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Convergent synthesis of an octasaccharide fragment of the O-specific polysaccharide of *Shigella dysenteriae* type 1 *

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Abstract

A stereocontrolled, convergent synthesis is described of the linear octasaccharide methyl glycoside α-L-Rha*p*-(1 → 2)-α-D-Gal*p*-(1 → 3)-α-Glc*p*NAc-(1 → 3)-α-L-Rha*p*-(1 → 3)-α-L-Rha*p*-(1 → 2)-α-D-Gal*p*-(1 → 3)-α-D-Glc*p*NAc-(1 → 3)-α-L-Rha*p*-OMe (**11**), which corresponds to two contiguous repeating units of the O-specific polysaccharide of *Shigella dysenteriae* type 1.

1. Introduction

Robbins and co-workers [2,3] suggested, that conjugate vaccines consisting of the O-specific polysaccharides (O-SP) of *Shigellae* and an immunogenic protein would confer protective immunity to humans against shigellosis. We assumed [1] that oligosaccharides, shorter than the native polysaccharide, may also be exploited to elicit high-avidity antibodies against the O-SP of *Sh. dysenteriae* type 1, provided that they have a high degree of conformational similarity to the native O-SP. Synthetic carbohydrate chemistry may provide suitable haptens, and the purpose of the present work is to further explore the feasibility of this approach [1,4–7].

The O-specific polysaccharide of *Sh. dysenteriae* type 1, is a heteropolysaccharide, characterized by the tetrasaccharide repeating-unit [8,9] **I**. The constituent

* For a preliminary communication, see ref 1.

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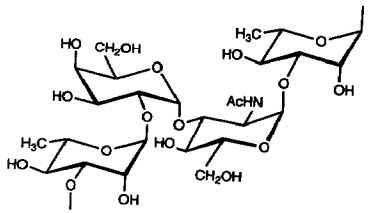


I

1 α-L-Rha*p*-(1 → 3)-α-L-Rha*p*-OMe

2 α-D-Glc*p*NHCOC$_2$H$_5$-(1 → 3)-α-L-Rha*p*-OMe

3 α-L-Rha*p*-(1 → 2)-α-D-Gal*p*-OMe

4 α-D-Gal*p*-(1 → 3)-α-D-Glc*p*NAc-OMe

5 α-D-Gal*p*-(1 → 3)-α-D-Glc*p*NAc-(1 → 3)-α-L-Rha*p*-OMe

6 α-L-Rha*p*-(1 → 2)-α-D-Gal*p*-(1 → 3)-α-D-Glc*p*NAc-(1 → 3)-α-L-Rha*p*-OMe

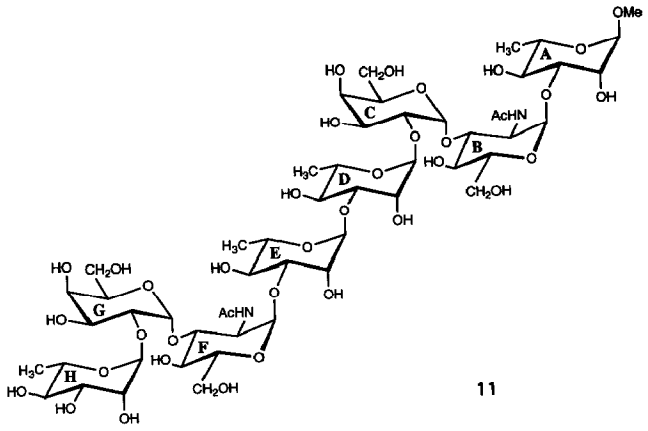
7 α-D-Gal*p*-(1 → 3)-α-D-Glc*p*NAc-(1 → 3)-α-L-Rha*p*-(1 → 3)-α-L-Rha*p*-OMe

8 α-D-Gal*p*-(1 → 3)-α-D-Glc*p*NHCOC$_2$H$_5$-(1 → 3)-α-L-Rha*p*-(1 → 3)-α-L-Rha*p*-OMe

9 α-L-Rha*p*-(1 → 3)-α-L-Rha*p*-(1 → 2)-α-D-Gal*p*-(1 → 3)-α-D-Glc*p*NAc-(1 → 3)-α-L-Rha*p*-OMe

10 α-L-Rha*p*-(1 → 3)-α-L-Rha*p*-(1 → 2)-α-D-Gal*p*-(1 → 3)-α-D-Glc*p*NAc-(1 → 3)-α-L-Rha*p*-(1 → 3)-α-L-Rha*p*-OMe

monosaccharide units are α-linked D-galactose, 2-acetamido-2-deoxy-D-glucose, and L-rhamnose. Hitherto we have prepared [1,4,5,10] the methyl glycosides of di- to hexa-saccharide fragments (**1–10**) of the O-SP. The use of these oligosaccharides as molecular probes in mapping the binding characteristics of a murine monoclonal antibody against the O-SP has been reported [11]. We have also described the synthesis of two fully protected, frame-shifted tetrasaccharides related to the O-specific polysaccharide, that can function both as glycosyl donors, and as glycosyl acceptors, after chemoselective removal of only one of their protecting groups [6,7]. These intermediates are now being used in our laboratory as building blocks for at the synthesis of extended epitopes of the O-SP. We are employing high resolution NMR spectroscopy to characterize the synthetic oligosaccharides and to estimate their similarity to the O-SP. To this end, we completely assigned the 500 or 600 MHz ^{1}H, and 100 MHz ^{13}C NMR spectra of oligosaccharides **1–10**, which have the natural, α anomeric configuration at their reducing end termini [4,5,10]. A comparison of selected NMR characteristics of oligosaccharides **1–10** with those of the O-SP led us to conclude, that short oligosaccharides fail to mimic the conformational features of the native polysaccharide [4,5]. They are, therefore, unlikely to elicit protective antibodies. Even the

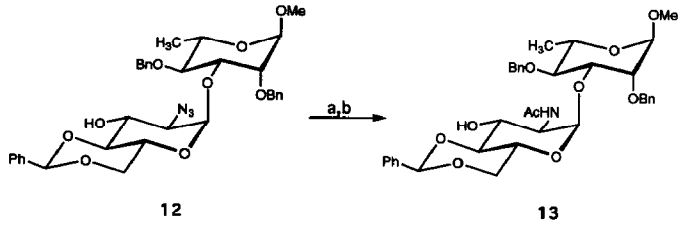


11

hexasaccharide **10** lacks a high degree of conformational similarity to the O-SP [5]. A more complex fragment is therefore needed for a conformational mimicry. Here we describe a convergent synthesis of the homologous octasaccharide methyl glycoside **11**, which corresponds to two contiguous repeating units of the O-SP.

2. Results and discussion

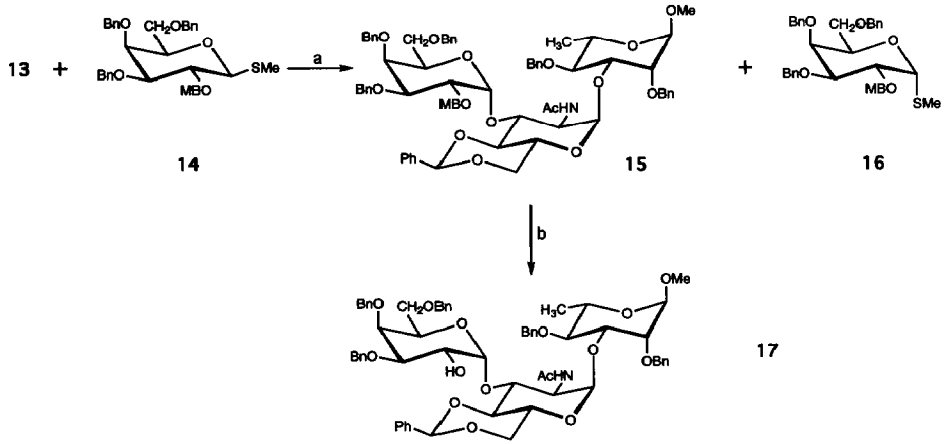
Experience gained during the preparation of the smaller homologues **1–10** indicated that the construction of the *trans* interglycosidic linkage between the two rhamnose residues (units **D** and **E**) is more convenient than that between any other two units in **11**. We based our strategy on condensation of two tetrasaccharide building blocks corresponding to the **ABCD** and **EFGH** segments. These blocks were constructed in a stepwise manner. The **ABCD** segment was prepared as follows. The disaccharide [4] **12** was converted to the acetamido derivative **13** by reduction of the azido group, followed by *N*-acetylation [12], in 79% (Scheme 1). Reaction of the glycosyl acceptor **13** with methyl 3,4,6-tri-*O*-benzyl-2-*O*-(4-methoxybenzyl)-1-thio-β-D-galactopyranoside [4,5] (**14**) under promotion by methyl trifluoromethanesulfonate [13] (MeOTf) afforded the **ABC** trisaccharide **15** in 86% yield (Scheme 2). The α stereochemistry of the newly formed interglycosidic linkage was inferred from the $^3J_{H\text{-}1,H\text{-}2}$ coupling constant for the galactosyl residue, which is 3.8 Hz. The glycosylation reaction was accompanied by partial anomerization of the thio-galactoside donor to **16**, which we noted and characterized earlier [4]. Next, the oxidative removal of the 4-methoxybenzyl group from **15** with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone [14] (DDQ) afforded the trisaccharide acceptor **17** in 57% yield. The strategy for the rhamnose unit **D** envisaged a temporary, selectively removable protecting group at O-3, and permanent groups



[a]Reagents: (a) $NiCl_2 \cdot 6\ H_2O$, H_3BO_3, $NaBH_4$ — $(MeOCH_2)_2$, EtOH; (b) Ac_2O — MeOH.

Scheme 1.

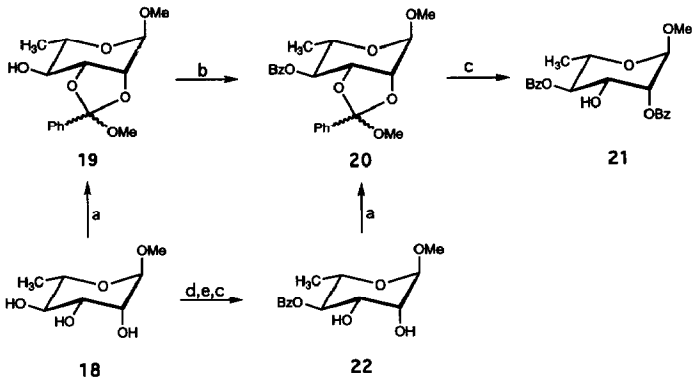
at O-2 and O-4. Compound **29** was selected for this purpose, in which the bromoacetyl group [15] fulfills our requirement, since it can be removed selectively, under essentially neutral conditions. We designed several approaches to this unit. In the first route, the starting compound was methyl α-L-rhamnopyranoside **18**, which was converted to the dibenzoate **21** in a three-step, one-pot reaction through the intermediacy of the cyclic orthoesters **19** and **20** (Scheme 3, reactions a and b). The combined yield from this protocol is 60%. The route follows the method of Garegg and Hultberg [16], which was adapted for **21** by Wessel and Bundle [17]. Reproduction of the published protocol [17] led to several experimental improvements, which made the method suitable also for the high-yielding syntheses of 2-*O*-mono- and 2,4-di-*O*-acyl-1-thio-rhamnosides [7,18]. As a result of these developments, **21** could now be obtained as a crystalline substance. Alternatively, **21** was



[a]Reagents: (a) CF_3SO_3Me, 2,6-di-*tert*-butyl-4-methyl-C_5H_2N — $(C_2H_5)_2O$; (b) 2,3-dichloro-5,6-dicyano-1,4-benzoquinone — CH_2Cl_2, H_2O.

MB = 4-methoxybenzyl

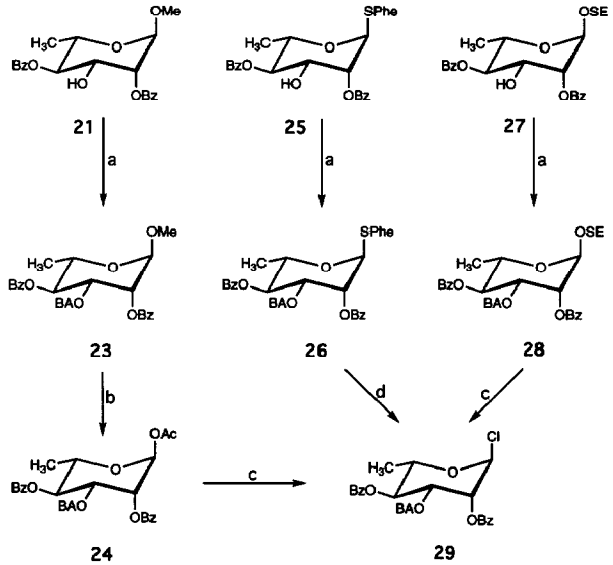
Scheme 2.



[a]Reagents: (a) $PhC(OMe)_3$, H^+; (b) BzCl — C_5H_5N; (c) AcOH — H_2O; (d) $(CH_3)_2C(OCH_3)_2$, 10-camphorsulfonic acid; (e) BzCl — C_5H_5N.

Scheme 3.

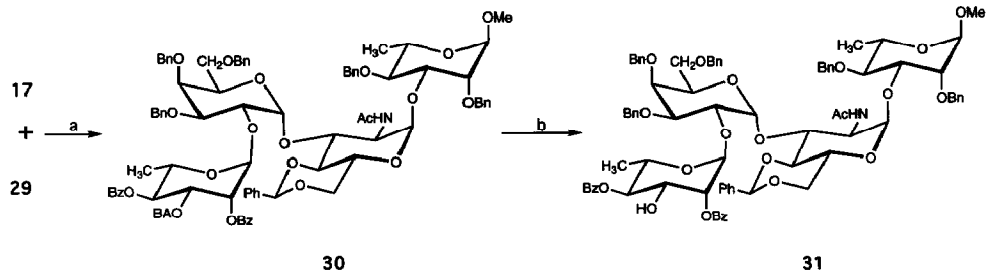
obtained from **18** through the diol [19] **22** in a combined yield of 66%. Bromoacetylation [15] of **21** afforded **23** [20] which was acetolyzed (H_2SO_4–Ac_2O) to give the acetate **24** (72% yield) (Scheme 4).



[a]Reagents: (a) $BrCH_2COBr$ — C_5H_5N; (b) Ac_2O, H_2SO_4; (c) CH_3OCHCl_2, $ZnCl_2$. Et_2O — CH_2Cl_2; (d) Cl_2 — CH_2Cl_2.

BA = bromoacetyl
SE = 2-(trimethylsilyl)ethyl

Scheme 4.

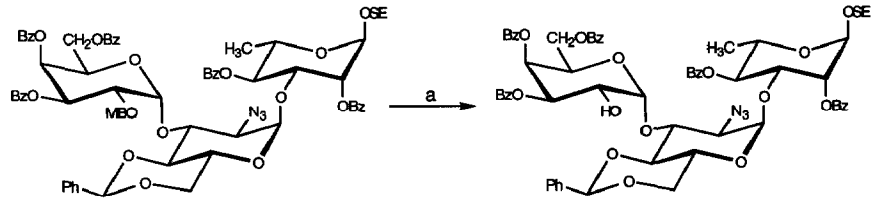


[a]Reagents: (a) CF_3SO_3Ag, 2,6-di-*tert*-butyl-4-methyl-C_5H_2N — CH_2Cl_2; (b) $CS(NH_2)_2$ — MeOH.
BA = bromoacetyl

Scheme 5.

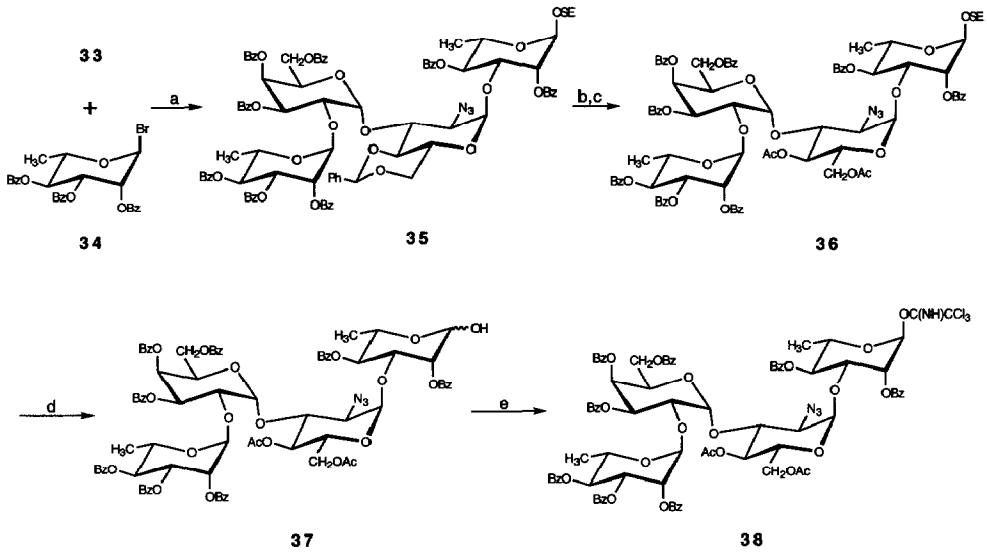
Treatment [21] of **24** with 1,1-dichloromethyl methyl ether and zinc chloride–diethyl ether complex [4] afforded the rhamnosyl chloride **29** in a nearly quantitative yield. The α anomeric configuration in **29** was ascertained by the 183 Hz $^1J_{C\text{-}1,H\text{-}1}$ coupling constant [22]. Alternative routes to **29** included the conversion of the known phenyl 1-thiorhamnoside [18] **25** and 2-(trimethylsilyl)ethyl rhamnoside [7] **27** into their *O*-bromoacetyled derivatives **26** and **28**, respectively, which were routinely transformed to **29** as shown in Scheme 4. Condensation of the **ABC** acceptor **17** with the rhamnosyl donor **29** in the presence of silver trifluoromethanesulfonate (AgOTf) and 2,6-di-*tert*-butyl-4-methylpyridine (DTBMP) gave the fully protected **ABCD** tetrasaccharide **30** in an excellent yield. Removal of the bromoacetyl group with thiourea [15] afforded the tetrasaccharide aceptor **31** in 94% yield (Scheme 5).

We chose the trisaccharide (trimethylsilyl)ethyl glycoside [6] **32** as the precursor to the **EFGH** block. 2-(Trimethylsilyl)ethyl glycosides of mono- and oligo-saccharides have been shown to be useful intermediates in oligosaccharide syntheses [23–25]. Whereas their glycosidic linkage is stable under a variety of reaction conditions, they can be converted to glycosyl donors in high yields either directly,



[a]Reagents: (a) 2,3-dichloro-5,6-dicyano-1,4-benzoquinone — CH_2Cl_2, H_2O.
MB = 4-methoxybenzyl
SE = 2-(trimethylsilyl)ethyl

Scheme 6.

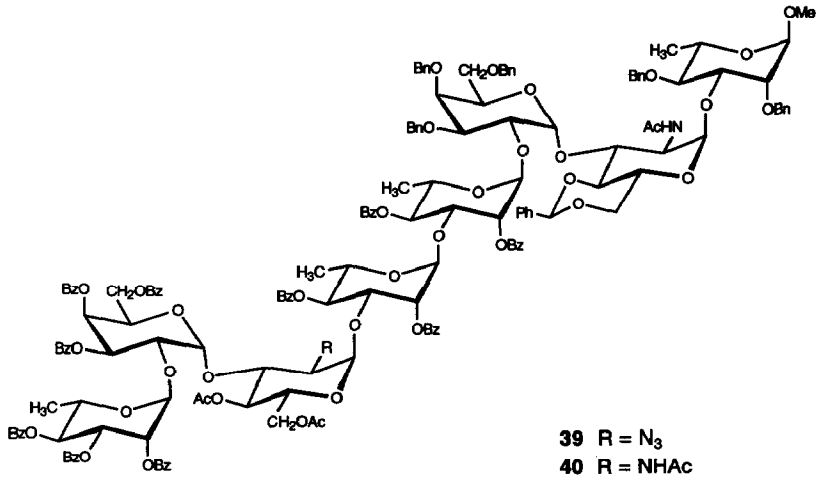


[a]Reagents: (a) CF_3SO_3Ag, 2,6-di-*tert*-butyl-4-methyl-C_5H_2N — CH_2Cl_2; (b) AcOH, H_2O; (c) Ac_2O — C_5H_5N; (d) CF_3COOH — CH_2Cl_2; (e) CCl_3CN, 1,8-diazabicyclo[5.4.0]undec-7-ene — CH_2Cl_2.

SE = 2-(trimethylsilyl)ethyl

Scheme 7.

or by way of the corresponding glycosyl hemiacetals [24]. Treatment of the compound **32** with DDQ afforded the alcohol **33** in 94% yield (Scheme 6). The trisaccharide acceptor **33** was glycosylated with 2,3,4-tri-*O*-benzoyl-α-L-rhamnopyranosyl bromide [26] **34** in the presence of AgOTf and DTBMP, to give the protected tetrasaccharide **35** in 94% yield (Scheme 7). We found, that the **34** or the corresponding chloride [7] are less likely to promote side-reactions, e.g., formation of an orthoester or a β-rhamnosyl linkage, than the corresponding *O*-acetylated counterparts. Next, the benzylidene-acetal function was replaced by acetyl groups [(*i*) H_3O^+, (*ii*) Ac_2O–Py] to afford **36**. An attempt to convert the tetrasaccharide glycoside **36** into the corresponding tetraosyl chloride proved to be abortive under the conditions (1,1-dichloromethyl methyl ether, $ZnCl_2$) reported for related transformations [23,24]. Although the 2-(trimethylsilyl)ethoxy group in **36** could be replaced by chlorine during this reaction, concurrent cleavage of residue *H* occurred, as shown by the isolation of 2,3,4-tri-*O*-benzoyl-α-L-rhamnopyranosyl chloride [7] in pure form from the mixture. An approximately equimolar amount of a glycotriosyl chloride was also isolated, which corresponds to the **EFG** sequence. An alternative approach was therefore sought for the transformation of **36** into a glycosyl donor. This was accomplished in a two-step sequence. First, the 2-(trimethylsilyl)ethyl group was removed by the treatment [23] of **36** with trifluoroacetic acid in CH_2Cl_2, to afford the hemiacetal **37** in 87% yield. Subsequently, compound **37** was converted to the trichloroacetimidate derivative **38** by reaction [27] with



trichloroacetonitrile in the presence of 1,8-diazabicyclo[5.4.0]undec-7-ene [28] in 94% yield. The α anomeric configuration of the reducing end unit in **38** was inferred from the chemical shift analogy of H-1_E with the corresponding proton in a closely related compound [6].

Condensation of the tetrasaccharide donor **38** with the tetrasaccharide acceptor **17** was performed in CH_2Cl_2, under catalysis by boron trifluoride etherate. The fully protected octasaccharide **39** could be isolated in 69% yield. The stereochemical integrity of **39** was indicated by NMR spectroscopy, which provided proof for the all-α stereochemistry of the interglycosidic linkages. The identity of compound **39** received further support from fast-atom bombardment mass spectroscopy (FABMS), using a mixture of dithiothreitol and dithioerythritol as the matrix. For **39** the measured mass of the protonated parent ion was 2994.028 amu. This is within 11 ppm from the calculated mass for $C_{167}H_{165}N_4O_{48}$ which is 2994.059. To achieve this accuracy, data from several scans were acquired in profile mode which allows averaging of peak shape before assignment of mass. A two-step conversion of **39** [(*i*) $NiCl_2$–H_3BO_3–$NaBH_4$; (*ii*) Ac_2O] afforded the acetamido derivative **40** in 44% yield. The measured mass of the protonated parent ion was 3010.059, which agrees within 7 ppm with the theoretical value calculated for $C_{169}H_{169}N_2O_{49}$. Routine deprotection of **40** [(*i*) NaOMe–MeOH, (ii) H_2–Pd–C] afforded the octasaccharide methyl glycoside **11**, which was characterized by NMR and FABMS. At this stage, partial assignment of the ^{1}H NMR spectrum of **11** was aided by the published spectra of the smaller homologues **1–10**. We compared the chemical shifts of the anomeric protons for **11** with those in the O-SP. The criterion for coincidence was set arbitrarily as less than 0.01 ppm difference in the chemical shifts [5]. This comparison revealed, that in **11** the chemical shifts of the anomeric

protons of five consecutive residues coincide with the corresponding chemical shifts for the O-SP. These are the residues **C**, **D**, **E**, **F**, and **G**. It is very likely that increasing spectral coincidence reflects increasing conformational similarities. Thus we believe, the octasaccharide **11** more closely approaches the conformational determinant of the O-SP than any of the smaller homologues **1–10**. In order to further probe the similarity between the octasaccharide **11** and the O-SP of *Sh. dysenteriae* type 1, a detailed analysis of their ^{1}H and ^{13}C NMR spectra is currently being carried out in our laboratory. These findings will be the subject of a future publication [29].

3. Experimental

General methods.—General experimental conditions are described in ref. 4. Optical rotations were measured for $CHCl_3$ solutions, except where indicated otherwise. The NMR data were obtained on a Gemini 300 (Varian) spectrometer, operating at 300 MHz for ^{1}H and at 75 MHz for ^{13}C. The fast-atom bombardment mass spectra were run on a Jeol SX102 mass spectrometer using 6 keV Xe atoms to ionize the samples which were desorbed from a "magic bullet" matrix (mixture of dithiothreitol and dithioerythritol). For low mass spectra (< 2000 amu), the instrument was calibrated against Ultramark 1621 (PCR Chemicals) and for higher mass samples, against cesium iodide. For the low resolution, chemical ionization mass spectra (CIMS) ammonia was used as the ionizing gas.

Methyl O-*(2-acetamido-4,6-*O*-benzylidene-2-deoxy-α-*D*-glucopyranosyl)-(1 → 3)-2,4-di-*O*-benzyl-α-*D*-rhamnopyranoside* (**13**).—To a solution of methyl *O*-(2-azido-4,6-*O*-benzylidene-2-deoxy-α-D-glucopyranosyl)-(1 → 3)-2,4-di-*O*-benzyl-α-L-rhamnopyranoside [4] (**12**, 2.9 g, 4.5 mmol) in EtOH (20 mL) was added a solution of $NiCl_2 \cdot 6H_2O$ (3.0 g, 12.6 mmol) and H_3BO_3 (1.8 g, 29 mmol) in EtOH (120 mL). To this solution was added, under stirring at 25°C, a 1% solution of $NaBH_4$ in EtOH (~ 40 mL) during 1 h. The mixture was cooled to 0°C, then treated with Ac_2O (2 mL). Extractive work-up, followed by column chromatography using EtOAc as eluant afforded **13** as an amorphous solid (2.35 g, 79%); $[\alpha]_D$ +15° (*c* 0.5). NMR ($CDCl_3$): ^{1}H, δ 7.15–7.45 (aromatic), 5.519 (s, 1 H, C*H*Ph), 4.932 (d, 1 H, $J_{1,2}$ 3.9 Hz, H-1_B), 4.771, 4.744, 4.586, and 4.507 (4 d, 4 H, 2 CH_2 of Bn), 3.337 (s, 3 H, CH_3O), 1.618 (s, 3 H, CH_3CO), and 1.373 (d, 1 H, $J_{5,6}$ 6.2 Hz, H-6_A); ^{13}C, δ 172.1 (*C*=O), 137.4–126.5 (aromatic), 101.9 (*C*HPh), 97.5 (C-1_A), 93.6 (C-1_B), 82.1 (C-4_B), 75.6 and 71.9 (CH_2 of Bn), 68.6 (C-6_B), 54.9 (CH_3O), 54.3 (C-2_B), 22.6 (*C*H_3CO), and 18.1 (C-6_A). CIMS: *m/z* 650 [$(M + H)^+$]. Anal. Calcd for $C_{36}H_{43}NO_{10}$: C, 66.54; H, 6.67; N, 2.16. Found: C, 66.45; H, 6.71; N, 2.13.

Methyl O-[3,4,6-tri-O-*benzyl-2-*O*-(4-methoxybenzyl)-α-*D*-galactopyranosyl]-(1 → 3)-*O*-(2-acetamido-4,6-*O*-benzylidene-2-deoxy-α-*D*-glucopyranosyl)-(1 → 3)-2,4-di-*O*-benzyl-α-*L*-rhamnopyranoside* (**15**).—Methyl trifluoromethanesulfonate (150 μL) was added to a stirred mixture of **13** (2.92 g, 4.5 mmol), methyl 3,4,6-tri-*O*-benzyl-2-*O*-(4-methoxybenzyl)-1-thio-β-D-galactopyranoside [4,5] (**14**, 5.0 g, 8.3 mmol), 2,6-di-*tert*-butyl-4-methylpyridine (1.5 g, 7.4 mmol), and 4A molecular sieves (3 g)

in diethyl ether (100 mL), at 25°C. The mixture was stirred for 60 h, during which time more MeOTf was added after 20 h (150 μL, 1.3 mmol), and 40 h (200 μL, 1.8 mmol). The reaction was terminated by the addition of Et_3N (3 mL). Work-up in the usual manner followed by chromatography (3:1 → 2:1 hexane–EtOAc) afforded first a mixture of **14** and **16** (Ref 4), from which **14** (1.5 g) was isolated by crystallization. Subsequent elution afforded **15** as an amorphous solid (4.70 g, 87%); $[\alpha]_D$ +48° (*c* 0.8). NMR ($CDCl_3$): ^1H, δ 7.4–6.63 (aromatic), 6.382 (d, 1 H, N*H*), 5.545 (d, 1 H, $J_{1,2}$ 3.8 Hz, H-1_C), 5.417 (s, 1 H, C*H*Ph), 5.082 (d, 1 H, $J_{1,2}$ 3.7 Hz, H-1_B), 3.746 (s, 3 H, CH_3O of 4-methoxybenzyl), 3.279 [s, 3 H, CH_3O (aglycon)], 1.701 (CH_3CO), 1.355 (d, 1 H, $J_{5,6}$ 6.2 Hz, H-6_A); ^{13}C, δ 158.9–113.4 (aromatic), 101.8 (*C*HPh), 98.1 and 97.1 (C-1_A, 1_C), 93.0 (C-1_B), 82.8 (C-4_B), 75.8, 74.3, 73.8, 73.7, 72.3, 71.0, 70.7, and 68.8 (C-6_B, 6_C, and CH_2 of Bn and 4-methoxybenzyl), 55.1 and 54.7 (CH_3O), 51.8 (C-2_B), 22.7 (CH_3CO), and 17.9 (C-6_A). FABMS: *m/z* 1202 $[(M + H)^+]$. Anal. Calcd for $C_{71}H_{79}NO_{16}$: C, 70.92; H, 6.62; N, 1.16. Found: C, 71.01; H, 6.91; N, 1.18.

Methyl O-*(3,4,6-tri-*O*-benzyl-α-*D*-galactopyranosyl)-(1 → 3)-*O*-(2-acetamido-4,6-*O*-benzylidene-2-deoxy-α-*D*-glucopyranosyl)-(1 → 3)-2,4-di-*O*-benzyl-α-*L*-rhamnopyranoside* (**17**).—2,3-Dichloro-5,6-dicyano-1,4-benzoquinone (0.8 g, 3.5 mmol) was added to a stirred mixture of **15** (3.3 g, 2.7 mmol) in CH_2Cl_2 (200 mL) and H_2O (10 mL) at 25°C. After 2 h, more 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (0.4 g, 1.8 mmol) was added, and the mixture was stirred for an additional period of 2 h. The usual work-up, followed by chromatography (1:1 hexane–EtOAc) gave **17** as an amorphous substance (1.7 g, 57%); $[\alpha]_D$ +43° (*c* 0.7). NMR ($CDCl_3$): ^1H, δ 5.543 (s, 1 H, C*H*Ph), 5.350 (d, 1 H, $J_{1,2}$ 4.2 Hz, H-1_C), 5.022 (m, 1 H, H-1_B), 3.295 (s, 3 H, CH_3O), and 1.375 (d, 1 H, $J_{5,6}$ 6.3 Hz, H-6_A); ^{13}C, δ 172.2 (*C*=O), 138.4–126.0 (aromatic), 101.1 (*C*HPh), 99.9 (C-1_A), 97.9 (C-1_C), 93.6 (C-1_B), 82.3 (C-4_B), 75.9, 74.5, 73.7, 73.2, and 72.3 (CH_2 of Bn), 68.8 and 68.7 (C-6_A,6_B), 55.8 (CH_3O), 52.1 (C-2_B), 22.9 (CH_3CO), and 18.2 (C-6_A). FABMS: *m/z* 1082 $[(M + H)^+]$. Anal. Calcd for $C_{63}H_{71}NO_{15}$: C, 69.91; H, 6.61; N, 1.29. Found: C, 69.70; H, 6.94; N, 1.26.

*Methyl 4-*O*-benzoyl-α-*L*-rhamnopyranoside* (**22**).—To a solution of methyl 2,3-*O*-isopropylidene-α-L-rhamnopyranoside, obtained from **18** (5 g, 28 mmol) as described in ref 30, in pyridine (8 mL) was added BzCl (3.6 mL) at 0°C. After 1 h, the mixture was concentrated. Extractive work-up ($CHCl_3$–5% aq HCl–H_2O) afforded a semicrystalline product, which was dissolved in 4:1 MeOH–H_2O (25 mL). To this mixture was added CF_3CO_2H (2 mL). After 30 min, the volatiles were evaporated under vacuum. The residue was dried by repeated addition and evaporation of toluene. Treatment of the syrupy residue with petroleum ether afforded crystalline **22** (5.7 g, 72%); mp 113–115°C; $[\alpha]_D$ − 106° (*c* 1.1), lit. [19] $[\alpha]_D$ − 82° ($CHCl_3$). NMR ($CDCl_3$): ^1H, δ 8.06–7.36 (aromatic), 5.090 (t, 1 H, $J_{3,4} = J_{4,5} = 9.4$ Hz, H-4), 4.753 (br d, 1 H, H-1), 4.04–3.98 (m, 2 H, H-2,3), 3.931 (dq, 1 H, H-5), 3.398 (s, 3 H, CH_3O), and 1.275 (d, 3 H, $J_{5,6}$ 6.2 Hz, H-6); ^{13}C, δ 167.3 (*C*=O), 133.4–128.4 (aromatic), 100.6 (C-1), 75.8 (C-4), 70.8 and 70.2 (C-2,3), 65.6 (C-5), 55.0 (CH_3O), and 17.4 (C-6). CIMS: *m/z* 300 $[(M + NH_4)^+]$. Anal. Calcd for $C_{14}H_{18}O_6$: C, 59.57; H, 6.43. Found: C, 59.40; H, 6.50.

Methyl 2,4-di-O-benzoyl-α-L-rhamnopyranoside (**21**).—(*a*) A mixture of **18** (25 g, 88 mmol), trimethyl orthobenzoate (43 mL, 250 mmol), and a catalytic amount of 10-camphorsulfonic acid was stirred at 25°C until the mixture became homogeneous (~ 30 min), then the by-product MeOH was removed at 30°C, under the vacuum of a water aspirator. The residue, containing the intermediate **19**, was dissolved in pyridine (50 mL). To this solution was added BzCl (24 mL), at 0°C. After 3 h, the mixture was treated with aq $NaHCO_3$ at 0°C, then extracted with $CHCl_3$. The organic phase was washed with H_2O, then concentrated to give a syrup, containing the intermediate **20**. Residual pyridine was removed by repeated addition and evaporation of H_2O. To a solution of the syrupy residue in CH_3CN (200 mL) was added aq 50% CF_3CO_2H (10 mL) at 0°C. After 3 min, the volatiles were removed under vacuum. Column chromatography (6:1 hexane–EtOAc) of the residue afforded a syrup which was crystallized from hexane to afford crystalline **21** (32.5 g, 60%); mp 84–86°C; $[\alpha]_D$ +64° (*c* 1.3), lit. [17] $[\alpha]_D$ +57° ($CHCl_3$), lit. [31] for the D isomer, $[\alpha]_D$ −59° ($CHCl_3$). CIMS: *m/z* 404 $[(M + NH_4)^+]$, 387 $[(M + H)^+]$, and 355 $[(M + H - MeOH)^+]$. Anal. Calcd for $C_{21}H_{22}O_7$: C, 65.27; H, 5.75. Found: C, 65.30; H, 5.78.

(*b*) To a mixture of **22** (5.0 g, 17.6 mmol) and trimethyl orthobenzoate (6 mL, 35 mmol) was added a catalytic amount of 10-camphorsulfonic acid. The mixture was shaken until it became homogeneous (~ 10 min). The by-product MeOH was removed as described in (*a*). To a solution of the intermediate orthoester **20** in CH_3CN (50 mL) at 0°C was added aq 50% CF_3CO_2H (2 mL). After 3 min, the mixture was processed as described in (*a*), to give **21** (6.3 g, 92%), which was identical to the product obtained in (*a*).

1-O-Acetyl-2,4-di-O-benzoyl-3-O-bromoacetyl-α-L-rhamnopyranose (**24**).—To a solution of methyl 2,4-di-*O*-benzoyl-3-*O*-bromoacetyl-α-L-rhamnopyranoside [20] (**23**, 5.5 g, 11 mmol), obtained from **21** by bromoacetylation essentially as described [15] in Ac_2O (40 mL) at 0°C was added conc H_2SO_4 (6 drops). After 3 h, solid $NaHCO_3$ was added, and the mixture was stirred for 5 min. The mixture was concentrated. Extractive work-up, followed by column chromatography using 5:1 hexane–EtOAc as eluant gave amorphous **24** (4.2 g, 72%); $[\alpha]_D$ +60° (*c* 1.2). NMR ($CDCl_3$): ^1H, δ 8.13–7.43 (aromatic), 6.238 (d, 1 H, $J_{1,2}$ 1.9 Hz, H-1), 5.645 (dd, 1 H, $J_{2,3}$ 3.6, $J_{3,4}$ 10.2 Hz, H-3), 5.572 (dd, 1 H, H-2), 5.551 (t, 1 H, H-4), 4.177 (dq, 1 H, H-5), 3.670 and 3.620 (2 d, 2 H, *J* ~ 11.9 Hz, CH_2Br), 2.236 (s, 3 H, CH_3CO), 1.355 (d, 3 H, $J_{5,6}$ 6.3 Hz, H-6); ^{13}C, δ 169.0 (*C*=O of Ac), 167.4 (*C*=O of $BrCH_2CO$), and 166.1 (2 C) (*C*=O of Bz), 133.9–128.6 (aromatic), 90.7 ($^1J_{C\text{-}1,H\text{-}1}$ 177 Hz, C-1), 70.8, 70.7, and 69.1 (2 C) (C-2,3,4,5), 24.9 (CH_2Br), 20.9 (CH_3CO), and 17.6 (C-6). CIMS: *m/z* 552 $([M + NH_4)^+]$ and 475 $[(M + H - AcOH)^+]$. Anal. Calcd for $C_{24}H_{23}BrO_9$: C, 53.84; H, 4.33; Br, 14.93. Found: C, 54.10; H, 4.55; Br, 14.79.

Phenyl 2,4-di-O-benzoyl-3-O-bromoacetyl-1-thio-α-L-rhamnopyranoside (**26**).—Phenyl 2,4-di-*O*-benzoyl-1-thio-α-L-rhamnopyranoside [18] (**25**) was bromoacetylated as described for the preparation of compound **23**, to afford **26** as a syrup (94%); $[\alpha]_D$ −28° (*c* 1.4). NMR ($CDCl_3$): ^1H, δ 8.12–7.24 (aromatic), 5.816 (dd, 1 H, $J_{1,2}$ 1.7, $J_{2,3}$ 2.9 Hz, H-2), 5.625–5.551 (m, 3 H, H-1,3,4), 4.602 (dq, 1 H, H-5),

3.667 and 3.625 (2 d, 2 H, CH_2Br), and 1.360 (d, 1 H, $J_{5,6}$ 6.2 Hz, H-6); ^{13}C, δ 166.4, 165.54, and 165.48 (C=O), 133.6–128.0 (aromatic), 85.8 (C-1), 71.8, 71.5, and 71.4 (C-2,3,4), 68.1 (C-5), 25.0 (CH_2Br) and 17.6 (C-6). CIMS: m/z 602 [$(M + NH_4)^+$]. Anal. Calcd for $C_{28}H_{25}BrO_7S$: C, 57.44; H, 4.30; Br, 13.65; S, 5.48. Found: C, 56.59; H, 4.39; Br, 13.49; S, 5.33.

2-(Trimethylsilyl)ethyl 2,4-di-O-benzoyl-3-O-bromoacetyl-α-L-rhamnopyranoside (**28**).—2-(Trimethylsilyl)ethyl 2,4-di-O-benzoyl-α-L-rhamnopyranoside [7] (**27**) was bromoacetylated as described for the preparation of **23**, to afford **28** as a syrup (71%); $[\alpha]_D$ +52° (c 1). NMR ($CDCl_3$): ^1H, δ 8.14–7.42 (aromatic), 5.658 (dd, 1 H, $J_{2,3}$ 3.4, $J_{3,4}$ 10.1 Hz, H-3), 5.516 (dd, 1 H, H-2), 5.503 (t, 1 H, $J_{3,4} = J_{4,5} = 10.1$ Hz, H-4), 4.970 (d, 1 H, H-1), 4.123 (dq, 1 H, H-5), 3.92–3.85 and 3.66–3.57 (m, 2 H, OCH_2), 3.652 and 3.601 (2 d, 2 H, CH_2Br), and 1.336 (d, 1 H, $J_{5,6}$ 6.2 Hz, H-6); ^{13}C, δ 166.5, 165.72, and 165.46 (C=O), 133.5–128.5 (aromatic), 100.0 (C-1), 71.6, 71.3, 70.6, 66.6, and 65.8 (C-2,3,4,5,OCH_2), 68.1 (C-5), 25.1 (CH_2Br), 17.9 (CH_2Si), 17.6 (C-6), and −1.4 ($SiMe_3$). CIMS: m/z 610 [$(M + NH_4)^+$]. Anal. Calcd for $C_{27}H_{33}BrO_8Si$: C, 54.63; H, 5.60; Br, 13.46. Found: C, 54.53; H, 5.64; Br, 13.53.

2,4-Di-O-benzoyl-3-O-bromoacetyl-α-L-rhamnopyranosyl chloride (**29**).—(*a*) To a stirred mixture of **24** (3.2 g, 6.0 mmol) and $ZnCl_2 \cdot Et_2O$ (1 mL of a 54% solution in CH_2Cl_2) in CH_2Cl_2 was added 1,1-dichloromethyl methyl ether (1.5 mL, 16.5 mmol). After 4 h aq $NaHCO_3$ was added. The $CHCl_3$ phase was washed with H_2O and concentrated. Column chromatographic purification (8:1 hexane–EtOAc) of the residue afforded **29** as a syrup (3.0 g, 98%); $[\alpha]_D$ +47°(c 1.6), lit. [20] +43°. NMR ($CDCl_3$): ^1H, δ 8.13–7.42 (aromatic), 6.160 (d, 1 H, H-1), 5.907 (dd, 1 H, $J_{2,3}$ 3.4, $J_{3,4}$ 10.2 Hz, H-3), 5.701 (dd, 1 H, $J_{1,2}$ 1.7 Hz, H-2), 5.558 (t, 1 H, H-4), 4.402 (dq, 1 H, H-5), 3.655 and 3.603 (2 d, 2 H, CH_2Br), and 1.385 (d, 1 H, $J_{5,6}$ 6.2 Hz, H-6); ^{13}C, δ 166.4, 165.5, and 165.2 (C=O), 133.9–128.5 (aromatic), 89.0 ($J_{C\text{-}1,H\text{-}1}$ 183 Hz, C-1), 72.3 (C-2), 70.7 (C-4), and 69.7 (C-3, 5), 24.8 (CH_2Br), and 17.3 (C-6). Anal. Calcd for $C_{12}H_{17}ClO_7$: C, 46.68 H, 5.55; Cl, 11.48. Found: C, 46.58; H, 5.60; Cl, 11.57.

(*b*) To a solution of **26** (280 mg) in CH_2Cl_2 (6 mL) was added a solution of Cl_2 in CCl_4 until the yellow color persisted, at 0°C. After 5 h, hex-1-ene (excess) was added and the solution concentrated. Column chromatography (8:1 hexane–EtOAc) afforded **29** as a syrup (226 mg, 92%) which was identical to the preparation obtained in (*a*).

(*c*) Treatment of **28** with 1,1-dichloromethyl methyl ether and $ZnCl_2 \cdot Et_2O$ as described in (*a*) afforded **29** (86%) which was identical to the preparation obtained in (*a*).

Methyl O-(2,4-di-O-benzoyl-3-O-bromoacetyl-α-L-rhamnopyranosyl)-(1 → 2)-O-(3,4,6-tri-O-benzyl-α-D-galactopyranosyl-(1 → 3)-O-(2-acetamido-4,6,-benzylidene-2-deoxy-α-D-glucopyranosyl)-(1 → 3)-2,4-di-O-benzyl-α-L-rhamnopyranoside (**30**).—A mixture of **17** (1.20 g, 1.1 mmol), **29** (1.14 g, 3.7 mmol), 2,6-di-*tert*-butyl-4-methylpyridine (0.4 g, 2 mmol), 4A molecular sieves (1 g), and dry CH_2Cl_2 (50 mL) was stirred for 1 h then cooled to −50°C. Silver trifluoromethanesulfonate (0.6 g, 2.7 mmol) was added. After 1 h more **29** (0.5 g, 1.6 mmol) and silver trifluoromethanesulfonate (0.4 g, 1.8 mmol) were added. The stirred mixture was allowed to reach

20°C in 3 h. Ice-cold, aq $NaHCO_3$ was added and the mixture was filtered. The organic phase was separated and concentrated. Column chromatography (1:1 hexane–EtOAc) of the residue afforded **30** as an amorphous solid (1.62 g, 94%); $[\alpha]_D$ +67° (*c* 0.9). NMR ($CDCl_3$): ^1H, δ 8.04–6.92 (aromatic), 6.197 (d, 1 H, $J_{NH\text{-}H\text{-}2}$ 9.6 Hz, N*H*), 5.741 (dd, 1 H, $J_{2,3}$ 3.3, $J_{3,4}$ 10.3 Hz, H-3_D), 5.707 (d, 1 H, $J_{1,2}$ 4.1 Hz, H-1_C), 5.662 (dd, 1 H, H-2_D), 5.657 (s, 1 H, C*H*Ph), 5.483 (d, 1 H, H-1_D), 5.250 (t, 1 H, H-4_D), 5.041 (d, 1 H, $J_{1,2}$ 3.9 Hz, H-1_B), 3.296 (s, 3 H, CH_3O), 1.706 (s, 3 H, CH_3CO), 1.340 and 0.529 (2 d, 2 H, $J_{5,6}$ ~ 6 Hz, H-6_A, 6_D); ^{13}C, δ 169.5 (*C*=O of Ac), 166.3, 165.6, and 165.0 (*C*=O of Bz and $BrCH_2CO$), 137.9–125.9 (aromatic), 100.4 (*C*HPh), 97.9 and 97.8 (C-1_A,1_D), 97.1 (C-1_C), 92.9 (C-1_B), 82.9 (C-4_B), 75.9, 74.4, 73.7, 73.2, and 72.2 (CH_2 of Bn), 70.5 and 68.6 (C-6_B,6_C), 54.8 (CH_3O), 51.6 (C-2_B), 25.4 (CH_2Br), 23.1 (CH_3CO), 18.1 and 17.3 (C-6_A,6_B). FABMS: *m/z* 1558 [$(C_{85}H_{90}\ ^{81}BrNO_{22}+H)^+$] and 1556 [$(C_{85}H_{90}\ ^{79}BrNO_{22}+H)^+$]. Anal. Calcd for $C_{85}H_{90}BrNO_{22}$: C, 65.54; H, 5.82; Br, 5.13; N, 0.90. Found: C, 64.82; H, 5.86; Br, 5.04; N, 0.84.

Methyl O-*(2,4-di-*O*-benzoyl-α-*L*-rhamnopyranosyl)-(1 → 2)-*O*-(3,4,6-tri-*O*-benzyl-α-*D*-galactopyranosyl)-(1 → 3)-*O*-(2-acetamido-4,6-*O*-benzylidene-2-deoxy-α-*D*-glucopyranosyl)-(1 → 3)-2,4-di-*O*-benzyl-α-*L*-rhamnopyranoside* (**31**).—Thiourea (0.5 g, 6.6 mmol) was added to a solution of **30** (1.5 g, 0.96 mmol) in 2:1 CH_3OH–CH_2Cl_2 (60 mL) at 25°C. After 1 h the solution was concentrated. The residue was treated with $CHCl_3$ (80 mL), the mixture filtered, and the insoluble part discarded. The $CHCl_3$ solution was washed with H_2O, dried (Na_2SO_4), and concentrated. Column chromatography (1:1 hexane–EtOAc) of the residue afforded amorphous **31** (1.30 g, 94%); $[\alpha]_D$ + 56° (*c* 0.4). NMR ($CDCl_3$): ^1H, δ 8.04–6.97 (aromatic), 6.172 (d, 1 H, $J_{NH\text{-}H\text{-}2}$ 9.5 Hz, N*H*), 5.702 (d, 1 H, $J_{1,2}$ 4.1 Hz, H-1_C), 5.636 (s, 1 H, C*H*Ph), 5.534 (dd, 1 H, H-2_D), 5.415 (d, 1 H, H-1_D), 5.094 (t, 1 H, H-4_D), 5.023 (d, 1 H, $J_{1,2}$ 3.8 Hz, H-1_B), 3.294 (s, 3 H, CH_3O), 1.683 (s, 3 H, CH_3CO), 1.344 and 0.651 (2 d, 2 H, $J_{5,6}$ ~ 6.0 Hz, H-6_A, 6_D); ^{13}C, δ 169.6 (*C*=O of Ac), 166.8 and 165.8 (*C*=O of Bz), 138.1–126.0 (aromatic), 100.5 (*C*HPh), 97.82 and 97.80 (C-1_A,1_D), 97.0 (C-1_C), 92.9 (C-1_B), 83.1 (C-4_B), 76.0, 74.4, 73.6, 73.5, and 72.3 (CH_2 of Bn), 70.5 and 68.7 (C-6_B,6_C), 54.8 (CH_3O), 51.6 (C-2_B), 23.0 (CH_3CO), 18.0 and 17.4 (C-6_A,6_B). FABMS: *m/z* 1436 [$(M+H)^+$]. Anal. Calcd for $C_{83}H_{84}NO_{21}$: C, 69.39; H, 6.24; N, 0.98. Found: C, 69.41; H, 6.34; N, 0.91.

2-(Trimethylsilyl)ethyl O-*(3,4,6-tri-*O*-benzoyl-α-*D*-galactopyranosyl)-(1 → 3)-*O*-(2-azido-4,6-*O*-benzylidene-2-deoxy-α-*D*-glucopyranosyl-(1 → 3)-2,4-di-*O*-benzoyl-α-*L*-rhamnopyranoside* (**33**).—A mixture of **32** (ref 6) (1.0 g, 0.75 mmol), 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (220 mg, 0.97 mmol), CH_2Cl_2 (100 mL), and H_2O (5 mL) was stirred at 25°C for 6 h. More 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (290 mg, 1.27 mmol) was added and stirring was continued for another 24 h. The mixture was extracted with aq $NaHCO_3$ and H_2O. The organic phase was concentrated. Column chromatography (2:1 hexane–EtOAc) of the residue afforded **33** as an amorphous solid (860 mg, 94%); $[\alpha]_D$ + 124° (*c* 0.2). NMR ($CDCl_3$): ^1H, δ 8.18–7.06 (aromatic protons), 5.856 (dd, 1 H, $J_{3,4}$ 3.2 Hz $J_{4,5}$ 1.9 Hz, H-4_C), 5.625 (dd, 1 H, $J_{1,2}$ 1.3, $J_{2,3}$ 3.3 Hz, H-2_A), 5.585 (t, 1 H, $J_{3,4}=J_{4,5}=10$ Hz, H-4_A), 5.520 (dd, 1 H, $J_{2,3}$ 10.5, $J_{2,3}$ 3.3 Hz, H-3_C), 5.347 (s, 1 H, *H*CPh), 5.250

(d, 1 H, $J_{1,2}$ 3.7 Hz, H-1_C), 5.167 (d, 1 H, $J_{1,2}$ 3.6 Hz, H-1_B), 4.998 (d, 1 H, $J_{1,2}$ 1.7 Hz, H-1_A), 3.106 (dd, 1 H, H-2_B), 1.350 (d, 3 H, H-6_A), 1.1–0.9 (m, 2 H, CH_2Si), and 0.084 [s, 9 H, $SiMe_3$]; ^{13}C, δ 166.0–165.3 (*C*=O), 136.2–123.7 (aromatic), 101.4 (*C*HPh), 101.3 (C-1_A), 97.1 (C-1_B), 95.3 (C-1_A), 81.0 (C-4_B), 68.3 (C-6_B), 65.8 (OCH_2CH_2), 61.7 (C-6_C), 18.0 (CH_2Si), 17.7 (C-6_A), and −1.3 ($SiMe_3$). FABMS: *m/z* 1222 [$(M + H)^+$] and 1196 [$(M + H_3 - N_3)^+$]. Anal. Calcd for $C_{65}H_{67}N_3O_{19}Si$: C, 63.87; H, 5.52; N, 3.44. Found: C, 63.74; H, 5.58; N, 3.41.

2-(Trimethylsilyl)ethyl O-*(2,3,4-tri-*O*-benzoyl-α-*L*-rhamnopyranosyl)-(1 → 2)-*O*-(3,4,6-tri-*O*-benzoyl-α-*D*-galactopyranosyl)-(1 → 3)-*O*-(2-azido-4,6-*O*-benzyldine-2-deoxy-α-*D*-glucopyranosyl)-(1 → 3)-2,4-di-*O*-benzoyl-α-*L*-rhamnopyranoside* (**35**).—A mixture of **33** (700 mg, 0.57 mmol), 2,3,4-tri-*O*-benzoyl-α-L-rhamnopyranosyl bromide [26] (**34**, 500 mg, 0.93 mmol), 2,6-di-*tert*-butyl-4-methylpyridine (190 mg, 0.93 mmol), 4A molecular sieves (0.5 g), and dry $(CH_2Cl)_2$ (20 mL) was stirred for 1 h then cooled to −20°C. Silver trifluoromethanesulfonate (250 mg, 1.13 mmol) was added. The stirred mixture was allowed to reach 20°C in 4 h. Ice-cold, aq $NaHCO_3$ was added and the mixture was filtered. The organic phase was separated and concentrated. Column chromatography (3:1 hexane–EtOAc) of the residue afforded **35** as an amorphous solid (905 mg, 94%); $[\alpha]_D$ + 149° (*c* 0.6). NMR ($CDCl_3$): ^1H, δ 8.62–6.82 (aromatic), 5.983 (dd, 1 H, $J_{3,4}$ 3.3, $J_{4,5}$ 2.1 Hz, H-4_C), 5.858 (dd, 1 H, $J_{2,3}$ 9.7 Hz, H-3_C), 5.738 (dd, 1 H, H-3_D), 5.723 (d, 1 H, $J_{1,2}$ 4.2 Hz, H-1_C), 5.686 (dd, 1 H, $J_{1,2}$ 1.8, $J_{2,3}$ Hz, 3.2 Hz, H-2_A), 5.598 (t, 1 H, $J_{3,4} = J_{4,5} = 9.8$ Hz, H-4_A), 5.523 (s, 1 H, *H*CPh), 5.439 (dd, 1 H, H-2_D), 5.005 (d, $J_{1,2}$ 1.7 Hz, H-1_A), 3.484 (dd, 1 H, $J_{2,3}$ 9.9 Hz, H-2_B), 1.342 and 0.611 (2 d, 6 H, H-6_A, 6_D), and 0.085 [s, 9 H, $SiMe_3$]; ^{13}C, δ 136.7–126.1 (aromatic carbons), 101.1 (*C*HPh), 97.3, 97.2, and 97.1 (C-1_A,1_C,1_D), 94.8 (C-1_B), 82.5 (C-4_B), 68.2 (C-6_B), 65.7 (OCH_2CH_2), 61.9 (C-6_C), 17.9 (CH_2Si), 17.6 and 17.2 (C-6_A,6_D) and −1.3 ($SiMe_3$). Anal. Calcd for $C_{92}H_{89}N_3O_{26}Si$: C, 65.74; H, 5.34; N, 2.50. Found: C, 65.52; H, 5.39; N, 2.44.

2-(Trimethylsilyl)ethyl O-*(2,3,4-tri-*O*-benzoyl-α-*L*-rhamnopyranosyl)-(1 → 2)-*O*-(3,4,6-tri-*O*-benzoyl-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* (**36**).—To a stirred solution of **35** (830 mg, 0.49 mmol) in AcOH (10 mL) was added H_2O at 70°C. After 5 h the mixture was concentrated. Toluene was added and evaporated from the residue. To a solution of the syrupy residue in pyridine (5 mL) were added Ac_2O (5 mL) and a catalytic amount of 4-dimethylaminopyridine. After 5 h the mixture was processed as usual, followed by column chromatographic purification (3:1 hexane–EtOAc) to give **36** as an amorphous solid (760 mg, 92%); $[\alpha]_D$ + 160° (*c* 0.5). NMR ($CDCl_3$): ^1H, δ 8.14–7.04 (aromatic), 5.955 (dd, 1 H, $J_{3,4}$ 3.4, $J_{4,5}$ 1.6 Hz, H-4_C), 5.744 (dd, 1 H, $J_{2,3}$ 10.6 Hz, H-3_C), 5.720 (dd, 1 H, H-3_D), 5.648 (dd, 1 H, $J_{1,2}$ 1.6, $J_{2,3}$ 3.5 Hz, H-2_A), 5.539 and 5.532 (2 t, 2 H, H-4_A, 4_D), 5.307 (d, 1 H, $J_{1,2}$ 3.5 Hz, H-1_B), 4.980 (d, 1 H, H-1_A), 3.553 (dd, 1 H, $J_{2,3}$ 10.0 Hz, H-2_B), 1.998 and 1.809 (2 s, 6 H, 2 CH_3CO), 1.341 and 1.239 (2 d, 6 H, H-6_A, 6_D), and 0.005 [s, 9 H, $SiMe_3$]; ^{13}C, δ 170.8 and 169.2 (*C*=O of Ac), 166.0, 165.9, 165.8, 165.3, 164.9 (2 C), 164.8, and 164.6 (*C*=O of Bz), 133.4–128.1 (aromatic carbons), 98.8, 97.2, and 97.0 (C-1_A,1_C,1_D), 93.9 (C-1_B), 65.8 (OCH_2CH_2), 61.9 and 61.1

(C-6_B, 6_C), 20.6 (CH_3CO), 18.1, 17.7, and 17.6 (CH_2Si, C-6_A, 6_D), and −1.4 ($SiMe_3$). FABMS: *m / z* 1651 $[(^{12}C_{88}{}^{13}CH_{89}N_3O_{28}Si - N_2 + H_3)^+]$, 1650 $[(^{12}C_{89}H_{89}N_3O_{28}Si - N_2 + H_3)^+]$, 1559 $[(^{12}C_{88}{}^{13}CH_{89}N_3O_{28}Si + H - SEOH)^+]$, and 1558 $[(^{12}C_{89}H_{89}N_3O_{28}Si + H - SEOH)^+]$. Anal. Calcd for $C_{89}H_{89}N_3O_{28}Si$: C, 63.75; H, 5.35; N, 2.51. Found: C, 63.64; H, 5.37; N, 2.42.

O-2,3,4-Tri-O-benzoyl-α-L-rhamnopyranosyl)-(1 → 2)-O-(3,4,6-tri-O-benzoyl-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-L-rhamnopyranose (**37**).—A solution of **36** (1.6 g, 0.95 mmol) in 1:4 CH_2Cl_2—CF_3CO_2H (40 mL) was kept at 25°C for 5 h. Toluene (3 × 5 mL) was added and the solution was concentrated under vacuum. Purification by column chromatography (3:2 hexane–EtOAc) afforded **37** as an amorphous solid (1.3 g, 87%); $[\alpha]_D$ +178° (*c* 0.3). NMR ($CDCl_3$): ^1H, δ 8.14–7.04 (aromatic), 5.963 (dd, 1 H, H-4_C), 5.783 (dd, 1 H, $J_{1,2}$ 3.7, $J_{2,3}$ 10.2 Hz, H-3_C), 5.723 (dd, 1 H, H-3_D), 5.551 and 5.539 (2 t, 2 H, H-4_A, 4_D), 5.438 (dd, 1 H, $J_{1,2}$ 1.7, $J_{2,3}$ 3.5 Hz, H-2_A), 5.399 (d, 1 H, $J_{1,2}$ 3.5 Hz, H-1_B), 2.010 and 1.816 (2 s, 6 H, 2 CH_3CO), 1.338 and 1.245 (2 d, 6 H, H-6_A,6_D); ^{13}C, δ 170.8 and 169.2 (*C*=O of Ac), 165.9–164.6 (*C*=O of Bz), 133.5–128.1 (aromatic carbons), 98.7, 97.1, 93.8, and 92.4 (C-1_A,1_B,1_C,1_D), 61.2 and 60.4 (C-6_B,6_C), 20.65 and 20.61 (CH_3CO), 17.7 and 17.6 (C-6_A,6_D). FABMS: *m/z* 1558 $[(M + H - H_2O)^+]$ and 1550 $[(M - N_2 + H_3)^+]$. Anal. Calcd for $C_{84}H_{77}N_3O_{28}$: C, 64.00; H, 4.92; N, 2.66. Found: C, 63.81; H, 5.01; N, 2.57.

O-(2,3,4-Tri-O-benzoyl-α-L-rhamnopyranosyl)-(1 → 2)-O-(3,4,6-tri-O-benzoyl-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-rhamnopyranosyl trichloroacetimidate (**38**).—To a stirred solution of **37** (1.5 g, 0.95 mmol) in CH_2Cl_2 (15 mL) were added at −20°C trichloroacetonitrile (3.0 mL, 30 mmol) and 1,8-diazabicyclo[5.4.0]undec-7-ene (80 μL, 0.53 mmol). The solution was stirred at −20°C for 1 h and was then allowed to reach ~ 20°C in 1 h. Removal of the volatiles followed by purification by column chromatography (2:1 hexane–EtOAc) gave **38** as an amorphous solid (1.54 g, 94%); $[\alpha]_D$ +151° (*c* 0.7). NMR ($CDCl_3$): ^1H, δ 8.823 (s, 1 H, *H*N=C), 8.16–7.04 (aromatic protons), 6.448 (d, 1 H, $J_{1,2}$ 1.9 Hz, H-1_A), 5.958 (dd, 1 H, $J_{3,4}$ 3.3, $J_{4,5}$ 2.0 Hz, H-4_C), 5.888 (dd, 1 H, H-2_A), 5.780 (dd, 1 H, $J_{2,3}$ 10.7 Hz, H-3_C), 5.725 (dd, 1 H, $J_{2,3}$ 3.4, $J_{3,4}$ 9.9 Hz, H-3_D), 5.636 (t, 1 H, $J_{3,4} = J_{4,5} = 9.7$ Hz, H-4_A), 5.536 (t, 1 H, $J_{3,4} = J_{4,5} = 9.7$ Hz, H-4_D), 5.436 (dd, 1 H, H-2_D), 5.311 (d, 1 H, $J_{1,2}$ 3.5 Hz, H-1_C), 5.262 (d, 1 H, $J_{1,2}$ 3.5 Hz, H-1_B), 5.205 (d, 1 H, $J_{1,2}$ 1.7 Hz, H-1_D), 5.187 (dd, 1 H, H-4_B), 3.611 (dd, 1 H, $J_{2,3}$ 10 Hz, H-2_B), 2.008 and 1.814 (3 s, 6 H, 3 CH_3CO), 1.390 (d, 3 H, $J_{5,6}$ 6.2 Hz, H-6_A), and 1.225 (d, 3 H, $J_{5,6}$ 6.1 Hz, H-6_D). FABMS: *m / z* 1559 $[(^{12}C_{85}{}^{13}CH_{77}Cl_3N_4O_{28} + H - C_2H_2Cl_3NO)^+]$ 1558 $[(C_{86}H_{77}Cl_3N_4O_{28} + H - C_2H_2Cl_3NO)^+]$, 1533 $[(1559 - N_2 + H_2)^+]$, and 1532 $[(1558 - N_2 + H_2)^+]$. Anal. Calcd for $C_{86}H_{77}Cl_3N_4O_{28}$: C, 60.02; H, 4.51; N, 3.26; Cl, 6.18. Found: C, 59.81; H, 4.54; N, 3.20; Cl, 6.28.

Methyl O-(2,3,4-tri-O-benzoyl-α-L-rhamnopyranosyl)-(1 → 2)-O-(3,4,6-tri-O-benzoyl-α-D-galactopyranosyl)-(1 → 3)-O-(4,6-di-O-acetyl-2-azido-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-benzyl-α-D-galactopyranosyl)-

(1 → 3)-O-(2-acetamido-4,6-O-benzylidene-2-deoxy-α-D-glucopyranosyl)-(1 → 3)-2,4-di-O-benzyl-α-L-rhamnopyranoside (**39**).—A mixture of **31** (250 mg, 0.174 mmol), **38** (200 mg, 0.116 mmol), and 4A molecular sieves (1.3 g) in dry CH_2Cl_2 (8 mL) was stirred for 1 h then cooled to −20°C. Boron trifluoride ethereate (20 μL) was added, then the mixture was allowed to reach ~ −5–0°C in 4 h. Triethylamine (~ 200 μL) was added. The mixture was filtered. The volatiles were removed under reduced pressure. Column chromatography (3:2 hexane–EtOAc) afforded **39** as an amorphous solid (252 mg, 69%); $[\alpha]_D$ +120° (*c* 0.7). NMR ($CDCl_3$): ^{1}H, δ 6.202 (d, 1 H, $J_{NH\text{-}H\text{-}2}$ 9.5 Hz, N*H*), 5.902 (dd, 1 H, $J_{3,4}$ 3.1, $J_{4,5}$ 1.1 Hz, H-4_G), 5.746–5.670 (m, 3 H, H-2_D,3_G,3_H), 5.641 (s, 1 H, C*H*Ph), 5.515 (t, 1 H, H-4_{Rha}), 5.412 (d, 1 H, $J_{1,2}$ 1.5 Hz, H-1_D), 5.356 and 5.346 (2 t, 2 H, 2 H-4_{Rha}), 5.081 (dd, 1 H, H-4_F), 5.019 (d, 1 H, $J_{1,2}$ 3.7 Hz, H-1_B), 3.293 (s, 3 H, CH_3O), 1.963 (s, 3 H, CH_3CON), 1.752 and 1.667 (2 s, 6 H, 2 CH_3CO), 1.335, 1.216, 1.186, and 0.656 (4 d, 12 H, $J_{5,6}$ ~ 6.2 Hz, H-6_A,6_D,6_E,6_H); ^{13}C, δ 170.5, 169.4, and 168.8 (*C*=O of Ac), 165.6–164.3 (*C*=O of Bz), 137.8–125.7 (aromatic), 100.5 (*C*HPh), 98.9, 98.6, 97.6, and 97.4 (C-1_A,1_D,1_E,1_H), 96.8 and 96.7 (C-1_C,1_G), 93.3 and 92.7 (C-1_B, 1_F), 82.7 (C-4_B), 75.7, 74.1, 73.4, 73.3, 72.0, 70.3, and 68.4 (CH_2 of Bn and C-6_B, 6_C), 54.6 (*C*H_3O), 51.3 (C-2_B), 22.8 (*C*H_3CON), 20.35 and 20.31 (*C*H_3COO), 17.8, 17.3, and 17.2 (2 C) (C-6_A,6_D,6_E,6_F). FABMS: *m/z* 2994.028 [($C_{167}H_{164}N_4O_{48}$ + H)$^+$]. Anal. Calcd for $C_{167}H_{164}N_4O_{48}$: C, 66.97; H, 5.52; N, 1.87. Found: C, 65.20; H, 5.43; N, 1.92.

Methyl 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 (**11**).—To a solution of **39** (240 mg, 0.08 mmol) in 1,2-dimethoxyethane (0.5 mL) was added a solution of $NiCl_2 \cdot 6\ H_2O$ (0.3 g, 1.26 mmol) and H_3BO_3 (0.15 g, 2.4 mmol) in EtOH (10 mL). To this solution was added, under stirring at 25°C, a 1% solution of $NaBH_4$ in EtOH (~ 40 mL) during 1 h. The mixture was cooled to 0°C, then treated with Ac_2O (2 mL). After 10 min the volatiles were removed under diminished pressure. The residue was equilibrated between $CHCl_3$ and H_2O. The $CHCl_3$ phase was concentrated. Column chromatography of the residue (1:1 hexane–EtOAc) afforded **40** as a solid glass (105 mg, 44%). NMR ($CDCl_3$): ^{1}H, δ 6.580 and 6.290 (2 d, 2 H, $J_{NH\text{-}H\text{-}2}$ 9.5 Hz, NH_B, NH_F), 5.935 (br d, 1 H, H-4_G), 5.587 (s, 1 H, C*H*Ph), 3.293 (s, 3 H, CH_3O), 1.946 and 1.927 (2 s, 6 H, 2 CH_3CON), 1.680 and 1.634 (2 s, 6 H, 2 CH_3CO), 1.337, 1.160, 1.000, and 0.648 (4 d, 12 H, $J_{5,6}$ ~ 6.1 Hz, H-6_A,6_D,6_E,6_H); ^{13}C, δ 170.8, 170.0, 169.8, and 168.9 (*C*=O of Ac), 165.9–164.4 (*C*=O of Bz), 100.8 (*C*HPh), 99.0 (2 C), 98.6, 97.8 (2 C), 97.6, 97.4, and 93.0 (C-1_A,1_B,1_C,1_D,1_E,1_F,1_G,1_H), 83.0 (C-4_B), 54.8 (*C*H_3O), 51.5 (C-2_B), 23.0 and 22.5 (*C*H_3CON), 20.8 and 20.6 (*C*H_3COO), 18.0, 17.5 (2 C), and 17.3 (C-6_A, 6_D, 6_E, 6_H). FABMS: *m/z* 3010.059 [($C_{169}H_{168}N_2O_{49}$ + H)$^+$]. A solution of **40** in MeOH was treated with NaOMe until the pH of the solution reached ~ 12–13 at 25°C. After the 12 h the solution was neutralized with Dowex 50 × 2 (H^+) and filtered, then the volatiles were removed. The residue was purified by column chromatography, using 3:1 EtOAc–CH_3OH as eluant. The resulting material was hy-

drogenolyzed in 10:1 EtOH–AcOH on 10% Pd–C (Degussa Type E101NE/W) at 25°C for 24 h, under atmospheric pressure. The usual work-up followed by gel filtration through Biogel P-2 using 0.02 M pyridinium acetate as eluant afforded **11** as an amorphous solid; $[\alpha]_D$ +77° (*c* 0.3, H_2O). NMR (D_2O): ^1H, δ 5.600 (d, 2 H, $J_{1,2}$ 3.5 Hz, H-1_C,1_G), 5.108 (d, 1 H, $J_{1,2}$ 1.5 Hz, H-1_E), 5.081 (d, 1 H, $J_{1,2}$ 1.8 Hz, H-1_H), 5.057 (d, 1 H, $J_{1,2}$ 1.5 Hz, H-1_D), 5.042 (d, 1 H, $J_{1,2}$ 3.2 Hz, H-1_F), 4.992 (d, 1 H, $J_{1,2}$ 3.3 Hz, H-1_B), 4.714 (d, 1 H, $J_{1,2}$ 1.6 Hz, H-1_A), 3.394 (s, 3 H, CH_3O), 2.060 and 2.052 (2 s, 6 H, 2 CH_3CO), 1.350–1.290 (4 d, 12 H, H-6_A,6_D,6_E,6_H); ^{13}C, δ174.76 and 174.70, (*C*=O), 102.9, 102.2, 102.1, and 101.4 (C-1_A, 1_D, 1_E, 1_H), 98.4 (2 C) (C-1_C,1_G), 94.8 (2 C) (C-1_B,1_F), 78.8 (C-3_D), 61.5 (2 C) (C-6_C,6_G), 60.76 and 60.71 (C-6_B,6_F), 55.5 (CH_3O), 52.7 (C-2_B, 2_F), 22.8 (CH_3CON), 17.6, 17.48, 17.42, and 17.36 (C-6_A,6_D,6_E,6_H). FABMS: *m/z* 1369 $[(C_{53}H_{90}N_2O_{37} + Na)^+]$ and 1347 $[(C_{53}H_{90}N_2O_{37} + H)^+]$.

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