexadecasaccharides, conventional deprotection of which led to di- (**2**), tri- (**3**), and tetrameric (**4**) repeating units of the *O*-polysaccharide of *Sh. dysenteriae* type 1,

The *O*-polysaccharides constitute the outer domain of the cell-surface lipopolysaccharides (endotoxins) of Gram-negative bacteria.[1] Structurally, these polysaccharides consist of repeating unit oligosaccharides containing two to seven monosaccharide residues, Although the purified *O*-polysaccharides have no known pharmacologic effects associated with the intact lipopolysaccharides, their unique properties make them of medical and scientific interest. First, they are the bacterial surface structures in contact with host tissues, Second, the diversity among the *O*-polysaccharides is so broad that they alone define the serogroup (serotype) specificity of *Enterobacteriaceae*. Third, their full expression is required for the virulence of Gram-negative bacteria that cause systemic infection. Lastly, increasing evidence supports the hypothesis that serum antibodies against the *O*-polysaccharides may confer protective immunity in humans,[2] While the *O*-polysaccharides are T-cell independent antigens[3] and alone are not immunogenic, they may be converted to immunogens by covalently binding them to proteins[4] or possibly to T-cell epitope peptides.[5] Recently, Robbins and co-workers found that protein conjugates of the *O*-polysaccharides of *Shigellae* induce circulating antibodies that can offer host protection to shigellosis caused by *Shigella sonnei* in adults.[6] Although the *molecular requirements* for such conjugates to induce lasting, protective antibodies including, for example, hapten size, hapten density, hapten/protein ratio, are not well-understood,[7] vaccines constructed along these lines are likely to be important tools to both *prevent and treat* Gram-negative bacterial infections which is increasingly more difficult due to the emergence of multiple drug-resistant microorganisms.[8] Lindberg and co-workers prepared protein conjugates of a heptasaccharide fragment of the *O*-antigenic polysaccharide of *Salmonella typhimurium* and reported studies of their immunogenicity in animal models,[9] We surmised[10] that extended fragments of the *O*-polysaccharides may be suitable for the induction of protective antibodies when coupled to immunogenic proteins, provided that the conformational ensemble of such saccharides approaches that of the conformational determinant of the native polysaccharide, Based

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(1) *Bacterial endotoxin: recognition and effector mechanisms*; Levin, J., Alving, C. R., Munford, R. S., Stutz, P. L., Eds.; Excerpta Medica: Amsterdam, 1993.

(2) (a) Robbins, J. B.; Schneerson, R. *J. Infect. Dis.* **1990**, *161*, 821. (b) Robbins, J. B.; Chu, C.; Schneerson, R. *Clin. Inf. Dis.* **1992**, *15*, 346.

(3) (a) Harding, C. V.; Kihlberg, J.; Elofsson, M.; Magnusson, G.; Unanue, E. R. *J. Immunol.* **1993**, *151*, 2419. (b) Ishioka, G. Y.; Lamont, A. G.; Thomson, D.; Bulbow, N.; Gaeta, F. C. A.; Sette, A.; Grey, H. M. *J. Immunol*, **1992**, *148*, 2446. and references therein.

(4) (a) Dick, W. E., Jr.; Beurret, M. *Contrib. Microbiol. Immunol.* **1989**, *10*, 48. (b) Egan, W. *Annu. Rep. Med. Chem.* **1993**, *28*, 257.

(5) For studies on the immunologic properties of T-cell epitope peptide–carbohydrate conjugates, not including *O*-polysaccharides, see: (a) Ishioka, G. Y.; Lamont, A. G.; Thompson, D.; Bulbow, F.; Gaeta, F. C. A.; Sette, A.; Grey, H. M. *J. Immunol.* **1992**, *148*, 2446. (b) Harding, C. V.; Kihlberg, J.; Elofsson, M.; Magnusson, G.; Unanue, E. R. *J. Immunol.* **1993**, *151*, 2419. (c) Paradiso, P. R.; Dermody, K.; Pillai, S. *Vaccine Res.* **1993**, *2*, 239. (d) Lett, E.; Gangloff, S.; Zimmermann, M.; Wachsmann, D.; Klein, J.-P. *Infect. Immun.*. **1994**, *62*, 785. (e) AlonsoDeVelasco, E.; Merkus, D.; Anderton, S.; Verheul, A. F. M.; Lizzio, E. F.; Van der Zee, R.; Van Eden, W.; Hoffmann, T.; Verhoef, J.; Snippe, H. *Infect. Immun.* **1995**, *63*, 961.

(6) Taylor, D. N.; Trofa, A. C.; Sadoff, J.; Chu, C.; Bryla, D.; Shiloach, J.; Cohen, D.; Ashkenazi, S.; Lerman, Y.; Egan, W.; Schneerson, R.; Robbins, J. B. *Infect. Immun.* **1993**, *61*, 3678.

(7) For studies on the relation between the size of native polysaccharide-derived saccharides and the immunogenicity of their protein conjugates, see: (a) Anderson, P. W.; Pichichero, M. E.; Stein, E. C.; Porcelli, S.; Betts, R. F.; Connuck, D. M.; Korones, D.; Insel, R. A.; Zahradnik, J. M.; Eby, R. *J. Immunol.* **1989**, *142*, 2464. (b) Paoletti, L. C.; Kasper, D.; Michon, F.; DiFabio, J.; Jennings, H. J.; Tosteson, T. D.; Wessels, M. R. *J. Clin. Invest.* **1992**, *89*, 203.

(8) Cohen, M. L. *Science* **1992**, *257*, 1050.

(9) (a) Svenson, S. B.; Nurminen, M.; Lindberg, A. A. *Infect. Immunol.* **1979**, *25*, 863. (b) Lindberg, A. A.; Wollin, R.; Bruse, G.; Ekwall, E.; Svenson, S. B. *ACS Symp. Ser.* **1983**, *231*, 83. (c) Svenson, S. B.; Lindberg, A. A. *Prog. Allergy* **1983**, *33*, 120. For the preparation and evaluation of the protective effect of a protein conjugate of the native *O*-polysaccharide of *S. typhimurium*, see: Watson, D. C.; Robbins, J. B.; Szu, S. C. *Infect. Immunol.* **1992**, *60*, 4679.

(10) Pozsgay, V.; Coxon, B. *Carbohydr. Res.* **1993**, *257*, 189.

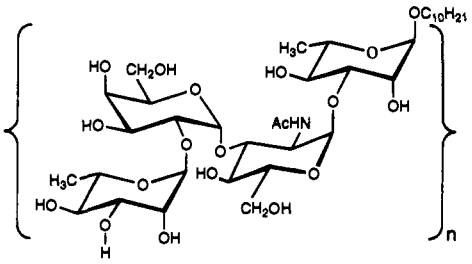
on this hypothesis we are currently developing immunogens using totally synthetic carbohydrate haptens. Because of the well-defined molecular characteristics of the conjugates containing entirely synthetic saccharides, such as hapten size, hapten density, and type of the connecting elements between the hapten and the immunogenic protein, such conjugates should be valuable reagents to probe basic immunologic phenomena. In addition, the use of synthetic saccharides of defined structure instead of polysaccharides of highly complex architecture is likely to offer practical advantages including enhanced uniformity of conjugates and elimination of the analytical difficulties associated with the established, polysaccharide–protein vaccines.[4] Since progress in this area will be determined by the availability of extended oligosaccharides related to bacterial polysaccharides,[11] we are exploring routes to such compounds,[12] Of particular importance to us is the Gram-negative bacterium *Shigella dysenteriae* type 1 which is the causative organism of epidemic and endemic diarrhea and dysentery in may parts of the world with high mortality and morbidity,[13] The *O*-polysaccharide of *Sh. dysenteriae* type 1 consists of the linear tetrasaccharide repeating unit **A**, containing α-linked *N*-acetyl-D-glucosamine, D-galactose, and L-rhamnose as the monosaccharide constituents,[14]

[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→]$_n$

A

A number of synthetic routes to methyl glycosides of di- to tetrasaccharide fragments of polysaccharide **A** have been reported,[15] The syntheses of deoxy and deoxyfluoro analogs of the disaccharide fragment Rha-Gal have also been described.[16] We have synthesized di- to octasaccharide fragments[17] and also reported initial approaches to glycosyl donor/acceptor derivatives of two frame-shifted tetrasaccharides corresponding to **A**.[18] As part of this project we report here a rapid assembly of the hexadecasaccharide **4** which represents four consecutive repeating units of the *O*-polysaccharide **A** and its fragments **1**–**3**. It is likely that the targeted hexadecasaccharide **4** expresses the conformational determinant of the *O*-polysaccharide **A** which we believe is necessary for the induction of high-avidity antibodies against the native antigen.[10,17b] The synthesis of saccharides of this size presents



1 n=1
2 n=2
3 n=3
4 n=4

unusual challenges, While the common problems encountered in the synthesis of complex oligosaccharides have been recognized,[19,20] a general solution to these challenges has not yet emerged and the synthesis of extended saccharides requires strategies tailored to the specifics of the targets,[21] The overall strategy to **4** utilized experience gained during our syntheses of smaller fragments of **A**,[10,17,18] including the development of an efficient method for the construction of the 2-(trimethylsilyl)-ethyl (SE) glycoside of L-rhamnose (Rha),[18a] the finding that the interglycosidic cleavage, which may occur during the direct conversion of SE glycosides of oligosaccharides to glycosyl donors, can be circumvented in a two-step procedure,[17d] the recognition that *O*-acetyl groups can be selectively cleaved in the presence of *O*-benzoyl groups by anhydrous HBF_4,[10] and an efficient route to partially acylated thioglycosides.[22]

Results and Discussion

Our plan was to construct a repeating unit block that can serve both as a glycosyl donor and as a glycosyl acceptor in a stepwise fashion from monosaccharide synthons and use it in an iterative manner, The key tetrasaccharide intermediate **23** was selected for this purpose, A major feature of this building block is that after its initial coupling with the aglycon under mildly acidic conditions that do not effect the functional/protecting groups, the site of the chain elongation can be unmasked by a minimal protecting group manipulation only involving hydrogenolytic removal of the *O*-benzyl group, The starting compound was the selectively functionalized L-rhamnose derivative[18a] **5** which is equipped with 2-(trimethylsilyl)ethyl group as the aglycon, This group serves as a temporary protecting group of the anomeric center, is stable under a variety of reaction conditions, and can be removed selectively under conditions that leave the interglycosidic linkages and most protecting groups unaffected,[23] A highly stereocontrolled reaction of **5** with the glucosamine synthon[24] **6** afforded disaccharide **7** (92%) having 1,2-*cis* interglycosidic linkage, due to the nonparticipating properties[21] of the azido group at C-2.

(11) By definition, saccharides consisting of two to ten monosaccharide residues are termed oligosaccharides (*Eur. J. Biochem.* **1982**, *126*, 433).

(12) For leading references on the chemical synthesis of oligosaccharide fragments of bacterial, cell-surface polysaccharides, see: (a) *ACS Symp. Ser.* **1993**, *519*. (b) Bundle, D. R. *Top. Curr. Chem.* **1990**, *154*, 1.

(13) (a) Chu, C.; Watson, D.; Szu, S.; Bryla, D.; Shiloach, J.; Schneerson, R.; Robbins, J. B. *Infect. Immunol.* **1991**, *59*, 4450. (b) Ries, A.; Wells, J. G.; Olivola, D.; Ntakibirora, M.; Nyandwi, S.; Ntibakivayo, M.; Ivey, C. B.; Greene, K. D.; Tenover, F. C.; Wahlquist, S. P.; Griffin, P. M.; Tauxe, R. V. *J. Infect. Dis.* **1994**, *169*, 1035.

(14) (a) Dmitriev, B. A.; Knirel, Y. A.; Kochetkov, N. K.; Hofman, I. L. *Eur. J. Biochem.* **1976**, *66*, 559. (b) Sturm, S.; Jann, B.; Fortnagel, P.; Timmis, K. N. *Microb. Pathog.* **1986**, *1*, 307.

(15) (a) Garegg, P. J.; Hällgren, C. *J. Carbohydr. Chem.* **1992**, *11*, 445. (b) Pavliak, V.; Kovac, P.; Glaudemans, C. P. J. *Carbohydr. Res.* **1992**, *229*, 103. (c) Kovac, P.; Edgar, K. J. *J. Org. Chem.* **1992**, *57*, 2455. (d) Fält, I. C.; Lindberg, A. A. *Microb. Pathog.* **1994**, *16*, 27.

(16) (a) Mulard, L. A.; Kovac, P.; Glaudemans, C. P. J. *Carbohydr. Res.* **1994**, *251*, 213. (b) Mulard, L. A.; Kovac, P.; Glaudemans, C. P. J. *Carbohydr. Res.* **1994**, *259*, 21.

(17) (a) Pozsgay, V.; Brisson, J.-R.; Jennings, H. J. *Can. J. Chem.* **1987**, *65*, 2764. (b) Pozsgay, V.; Glaudemans, C. P. J.; Robbins, J. B.; Schneerson, R. *Bioorg. Med. Chem. Lett.* **1992**, *2*, 255. (c) Pozsgay, V.; Coxon, B.; Yeh, H. *Bioorg. Med. Chem.* **1993**, *1*, 237. (d) Pozsgay, V.; Pannell, L. *Carbohydr. Res.* **1994**, *258*, 105. (e) Pozsgay, V.; Coxon, B. *Carbohydr. Res.* In press,

(18) (a) Pozsgay, V.; Glaudemans, C. P. J.; Robbins, J. B.; Schneerson, R. *Tetrahedron* **1992**, *48*, 10249. (b) Pozsgay, V.; Glaudemans, C. P. J.; Robbins, J. B.; Schneerson, R. *Carbohydr. Res.* **1993**, *244*, 259.

(19) Nicolaou, K. C.; Dolle, R. E.; Papahatjis, D. P.; Randall, J. L. *J. Am. Chem. Soc.* **1984**, *106*, 4189.

(20) For recent reviews of glycosylation methods and their application in oligosaccharide synthesis, see: (a) Toshima, K.; Tatsuta, K. *Chem. Rev.* **1993**, *93*, 1503. (b) Banoub, J.; Boullanger, P.; Lafont, D. *Chem. Rev.* **1992**, *92*, 1167. (c) Kanie, O.; Hindsgaul, O. *Curr. Opin. Struct. Biol.* **1992**, *2*, 674. (d) Lockhoff, O. in *Methoden der organischen Chemie (Houben-Weyl)*; Hagemann, H., Klamann, D., Eds.; G. Thieme Verlag: Stuttgart, 1992; *E 14a/3*, 621. (e) Schmidt, R. R. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon Press, New York, 1991; Vol. 6, p 33.

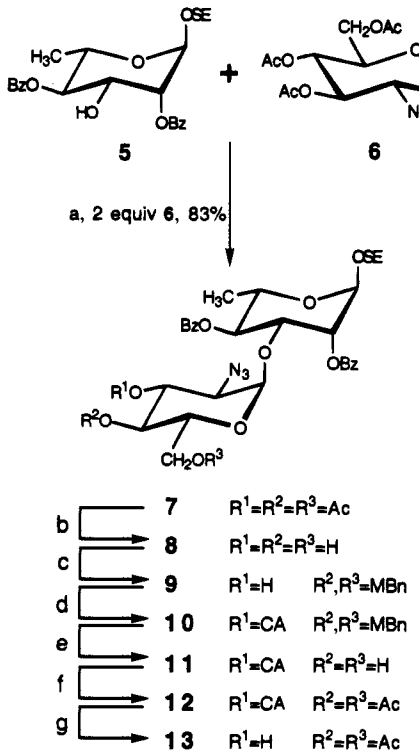
(21) Paulsen, H. *Angew. Chem., Int. Ed. Engl.* **1982**, *21*, 155.

(22) Pozsgay, V. *Carbohydr. Res.* **1992**, *235*, 295.

(23) For a review on the preparation and the use of 2-(trimethylsilyl)-ethyl glycosides in oligosaccharide synthesis, see: Magnusson, G. *Trends Glycosci. Glycotechnol.* **1992**, *4*, 358. For observations on the limited stability of the interglycosidic linkage of deoxysugars during the direct conversion of 2-(trimethylsilyl)ethyl glycosides into glycosyl chlorides, see: (a) Reference 17d. (b) Zhiyuan, Z.; Magnusson, G. *Carbohydr. Res.* **1994**, *262*, 79.

(24) Paulsen, H.; Richter, A.; Sinnwell, V.; Stenzel, W. *Carbohydr. Res.* **1978**, *64*, 339.

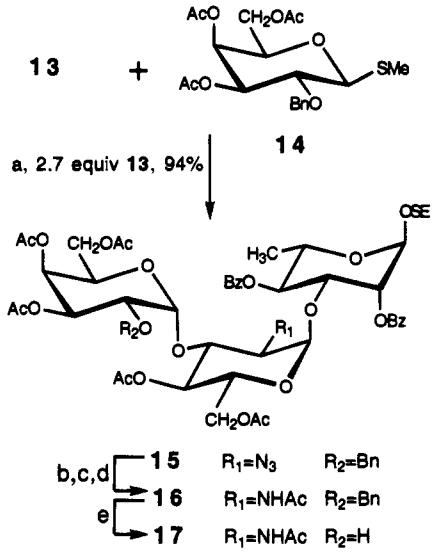
Scheme 1[a]



[a] Ac = acetyl, Bz = benzoyl, CA = chloroacetyl, MBr = 4-methoxybenzylidene, SE = 2-(trimethylsilyl)ethyl, Reagents and conditions: (a) 1.3 equiv of CF_3SO_2OAg, 1.1 equiv of 2,6-di-*tert*-butyl-4-methylpyridine, CH_2Cl_2, 0 °C, 2 h, 92%; (b) $HBF_4{\cdot}Et_2O$, MeOH, 25 °C, 48 h; (c) 5 equiv of 4-methoxybenzaldehyde dimethyl acetal, 4-toluenesulfonic acid (cat.), DMF, 25 °C, 3 h, 92%; (d) 1.9 equiv of $(ClCH_2CO)_2O$, C_5H_5N, 0 °C, 1 h, 89%; (e) $HBF_4{\cdot}Et_2O$, MeOH, 0 °C, 30 min; (f) Ac_2O, C_5H_5N, 4-(dimethylamino)pyridine (cat.), 0 °C, 1 h, 70% for two steps; (g) 5 equiv of thiourea, MeOH, 25 °C, 24 h, 86%.

Transformation of **7** to the partially protected acceptor **13** was achieved in six steps as outlined in Scheme 1, As the first step (**7** → **8**) of this sequence, chemoselective removal of the *O*-acetyl groups in the presence of the *O*-benzoyl groups proceeded smoothly with anhydrous HBF_4 in MeOH,[25] The goal of the subsequent transformations was the installation of acetyl groups at O-4 and O-6 of the azido-deoxy glucose moiety. These conversions included the introduction of two orthogonal protecting groups to provide the intermediate **10**. Selective, acidolytic removal of the 4-methoxybenzylidene acetal afforded the diol **11**, Interestingly, the monochloroacetyl group in **11** migrated to O-6 during attempted chromatographic purification (^1H NMR). Therefore, **11** was acetylated *in situ* to provide the diacetate **12** from which the chloroacetyl group was removed[26] with thiourea (→**13**). Methyl trifluoromethanesulfonate-promoted reaction[27] of thiogalactoside[28] **14** with the acceptor **13** afforded the trisaccharide **15** in an exclusive stereoselective manner in 94% yield (Scheme 2).

Scheme 2[a]



[a] Reagents and conditions: (a) 4.5 equiv of CF_3SO_2OMe, 6 equiv of 2,6-di-*tert*-butyl-4-methylpyridine, Et_2O, 4 Å molecular sieves, 25 °C, 54 h; (b) 5 equiv of PPh_3, CH_2Cl_2, 35-40 °C, 28 h; (c) H_2O, 35–40 °C, 24 h; (d) Ac_2O, C_5H_5N, 0 °C, 30 min, 82% for three steps; (e) H_2/Pd–C, EtOH, AcOH, 25 °C, 24 h, 98%.

Introduction of the acetamido functionality by reduction of the azido group[29] with PPh_3 followed by N-acetylation led to compound **16**, from which hydrogenolysis removed the benzyl group to afford the trisaccharide **17** (98%), The rhamnosyl donor **20** (Scheme 3) was prepared from the known glycoside[30] **18** by acetolysis (→**19**) followed by treatment with 1,1-dichloromethyl methyl ether[31] using $ZnCl_2{\cdot}Et_2O$ as catalyst,[17c] As the next step to the tetrasaccharide block **23** (Scheme 4), alcohol **17** was condensed with the rhamnosyl donor **20** in the presence of AgOTf and the hindered base 2,6-di-*tert*-butyl-4-methylpyridine[32] to give the glycoside **21**, Sequential treatment[23] of **21** with CF_3CO_2H (→**22**, 77%) and then with CCl_3CN/DBU[33,34] furnished the key tetrasaccharide donor/acceptor intermediate **23** (82%). Exposure of a solution of **23** and 1-decanol[35] in CH_2Cl_2 to TMSOTf according to Schmidt[33] afforded the tetrasaccharide glycoside **24** (91%) (Scheme 5), It is noted that attempted Koenings–Knorr type coupling[21] of the tetraosyl chloride derived from hemiacetal **22** [$(COCl)_2$/DMF][36] with 1-decanol invariably afforded an ortho ester as the major product together with a minor amount (<5%) of the glycoside **24**, Liberation of the 3-HO group or the nonreducing terminal rhamnose residue by hydrogenolytic cleavage of the benzyl group in **24** gave the acceptor **25** (87%). Iteration of the glycosylation procedure with the key tetrasaccharide donor **23** (→**26**) followed by regioselective deprotection of the reducing-end terminal rhamnose unit afforded the partially protected

(25) We found (ref 10) this reagent to be superior to HCl/MeOH which has been the standard reagent for the removal of *O*-acetyl in the presence of *O*-benzoyl groups: (a) Corey, E. J.; Clark, D. A.; Goto, G.; Marfat, A.; Mioskowski, C.; Samuelsson, B.; Hammarström, C. *J. Am. Chem. Soc.* **1980**, *102*, 1436. (b) Byramova, N. E.; Ovchinnikov, M. V.; Backinowsky, L. V.; Kochetkov, N. K. *Carbohydr. Res.* **1983**, *124*, C8.

(26) Selective reagents for the removal of the *O*-monochloroacetyl group include thiourea (Cook, A. F.; Maichuk, D. T. *J. Org. Chem.* **1970**, *35*, 1940; Bertolini, M. J.; Glaudemans, C. P. J. *Carbohydr. Res.*, **1970**, *15*, 263), hydrazine dithiocarbonate (Van Boeckel, C. A. A. Beetz, T. *Tetrahedron Lett.* **1983**, *24*, 3775), and hydrazine acetate (Udodong, U. E.; Rao, C. S.; Fraser-Reir, B. *Tetrahedron* **1992**, *48*, 4713).

(27) Lönn, H. *Carbohydr. Res.* **1985**, *139*, 105.

(28) Pozsgay, V.; Trinh, L.; Shiloach, J.; Robbins, J. B. *Bioconjugate Chem.* Submitted.

(29) For numerous methods for the reduction of the azido group, see: (a) Scriven, E. F. V.; Turnbull, K. *Chem. Rev.* **1988**, *88*, 298. (b) Ranu, B. C.; Sarkar, A.; Chakraborty, R. *J. Org. Chem.* **1994**, *59*, 4114.

(30) Wessel, H. P.; Bundle, D. R. *Carbohydr. Res.* **1983**, *124*, 301.

(31) Gross, H.; Farkas, I.; Bognár, R. *Z. Chem.* **1978**, *18*, 201.

(32) Kronzer, F. J.; Schuerch, C. *Carbohydr. Res.* **1973**, *27*, 379.

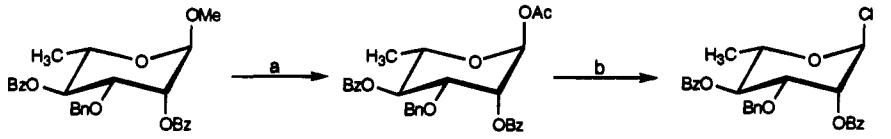
(33) Schmidt, R. R.; Michel, J. *Angew. Chem., Int. Ed. Engl.* **1980**, *19*, 731.

(34) Numata, M.; Sugimoto, M.; Koike, K.; Ogawa, T. *Carbohydr. Res.* **1987**, *163*, 209.

(35) The aglycon selected is expected to enable reversible adsorption of the target saccharides to hydrophobic surfaces, such as plastic wells, Sep-Pak C_{18} particles (e.g., Lowary, T. L.; Swiedler, S. J.; Hindsgaul, O. *Carbohydr. Res.* **1994**, *256*, 257. and references therein), and noncovalent attachment to red blood cells (e.g., Grossman, N.; Svenson, S. B.; Leive, L.; Lindberg, A. A. *Mol. Immunol.* **1990**, *27*, 859.).

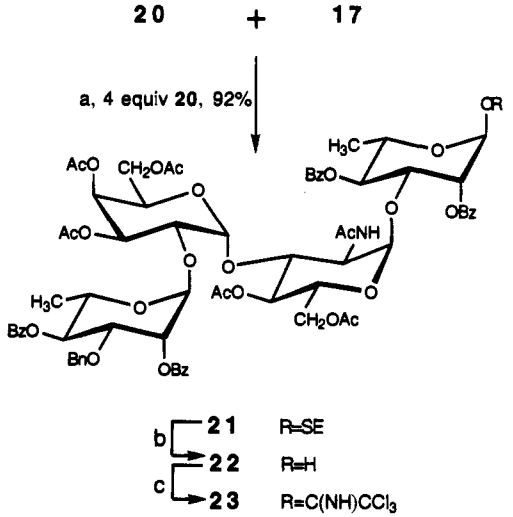
(36) Iversen, T.; Bundle, D. R. *Carbohydr. Res.* **1982**, *103*, 29.

Scheme 3[a]



[a] Reagents and conditions: (a) Ac_2O, H_2SO_4, 0 °C, 1 h, 87%; 1 h, 87%; (b) Cl_2HCOMe, $ZnCl_2{\cdot}Et_2O$, CH_2Cl_2, 0 → 23 °C, 1 h, 91%.

Scheme 4[a]



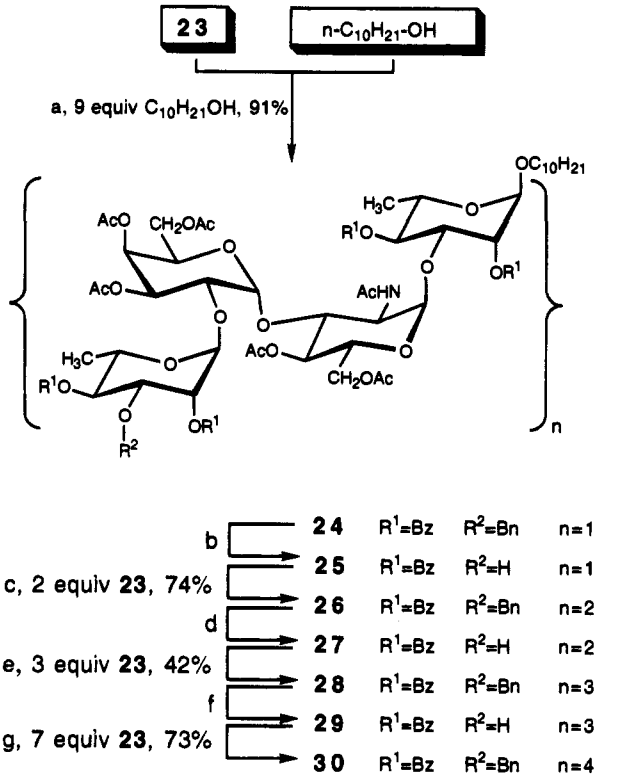
[a] Reagents and conditions: (a) 1.25 equiv of CF_3SO_2OAg, 1.35 equiv of 2,6-di-*tert*-butyl-4-methylpyridine, CH_2Cl_2, 4 Å molecular sieves, −20 °C, 30 min; (b) CF_3CO_2H, CH_2Cl_2, 25 °C, 18 h, 77%; (c) CCl_3CN, 1,8-diazabicyclo[5.4.0]undec-7-ene, CH_2Cl_2, −20 → +20 °C, 2 h, 82%.

octasaccharide glycoside **27**. Two subsequent iterations of the coupling and deblocking steps afforded the fully protected trimer (**28**) and tetramer (**30**) of the repeating unit of the *O*-polysaccharide of *Sh. dysenteriae* type 1. Exposure of the intermediates **24**, **26**, **28**, and **30** to H_2−Pd/C followed by treatment with NaOMe/MeOH afforded the lipid-anchored tetra- (**1**), octa- (**2**), dodeca- (**3**), and hexadecasaccharides (**4**).[37] The identity and purity of the synthetic intermediates and the target saccharides were established by elemental analysis, TLC, ^1H and ^{13}C NMR, chemical ionization, and fast atom bombardment mass spectroscopy. Particular support was provided by the ^{13}C NMR spectra of the dodeca- (**3**) and hexadecasaccharides (**4**), in the latter of which the anomeric resonances for the four Gal residues, three and four Rha residues, and three GlcNAc residues, respectively, coincide with the corresponding resonances of the native, *O*-polysaccharide of *Sh. dysenteriae* 1[38] (Table 1), This coincidence not only establishes the stereochemical integrity of the interglycosidic linkages but also indicates that compounds **3** and **4** express a high degree of conformational similarity to the native polysaccharide,

Conclusion

In conclusion, a concise technology was developed for the total synthesis of oligomeric repeating unit glycosides corresponding to the immunodeterminant, *O*-polysaccharide of *Sh. dysenteriae* type 1. This strategy renders extended saccharide

Scheme 5[a]



[a] Reagents and conditions: (a) $CF_3SO_2OSiMe_3$ (cat.), CH_2Cl_2, 4 Å molecular sieves, 23 °C, 2 h; (b) H_2/Pd−C, EtOH, AcOH, 23 °C, 16 h, 86%; (c) $CF_3SO_2OSiMe_3$ (cat.), CH_2Cl_2, 23 °C, 4 h; (d) H_2/Pd−C, EtOH, AcOH, 23 °C, 24 h, 95%; (e) $CF_3SO_2OSiMe_3$ (cat.), CH_2Cl_2, 23 °C, 4 h; (f) (d) H_2/Pd−C, EtOH, AcOH, 23 °C, 48 h, 66%; (g) $CF_3SO_2OSiMe_3$ (cat.), CH_2Cl_2, 23 °C, 6 h.

structures now available in aglycon-linked form in sufficient quantities for conformational and immunochemical studies and makes the preparation of a glycoconjugate vaccine containing totally synthetic carbohydrate haptens feasible, These experiments are progressing on our laboratory.

Experimental Section

General Methods. All chemicals were commercial grade and were used without purification. Solvents for chromatography were distilled prior to use. Anhydrous solvents were obtained from Aldrich. Column chromatography was performed on silica gel 60 (0.040−0.063 mm). Melting points were taken on a Meltemp capillary melting point apparatus and are uncorrected. Optical rotations were measured at 23 °C with a Perkin-Elmer Type 341 polarimeter. The ^1H and ^{13}C NMR spectra were recorded with an XL-300 or Gemini-300 (Varian) spectrometer at 300 and 75.5 MHz, respectively. The internal references were TMS (0.000 ppm for ^1H for solutions in $CDCl_3$), acetone (2.225 ppm for ^1H and 31.00 ppm for ^{13}C for solutions in D_2O), and $CDCl_3$ (77.00 ppm for ^{13}C for solutions in $CDCl_3$). 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 with a JEOL SX102 mass spectrometer using 6 keV Xe atoms to ionize samples from dithiothreitol/dithioerythritol,

(37) Saccharide fragments of comparable dimensions, corresponding to the *O*-polysaccharide of another Gram-negative bacterium, were previously obtained from its native polysaccharide by bacteriophage-associated endoglycanase cleavage: Svenson, S. B.; Lönngren, J.; Carlin, N.; Lindberg, A. A. *J. Virol.* **1979**, *32*, 583.

(38) Chu, C.; Liu, B.; Watson, D.; Szu, S.; Bryla, D.; Shiloach, J.; Schneerson, R.; Robbins, J. B. *Infect. Immunol.* **1991**, *59*, 4450.

Table 1. Chemical Shifts (ppm) of the Anomeric Carbon Atoms of the *O*-Polysaccharide of *Sh. dysenteriae* Type 1 and the Synthetic Saccharides **1**–**4**[a]

$$(Rha_D \rightarrow Gal_C \rightarrow Glc pNAc_B \rightarrow Rha_A \rightarrow)_n$$

compound	chemical shift[b]			
	Rha_D	Gal_C	$GlcNAc_B$	Rha_A
O-polysaccharide[38]	102.32	98.94	95.21	103,06
4 ($n = 4$)	**102.33**	**99.00**	**95.25**	**103.06**
	(3 C)	(3 C)	(3 C)	(3 C)
	102.46	**98.89**	*95.35*	*100.77*
3 ($n = 3$)	**102.24**	**99.03**	**92.25**	**103.05**
	(2 C)	(2 C)	(2 C)	(2 C)
	102.46	**98.93**	*95.39*	*100.79*
2 ($n = 2$)	**102.37**	**98.88**	**95.19**	**103.03**
	102.45	98.83	*95.50*	*100.78*
1 ($n = 1$)	102.46	**98.87**	*95.39*	*100.76*

[a] At 75.5 MHz, in 1:1 MeOH-d_4–D_2O at 295 K, internal acetone = 31.00 ppm. [b] Chemical shifts of the saccharides **1**–**4** that differ by less than 0.1 ppm from the corresponding resonances of the *O*-polysaccharide are shown in boldface. The resonances corresponding to the reducing end terminus Rha residue and the GlcNAc residue directly linked to it are shown in italics.

3-nitrobenzyl alcohol, or glycerol as the matrix. Elemental analyses were performed by Atlantic Microlab, Inc., Norcross, GA. Abbreviations: Ac = acetyl, Bz = benzoyl, Bn = benzyl, CA = chloroacetyl, MP = 4-methoxyphenyl, SE = 2-(trimethylsilyl)ethyl. Subscripts A–P refer to individual sugar residues with A standing for the reducing end unit.

2-(Trimethylsilyl)ethyl *O*-(3,4,6-Tri-*O*-acetyl-2-azido-2-deoxy-α-D-glucopyranosyl)-(1→3)-2,4-di-*O*-benzoyl-α-L-rhamnopyranoside (7). A stirred solution of **5**[18a] (13.0 g, 27 mmol), **6**[24] (19.0 g, 54 mmol), and 2,6-di-*tert*-butyl-4-methylpyridine (12.0 g, 58 mmol) in CH_2Cl_2 (150 mL) was treated under argon with CF_3SO_2OAg (18.0 g, 70 mmol) at −70 °C. The mixture was allowed to reach 0 °C in 2 h before treatment with saturated aqueous $NaHCO_3$ solution. The mixture was filtered, and the solids were washed thrice with $CHCl_3$. The organic phase was extracted with H_2O and concentrated, Column chromatography of the residue (4:1 hexane–EtOAc) afforded **7** (20.0 g, 92%) as a syrup: [α]D + 150° (*c* 1.3, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 8.17–7.30 (aromatic protons), 5.610 (dd, 1 H, H-2 of Rha_A), 5.556 (dd, 1 H, $J_{3,4} = J_{4,5} = 9.8$ Hz, H-4 of Rha_A), 5.208 (d, 1 H, $J_{1,2} = 3.6$ Hz, H-1 of $GlcN_B$), 5.066 (dd, 1 H, $J_{2,3} + J_{3,4} = 19.8$ Hz, H-3 of $GlcN_B$), 4.990 (d, 1 H, $J_{1,2} = 1.6$ Hz, H-1 of Rha_A), 4.817 (dd, 1 H, H-4 of $GlcN_B$), 4.403 (dd, 1 H, $J_{2,3} = 3.4$ Hz, $J_{3,4} = 9.9$ Hz, H-3 of Rha_A), 4.099 (dq, 1 H, H-5 of Rha_A), 3.238 (dd, 1 H, $J_{2,3} = 10.5$ Hz, H-2 of $GlcN_B$), 2.054, 1.922, and 1.611 (CH_3CO), 1.357 (d, 1 H, $J_{5,6} = 6.2$ Hz, H-6 of Rha_A), 1.1–0.9 (m, 2 H, CH_2Si), and 0.074 (s, 9 H, $SiMe_3$); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 170.3, 169.2, and 169.1 (*C*=O of Ac), 165.9 and 164.8 (*C*=O of Bz), 133.3–128.2 (aromatic), 97.0 and 93.6 (C-1 of Rha_A and $GlcN_B$), 65.7 (OCH_2CH_2), 61.1 (C-6 of $GlcN_B$), 20.6, 20.4, and 20.2 (CH_3CO), 18.0 (CH_2Si), 17.6 (C-6_A), and −1.4 ($SiMe_3$). Anal. Calcd for $C_{37}H_{47}N_3O_{14}Si$: C, 56.55; H, 6.03; N, 5.35. Found: C, 56.39; H, 6.08; N, 5.34.

2-(Trimethylsilyl)ethyl *O*-(2-Azido-2-deoxy-α-D-glucopyranosyl)-(1→3)-2,4-di-*O*-benzoyl-α-L-rhamnopyranoside (8). A solution of **7** (18.0 g, 23 mmol) in MeOH (200 mL) was treated[10] with HBF_4 (~54% in Et_2O, 10 mL) at 23 °C. After 48 h the solution was concentrated to ~50 mL under vacuum. The residue was treated with Et_3N at 0 °C, and then most of the volatiles were removed under vacuum. Column chromatography (1:1 hexane–EtOAc) afforded **8** (12.4 g, 83%) as a syrup: [α]D + 115° (*c* 1.7, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 8.15–7.36 (aromatic protons), 5.550 (dd, 1 H, $J_{1,2} = 1.9$ Hz, $J_{2,3} = 3.3$ Hz, H-2 of Rha_A), 5.466 (dd, 1 H, $J_{3,4} = J_{4,5} = 9.9$ Hz, H-4 of Rha_A), 4.975 (d, 1 H, $J_{1,2} = 3.6$ Hz, H-1 of $GlcN_B$), 4.970 (d, 1 H, H-1 of Rha_A), 4.336 (dd, 1 H, H-3 of Rha_A), 4.045 (dq, 1 H, H-5 of Rha_A), 3.480 (dd, 1 H, $J_{2,3} = 10.2$ Hz, $J_{3,4} = 8.5$ Hz, H-3 of $GlcN_B$), 2.940 (dd, 1 H, H-2 of $GlcN_B$), 1.312 (d, 1 H, $J_{5,6} = 6.3$ Hz, H-6 of Rha_A), 1.1–0.9 (m, 2 H, CH_2Si), and 0.066 (s, 9 H, $SiMe_3$); ^{13}C NMR δ 133.6–128.4 (aromatic), 97.0 and 94.9 (C-1 of Rha_A and $GlcN_B$), 65.7 (OCH_2CH_2), 60.8 (C-6 of $GlcN_B$), 17.9 (CH_2Si), 17,7 (C-6 of Rha_A), and −1.4 ($SiMe_3$); mass spectrum (FAB) *m/z* 660 [(M + H)$^+$], 632 [(M + H − N_2)$^+$], and 542 [(M + H − $Me_3Si(CH_2)_2OH$)$^+$], Anal. Calcd for $C_{31}H_{41}N_3O_{11}Si$: C, 56.43; H, 6.27; N, 6.37. Found: C, 56,22; H, 6.28; N, 6.30,

2-(Trimethylsilyl)ethyl *O*-[2-Azido-2-deoxy-4,6-*O*-(4-methoxybenzylidene)-α-D-glucopyranosyl]-(1→3)-2,4-di-*O*-benzoyl-α-L-rhamnopyranoside (9). To a solution of the triol **8** (12.0 g, 18 mmol) and 4-methoxybenzaldehyde dimethyl acetal (15 mL, 87 mmol) in DMF (10 mL) was added a catalytic amount of 10-camphorsulfonic acid at 23 °C. After 3 h the reaction was quenched with Et_3N. The reaction mixture was stirred with hexane for 10 min (2 × 200 mL). The hexane layer was decanted and the residue chromatographed (5:1 hexane–EtOAc) to give **9** (13.2 g, 92%) as an amorphous solid: [α]D + 92° (*c* 1,5, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 8.18–6.76 (aromatic protons), 5.599 (dd, 1 H, H-2 of Rha_A), 5,546 (dd, 1 H, $J_{3,4} = J_{4,5} = 9,8$ Hz, H-4 of Rha_A), 5.220 (s, 1 H, *CH*MP), 5.081 (d, 1 H, $J_{1,2} = 3.7$ Hz, H-1 of $GlcN_B$), 4.979 (d, 1 H, $J_{1,2} = 1.6$ Hz, H-1 of Rha_A), 4.427 (dd, 1 H, $J_{2,3} = 3.5$ Hz, $J_{3,4} = 9.8$ Hz, H-3 of Rha_A), 4.073 (dq, 1 H, H-5 of Rha_A), 3.789 (s, 3 H, CH_3O), 3.021 (dd, 1 H, $J_{2,3} = 10.0$ Hz, H-2 of $GlcN_B$), 1.312 (d, 1 H, $J_{5,6} = 6.2$ Hz, H-6 of Rha_A), 1.1–0.9 (m, 2 H, CH_2Si), and 0.069 (s, 9 H, $SiMe_3$); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 133.2–113.3 (aromatic), 101.7 (*CH*MP), 97.0 and 94.9 (C-1 of Rha_A and $GlcN_B$), 65.7 (OCH_2CH_2), 62.7 (C-6 of $GlcN_B$), 55.3 (CH_3O), 18.0 (CH_2Si), 17.7 (C-6 of Rha_A), and −1.3 ($SiMe_3$); mass spectrum (FAB) *m/z* 778 [(M + H)$^+$], 750 [(M + H − N_2)$^+$], and 660 [(M + H − $Me_3Si(CH_2)_2OH$)$^+$]. Anal. Calcd for $C_{39}H_{47}N_3O_{12}Si$: C, 60.22; H, 6.09; N, 5.40. Found: C, 60.10; H, 6.15; N, 5.45.

2-(Trimethylsilyl)ethyl *O*-[2-Azido-3-*O*-(chloroacetyl)-2-deoxy-4,6-*O*-(4-methoxybenzylidene)-α-D-glucopyranosyl]-(1→3)-2,4-di-*O*-benzoyl-α-L-rhamnopyranoside (10). To a stirred solution of alcohol **9** (12.0 g, 15.4 mmol) in pyridine (30 mL) at 0 °C was added chloroacetic anhydride (4.8 g, 28 mmol). After 15 min the solution was concentrated under vacuum. Residual pyridine was removed by addition and evaporation of toluene thrice, The residue was dissolved in $CHCl_3$. Extraction of the solution with aqueous $NaHCO_3$ solution at 0 °C followed by concentration and chromatography of the residue (6:1 hexane–EtOAc) afforded **10** as a syrup (11.8 g, 89%): [α]D + 124° (*c* 0.6, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 8.18–6.80 (aromatic protons), 5.621 (dd, 1 H, H-2 of Rha_A), 5.577 (dd, 1 H, $J_{3,4} = J_{4,5} = 9.8$ Hz, H-4 of Rha_A), 5.225 (d, 1 H, $J_{1,2} = 3.8$ Hz, H-1 of $GlcN_B$), 5.208 (s, 1 H, *CH*MP), 5.204 (dd, 1 H, H-3 of $GlcN_B$), 4.984 (d, 1 H, $J_{1,2} = 1.6$ Hz, H-1 of Rha_A), 4.453 (dd, 1 H, $J_{2,3} = 3.4$ Hz, $J_{3,4} = 9.9$ Hz, H-3 of Rha_A), 3.960 (s, 2 H, CH_2Cl), 3.809 (s, 3 H, CH_3O), 3.443 (dd, 1 H, H-4 of $GlcN_B$), 3.143 (dd, 1 H, $J_{2,3} = 10.1$ Hz, H-2 of $GlcN_B$), 1.345 (d, 1 H, $J_{5,6} = 6.2$ Hz, H-6 of Rha_A), 1.1–0.9 (m, 2 H, CH_2Si), and 0.073 (s, 9 H, $SiMe_3$); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 166.0, 165.7, and 165,2 (*C*=O), 159.9–113.7 (aromatic), 101.3 (*CH*MP), 97.1 and 94.8 (C-1 of Rha_A and $GlcN_B$), 65.7 (OCH_2CH_2), 61.0 (C-6 of $GlcN_B$), 55.3 (CH_3O), 40.5 (CH_2Cl), 18.0 (CH_2Si), 17.7 (C-6 of Rha_A), and −1.3 ($SiMe_3$); mass spectrum (FAB) *m/z* 794 [(M + H_3 − N_2)$^+$] and 702 [(M + H − $Me_3Si(CH_2)_2OH$)$^+$].

2-(Trimethylsilyl)ethyl *O*-[4,6-Di-*O*-acetyl-2-azido-3-*O*-(chloroacetyl)-2-deoxy-α-D-glucopyranosyl]-(1→3)-2,4-di-*O*-benzoyl-α-L-rhamnopyranoside (12). To a solution of **10** (28.0 g, 33 mmol) in MeOH (200 mL) at 0 °C was added HBF_4 (~54% in Et_2O, 1 mL) at 0 °C. The solution was allowed to reach 23 °C in ~30 min. The solution was cooled to 0 °C and treated with aqueous $NaHCO_3$ solution under stirring until its pH reached ~5–6 as detected with indicator paper. The mixture was concentrated to a volume of 100 mL, and the residue was equilibrated between $CHCl_3$ and H_2O. The $CHCl_3$ layer was dried (Na_2SO_4) and concentrated to give **11** [^1H NMR (300 MHz, $CDCl_3$) δ 5.599 (dd, 1 H, H-2 of Rha_A), 5.538 (dd, 1 H, H-4 of Rha_A), 5.179 (d, 1 H, H-1 of $GlcN_B$), 4.978 (d, 1 H, H-1 of Rha_A), 4.882 (dd, 1 H, H-3 of $GlcN_B$), 4.388 (dd, 1 H, H-3 of Rha_A)]. A solution of the residue in pyridine (40 mL) at 0 °C was treated with Ac_2O (40 mL) and a catalytic amount of 4-(dimethylamino)pyridine. After 1 h the solution was concentrated under vacuum. Chromatographic purification of the residue (4:1 hexane–EtOAc) provided **12** (19.0 g, 70% for two steps) as a syrup: [α]D + 156° (*c* 1, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 8.17–7.75 (aromatic protons), 5.617 (dd, 1 H, $J_{1,2} = 1.9$ Hz, $J_{2,3} = 3.3$ Hz, H-2 of Rha_A), 5.547 (dd, 1 H, $J_{3,4} = J_{4,5} = 9.8$ Hz, H-4 of Rha_A), 5.246 (d, 1 H, $J_{1,2} = 3.6$ Hz, H-1 of $GlcN_B$), 5.090 (dd,

1 H, $J_{2,3}$ = 10.6 Hz, $J_{3,4}$ = 9,9 Hz, H-3 of $GlcN_B$), 4.981 (d, 1 H, H-1 of Rha_A), 4.846 (dd, 1 H, $J_{4,5}$ = 9.1 Hz, H-4 of $GlcN_B$), 4.397 (dd, 1 H, H-3 of Rha_A), 4.097 (dq, 1 H, H-5 of Rha_A), 3.94 and 3.87 (2 d, 2 H, $J \sim 15$ Hz, CH_2Cl), 3.251 (dd, 1 H, H-2 of $GlcN_B$), 2.056 and 1.610 (CH_3CO), 1.357 (d, 1 H, $J_{5,6}$ = 6.2 Hz, H-6 of Rha_A), 1.1−0.9 (m, 2 H, CH_2Si), and 0.070 (s, 9 H, $SiMe_3$); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 170.4 and 169,3 (C=O of Ac), 166.0 and 164.8 (C=O of Bz and CA), 133.4−128.4 (aromatic), 97.1 and 93,4 (C-1 of Rha_A and $GlcN_B$), 65.8 (CH_2CH_2Si), 60.2 (C-6 of $GlcN_B$), 40.3 (CH_2Cl), 20.6 and 20.2 (CH_3CO), 18.0 (CH_2Si), 17.6 (C-6 of Rha_A), and −1.4 ($SiMe_3$); mass spectrum (FAB) *m/z* 794 [$(M + H_3 - N_2)^+$] and 702 [$(M + H - Me_3Si(CH_2)_2OH)^+$].

2-(Trimethylsilyl)ethyl *O*-(4,6-Di-*O*-acetyl-2-azido-2-deoxy-α-D-glucopyranosyl)-(1→3)-2,4-di-*O*-benzoyl-α-L-rhamnopyranoside (13). A solution of **12** (4.5 g, 5.5 mmol) and thiourea (2.0 g, 26 mmol) in MeOH (50 mL) was stirred at 23 °C for 24 h and then was concentrated under vacuum. The residue was equilibrated between $CHCl_3$ and H_2O. Column chromatography (3:1 hexane−EOAc) of the residue obtained after concentration of the $CHCl_3$ layer afforded the diacetate **13** (3,5 g, 86%) as an amorphous solid: [α]D + 134° (*c* 1.6, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 8.17−7.45 (aromatic protons), 5,603 (dd, 1 H, $J_{1,2}$ = 1.7 Hz, $J_{2,3}$ = 3.3 Hz, H-2 of Rha_A), 5.512 (dd, 1 H, $J_{3,4} = J_{4,5}$ = 9.8.Hz, H-4 of Rha_A), 5.132 (d, 1 H, $J_{1,2}$ = 3.4 Hz, H-1 of $GlcN_B$), 4.973 (d, 1 H, H-1 of Rha_A), 4.675 (dd, 1 H, $J_{3,4} + J_{4,5}$ = 19.3 Hz, H-4 of $GlcN_B$), 4.379 (dd, 1 H, $J_{2,3}$ = 3.3 Hz, $J_{3,4}$ = 9.8 Hz, H-3 of Rha_A), 4.075 (dq, 1 H, H-5 of Rha_A), 3.89−3.56 (m, H-3,5,6,6' of $GlcN_B$, and CH_2CH_2Si), 3,143 (dd, 1 H, $J_{2,3}$ = 10.2 Hz, H-2 of $GlcN_B$), 2.056, 1.671 (2 s, 6 H, 2 CH_3CO), 1.336 (d, 3 H, $J_{5,6}$ = 6.3 Hz, H-6 of Rha_A), 1.1−0.9 (m, 2 H, CH_2Si), and 0.068 (s, 9 H, $SiMe_3$); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 170.5 and 170.2 (C=O of Ac), 165.9 and 165.0 (C=O of Bz), 133.4−128,4 (aromatic), 97.1 and 93.5 (C-1 of Rha_A and $GlcN_B$), 65.7 (OCH_2CH_2), 61.4 (C-6 of $GlcN_B$), 20,6 and 20.4 (CH_3CO), 18.0 (CH_2Si), 17.6 (C-6_A), and −1.4 ($SiMe_3$); mass spectrum (FAB) *m/z* 718 [$(M + H_3 - N_2)^+$] and 626 [$(M + H - Me_3Si(CH_2)_2OH)^+$]. Anal. Calcd for $C_{35}H_{45}N_3O_{13}Si$: C, 56.52; H, 6.10; N, 5.65. Found: C, 57.25; H, 6.33; N, 5.59.

2-(Trimethylsilyl)ethyl *O*-(3,4,6-Tri-*O*-acetyl-2-*O*-benzyl-α-D-galactopyranosyl)-(1→3)-*O*-(4,6-di-*O*-acetyl-2-azido-2-deoxy-α-D-glucopyranosyl)-(1→3)-2,4-di-*O*-benzoyl-α-L-rhamnopyranoside (15). A mixture of the alcohol **13** (30.0 g, 40 mmol), methyl 3,4,6-tri-*O*-acetyl-2-*O*-benzyl-1-thio-β-D-galactopyranoside[28] (**14**) (32,0 g, 70 mmol), 2,6-di-*tert*-butyl-4-methylpyridine (25.0 g, 122 mmol), and 4 Å molecular sieves (~20 g) in dry ether (200 mL) was stirred for 2 h at 23 °C before treatment with CF_3SO_2OMe[27] (10 g). The mixture was stirred for 66 h during which additional amounts of **14** (19.0 g, 41 mmol), 2,6-di-*tert*-butyl-4-methylpyridine (25.0 g, 122 mmol), and CF_3SO_2OMe (20 g) were added in portions. The reaction was quenched with aqueous $NaHCO_3$ solution. Extractive workup ($CHCl_3/H_2O$) followed by chromatographic purification (3:1 hexane−EtOAc) afforded **15** (42.5 g, 94%) as a syrup: [α]D + 135° (*c* 0.5, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 8.18−7.19 (aromatic protons), 5.654 (dd, 1 H, H-2 of Rha_A), 5.534 (dd, 1 H, $J_{3,4} = J_{4,5}$ = 9.8.Hz, H-4 of Rha_A), 5.310 (br d, 1 H, H-4 of Gal_C), 5.281 (d, 1 H, $J_{1,2}$ = 3.5 Hz, H-1 of $GlcN_B$), 5.151 (dd, 1 H, $J_{2,3}$ = 10.7 Hz, $J_{3,4}$ = 3.2 Hz, H-3 of Gal_C), 4.968 (d, 1 H, $J_{1,2}$ = 1.6 Hz, H-1 of Rha_A), 4.923 (dd, 1 H, $J_{3,4} + J_{4,5}$ = 19.2 Hz, H-4 of $GlcN_B$), 4.909 (d, 1 H, $J_{1,2}$ = 3.6 Hz, H-1 of Gal_C), 4.552 and 4.455 (2 d, 2 H, $J \sim 11$ Hz for each, CH_2 of Bn), 4.415 (dd, 1 H, $J_{2,3}$ = 3.2 Hz, H-3 of Rha_A), 3.120 (dd, 1 H, $J_{2,3}$ = 10.2 Hz, H-2 of $GlcN_B$), 2.083, 2.023, 1.861, 1.823, and 1.410 (CH_3CO), 1.348 (d, 3 H, $J_{5,6}$ = 6.2 Hz, H-6 of Rha_A), 1.1−0.9 (m, 2 H, CH_2Si), and 0.060 (s, 9 H, $SiMe_3$); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 170,5, 170.4, 169.9, 169.5, and 168.7 (C=O of Ac), 165.8 and 164.9 (C=O of Bz), 137.8−127.4 (aromatic), 99.0 and 97.0 (2C) (C-1 of Rha_A, $GlcNAc_B$, and Gal_C), 72.7 (CH_2 of Bn), 65.8 (CH_2CH_2Si), 62.1 and 61.4 (C-6 of $GlcNAc_B$ and Gal_C), 20.7, 20.6, and 20.3 (CH_3CO), 18.0 (CH_2Si), 17.7 (C-6 of Rha_A), and −1.4 ($SiMe_3$); mass spectrum (FAB) *m/z* 1194 [$(M + SiMe_3)^+$], 1122 [$(M + H)^+$], 1093 [$(M + H - (CH_2)_2)^+$] and 1004 [$(M + H - Me_3Si(CH_2)_2OH)^+$].

2-(Trimethylsilyl)ethyl *O*-(3,4,6-Tri-*O*-acetyl-2-*O*-benzyl-α-D-galactopyranosyl)-(1→3)-*O*-(2-acetamido-4,6-di-*O*-acetyl-2-deoxy-α-D-glucopyranosyl)-(1→3)-2,4-di-*O*-benzoyl-α-L-rhamnopyranoside (16). A solution of the azide **15** (1.8 g, 1.6 mmol) and triphenylphospine[39] (2,0 g, 7,4 mmol) in dry CH_2Cl_2 (100 mL) was stirred at 35−40 °C for 28 h. The solution was treated with H_2O (10 mL) followed by stirring at 35−40 °C for 24 h. The dried (Na_2SO_4) organic phase was concentrated. The residue was treated with pyridine (10 mL) and acetic anhydride (2 mL) at 0 °C for 30 min. Removal of the volatiles under vacuum followed by column chromatographic purification (1:1 hexane−EtOAc) of the residue afforded **16** (1.5 g, 82% for three steps) as an amorphous solid: [α]D + 98° (*c* 1.2, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 8.18−7.16 (aromatic protons), 6.240 (d, 1 H, *J* = 9.4 Hz, *H*NAc), 5.523 (dd, 1 H, H-2 of Rha_A), 5.449 (dd, 1 H, $J_{3,4} = J_{4,5}$ = 9.8 Hz, H-4 of Rha_A), 5,305 (dd, 1 H, H-4 of Gal_C), 5.105 (dd, 1 H, $J_{2,3}$ = 10.5, $J_{3,4}$ = 3.3 Hz, H-3 of Gal_C), 4.998 (dd, 1 H, H-4 of $GlcNAc_B$), 4.970 (d, 1 H, $J_{1,2}$ = 3.5 Hz, H-1 of $GlcNAc_B$), 4.944 (d, 1 H, H-1 of Rha_A), 4.852 (d, 1 H, $J_{1,2}$ = 3.3 Hz, H-1 of Gal_C), 4.458 and 4.400 (2 d, 2 H, $J \sim 12$ Hz for each, CH_2 of Bn), 4.338 (ddd, 1 H, H-2 of $GlcNAc_B$), 2.045, 1.998, 1.959, 1.859, 1.651, and 1.464 (CH_3CO), 1.346 (d, 1 H, $J_{5,6}$ = 6.3 Hz, H-6 of Rha_A), 1.1−0.9 (m, 2 H, CH_2Si), and 0.064 (s, 9 H, $SiMe_3$); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 170.5, 170.3, 170.0, 169.8, 169.3, and 168.8 (C=O of Ac), 166.0 and 165.7 (C=O of Bz), 137.7−127.5 (aromatic), 99.0 and 97.0 (2C) (C-1 of Rha_A, $GlcNAc_B$, and Gal_C), 72.7 (CH_2 of Bn), 65,8 (CH_2CH_2Si), 61.1 and 60.4 (C-6 of $GlcNAc_B$ and Gal_C), 51.9 (C-2 of $GlcNAc_B$), 22.7 (CH_3CON), 20.6 and 20.3 (CH_3CO), 17.9 (CH_2Si), 17.6 (C-6 of Rha_A), and −1.4 ($SiMe_3$); mass spectrum (FAB) *m/z* 1210 [$(M + SiMe_3)^+$], 1138 [$(M + H)^+$], 1109 [$(M + H - (CH_2)_2)^+$], and 1020 [$(M + H - Me_3Si(CH_2)_2OH)^+$]. Anal. Calcd for $C_{56}H_{71}NO_{22}Si$: C, 59.09; H, 6.29; N, 1.23. Found: C, 59.34; H, 6.40; N, 1.17.

2-(Trimethylsilyl)ethyl *O*-(3,4,6-Tri-*O*-acetyl-α-D-galactopyranosyl)-(1→3)-*O*-(2-acetamido-4,6-di-*O*-acetyl-2-deoxy-α-D-glucopyranosyl)-(1→3)-2,4-di-*O*-benzoyl-α-L-rhamnopyranoside (17). Compound **16** (1.30 g, 1.14 mmol) in a mixture of EtOH (20 mL) and AcOH (1 mL) was hydrogenolyzed over Pd−C (10%, ~0.2 g) at 100 psi for 24 h. Filtration through a layer of silica gel followed by concentration afforded **17** (1.17 g, 98%) as an amorphous solid: [α]D + 126° (*c* 1, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 8.17−7.47 (aromatic protons), 6.380 (d, 1 H, *J* = 10.5 Hz, *H*NAc), 5.527 (dd, 1 H, H-2 of Rha_A), 5.418 (dd, 1 H, $J_{3,4} = J_{4,5}$ = 9.9 Hz, H-4 of Rha_A), 5.305 (br d, 1 H, H-4 of Gal_C), 5.040 (d, 1 H, $J_{1,2}$ = 3.5 Hz, H-1 of $GlcNAc_B$), 4.934 (dd, 1 H, $J_{3,4} + J_{4,5}$ = 22.9 Hz, H-4 of $GlcNAc_B$), 4.936 (d, 1 H, H-1 of Rha_A), 4.92 (dd, 1 H, H-3 of Gal_C), 4.732 (d, 1 H, H-1 of Gal_C), 4.265 (ddd, 1 H, H-2 of $GlcNAc_B$), 2.109, 2.017, 1.983, 1.967, 1.702, and 1.668 (CH_3CO), 1.345 (d, 1 H, $J_{5,6}$ = 6.3 Hz, H-6 of Rha_A), 1.1−0.9 (m, 2 H, CH_2Si), and 0.062 (s, 9 H, $SiMe_3$); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 170.5, 170.3, 170.1 (2 C), 169.9, and 169.7 (C=O of Ac), 165.9 and 165.6 (C=O of Bz), 133.9−128.6 (aromatic), 100.3 (C-1 of Rha_A), 97.1 and 96.2 (C-1 of $GlcNAc_B$, and Gal_C), 65.8 (CH_2CH_2Si), 61.0 and 60.7 (C-6 of $GlcNAc_B$ and Gal_C), 51.6 (C-2 of $GlcNAc_B$), 22.4 (CH_3CON), 20.6 (CH_3CO), 18.0 (CH_2Si), 17.6 (C-6 of Rha_A), and −1.4 ($SiMe_3$); mass spectrum (FAB) *m/z* 1120 [$(M + SiMe_3)^+$], 1048 [$(M + H)^+$], 1020 [$(M + H - (CH_2)_2)^+$], and 930 [$(M + H - Me_3Si(CH_2)_2OH)^+$]. Anal. Calcd for $C_{49}H_{65}NO_{22}Si$: C, 56.15; H, 6.25; N, 1.34. Found: C, 55.63; H, 5.30; N, 1.27.

1-*O*-Acetyl-2,4-di-*O*-benzoyl-3-*O*-benzyl-α-L-rhamnopyranose (19). A solution of methyl 2,4-di-*O*-benzoyl-3-*O*-benzyl-α-L-rhamnopyranoside[30] (**18**) (6.0 g, 12.6 mmol) in acetic anhydride (30 mL) was treated at 0 °C with concentrated sulfuric acid (0.3 mL). After 1 h the solution was poured into aqueous $NaHCO_3$ solution at 0 °C. Extractive workup ($CHCl_3/H_2O$) followed by chromatographic purification (6:1 hexane−EtOAc) afforded **19** (5.5 g, 87%): [α]D + 106° (*c* 1.4, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 8.16−7.07 (aromatic protons), 6.237 (d, 1 H, $J_{1,2}$ = 1.9 Hz, H-1), 5.641 (dd, 1 H, $J_{2,3}$ = 3.4 Hz, H-2), 5.500 (dd, 1 H, $J_{3,4} = J_{4,5}$ = 9.9 Hz, H-4), 4.683 and 4.515 (2 d, 2 H, $J \sim 12.4$ Hz for each, CH_2 of Bn), 4.073 (dd, 1 H, H-3), 4.062 (dq, 1 H, H-5), and 1.334 (d, 3 H, $J_{5,6}$ = 6.3 Hz, H-6_A); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 168.3 (C=O of Ac), 165.5 (C=O of Bz), 137.3−127.6 (aromatic), 91.2 ($J_{C\text{-}1,H\text{-}1}$ = 176 Hz) (C-1), 73.8 (C-3), 72.5 (C-4), 71.0 (CH_2 of Bn), 69.1 (C-5), 67.9 (C-2), and 17.7 (C-6); mass spectrum (CI) *m/z* 522 [$(M + NH_4)^+$]. Anal. Calcd for $C_{29}H_{28}O_8$: C, 69.04; H, 5.59. Found: C, 69.01; H, 5.66.

(39) Classon, B.; Garegg, P. J.; Oscarson, P. J.; Tiden, A.-K. *Carbohydr. Res.* **1986**, *150*, 63.

2,4-Di-*O*-benzoyl-3-*O*-benzyl-α-L-rhamnopyranosyl Chloride (20). To a stirred solution of the acetate **19** (5.0 g, 1 mmol) and 1,1-dichloromethyl methyl ether (5 mL, 55 mmol) in dry CH_2Cl_2 (50 mL) was added $ZnCl_2$·Et_2O (~0,3 mL, 2.2 M in CH_2Cl_2). The mixture was allowed to reach 23 °C and then was treated with aqueous, ice-cold $NaHCO_3$ solution. The organic phase was washed with H_2O and concentrated. Column chromatography (8:1 hexane−EtOAc) of the residue afforded **20** (4.3 g, 90%); mp 66−68 °C; $[\alpha]_D$ + 71° (*c* 1.4, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 8.14−7.06 (aromatic protons), 6.173 (d, 1 H, $J_{1,2}$ = 1.5 Hz, H-1), 5.774 (dd, 1 H, $J_{2,3}$ = 3,3 Hz, H-2), 5.511 (dd, 1 H, $J_{3,4}$ = $J_{4,5}$ = 9.9 Hz, H-4), 4,633 and 4.490 (2 d, 2 H, J ~ 12.4 Hz for each, CH_2 of Bn), 4.344 (dd, 1 H, H-3), 4.240 (dq, 1 H, H-5), and 1.334 (d, 3 H, $J_{5,6}$ = 6.3 Hz, H-6$_A$); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 165.5 (*C*=O), 137.1−127.8 (aromatic), 90,1 ($J_{C\text{-}1,H\text{-}1}$ = 183 Hz) (C-1), 72.7 (C-3), 72.3 (C-4), 71.2 (2 C) (C-2 and CH_2 of Bn), 69,9 (C-5), and 17.4 (C-6); mass spectrum (CI) *m/z* 498 [$(M + NH_4)^+$] and 445 [$(M + H)^+$]. Anal. Calcd for $C_{27}H_{25}ClO_6$: C, 67.43; H, 5.24; Cl, 7.37. Found: C, 67.50; H, 5.30; Cl, 7,26.

2-(Trimethylsilyl)ethyl *O*-(2,4-Di-O-benzoyl-3-*O*-benzyl-α-L-rhamnopyranosyl)-(1→2)-*O*-(3,4,6-tri-*O*-acetyl-α-D-galactopyranosyl)-(1→3)-*O*-(2-acetamido-4,6-di-*O*-acetyl-2-deoxy-α-D-glucopyranosyl)-(1→3)-2,4-di-*O*-benzoyl-α-L-rhamnopyranoside (21). A mixture of the trisaccharide **17** (19.5 g, 19 mmol), chloride **20** (38.0 g, 79 mmol), 2,6-di-*tert*-butyl-4-methylpyridine (22.0 g, 107 mmol), and 4 Å molecular sieves (~10 g) in dry CH_2Cl_2 (300 mL) was stirred for 2 h at 23 °C and then cooled to −20 °C and treated with CF_3SO_2OAg (25.0 g, 99 mmol). The mixture was allowed to reach ~−10 °C in 30 min. The reaction was quenched with aqueous $NaHCO_3$ solution. Extractive workup ($CHCl_3$/H_2O) followed by chromatographic purification (2;1 hexane−EtOAc) afforded **21** (25.5 g, 92%): $[\alpha]_D$ + 110° (*c* 0.7, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 8,17−7.02 (aromatic protons), 6.300 (d, 1 H, J = 10 Hz, *H*NAc), 5.550 (dd, 1 H, H-2 of Rha$_A$), 5.449 and 5.390 (2 dd, 2 H, J ~9.8 Hz, H-4 of Rha$_A$ and Rha$_D$), 5,42 (br d, 1 H, H-2 of Rha$_D$), 5.350 (br d, 1 H, H-4 of Gal$_C$), 5.050 (d, 1 H, $J_{1,2}$ = 3.5 Hz, H-1 of GlcNAc$_B$), 4.950 (d, 1 H, H-1 of Gal$_C$), 4,942 (d, 1 H, H-1 of Rha$_A$), 2.109, 2.016, 1.987, 1.910, 1.724, and 1.586 (*CH*$_3$-CO), 1.340 and 1.160 (2 d, 2 H, $J_{5,6}$ = 6.3 Hz, H-6 of Rha$_A$ and Rha$_D$), 1.1−0.9 (m, 2 H, CH_2Si), and 0.068 (s, 9 H, $SiMe_3$); ^{13}C NMR (75,5 MHz, $CDCl_3$) δ 170.6, 170.4, 170,0, 169.8 (2C), and 168.4 (*C*=O of Ac), 165.8, 165.7, 165.4, and 165.2 (*C*=O of Bz), 137.6−127.2 (aromatic), 98.5 ($J_{C\text{-}1,H\text{-}1}$ = 173 Hz), 97.2 ($J_{C\text{-}1,H\text{-}1}$ = 171 Hz), 96.7 ($J_{C\text{-}1,H\text{-}1}$ = 173 Hz), and 95.8 ($J_{C\text{-}1,H\text{-}1}$ = 172 Hz) (C-1 of Rha$_A$, GlcNAc$_B$, Gal$_C$, and Rha$_D$), 71.6 (CH_2 of Bn), 65.9 (*C*H_2CH$_2$Si), 61.0 and 60.8 (C-6 of GlcNAc$_B$ and Gal$_C$), 51.1 (C-2 of GlcNAc$_B$), 22.5 (*C*H_3CON), 20.7 and 20.6 (*C*H_3CO), 18.1 (*C*H_2Si), 17.85 and 17.78 (C-6 of Rha$_A$ and Rha$_D$), and −1.2 ($SiMe_3$); mass spectrum (FAB) *m/z* 1565 [$(M + SiMe_3)^+$], 1514 [$(M + Na)^+$], and 1492 [$(M + H)^+$]. Anal. Calcd for $C_{71}H_{77}NO_{28}$: C, 61.25; H, 5.57; N, 1.01. Found: C, 61.11; H, 5.92; N, 0.94.

***O*-(2,4-Di-*O*-benzoyl-3-*O*-benzyl-α-L-rhamnopyranosyl)-(1→2)-*O*-(3,4,6-tri-*O*-acetyl-α-D-galactopyranosyl)-(1→3)-*O*-(2-acetamido-4,6-di-*O*-acetyl-2-deoxy-α-D-glucopyranosyl)-(1→3)-2,4-di-*O*-benzoyl-α-L-rhamnopyranose (22).** A solution of the glycoside **21** (28.5g, 19 mmol) in dry CH_2Cl_2 (60 mL) was treated[23] at 23 °C with CF_3COOH (50 mL). After 18 h the volatiles were removed under the vacuum of a water aspirator. Column chromatographic purification (2:1 EtOAc−hexane) of the residue afforded the hemiacetal **22** (20,5 g, 77%): $[\alpha]_D$ + 137° (*c* 0.5, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 8,22−6.96 (aromatic protons), 6.438 (d, 1 H, J = 10 Hz, *H*NAc), 5.734 [br d, H-2 of Rha$_A$ (β)], 5.630 [br d, H-2 of Rha$_A$ (α)], 2.104, 2.009 (2 C), 1.874, 1.747, and 1.528 (*CH*$_3$CO), 1.328, and 1.168 (2 d, 2 H, $J_{5,6}$ = 6.2 Hz, H-6 of Rha$_A$ and Rha$_D$); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 170.9−168.7 (*C*=O of Ac), 166.0−165.5 (*C*=O of Bz), 137.7−127.3 (aromatic), 98.5 ($J_{C\text{-}1,H\text{-}1}$ = 173 Hz), 96.6 ($J_{C\text{-}1,H\text{-}1}$ = 173 Hz), 95.2 ($J_{C\text{-}1,H\text{-}1}$ = 172 Hz), and 92.3 ($J_{C\text{-}1,H\text{-}1}$ = 171 Hz) (C-1 of Rha$_A$, GlcNAc$_B$, Gal$_C$, and Rha$_D$), 71.6 (CH_2 of Bn), 61.2 and 60.8 (C-6 of GlcNAc$_B$ and Gal$_C$), 51,1 (C-2 of GlcNAc$_B$), 22.4 (*C*H_3CON), 20.6 (*C*H_3CO), and 17.7 (C-6 of Rha$_A$ and Rha$_D$); mass spectrum (FAB) *m/z* 1391 [$(M + 1)^+$]. Anal. Calcd for $C_{71}H_{77}NO_{28}$: C, 61.25; H, 5.57; N, 1.01. Found: C, 61.11; H, 5.92; N, 0.94.

***O*-(2,4-Di-*O*-benzoyl-3-*O*-benzyl-α-L-rhamnopyranosyl)-(1→2)-*O*-(3,4,6-tri-*O*-acetyl-α-D-galactopyranosyl)-(1→3)-*O*-(2-acetamido-4,6-di-*O*-acetyl-2-deoxy-α-D-glucopyranosyl)-(1→3)-2,4-di-*O*-benzoyl-α-L-rhamnopyranosyl Trichloroacetimidate (23).** To a solution of compound **22** (5.0 g, 3.6 mmol) in dry CH_2Cl_2 (30 mL) were sequentially added CCl_3CN (6 mL, 50 mmol) and 1,8-diazabicyclo-[5.4,0]undec-7-ene (400 μL, 2.7 mmol).[33,34] The solution was allowed to reach 23 °C in 2 h and then was applied to a column of silica gel (15 × 5 cm) made in 5:1 hexane−EtOAc. Elution with the same solvent afforded **23** (4.50 g, 82%): $[\alpha]_D$ + 106° (*c* 1.1, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 6.409 (d, 1 H, $J_{1,2}$ = 1.7 Hz, H-1 of Rha$_A$), 6.360 (d, 1 H, J ~ 10 Hz, *H*NAc), 5.817 (br dd, 1 H, H-2 of Rha$_A$), 5.573 (dd, 1 H, J = 9.8 Hz, H-4 of Rha$_A$), 5.44 (H-2 of Rha$_D$), 5.404 (dd, 1 H, $J_{3,4}$ = $J_{4,5}$ = 9.8 Hz, H-4 of Rha$_D$), 5.350 (br d, 1 H, H-4 of Gal$_C$), 5.154 (br d, 1 H, H-1 of Rha$_D$), 4.946 (d, 1 H, $J_{1,2}$ = 3.3 Hz, H-1 of Gal$_C$), 4.648 and 4.511 (2 d, 2 H, J ~ 12 Hz for each, CH_2 of Bn), 2.114, 2.021, 2.011, 1.878, 1.734, and 1.590 (*CH*$_3$CO), 1.401, and 1.180 (2 d, 2 H, $J_{5,6}$ ~ 6.2 Hz, H-6 of Rha$_A$ and Rha$_D$); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 170.8−168.5 (*C*=O of Ac), 165.8−165.1 (*C*=O of Bz), 137.8−127.2 (aromatic), 98.5 ($J_{C\text{-}1,H\text{-}1}$ = 170 Hz), 96.7 ($J_{C\text{-}1,H\text{-}1}$ = 173 Hz), and 96.2 ($J_{C\text{-}1,H\text{-}1}$ = 170 Hz) (C-1 of GlcNAc$_B$, Gal$_C$, and Rha$_D$), 95.0 ($J_{C\text{-}1,H\text{-}1}$ = 180 Hz) (C-1 of Rha$_A$), 61.2 and 61.1 (C-6 of GlcNAc$_B$, and Gal$_C$), 51.0 (C-2 of GlcNAc$_B$), 22.5 (*C*H_3CON), 20.7 (*C*H_3COO), and 17.8 (C-6 of Rha$_A$ and Rha$_D$); mass spectrum (FAB) *m/z* 1535 [$(M + 1)^+$], 1374 [$(M + H - C_2H_2Cl_3NO)^+$]. Anal. Calcd for $C_{73}H_{77}Cl_3N_2O_{28}$: C, 57.06; H, 5.05; Cl, 6.92; N, 1.82. Found: C, 57.29; H, 5.22; Cl, 6.91; N, 1.75.

Decyl *O*-(2,4-Di-O-benzoyl-3-*O*-benzyl-α-L-rhamnopyranosyl)-(1→2)-*O*-(3,4,6-tri-*O*-acetyl-α-D-galactopyranosyl)-(1→3)-*O*-(2-acetamido-4,6-di-*O*-acetyl-2-deoxy-α-D-glucopyranosyl)-(1→3)-2,4-di-*O*-benzoyl-α-L-rhamnopyranoside (24). A mixture of the imidate **23** (1.136 g, 0.755 mmol), 1-decanol (1.1 g, 6.9 mmol), and 4 Å molecular sieves (1.2 g) in dry CH_2Cl_2 (40 mL) was stirred for 1 h at 23 °C and then was treated[33] with $CF_3SO_2OSiMe_3$ (40 μL, 0.21 mmol). The reaction was quenched after 2 h with aqueous $NaHCO_3$ solution. Filtration, followed by concentration of the organic phase, afforded a syrup which was purified by chromatography (2:1 hexane−EtOAc) to give **24** (1.033 g, 91%): $[\alpha]_D$ + 102° (*c* 1, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 8.18−7.00 (aromatic protons), 6.273 (d, 1 H, J = 10 Hz, *H*NAc), 5.564 (dd, 1 H, H-2 of Rha$_A$), 5.450 (dd, 1 H, J = 9.8 Hz, H-4 of Rha$_A$), 5.420 (H-2 of Rha$_D$), 5.388 (dd, 1 H, $J_{3,4}$ = $J_{4,5}$ = 9.8 Hz, H-4 of Rha$_D$), 5.352 (br d, 1 H, H-4 of Gal$_C$), 5.135 (d, 1 H, $J_{1,2}$ = 1.8 Hz, H-1 of Rha$_D$), 5.106 (dd, 1 H, H-3 of Gal$_C$), 5.091 (dd, 1 H, H-4 of GlcNAc$_B$), 5.060 (d, 1 H, $J_{1,2}$ = 3.3 Hz, H-1 of GlcNAc$_B$), 4.953 (d, 1 H, $J_{1,2}$ = 3.2 Hz, H-1 of Gal$_C$), 4.905 (d, 1 H, $J_{1,2}$ = 1.7 Hz, H-1 of Rha$_A$), 4.639 and 4.497 (2 d, 2 H, J ~ 12 Hz for each, CH_2 of Bn), 2.110, 2.014, 1.988, 1.913, 1.740, and 1.596 (*CH*$_3$CO), 1.336 and 1.153 (2 d, 2 H, $J_{5,6}$ ~ 6.3 Hz, H-6 of Rha$_A$ and Rha$_D$), and 0.92−0.85 (m, 3 H, CH_3 of decyl); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 170.8, 170.5, 170.1, 169.9, 169.8, and 168.5 (*C*=O of Ac), 166.0, 165.8, 165.6, and 165.3 (*C*=O of Bz), 133.9−128.6 (aromatic), 98.6, 97.7, 96.7, and 96.0 (C-1 of Rha$_A$, GlcNAc$_B$, Gal$_C$, and Rha$_D$), 61.0 and 60.8 (C-6 of GlcNAc$_B$ and Gal$_C$), 51.1 (C-2 of GlcNAc$_B$), 31.9, 29.6 (2 C), 29.4 (2 C), 29.3, 26.1, and 22.7 (CH_2 of decyl), 22.4 (*C*H_3CON), 20.6 and 20.5 (*C*H_3CO), 17.76 and 17.66 (C-6 of Rha$_A$ and Rha$_D$), and 14.1 (CH_3 of decyl); mass spectrum (FAB) *m/z* 1532 [$(M + 1)^+$].

Decyl *O*-(2,4-Di-*O*-benzoyl-α-L-rhamnopyranosyl)-(1→2)-*O*-(3,4,6-tri-*O*-acetyl-α-D-galactopyranosyl)-(1→3)-*O*-(2-acetamido-4,6-di-*O*-acetyl-2-deoxy-α-D-glucopyranosyl)-(1→3)-2,4-di-*O*-benzoyl-α-L-rhamnopyranoside (25). The tetrasaccharide (**24**) was hydrogenolyzed under conditions described for compound **17** to afford the alcohol **25** (86%): $[\alpha]_D$ + 85° (*c* 0.7, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 8.25−7.33 (aromatic protons), 6.145 (d, 1 H, J = 10 Hz, *H*NAc), 5.548 (dd, 1 H, H-2 of Rha$_A$), 5.471 (dd, 1 H, J = 9.8 Hz, H-4 of Rha$_A$), 5.361 (br d, 1 H, H-4 of Gal$_C$), 5.254 (dd, 1 H, $J_{1,2}$ = 1.6 Hz, $J_{2,3}$ = 3.3 Hz, H-2 of Rha$_D$), 5.240 (dd, 1 H, $J_{3,4}$ = $J_{4,5}$ = 9.8 Hz, H-4 of Rha$_D$), 5.133 (br d, 1 H, H-1 of Rha$_D$), 5.120 (dd, 1 H, $J_{3,4}$ = $J_{4,5}$ = 9.8 Hz, H-4 of GlcNAc$_B$), 5.119 (dd, 1 H, $J_{2,3}$ = 10.4 Hz, $J_{3,4}$ = 3.2 Hz, H-3 of Gal$_C$), 5.041 (d, 1 H, $J_{1,2}$ = 3.5 Hz, H-1 of GlcNAc$_B$), 4.938 (d, 1 H, $J_{1,2}$ = 3.3 Hz, H-1 of Gal$_C$), 4.910 (d, 1 H, $J_{1,2}$ = 1.6 Hz, H-1 of Rha$_A$), 4.468 (ddd, 1 H, H-2 of GlcNAc$_B$), 2.380 (d, J ~ 8 Hz, *HO*), 2.109, 2.040, 2.020, 1.918, 1.708, and 1.700 (*CH*$_3$CO), 1.71−1.25 (m, 2 H, CH_2 of decyl), 1.38−1.25 (m, 14 H, CH_2 of decyl), 1.336 and 1.190 (2 d, 2 H, $J_{5,6}$ ~6.2 Hz, H-6 of Rha$_A$ and Rha$_D$), and 0.92−0.85

(m, 3 H, CH_3 of decyl); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 133.9−128,6 (aromatic), 98.2, 97.7, 97.1, and 96.0 (C-1 of Rha_A, $GlcNAc_B$, Gal_C, and Rha_D), 68.6 (C-1 of decyl), 61.0 and 60.7 (C-6 of $GlcNAc_B$ and Gal_C), 51,4 (C-2 of $GlcNAc_B$), 31.8, 29.6 (2 C), 29.3 (2 C), 29.2, 26.0, and 22.6 (CH_2 of decyl), 22.4 (CH_3CON), 20.6 and 20.5 (CH_3CO), 17,65 and 17.59 (C-6 of Rha_A and Rha_D), and 14.2 (CH_3 of decyl); mass spectrum (FAB) *m/z* 1442 [(M + 1)$^+$].

Decyl *O*-(2,4-Di-*O*-benzoyl-3-*O*-benzyl-α-L-rhamnopyranosyl)-(1→2)-*O*-(3,4,6-tri-*O*-acetyl-α-D-galactopyranosyl)-(1→3)-*O*-(2-acetamido-4,6-di-*O*-acetyl-2-deoxy-α-D-glucopyranosyl)-(1→3)-*O*-(2,4-di-*O*-benzoyl-α-L-rhamnopyranosyl)-(1→3)-*O*-(2,4-di-*O*-benzoyl-α-L-rhamnopyranosyl)-(1→2)-*O*-(3,4,6-tri-*O*-acetyl-α-D-galactopyranosyl)-(1→3)-*O*-(2-acetamido-4,6-di-*O*-acetyl-2-deoxy-α-D-glucopyranosyl)-(1→3)-2,4-di-*O*-benzoyl-α-L-rhamnopyranoside (26). To a stirred solution of the tetrasaccharide **25** (1.38 g, 0.957 mmol) and the imidate **23** (3.15 g, 2.04 mmol) in dry CH_2Cl_2 (60 mL) was added at 23 °C $CF_3SO_2OSiMe_3$ (5 μL, 0.026 mmol). After 1 h an additional amount of $CF_3SO_2OSiMe_3$ (10 μL, 0.052 mmol) was added, and the reaction was quenched after 3 h with aqueous $NaHCO_3$ solution. Extractive workup followed by chromatography (3:2 hexane−EtOAc) gave **26** (1.98 g, 74%): $[\alpha]_D$ + 111° (*c* 0.4); ^1H NMR (300 MHz, $CDCl_3$) δ 6.156 and 6,138 (2 d, 2 H, J = 10 Hz, *H*NAc of $GlcNAc_B$ and $GlcNAc_F$); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 170.6−168.4 (*C*=O of Ac), 165.7−164.9 (*C*=O of Bz), 133.6−127.1 (aromatic), 98.8 ($J_{C\text{-}1,H\text{-}1}$ = 172 Hz), 98.4 ($J_{C\text{-}1,H\text{-}1}$ = 173 Hz), 97.7 ($J_{C\text{-}1,H\text{-}1}$ = 170 Hz), 97.5 ($J_{C\text{-}1,H\text{-}1}$ = 170 Hz), 96.8 ($J_{C\text{-}1,H\text{-}1}$ = 169 Hz), 96.6 ($J_{C\text{-}1,H\text{-}1}$ = 172 = Hz), 96.3 ($J_{C\text{-}1,H\text{-}1}$ = 172 Hz), and 95.5 (C-1 of Rha_A, $GlcNAc_B$, Gal_C, Rha_D, Rha_E, $GlcNAc_F$, Gal_G, and Rha_H), 60.6 and 60.4 (C-6 of $GlcNAc_B$, Gal_C, $GlcNAc_F$, and Gal_G), 50.7 (C-2 of $GlcNAc_B$ and $GlcNAc_F$), 31.6, 29.4 (2 C), 29.1 (3 C), 25.8, and 22.4 (CH_2 of decyl), 22.1 (CH_3CON), 20.4 (CH_3COO), 17.4 (C-6 of Rha_A, Rha_D, Rha_E, and Rha_H), and 13.9 (CH_3 of decyl); mass spectrum (FAB) for $C_{145}H_{167}N_2O_{55}$ [(M + 1)$^+$] *m/z* calcd 2816.03, found 2816.03.

Decyl *O*-(2,4-Di-*O*-benzoyl-α-L-rhamnopyranosyl)-(1→2)-*O*-(3,4,6-tri-*O*-acetyl-α-D-galactopyranosyl)-(1→3)-*O*-(2-acetamido-4,6-di-*O*-acetyl-2-deoxy-α-D-glucopyranosyl)-(1→3)-*O*-(2,4-di-*O*-benzoyl-α-L-rhamnopyranosyl)-(1→3)-*O*-(2,4-di-*O*-benzoyl-α-L-rhamnopyranosyl)-(1→2)-*O*-(3,4,6-tri-*O*-acetyl-α-D-galactopyranosyl)-(1→3)-*O*-(2-acetamido-4,6-di-*O*-acetyl-2-deoxy-α-D-glucopyranosyl)-(1→3)-2,4-di-*O*-benzoyl-α-L-rhamnopyranoside (27) was obtained from **26** under conditions described for **17** in 95% yield: $[\alpha]_D$ + 105° (*c* 0.4, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 8.17−7.30 (aromatic), 6.203 and 6.078 (2 d, 2 H, J = 9.9 Hz, *H*NAc of $GlcNAc_B$ and $GlcNAc_F$), 5.553 (dd, 1 H, H-2 of Rha_A), 5.360 and 5.317 (2 br d, 2 H, H-4 of Gal_C and Gal_G), 4.898 (d, 1 H, $J_{1,2}$ = 1.5 Hz, H-1 of Rha_A), 2.111, 2.079, 2.047, 2.021, 2.002, 1.904, 1.891, 1.836, 1.708, 1.675, 1.637, and 1.633 (CH_3CO), 1.336, 1.243, 1.125, and 1.090 (4 d, J ~ 6.3 Hz for each, H-1 of Rha_A, Rha_D, Rha_E, and Rha_H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 170.9−165.4 (*C*=O), 133.7−128.4 (aromatic), 99.0, 98.1, 97.9, 97.7, 97.1, 96.6, 96.4, and 95.5 (C-1 of Rha_A, $GlcNAc_B$, Gal_C, Rha_D, Rha_E, $GlcNAc_F$, Gal_G, and Rha_H), 68.5 (C-1 of decyl), 60.8 and 60.6 (3 C) (C-6 of $GlcNAc_B$, Gal_C, $GlcNAc_F$, and Gal_G), 51.0 and 50.9 (C-2 of $GlcNAc_B$ and $GlcNAc_F$), 31.8, 29.5 (2 C), 29.2 (3 C), 26.0, and 22.6 (CH_2 of decyl), 22.3 (2 C) (CH_3CON), 20.5 (CH_3COO), 17.6 and 17.3 (C-6 of Rha_A, Rha_D, Rha_E, and Rha_H), and 14,0 (CH_3 of decyl); mass spectrum (FAB) for $C_{138}H_{161}N_2O_{55}$ [(M + 1)$^+$] *m/z* calcd 2725.99, found 2726.0. Anal. Calcd for $C_{138}H_{160}N_2O_{55}$: C, 60.75; H, 5.95; N, 1.03. Found: C, 60.71; H, 6.04; N, 1.00.

Decyl *O*-(2,4-Di-*O*-benzoyl-3-*O*-benzyl-α-L-rhamnopyranosyl)-(1→2)-*O*-(3,4,6-tri-*O*-acetyl-α-D-galactopyranosyl)-(1→3)-*O*-(2-acetamido-4,6-di-*O*-acetyl-2-deoxy-α-D-glucopyranosyl)-(1→3)-*O*-(2,4-di-*O*-benzoyl-α-L-rhamnopyranosyl)-(1→3)-*O*-(2,4-di-*O*-benzoyl-α-L-rhamnopyranosyl)-(1→2)-*O*-(3,4,6-tri-*O*-acetyl-α-D-galactopyranosyl)-(1→3)-*O*-(2-acetamido-4,6-di-*O*-acetyl-2-deoxy-α-D-glucopyranosyl)-(1→3)-*O*-(2,4-di-*O*-benzoyl-α-L-rhamnopyranosyl)-(1→3)-*O*-(2,4-di-*O*-benzoyl-α-L-rhamnopyranosyl)-(1→2)-*O*-(3,4,6-tri-*O*-acetyl-α-D-galactopyranosyl)-(1→3)-*O*-(2-acetamido-4,6-di-*O*-acetyl-2-deoxy-α-D-glucopyranosyl)-(1→3)-2,4-di-*O*-benzoyl-α-L-rhamnopyranoside (28). To a solution of **27** (670 mg, 0.246 mmol) and the imidate **23** (1.2 g, 0.781 mmol) in CH_2Cl_2 (45 mL) was added at 23 °C $CF_3SO_2OSiMe_3$ (16 μL, 0.083 mmol). After 6 h the reaction was terminated by the addition of *N*-ethyldiisopropylamine (200 μL) followed by removal of the volatiles under vacuum. Column chromatography (3:2 EtOAc−hexane) of the residue afforded **28** (~500 mg, fraction 1), containing ~10% of an impurity (^1H NMR, assuming that the molecular weight of the contaminant is similar to that of **28**). Also obtained was an impure fraction containing **28** which was rechromatographed to give 92 mg of **28** and a minor contaminant (fraction 2). Fractions 1 and 2 were combined and treated with pyridine (2 mL), acetic anhydride (2 mL), and a catalytic amount of 4-(dimethylamino)-pyridine at 23 °C for 3 h. Removal of the volatiles under vacuum followed by column chromatography (3:2 EtOAc−hexane) of the residue afforded pure **28** (426 mg, 42%): $[\alpha]_D$ + 117° (*c* 0.9, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 6.175, 6.142, and 6.020 (3 d, 3 H, J = 9.9 Hz, *H*NAc of $GlcNAc_B$ $GlcNAc_F$, and $GlcNAc_J$); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 171.8−168.6 (*C*=O of Ac), 165.9−165,1 (*C*=O of Bz), 99.0 (2 C), 98.6, 97.9, 97.8, 97.7, 97.0, 96,8, 96.4 (2 C), 96.3, and 95.7 (C-1 of Rha_A, $GlcNAc_B$, Gal_C, Rha_D, Rha_E, $GlcNAc_F$, Gal_G, Rha_H, Rha_I, $GlcNAc_J$, Gal_K, and Rha_L), 71.7 (CH_2 of Bn), 68.5 (C-1 of decyl), 60.8 (2 C), 60.6 (3 C), and 60.2 (C-6 of $GlcNAc_B$, Gal_C, $GlcNAc_F$, Gal_G, $GlcNAc_J$, and Gal_K), 50.9 (2 C) and 50,7 (C-2 of $GlcNAc_B$, $GlcNAc_F$, and $GlcNAc_J$), 31.9, 29.6 (2 C), 29.3 (3 C), 26.0, and 22.7 (CH_2 of decyl), 22.3 (3 C) (CH_3CON), 20.6−20.4 (CH_3COO), 17.6, 17.5, and 17.4 (C-6 of Rha_A, Rha_D, Rha_E, Rha_H, Rha_I, and Rha_L), and 14.1 (CH_3 of decyl); mass spectrum (FAB) for $C_{209}H_{236}N_3O_{82}$ [(M + 1)$^+$] *m/z* calcd 4099.4, found 4099.3.

Decyl *O*-(2,4-Di-*O*-benzoyl-α-L-rhamnopyranosyl)-(1→2)-*O*-(3,4,6-tri-*O*-acetyl-α-D-galactopyranosyl)-(1→3)-*O*-(2-acetamido-4,6-di-*O*-acetyl-2-deoxy-α-D-glucopyranosyl)-(1→3)-*O*-(2,4-di-*O*-benzoyl-α-L-rhamnopyranosyl)-(1→3)-*O*-(2,4-di-*O*-benzoyl-α-L-rhamnopyranosyl)-(1→2)-*O*-(3,4,6-tri-*O*-acetyl-α-D-galactopyranosyl)-(1→3)-*O*-(2-acetamido-4,6-di-*O*-acetyl-2-deoxy-α-D-glucopyranosyl)-(1→3)-*O*-(2,4-di-*O*-benzoyl-α-L-rhamnopyranosyl)-(1→3)-*O*-(2,4-di-*O*-benzoyl-α-L-rhamnopyranosyl)-(1→2)-*O*-(3,4,6-tri-O-acetyl-α-D-galactopyranosyl)-(1→3)-*O*-(2-acetamido-4,6-di-*O*-acetyl-2-deoxy-α-D-glucopyranosyl)-(1→3)-2,4-di-*O*-benzoyl-α-L-rhamnopyranoside (29). Catalytic hydrogenolysis of **28** under conditions described for **17** followed by column chromatographic purification (3:2 EtOAc-hexane) afforded **29** in 66% yield: $[\alpha]_D$ + 119° (*c* 0.3, $CHCl_3$); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 170.8−168.6 (*C*=O of Ac), 167.0−165.1 (*C*=O of Bz), 99.0 (2 C), 98.1, 97.9, 97.8, 97.7, 97.1, 96.7, 96.4 (2 C), 96.1, and 95.6 (C-1 of Rha_A, $GlcNAc_B$, Gal_C, Rha_D, Rha_E, $GlcNAc_F$, Gal_G, Rha_H, Rha_I, $GlcNAc_J$, Gal_K, and Rha_L), 68.5 (C-1 of decyl), 60.8 (2 C), 60.6 (3 C), and 60.2 (C-6 of $GlcNAc_B$, Gal_C, $GlcNAc_F$, Gal_G, $GlcNAc_J$, and Gal_K), 51.0, 50.9, and 50.7 (C-2 of $GlcNAc_B$, $GlcNAc_F$, and $GlcNAc_J$), 31.8, 29.5 (2 C), 29.3 (3 C), 26.0, and 22.6 (CH_2 of decyl), 22.35 and 22.30 (2 C) (CH_3CON), 20.6−20.3 (CH_3COO), 17.6 (3 C) and 17.3 (C-6 of Rha_A, Rha_D, Rha_E Rha_H, Rha_I, and Rha_L), and 14.0 (CH_3 of decyl); mass spectrum (FAB) for $C_{202}H_{230}N_3O_{82}$ [(M + 1)$^+$] *m/z* calcd 4009.40, found 4009.25. Anal. Calcd for $C_{276}H_{229}N_3O_{82}$: C, 60.47; H, 5.76; N, 1.05. Found: C, 60.30; H, 5.82; N, 1.03.

Decyl *O*-(2,4-Di-*O*-benzoyl-3-*O*-benzyl-α-L-rhamnopyranosyl)-(1→2)-*O*-(3,4,6-tri-*O*-acetyl-α-D-galactopyranosyl)-(1→3)-*O*-(2-acetamido-4,6-di-*O*-acetyl-2-deoxy-α-D-glucopyranosyl)-(1→3)-*O*-(2,4-di-*O*-benzoyl-α-L-rhamnopyranosyl)-(1→3)-*O*-(2,4-di-*O*-benzoyl-α-L-rhamnopyranosyl)-(1→2)-*O*-(3,4,6-tri-*O*-acetyl-α-D-galactopyranosyl)-(1→3)-*O*-(2-acetamido-4,6-di-*O*-acetyl-2-deoxy-α-D-glucopyranosyl)-(1→3)-*O*-(2,4-di-*O*-benzoyl-α-L-rhamnopyranosyl)-(1→3)-*O*-(2,4-di-*O*-benzoyl-α-L-rhamnopyranosyl)-(1→2)-*O*-(3,4,6-tri-*O*-acetyl-α-D-galactopyranosyl)-(1→3)-*O*-(2-acetamido-4,6-di-*O*-acetyl-2-deoxy-α-D-glucopyranosyl)-(1→3)-2,4-di-*O*-benzoyl-α-L-rhamnopyranoside (30). To a solution of **29** (230 mg, 0.0573 mmol) and the imidate **23** (630 mg, 0.41 mmol) in CH_2Cl_2 (20 mL) was added at 23 °C $CF_3SO_2OSiMe_3$ (16 μL, 0.13 mmol). After 6 h the reaction was terminated by the addition of *N*-ethyldiisopropylamine (200 μL) followed by removal of the volatiles under vacuum. Column chromatography (3:2 EtOAc−hexane) of the residue afforded **30** (227 mg, 73%). The purity of the product is >95% as judged by the intensity of the *H*NAc signals in the ^1H NMR spectrum: $[\alpha]_D$ + 110° (*c* 0.2); ^1H NMR (300 MHz, $CDCl_3$) δ 6.277

and 6.241 (2.2 H), and 6.122 (2 H) (3 d, 4.2 H, $J \sim 9$ Hz, *H*NAc of $GlcNAc_B$, $GlcNAc_F$, $GlcNAc_J$, and $GlcNAc_N$); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 170.8−168.5 (*C*=O of Ac), 165,9−165.1 (*C*=O of Bz), 98.9 (3 C), 98.6, 97.9, 97,8 (2 C), 97.7, 96.7 (2 C), 96.4 (3 C), 96,0 (2 C), and 95.4 (C-1 of Rha_A, $GlcNAc_B$, Gal_C, Rha_D, Rha_E, $GlcNAc_F$, Gal_G, Rha_H, Rha_I, $GlcNAc_J$, Gal_K, Rha_L, Rha_M, $GlcNAc_N$, Gal_O, and Rha_P), 60.7, 60.6, and 60.2 (C-6 of $GlcNAc_B$, Gal_C, $GlcNAc_F$, Gal_G, $GlcNAc_J$, Gal_K, $GlcNAc_N$, and Gal_O), 50.9 (2 C) and 50,7 (2 C) (C-2 of $GlcNAc_B$, $GlcNAc_F$, $GlcNAc_J$, and $GlcNAc_N$), 31.9, 29.5 (2 C), 29.3 (3 C), 26,0, and 22.7 (CH_2 of decyl), 22.3 (CH_3CON), 20.6−20.3 (CH_3COO), 17.6−17.4 (C-6 of Rha_A, Rha_D, Rha_E, Rha_H, Rha_I, Rha_L, Rha_M, and Rha_P), and 14.1 (CH_3 of decyl); mass spectrum (FAB) for $C_{273}H_{305}N_4O_{109}$ [(M + 1)$^+$] *m/z* calcd 5386.4, found 5385.9.

Decyl *O*-α-L-Rhamnopyranosyl-(1→2)-*O*-α-D-galactopyranosyl-(1→3)-*O*-(2-acetamido-2-deoxy-α-D-glucopyranosyl)-(1→3)-α-L-rhamnopyranoside (1). To a solution of **25** (150 mg, 0.1 mmol) in dry MeOH (25 mL) was added at 23 °C NaOMe (100 mg). After 72 h the solution was treated with Dowex 50 × 8-100 (H^+) and then was concentrated. The residue was equilibrated between $CHCl_3$ and H_2O. Freeze-drying of the aqueous phase afforded an amorphous residue, which was purified by gel filtration through Biogel P-2 using 0.02 M pyridine−acetic acid, containing 0.01% 1,1,1-trichloro-2-methyl-2-propanol to give **1** (72 mg, 86%): $[\alpha]_D$ + 65° (*c* 0.5, H_2O); ^1H NMR (300 MHz, D_2O) δ 5.605 (br, 1 H, H-1 of Gal_C), 5.092 (br, 1 H, H-1 of Rha_D), 4.938 (br, 1 H, H-1 of $GlcNAc_B$), 4.752 (br, 1 H, H-1 of Rha_A), 2.068 (s, 3 H, CH_3CON), 1.656−1.54 (br m, 2 H, CH_2 of decyl), 1.40−1.19 (m, H-6 of Rha_A, Rha_D, and CH_2 of decyl), and 0.93−0.83 (br m, 3 H, CH_3 of decyl); ^{13}C NMR (75.5 MHz, D_2O) δ 174.1 (*C*=O of Ac), 102.1 (C-1 of Rha_D), 100.5 (C-1 of Rha_A), 98.3 (C-1 of Gal_C), 95.4 (C-1 of $GlcNAc_B$), 61.6 (C-6 of Gal_C), 60.9 (C-6 of $GlcNAc_B$), 52.7 (C-2 of $GlcNAc_B$), 32.6, 30.4 (2 C), 30.1 (2 C), 29.9, 26.7, and 23.4 (8 CH_2 of decyl), 23.0 (CH_3CO), 18.1 and 17.6 (C-6 of Rha_A and Rha_D), and 14.7 (CH_3 of decyl); mass spectrum (FAB) *m/z* 838 [(M + Na)$^+$] and 816 [(M + H)$^+$].

Decyl *O*-α-L-Rhamnopyranosyl-(1→2)-*O*-α-D-galactopyranosyl-(1→3)-*O*-(2-acetamido-2-deoxy-α-D-glucopyranosyl)-(1→3)-*O*-α-L-rhamnopyranosyl-(1→3)-*O*-α-L-rhamnopyranosyl-(1→2)-*O*-α-D-galactopyranosyl-(1→3)-*O*-(2-acetamido-2-deoxy-α-D-glucopyranosyl)-(1→3)-α-L-rhamnopyranoside (2) was obtained from **27** as described for **1** in 78% yield: $[\alpha]_D$ + 71° (*c* 0.5, H_2O); ^1H NMR (300 MHz, D_2O) δ 5.607 (br, 2 H, H-1 of Gal_C and Gal_G), 5.124, 5.080, and 5.050 (br, 3 H, H-1 of Rha_D, Rha_E, and Rha_H), 5.027 (br, 1 H, H-1 of $GlcNAc_F$), 4.955 (br, 1 H, H-1 of $GlcNAc_B$) 4.76 (br, 1 H, H-1 of Rha_A), 2.065 (s, 9 H, 3 CH_3CON), 1.65−1.50 (br m, 2 H, CH_2 of decyl), 1.40−1.19 (m, H-6 of 4 Rha and CH_2 of decyl), and 0.856 (br m, 3 H, CH_3 of decyl); ^{13}C NMR (75.5 MHz, D_2O) δ 174.6 and 174.1 (*C*=O of Ac), 102.5, 102.4, and 102.2 (C-1 of Rha_D, Rha_E, and Rha_H), 100.5 (C-1 of Rha_A), 98.3 (2 C) (C-1 of Gal_C and Gal_G), 95.5 (C-1 of $GlcNAc_B$), 94.6 (C-1 of $GlcNAc_F$), 61.5 and 60.7 (4 C) (C-6 of $GlcNAc_B$, Gal_C, $GlcNAc_F$, and Gal_G), 52.7 (2 C) (C-2 of $GlcNAc_B$ and $GlcNAc_F$), 32.6, 30.3 (2 C), 30.0 (2 C), 29.9, 26.6, and 23,3 (8 CH_2 of decyl), 22.96 and 22.94 (2 C, 2 CH_3CO), 18.0, 17.7 (2 C), and 17.4 (C-6 of 4 Rha), and 14.7 (CH_3 of decyl); mass spectrum (FAB) *m/z* 1495 [(M + Na)$^+$] and 1473 ([M + H)$^+$].

Decyl *O*-α-L-Rhamnopyranosyl-(1→2)-*O*-α-D-galactopyranosyl-(1→3)-*O*-(2-acetamido-2-deoxy-α-D-glucopyranosyl)-(1→3)-*O*-α-L-rhamnopyranosyl-(1→3)-*O*-α-L-rhamnopyranosyl-(1→2)-*O*-α-D-galactopyranosyl-(1→3)-*O*-(2-acetamido-2-deoxy-α-D-glucopyranosyl)-(1→3)-*O*-α-L-rhamnopyranosyl-(1→3)-*O*-α-L-rhamnopyranosyl-(1→2)-*O*-α-D-galactopyranosyl-(1→3)-*O*-(2-acetamido-2-deoxy-α-D-glucopyranosyl)-(1→3)-α-L-rhamnopyranoside (3) was obtained from **29** as described for **1**: $[\alpha]_D$ + 75° (*c* 0.4, H_2O); ^1H NMR (300 MHz, D_2O) δ 5.601 (br, 3 H, H-1 of 3 Gal), 5.153−5.000 (br m, 7 H, H-1 of 5 Rha and H-1 of 2 GlcNAc), 4.94 (br, 1 H, H-1 of $GlcNAc_B$), 4.79 (br, 1 H, H-1 of Rha_A), 2.064 (s, 9 H, 3 CH_3CON), 1.66−1.52 (br m, 2 H, CH_2 of decyl), 1.40−1.20 (m, H-6 of 6 Rha and CH_2 of decyl), and 0.878 (br m, 3 H, CH_3 of decyl); ^{13}C NMR (75.5 MHz, D_2O) δ 175.0 and 174.5 (*C*=O of Ac), 102.8 (2 C) and 102.4 (3 C) (C-1 of 5 Rha), 100.6 (C-1 of Rha_A), 98.5 (3 C) (C-1 of 3 Gal), 95.6 (C-1 of $GlcNAc_B$), 94.9 (2 C) (C-1 of 2 GlcNAc), 61.5 (3 C) (C-6 of 3 Gal), 60.9 and 60.8 (2 C) (C-6 of 3 GlcNAc), 52.7 (3 C) (C-2 of 3 GlcNAc), 32.5, 30.2 (2 C), 29.9 (2 C), 29.8, 26.6, and 23.3 (8 CH_2 of decyl), 22.91 and 22.86 (3 C, 3 CH_3CO), 17.9, 17.6 (3 C), 17.5, and 17.4 (C-6 of 6 Rha), and 14.6 (CH_3 of decyl); mass spectrum (FAB) for $C_{88}CH_{152}N_3O_{55}$ [(M + 1)$^+$] *m/z* calcd 2130.90, found 2130.88.

Decyl *O*-α-L-Rhamnopyranosyl-(1→2)-*O*-α-D-galactopyranosyl-(1→3)-*O*-(2-acetamido-2-deoxy-α-D-glucopyranosyl)-(1→3)-*O*-α-L-rhamnopyranosyl-(1→3)-*O*-α-L-rhamnopyranosyl-(1→2)-*O*-α-D-galactopyranosyl-(1→3)-*O*-(2-acetamido-2-deoxy-α-D-glucopyranosyl)-(1→3)-*O*-α-L-rhamnopyranosyl-(1→3)-*O*-α-L-rhamnopyranosyl-(1→2)-*O*-α-D-galactopyranosyl-(1→3)-*O*-(2-acetamido-2-deoxy-α-D-glucopyranosyl)-(1→3)-α-L-rhamnopyranoside (4). Compound **30** was treated with NaOMe in MeOH at 35−40 °C for 48 h as described for **1** followed by purification on a Sephadex G-100 column, using 0.02 N pyridine−acetic acid as the eluant. The product thus obtained was hydrogenolyzed as described for **17** at 23 °C at 230 psi for 48 h followed by gel filtration as above to afford **4** as an amorphous solid: $[\alpha]_D$ + 68° (*c* 0.2, H_2O); ^1H NMR (300 MHz, D_2O) δ 5.598 (br, 4 H, H-1 of 4 Gal), 5.106 (br, 3 H, H-1 of 3 Rha), 5.072 and 5.047 (br m, 7 H, H-1 of 4 Rha and 3 GlcNAc), 4.94 (br, 1 H, H-1 of $GlcNAc_B$), 4.75 (br, 1 H, H-1 of Rha_A), 2.060 (s, 12 H, 4 CH_3CON), 1.590 (br m, 2 H, CH_2 of decyl), 1.4−1.2 (m, H-6 of 8 Rha and CH_2 of decyl), and 0.880 (br m, 3 H, CH_3 of decyl); ^{13}C NMR (75.5 MHz, D_2O) δ 174.8 and 174.3 (*C*=O of Ac), 102.7 (3C) and 102.3 (4 C) (C-1 of 7 Rha), 100.4 (C-1 of Rha_A), 98.3 (4 C) (C-1 of 4 Gal), 95.5 (C-1 of $GlcNAc_B$), 94.8 (3 C) (C-1 of 3 GlcNAc), 61.5 (4 C) (C-6 of 4 Gal), 60.8 and 60.7 (3 C) (C-6 of 4 GlcNAc), 52.7 (4 C) (C-2 of 4 GlcNAc), 32.5, 30.2 (2 C), 29.9 (2 C), 29,8, 26.6, and 23.3 (8 CH_2 of decyl), 22.85 and 22.83 (4 C, 4 CH_3CO), 17.9, 17.6 (4 C), and 17.4 (3 C) (C-6 of 8 Rha), and 14.7 (CH_3 of decyl); mass spectrum (FAB) for $C_{114}H_{195}N_4O_{73}$ [(M + 1)$^+$] *m/z* calcd 2788.17, found 2788.12.

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Supplementary Material Available: The ^1H and the ^{13}C NMR spectra for compounds **1**−**4** recorded at 300 and 75,5 MHz, respectively (8 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, can be ordered from the ACS, and can be downloaded from the Internet; see any current masthead page for ordering information and Internet access instructions.

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