Synthesis and NMR spectroscopy of nine stereoisomeric 5,7-diacetamido-3,5,7,9-tetradeoxynon-2-ulosonic acids

Yury E. Tsvetkov, a,* Alexander S. Shashkov, a Yuriy A. Knirel, a Ulrich Zähringer b

a N.D. Zelinsky Institute of Organic Chemistry, Russian Academy of Sciences, Leninsky Prospekt 47, 119991 Moscow, Russian Federation
b Forschungszentrum Borstel, Zentrum für Medizin und Biowissenschaften, Parkallee 22, D-23845 Borstel, Germany

Received 28 June 2001; accepted 15 August 2001

Abstract

Derivatives of 5,7-diamino-3,5,7,9-tetradeoxynon-2-ulosonic acids are essential constituents of some bacterial polysaccharides and glycoproteins. In order to establish reliably the configuration of the natural sugars, nine stereoisomeric 5,7-diacetamido-3,5,7,9-tetradeoxynon-2-ulosonic acids were synthesized, including di-N-acetyl-legionaminic and -pseudaminic acids (the D-glycero-D-galacto and L-glycero-L-manno isomers, respectively) and their isomers at C-4, C-5, C-7, and C-8 having the L-glycero-D-galacto, D-glycero-D-talo, L-glycero-D-talo, D-glycero-L-altro, L-glycero-L-altro, D-glycero-L-manno, and L-glycero-L-gluco configurations. Synthesis was performed by condensation of 2,4-diacetamido-2,4,6-trideoxy-L-gulose, -D-mannose, -D-talose, and -D-allose with oxalacetic acid under basic conditions, the reaction of the last two precursors being accompanied by epimerisation at C-2. The 1H and 13C NMR data of the synthetic compounds are discussed. Acetylated methyl esters of the C-7 and C-8 isomeric nonulosonic acids were prepared and used for analysis of the side-chain conformation by NMR spectroscopy. © 2001 Published by Elsevier Science Ltd.

Keywords: 5,7-Diacetamido-3,5,7,9-tetradeoxynon-2-ulosonic acids, synthesis; 2,4-Diacetamido-2,4,6-trideoxyhexoses; Legionaminic acid; Pseudaminic acid; Lipopolysaccharide components

1. Introduction

N-Acyl and O-acetyl derivatives of various 5,7-diamino-3,5,7,9-tetradeoxynon-2-ulosonic acids are known as components of glycopeptides of Gram-negative bacteria, including lipopolysaccharides, a capsular polysaccharide, and glycoproteins. They play a role in immunospecificity, endow the cell surface with peculiar physicochemical properties, and are likely involved in bacterial virulence. Whereas the relative configuration within the conformationally rigid pyranose ring (C-4, 5, 6) of the higher sugars could be easily established using 1H NMR and NOE spectroscopy, reliable determination of the configuration in the flexible side chain (C-7, 8) required data from model compounds. To solve this problem, we synthesised, for the first time, nine stereoisomeric 5,7-diacetamido-3,5,7,9-tetradeoxynon-2-ulosonic acids. Synthesis of four of these sugars has been reported in preliminary communications.

* Corresponding author. Tel.: +7-95-9383686; fax: +7-95-1355328.
E-mail address: tsvetkov@ioc.ac.ru (Y.E. Tsvetkov).
2. Results and discussion

By analogy with the synthesis of N-acetylneuraminic acid, di-N-acetyl derivatives of 5,7-diamino-3,5,7,9-tetrahydroxynon-2-ulosonic acids could be obtained by condensation of 2,4-diacetamido-2,4,6-trideoxyhexoses with oxalacetic acid under basic conditions. Four chiral centers in the C₆ precursors, C-2,3,4,5, correspond to the centers C-5,6,7,8 in the target C₉ acids, and the fifth asymmetric center, C-4, is formed on condensation. 2,4-Diacetamido-2,4,6-trideoxy-L-gulose (15), -D-talose (25), -D-mannose (32), and -L-allose (48) were used as the C₆ precursors (See Schemes 1–4). They possess the same, L,L configuration at C-2 and C-3 (C-5 and C-6 in the expected C₉ acids), whereas the configurations at C-4 and C-5 vary, thus adopting all possible stereochemical combinations at C-7 and C-8 in the higher sugars (D,L; L,D; D,D; and L,L; respectively).

The 2,4-diacetamido-2,4,6-trideoxyhexoses 15, 25, 32, and 48 were synthesized as follows. L-Rhamnose, the most readily available 6-deoxyhexose, served as the progenitor of 15. Since introduction of an azido group (as a precursor of the acetamido function) is accompanied by inversion of the configuration, azidation at positions 2 and 4 would lead directly to the desirable configurations of C-2 and C-4. Hence, one additional inversion at C-3 has to be performed to achieve the target L-gulo configuration.

The prerequisite for successful S_N2 substitution of an axial sulfonate group at C-2 is that the substituent at C-1 is equatorial (see Ref. 10 and references cited therein). Therefore, benzyl β-L-rhamnopyranoside was thought to be the precursor of choice. This was prepared by Bu₂SnO-mediated benzylation of 1,2-diol 11 (Scheme 1). As expected, the reaction occurred in a regio- and stereoselective manner, though it was accompanied by migration of benzoyl protecting groups. As a result, a mixture of benzyl β-rhamnopyranoside dibenzoates 2–4 was obtained in total yield of 90–95% and 2:3:4 ratios of ~4:3:1. These compounds were separated and their structures proved by ¹H NMR spectroscopy. Most importantly, the β-configuration of 2–4 was demonstrated by a relatively high-field posi-
tion at $\delta$ 3.5–3.8 of the signal for H-5 (in $\alpha$-rhamnopyranosides H-5 would resonate at $\delta$ 4.1–4.3\(^3\)). The positions of the benzoyl groups in 2–4 were inferred from the low-field chemical shifts of the signals for H-3,4, H-2,4, and H-2,3, respectively. Debenzoylation of the mixture of 2–4 with sodium methoxide in methanol yielded 5.

Treatment of 5 with trimethyl orthoacetate in the presence of TsOH, followed by acetylation of OH-4 and hydrolytic opening of the orthoester ring in the 2,3-orthoester, yielded 2,4-diacetate 6. Low-field positions of the signals for H-2 and H-4 in the $^1H$ NMR spectrum proved the location of the acetyl groups in 6. Reaction of 6 with triflic anhydride in the presence of pyridine led to triflate 7, which readily gave the 3,4-anhydro-L-altroside 8 on treatment with sodium methoxide in methanol. The structure of 8, particularly the position of the epoxy group, was confirmed by NMR analysis of 8 and its acetate 9. The transformation of 8 into 9 resulted in a downfield shift of the signal for H-2 ($\delta$ 4.02 →
5.25), thus indicating the position of the hydroxy group in 8. This finding excluded conversion of the 3,4-L-altro-epoxide into the 2,3-L-manno-isomer that might proceed under basic conditions. Compound 8 had the necessary configuration of C-3, a free OH-2 group required for subsequent introduction of an azido group, and a 3,4-epoxy function suitable for introduction of the second azido group at position 4.

As anticipated, conversion of 8 into triflate 10 and subsequent reaction with sodium azide in DMF resulted in a high yield of azide 11. A large $J_{1,2}$ coupling constant value of 7.6 Hz in the $^1$H NMR spectrum of 11 showed that the azido group was pseudo-equatorial. Opening of the epoxide ring in 11 by treatment with sodium azide in the presence of ammonium chloride in boiling aqueous ethanol furnished diazide 12. Large $J_{1,2}$ and small $J_{2,3}$, $J_{3,4}$, and $J_{4,5}$ coupling constant values in the $^1$H NMR spectra of 12 and the derived acetate 13 were in accordance with the β-L-gulo configuration. Chemical shifts for H-2 ($\delta$ 3.69), H-3 ($\delta$ 5.33), and H-4 ($\delta$ 3.48) in the spectrum of 13 demonstrated that the azido groups were at C-2 and C-4. Hydrogenolysis of 12 over Pd(OH)$_2$/C reduced the azido groups, whereas the benzyl group remained intact (compare published data). Following N-acetylation, hydrogenolysis of the diacetamido derivative 14 proceeded smoothly providing the target sugar 15 in high yield. According to $^1$H NMR data, 15 exists in aqueous solution in the pyranose form as a mixture of α- and β-anomers in a ratio of ~1:5.

2-Azido-2-deoxy derivative 16 was used as a starting compound for preparation of 2,4-di-acetamido-2,4,6-trideoxy-D-talose (25).
Table 1
NMR data for 2,4-diacetamido-2,4,6-trideoxy-\(\alpha\)-talose 25 (D\(_2\)O, 30 °C)

<table>
<thead>
<tr>
<th>Form</th>
<th>(\alpha)-25p</th>
<th>(\beta)-25p</th>
<th>(\alpha)-25f</th>
<th>(\beta)-25f</th>
</tr>
</thead>
<tbody>
<tr>
<td>Content (%)</td>
<td>1H NMR data</td>
<td>13C NMR data</td>
<td>1H NMR data</td>
<td>13C NMR data</td>
</tr>
<tr>
<td></td>
<td>((J_{1,2}),(\delta))</td>
<td>((J_{1,2}),(\delta))</td>
<td>((J_{1,2}),(\delta))</td>
<td>((J_{1,2}),(\delta))</td>
</tr>
<tr>
<td>(\alpha)-25p</td>
<td>5.18 (4.12)</td>
<td>4.43 (4.18)</td>
<td>1.18 (4.43)</td>
<td>94.2 (52.8)</td>
</tr>
<tr>
<td>(18)</td>
<td>(4.24)</td>
<td>(4.12)</td>
<td>(4.24)</td>
<td>66.7 (52.7)</td>
</tr>
<tr>
<td>(\beta)-25p</td>
<td>4.97 (4.36)</td>
<td>3.91 (4.12)</td>
<td>1.18 (4.43)</td>
<td>94.6 (53.4)</td>
</tr>
<tr>
<td>(32)</td>
<td>(4.12)</td>
<td>(4.12)</td>
<td>(4.12)</td>
<td>69.6 (52.0)</td>
</tr>
<tr>
<td>(\alpha)-25f</td>
<td>5.38 (4.51)</td>
<td>4.04 (4.09)</td>
<td>1.24 (4.04)</td>
<td>86.9 (60.9)</td>
</tr>
<tr>
<td>major</td>
<td>(5.0)</td>
<td>(4.29)</td>
<td>(4.09)</td>
<td>71.6 (70.6)</td>
</tr>
<tr>
<td>(20)</td>
<td>(4.2)</td>
<td>(4.29)</td>
<td>(4.09)</td>
<td>69.0 (60.5)</td>
</tr>
<tr>
<td>(\beta)-25f</td>
<td>5.47 (4.38)</td>
<td>3.91 (4.25)</td>
<td>1.33 (3.91)</td>
<td>84.9 (59.9)</td>
</tr>
<tr>
<td>major</td>
<td>(5.0)</td>
<td>(4.25)</td>
<td>(4.25)</td>
<td>72.1 (71.3)</td>
</tr>
<tr>
<td>(14)</td>
<td>(4.8)</td>
<td>(4.25)</td>
<td>(4.25)</td>
<td>73.9 (73.8)</td>
</tr>
<tr>
<td>(\alpha)-25f</td>
<td>5.51 (4.45)</td>
<td>4.16 (4.31)</td>
<td>1.11 (4.16)</td>
<td>82.0 (55.0)</td>
</tr>
<tr>
<td>minor</td>
<td>(5.6)</td>
<td>(4.31)</td>
<td>(4.31)</td>
<td>71.3 (70.5)</td>
</tr>
<tr>
<td>(13.5)</td>
<td>(4.9)</td>
<td>(4.31)</td>
<td>(4.31)</td>
<td>75.0 (74.7)</td>
</tr>
<tr>
<td>(\beta)-25f</td>
<td>5.58 (4.38)</td>
<td>3.77 (4.25)</td>
<td>1.25 (3.77)</td>
<td>80.0 (53.4)</td>
</tr>
<tr>
<td>minor</td>
<td>(6.2)</td>
<td>(4.25)</td>
<td>(4.25)</td>
<td>72.8 (71.9)</td>
</tr>
<tr>
<td>(2.5)</td>
<td>(4.3)</td>
<td>(4.25)</td>
<td>(4.25)</td>
<td>71.9 (71.9)</td>
</tr>
</tbody>
</table>

Oxygcnation at C-6 and introduction of an amino function with inversion of the configuration at C-4 had to be carried out to obtain the desired structure. To this aim, the benzylidene group in 16 was removed by treatment with pyridinium perchlorate\(^{18}\) in aqueous acetonitrile (Scheme 2). Selective tosylation of the resulting diol 17, followed by substitution of the toslyoxy group in 18 with iodide, afforded the 6-iodo derivative, 19. Simultaneous reduction of the azido group and deiodination without affecting the benzyl protective groups occurred on hydrogenation over Pd(OH)\(_2\)/C in the presence of \(N,N\)-diisopropylethylamine. Following N-acetylation, the 2-acetamido-2,6-dideoxy derivative 20 was obtained in 84% yield. The use of LiAlH\(_4\) in THF for reduction of 19 was less effective giving only 49% of 20. A direct S\(_\text{N}2\) substitution at C-4 in the manno series is known to be complicated;\(^{19}\) therefore, the reaction sequence oxidation-oximation-reduction was applied to introduce the second amino group into 20. Swern oxidation of 20 gave the ketone 21, which was converted, without isolation, into the oxime 22. Reduction of the latter with NaBH\(_4\)–NiCl\(_2\) in methanol at \(-35 \degree C\)\(^{20}\) and subsequent N-acetylation gave a mixture of talo and manno isomers 23 and 24 in a ratio of 8:1. The structures of 23 and 24 were proved by \(^1\)H NMR spectroscopy. Large \(J_{3,4}\) and \(J_{4,5}\) coupling constant values (each of \(~10 \text{ Hz}\)) and a small \(J_{2,3}\) value (4.2 Hz) showed 24 to have the manno configuration. No well-resolved spectrum could be obtained for 23 even at elevated temperatures that could be accounted for by a restricted internal rotation of spatially close axial acetamido groups at C-2 and C-4 and the 3-\(O\)-benzyl group. Nevertheless, based on the line width for H-3 and H-5, it was concluded that \(J_{2,3}\) and \(J_{3,4}\) coupling constant values did not exceed 4 Hz and \(J_{4,5}\) was less than 2 Hz. These data were in good agreement with the expected talo configuration of 23.\(^{21}\) Hydrogenolysis of 23 over Pd(OH)\(_2\)/C afforded the target hexose 25.

The behaviour of 25 in aqueous solution is noteworthy. The \(^1\)H and \(^{13}\)C NMR spectra of 25, which were assigned using 2D COSY, TOCSY, and HSQC techniques (Table 1), contained six anomeric signals. Comparison with published data for talopyranose and its derivatives, including \(^{13}\)C NMR chemical shifts and coupling constant values,\(^{21,22}\) enabled identification of \(\alpha\)- and \(\beta\)-pyranoses \(\alpha\)-25p and \(\beta\)-25p. The four other signals belonged to \(\alpha\)- and \(\beta\)-furanoses \(\alpha\)-25f and \(\beta\)-25f, as followed from the coupling constant values (compare published data\(^{23}\)) and characteristic changes in the \(^{13}\)C NMR chemical shifts, especially those for C-1 and C-4, compared to the data of talofuranose\(^{22}\) and 25p (Table 1). Each of \(\alpha\)-25f and \(\beta\)-25f existed as two stereoisomers (\(E\) and \(Z\)) at the 4-acetamido group,\(^{24}\) which were not assigned, and designated as major and minor (Table 1). The
1H NMR signals for the stereoisomers within each anomic pair coalesced when the spectrum was run at 90 °C. Therefore, 2,4-diacetamido-2,4,6-trideoxy-D-talose (25) represents a rare example of a 4-acylamino-4-deoxyhexose that exists in aqueous solution exclusively in the pyranose form (32) and small 1,3-diaxial interaction of the acetamido groups.

2,4-Diacetamido-2,4,6-trideoxy-D-mannose (32) was prepared from benzyl β-D-fucopyranoside (26)25 using at the key step the known approach to β-mannosides based on simultaneous substitution with inversion at positions 2 and 4 in β-galactosides26 (Scheme 3). Bu₃SnO-mediated selective benzylation of 26 gave 3-benzoate 27, as followed from a low-field position of the signal for H-3 in the 1H NMR spectrum. Conversion of 27 into triflate 28 and its subsequent reaction with tetra-butylammonium azide in toluene resulted in diazide 29 in high yield. Large J₃,4 and J₄,5 coupling constant values (each of ~10 Hz) and small J₁,₂ and J₂,₃ values (<1 and 2.5 Hz, respectively) in the 1H NMR spectrum confirmed the manno configuration of 29. Conventional debenzylation of 29 afforded 30. Further transformations of 30 were similar to those described above in synthesis of 15 and included reduction of the azido groups by hydrogenation, N-acetylation (30 → 31), and removal of the benzyl protecting group (31 → 32). According to NMR data, the hexose 32 exists in aqueous solution exclusively in the pyranose form (α,β ratio ~1:1). Benzy l β-L-rhamnopurranoside 5 was chosen as the starting compound for preparation of 2,4-diacetamido-2,4,6-trideoxy-L-allose (48). To provide the proper D configuration at C-4, which would lead to the necessary L configuration on azidation, the L-rhamnoside 5 was converted into L-taloside 35 (Scheme 4). Conventional isopropylideneation of 5 gave 33, which was subjected to the known oxidations—reduction procedure to afford, via ketone 34, L-taloside 35 in nearly quantitative yield. In an attempt to apply the same approach that was successively used for the synthesis of the manno isomer 32, the isopropylidene group was removed and the resulting triol 36 was selectively benzyolated via dibutylstannylene derivative to yield monobenzoate 37. However, instead of the expected diazide 39, reaction of 2,4-ditriflate 38 obtained from 37 with tetra-butylammonium azide gave a complex mixture of products that was not further investigated. Therefore, another approach based on a consecutive introduction of azido groups to positions 4 and 2 was exploited. Azidation of 4-triflate 40 with sodium azide in DMF in the presence of a crown ether28 furnished azide 41 with the necessary configuration of C-4. To liberate HO-2 for introduction of the second azido group, 41 was subjected to deacetalation followed by Bu₃SnO-mediated selective 3-O-benzyolation of diol 42. Monobenzoate 43 thus obtained was converted into triflate 44, which was then converted to the target diazide 39 by reaction with sodium azide in DMF. Large values of all coupling constants in the 1H NMR spectrum proved unambiguously the L-gluco configuration of 39. LiAlH₄ reduction of azido groups in 39 with concomitant removal of the benzyl group and subsequent N-acetylation resulted in the diacetamido derivative 45. Mesitylation of 45 afforded mesylate 46. Inversion of the configuration at C-3 mediated by participation of a neighbouring acetamido group(s) was achieved by heating of 46 in aqueous 2-methoxyethanol in the presence of sodium acetate16 to give the L-allo derivative 47 in high yield. The configuration of 47 was confirmed by large J₁,₂ and J₄,₅ coupling constant values (8.6 and 10.2 Hz) and small J₂,₃ and J₃,₄ values (2.8 and 2.3 Hz, respectively). Conventional removal of the anumeric benzyl group afforded hexose 48, which occurred in the pyranose form (α,β ratio of 1:3.3, NMR data).

Condensation of compounds 15, 25, 32, and 48 with oxalacetic acid was performed in the presence of sodium tetraborate at pH 10.59 (Scheme 5). Acidic reaction products were isolated by anion exchange chromatography, and the individual isomers of 5,7-diacetamido-3,5,7,9-tetraoxynon-2-ulosonic acids were separated by reversed-phase C₁₈ HPLC.
Scheme 5. Reagents and conditions: i, oxalacetic acid, Na₂B₄O₇, pH 10.5, rt Only main isomers of acids 49–57 with an equatorial carboxyl group are shown.

Compounds 15 and 32 with the threeo configuration of the fragment C-3–C-4 afforded pairs of epimers at C-4 having the L-glycero-D-galacto/D-talo (49/50) and D-glycero-D-galacto/D-talo (53/54) configurations, respectively, in a nearly 1:1 ratio. Compounds 25 and 48 with the erythro configuration of the fragment C-3–C-4 gave the equatorial HO-4 epimers having the D-glycero-L-altro (51) and L-glycero-L-altro (55) configuration, respectively, with no axial HO-4 epimers. The reason for this unexpected stereoselectivity is not clear. In addition to 51 and 55, compounds 25 and 48 afforded, as minor products, isomeric nonulosonic acids with an axial AcNH-5 group having the D-glycero-L-manno (52), L-glycero-L-manno (56), and L-glycero-L-gluco (57) configuration. They evidently resulted from epimerisation at C-2 in the starting monosaccharides prior to condensation.

The structures of the synthesised acids were proved by ESIMS and NMR spectral data. Major peaks corresponding to either [M + Na]⁺ (positive mode) or [M − H]⁻ (negative mode) pseudomolecular ions were observed in the ESIMS spectra of 49–57. The data of the ¹H and ¹³C NMR spectra of both free acids and sodium salts are given in Tables 2 and 3.

They demonstrated the pyranose form of all sugars, which existed in aqueous solution as mixtures of anomers with a high predominance of the anomer having an equatorial carboxyl group (β for 49, 50, 53, and 54, and α for 51, 52, 55–57). The ratios of the free acids anomers are given in Table 2. The configuration within the pyranose ring followed from the ³ J H,H coupling constant values determined from the ¹H NMR spectra. Large ³ J 3a,4, ³ J 4,5, and ³ J 5,6 values for 49, 51, 53, and 55 indicated equatorial substituents at C-4, C-5, and C-6. Large ³ J 5,6 and small ³ J 3a,4 and ³ J 4,5 values for 50 and 54 showed that the OH-4 group is axial. In contrast, large ³ J 3a,4 and small ³ J 4,5 and ³ J 5,6 values for 52 and 56 confirmed the axial orientation of the AcNH-5 group. Finally, small ³ J 3a,4, ³ J 4,5, and ³ J 5,6 values for 57 demonstrated that both OH-4 and AcNH-5 are axial.

Four of the synthesised isomers occur in nature. These are the D-glycero-D-galacto and L-glycero-L-manno isomers called legionaminic³,⁸ and pseudaminic¹ acid, respectively, as well as C-4 and C-8 epimers of legionaminic acid having the D-glycero-D-talo and L-glycero-D-galacto configuration (4- and
Table 2

<table>
<thead>
<tr>
<th>Compound</th>
<th>( \alpha: \beta ) ratio</th>
<th>Form</th>
<th>H-3e ((J_{3b,3a}))</th>
<th>H-3a ((J_{3a,4}))</th>
<th>H-4 ((J_{4b,4a}))</th>
<th>H-5 ((J_{5b,5a}))</th>
<th>H-6 ((J_{6b,6a}))</th>
<th>H-7 ((J_{7b,7a}))</th>
<th>H-8</th>
<th>H-9</th>
<th>CH(_2)CON</th>
</tr>
</thead>
<tbody>
<tr>
<td>49(^a)</td>
<td>1:19 H</td>
<td>2.69</td>
<td>1.71</td>
<td>3.82</td>
<td>3.67</td>
<td>3.85</td>
<td>3.93</td>
<td>4.00</td>
<td>1.20</td>
<td>1.98, 2.02</td>
<td></td>
</tr>
<tr>
<td>49(^a)</td>
<td>1:19 Na</td>
<td>2.62</td>
<td>1.61</td>
<td>3.83</td>
<td>3.63</td>
<td>3.82</td>
<td>3.90</td>
<td>3.98</td>
<td>1.17</td>
<td></td>
<td></td>
</tr>
<tr>
<td>49(^b)</td>
<td>1:19 H</td>
<td>3.22</td>
<td>1.86</td>
<td>3.95</td>
<td>3.73</td>
<td>4.16</td>
<td>3.95</td>
<td>3.91</td>
<td>1.18</td>
<td>1.96, 2.00</td>
<td></td>
</tr>
<tr>
<td>49(^b)</td>
<td>1:19 Na</td>
<td>2.20</td>
<td>1.79</td>
<td>3.89</td>
<td>3.70</td>
<td>4.06</td>
<td>3.89</td>
<td>3.90</td>
<td>1.15</td>
<td>1.97, 2.01</td>
<td></td>
</tr>
<tr>
<td>50(^a)</td>
<td>1:8 H</td>
<td>2.65</td>
<td>1.94</td>
<td>4.08</td>
<td>3.84</td>
<td>4.47</td>
<td>3.89</td>
<td>4.08</td>
<td>1.28</td>
<td>1.96, 2.04</td>
<td></td>
</tr>
<tr>
<td>50(^b)</td>
<td>1:8 Na</td>
<td>2.40</td>
<td>2.03</td>
<td>3.97</td>
<td>3.84</td>
<td>4.26</td>
<td>3.87</td>
<td>3.95</td>
<td>1.18</td>
<td></td>
<td></td>
</tr>
<tr>
<td>50(^b)</td>
<td>1:8 H</td>
<td>2.18 (a)</td>
<td>2.13 (a)</td>
<td>4.11</td>
<td>3.89</td>
<td>4.48</td>
<td>3.95</td>
<td>3.96</td>
<td>1.21</td>
<td>1.97, 2.01</td>
<td></td>
</tr>
<tr>
<td>50(^b)</td>
<td>1:8 Na</td>
<td>2.10 (a)</td>
<td>2.06 (a)</td>
<td>4.09</td>
<td>3.88</td>
<td>4.42</td>
<td>3.90</td>
<td>3.98</td>
<td>1.20</td>
<td>1.97, 2.01</td>
<td></td>
</tr>
<tr>
<td>51(^b)</td>
<td>13.3:1 H</td>
<td>2.71</td>
<td>1.75</td>
<td>3.82</td>
<td>3.81</td>
<td>3.56</td>
<td>3.91</td>
<td>4.40</td>
<td>1.08</td>
<td></td>
<td></td>
</tr>
<tr>
<td>51(^b)</td>
<td>13.3:1 Na</td>
<td>2.70</td>
<td>1.68</td>
<td>3.75</td>
<td>3.79</td>
<td>3.42</td>
<td>3.93</td>
<td>4.41</td>
<td>1.05</td>
<td></td>
<td></td>
</tr>
<tr>
<td>51(^b)</td>
<td>13.3:1 H</td>
<td>2.34</td>
<td>1.93</td>
<td>3.99</td>
<td>3.86</td>
<td>3.90</td>
<td>3.92</td>
<td>4.42</td>
<td>1.08</td>
<td>2.06</td>
<td></td>
</tr>
<tr>
<td>51(^b)</td>
<td>13.3:1 Na</td>
<td>2.24</td>
<td>1.86</td>
<td>3.95</td>
<td>3.83</td>
<td>3.83</td>
<td>3.89</td>
<td>4.43</td>
<td>1.05</td>
<td>2.05</td>
<td></td>
</tr>
<tr>
<td>51(^b)</td>
<td>13.3:1 H</td>
<td>2.32</td>
<td>1.79</td>
<td>3.89</td>
<td>3.70</td>
<td>4.06</td>
<td>3.89</td>
<td>3.90</td>
<td>1.15</td>
<td>1.97, 2.01</td>
<td></td>
</tr>
<tr>
<td>51(^b)</td>
<td>13.3:1 Na</td>
<td>2.22</td>
<td>1.91</td>
<td>3.93</td>
<td>3.82</td>
<td>3.85</td>
<td>3.88</td>
<td>4.39</td>
<td>1.06</td>
<td>2.05</td>
<td></td>
</tr>
<tr>
<td>52(^b)</td>
<td>12.5:1 H</td>
<td>2.50</td>
<td>1.64</td>
<td>4.10</td>
<td>4.22</td>
<td>4.14</td>
<td>4.13</td>
<td>4.36</td>
<td>2.45</td>
<td>1.10</td>
<td></td>
</tr>
<tr>
<td>52(^b)</td>
<td>12.5:1 Na</td>
<td>2.50</td>
<td>1.64</td>
<td>4.10</td>
<td>4.22</td>
<td>4.14</td>
<td>4.13</td>
<td>4.36</td>
<td>2.45</td>
<td>1.10</td>
<td></td>
</tr>
<tr>
<td>52(^a)</td>
<td>12.5:1 H</td>
<td>2.03</td>
<td>1.82</td>
<td>4.25</td>
<td>4.29</td>
<td>4.27</td>
<td>3.82</td>
<td>4.12</td>
<td>1.09</td>
<td></td>
<td></td>
</tr>
<tr>
<td>52(^a)</td>
<td>12.5:1 Na</td>
<td>1.99</td>
<td>1.79</td>
<td>4.18</td>
<td>4.24</td>
<td>4.19</td>
<td>3.77</td>
<td>4.12</td>
<td>1.07</td>
<td></td>
<td></td>
</tr>
<tr>
<td>53(^b)</td>
<td>1:18 H</td>
<td>2.73</td>
<td>1.71</td>
<td>3.82</td>
<td>3.68</td>
<td>3.93</td>
<td>3.94</td>
<td>1.16</td>
<td>1.97</td>
<td></td>
<td></td>
</tr>
<tr>
<td>53(^b)</td>
<td>1:18 Na</td>
<td>2.75</td>
<td>1.61</td>
<td>3.66</td>
<td>3.67</td>
<td>3.77</td>
<td>3.82</td>
<td>3.93</td>
<td>1.16</td>
<td>1.95</td>
<td></td>
</tr>
<tr>
<td>53(^b)</td>
<td>1:18 H</td>
<td>2.31</td>
<td>1.87</td>
<td>3.98</td>
<td>3.72</td>
<td>4.31</td>
<td>3.91</td>
<td>3.85</td>
<td>1.16</td>
<td>1.99, 2.00</td>
<td></td>
</tr>
<tr>
<td>53(^b)</td>
<td>1:18 Na</td>
<td>2.19</td>
<td>1.82</td>
<td>3.94</td>
<td>3.70</td>
<td>4.23</td>
<td>3.85</td>
<td>3.85</td>
<td>1.15</td>
<td>1.99, 2.00</td>
<td></td>
</tr>
<tr>
<td>54(^a)</td>
<td>1:5.4 H</td>
<td>2.69</td>
<td>1.94</td>
<td>4.10</td>
<td>3.86</td>
<td>4.55</td>
<td>3.88</td>
<td>4.00</td>
<td>1.20</td>
<td>1.96, 2.00</td>
<td></td>
</tr>
<tr>
<td>54(^b)</td>
<td>1:5.4 Na</td>
<td>2.54</td>
<td>1.95</td>
<td>4.02</td>
<td>3.85</td>
<td>4.42</td>
<td>3.82</td>
<td>3.93</td>
<td>1.16</td>
<td>1.96</td>
<td></td>
</tr>
<tr>
<td>54(^b)</td>
<td>1:5.4 H</td>
<td>2.19</td>
<td>2.14</td>
<td>4.13</td>
<td>3.90</td>
<td>4.63</td>
<td>3.92</td>
<td>3.92</td>
<td>1.18</td>
<td>1.98, 1.99</td>
<td></td>
</tr>
<tr>
<td>54(^b)</td>
<td>1:5.4 Na</td>
<td>2.11</td>
<td>2.07</td>
<td>4.10</td>
<td>3.88</td>
<td>4.56</td>
<td>3.86</td>
<td>3.91</td>
<td>1.17</td>
<td>1.98, 1.99</td>
<td></td>
</tr>
<tr>
<td>55(^b)</td>
<td>8:3:1 H</td>
<td>2.70</td>
<td>1.72</td>
<td>3.79</td>
<td>3.85</td>
<td>3.57</td>
<td>4.13</td>
<td>4.07</td>
<td>1.21</td>
<td></td>
<td></td>
</tr>
<tr>
<td>55(^b)</td>
<td>8:3:1 Na</td>
<td>2.61</td>
<td>1.61</td>
<td>3.81</td>
<td>3.82</td>
<td>3.54</td>
<td>4.08</td>
<td>4.06</td>
<td>1.19</td>
<td>2.03, 2.05</td>
<td></td>
</tr>
</tbody>
</table>

\(^{a}\) Ref. 243228.
8-epilegionaminic acid, respectively). Using the synthetic models 53, 54, and 49, the configurations of legionaminic, 4- and 8-epilegionaminic acids were confirmed in some bacterial polysaccharides and revised in others.8

The 1H and 13C NMR spectroscopy and specific optical rotation data of the compound 56 fitted reasonably well those of pseudaminic acid derivatives isolated from bacterial polysaccharides4,29, thus confirming the L-glycero-L-manno configuration of the natural monosaccharide.

Comparison of the NMR data of various isomers (Tables 2 and 3, free acids) revealed several regularities, which can be useful for determination of the configuration of naturally occurring compounds of this class. Thus, the J6,7 coupling constant is dependent on the configuration at C-5: it is small (1.3–3.3 Hz) when AcNH-5 is equatorial (49–51, 53–55) and large (10.1–10.7 Hz) when it is axial (52, 56, 57), indicating the syn (gauche)- and trans-like relationship for H-6 and H-7, respectively. In the D-galacto and D-talo isomers, when C-8 had the D configuration (53, 54), the C-6 and C-8 signals appeared upfield by 2.0–2.3 and 1.4–2.0 ppm, respectively, compared to the corresponding L epimers (49, 50). In the L-manno isomers, a significant difference was observed for the C-9 signal, which appeared at 20.0 ppm in the D epimer (52) at C-8 but at 16.7 ppm in the L epimer (56).

The chemical shifts are influenced also by the anomeric configuration. In the sugars with an equatorial OH-4 (49, 51–53, 55, 56), the difference between the 1H NMR resonances for H-3eq and H-3ax was 0.86–1.02 ppm for the anomer with an axial carboxyl group but only 0.21–0.46 ppm for the other anomer, independently of whether AcNH-5 is axial or equatorial. When OH-4 was axial and AcNH-5 equatorial (50, 54), a typical difference of 0.71–0.75 or 0.05 ppm was observed for the anomers with an axial or an equatorial carboxyl group, respectively. In the 13C NMR spectra, the clearest dependence was shown by the C-3 and C-6 resonances. Compared to the other anomer, in the anomer with an axial carboxyl group they both appeared upfield by 0.8–1.3 and 1.6–2.9 ppm when OH-4 was equatorial (49, 51–53, 55, 56) or by 2.3–2.6 and 3.8–4.7 ppm, respectively, when OH-4 was axial (50, 54, 57).

For conformational studies by NMR spectroscopy, the L-glycero-D-galacto (49), D-glycero-L-altro (51), D-glycero-D-galacto (53), and

<table>
<thead>
<tr>
<th>Compound</th>
<th>z:β ratio</th>
<th>Form</th>
<th>H-3e (J3eq)</th>
<th>H-3a (J3ax)</th>
<th>H-4 (J4ax)</th>
<th>H-5 (J5ax)</th>
<th>H-6 (J6ax)</th>
<th>H-7 (J7ax)</th>
<th>H-8 (J8ax)</th>
<th>H-9 (J9ax)</th>
<th>CH3CON</th>
</tr>
</thead>
<tbody>
<tr>
<td>55α</td>
<td>H</td>
<td>2.32</td>
<td>1.93</td>
<td>3.94</td>
<td>3.91</td>
<td>3.94</td>
<td>4.16</td>
<td>4.06</td>
<td>1.18</td>
<td>2.04, 2.08</td>
<td></td>
</tr>
<tr>
<td></td>
<td>(13.3)</td>
<td>(12.5)</td>
<td>(4.4)</td>
<td>(10.2)</td>
<td>(10.2)</td>
<td>(2.8)</td>
<td>(5.8)</td>
<td>(6.4)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>55α</td>
<td>Na</td>
<td>2.21</td>
<td>1.89</td>
<td>3.89</td>
<td>3.88</td>
<td>3.84</td>
<td>4.13</td>
<td>4.08</td>
<td>1.16</td>
<td>2.02, 2.07</td>
<td></td>
</tr>
<tr>
<td></td>
<td>(13.2)</td>
<td>(11.3)</td>
<td>(4.3)</td>
<td></td>
<td>(11.0)</td>
<td>(3.0)</td>
<td>(6.0)</td>
<td>(6.3)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>56β</td>
<td>7.5:1</td>
<td>H</td>
<td>2.48</td>
<td>1.62</td>
<td>4.08</td>
<td>4.29</td>
<td>3.96</td>
<td>4.15</td>
<td>4.18</td>
<td>1.12</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>(13.0)</td>
<td>(12.9)</td>
<td>(4.7)</td>
<td>(3.6)</td>
<td>(2.4)</td>
<td>(10.5)</td>
<td>(3.4)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>56β</td>
<td>Na</td>
<td>2.41</td>
<td>1.55</td>
<td>4.08</td>
<td>4.26</td>
<td>3.75</td>
<td>4.01</td>
<td>4.04</td>
<td>1.125</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>(13.1)</td>
<td>(12.2)</td>
<td>(4.9)</td>
<td>(3.7)</td>
<td>(&lt;2)</td>
<td>(10.5)</td>
<td>(3.4)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>56α</td>
<td>H</td>
<td>2.01</td>
<td>1.80</td>
<td>4.20</td>
<td>4.27</td>
<td>4.08</td>
<td>4.17</td>
<td>4.10</td>
<td>1.10</td>
<td>1.90, 2.01</td>
<td></td>
</tr>
<tr>
<td></td>
<td>(12.8)</td>
<td>(12.0)</td>
<td>(4.6)</td>
<td>(3.7)</td>
<td>(&lt;2)</td>
<td>(10.7)</td>
<td>(3.3)</td>
<td>(6.5)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>56α</td>
<td>Na</td>
<td>1.92</td>
<td>1.78</td>
<td>4.16</td>
<td>4.24</td>
<td>4.02</td>
<td>4.13</td>
<td>4.11</td>
<td>1.11</td>
<td>1.97, 2.00</td>
<td></td>
</tr>
<tr>
<td></td>
<td>(13.2)</td>
<td>(12.0)</td>
<td>(5.2)</td>
<td>(3.7)</td>
<td>(1.0)</td>
<td>(10.7)</td>
<td>(3.3)</td>
<td>(6.5)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>57β</td>
<td>4:1</td>
<td>H</td>
<td>2.48</td>
<td>1.92</td>
<td>4.00</td>
<td>3.85</td>
<td>4.36</td>
<td>4.15</td>
<td>4.24</td>
<td>1.21, 1.95, 1.99</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>(14.8)</td>
<td>(2.9)</td>
<td>(3.1)</td>
<td>(2.6)</td>
<td>(2.2)</td>
<td>(10.3)</td>
<td>(4.0)</td>
<td>(6.5)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>57β</td>
<td>Na</td>
<td>2.22</td>
<td>1.97</td>
<td>3.90</td>
<td>3.82</td>
<td>4.16</td>
<td>4.16</td>
<td>4.08</td>
<td>1.11</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>(15.2)</td>
<td>(3.7)</td>
<td>(3.3)</td>
<td>(2.1)</td>
<td>(10.5)</td>
<td>(3.5)</td>
<td>(6.6)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>57α</td>
<td>H</td>
<td>1.95</td>
<td>2.13</td>
<td>4.00</td>
<td>3.91</td>
<td>4.42</td>
<td>4.22</td>
<td>4.16</td>
<td>1.15</td>
<td>1.97, 1.98</td>
<td></td>
</tr>
<tr>
<td></td>
<td>(15.2)</td>
<td>(3.6)</td>
<td>(3.3)</td>
<td>(2.1)</td>
<td>(10.5)</td>
<td>(4.0)</td>
<td>(6.5)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>57α</td>
<td>Na</td>
<td>1.85</td>
<td>2.09</td>
<td>3.97</td>
<td>3.88</td>
<td>4.42</td>
<td>4.17</td>
<td>4.17</td>
<td>1.14</td>
<td>1.97, 1.98</td>
<td></td>
</tr>
<tr>
<td></td>
<td>(15.2)</td>
<td>(3.6)</td>
<td>(3.3)</td>
<td>(2.1)</td>
<td>(10.5)</td>
<td>(4.0)</td>
<td>(6.5)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* Assignment could be interchanged.
The L- and D-glycero-D-galacto esters (55) isomers were converted to methyl esters (58–61) and then acetylated to 2,4,8-tri-O-acetyl derivatives (62–65), respectively. These compounds were more convenient to analyze than the free acids because of a wider range of 1H NMR chemical shifts and easier observation of signals for NH protons.

The L- and D-glycero-D-galacto esters (58 and 60) afforded mixtures of α- and β-acetates, 62 and 64, in a 1:1 ratio. The D- and L-glycero-L-altro esters (59 and 61), which differed from 58 and 60 in the configuration of C-7, gave predominantly α-acetates (α:β ratios were 13:1 for 63 and 65, respectively). The anomeric configurations in 62–65 were assigned based on the 1H and 13C NMR data (Table 4) by analogy with anomers of methyl N-acetylneuraminic pentaacetate. The $J_{HH}$ coupling constant values in the acetates 62–65 and the parent free acids were essentially the same, and, hence, O-acetylation did not significantly change the conformation of the molecules.

### Table 3

<table>
<thead>
<tr>
<th>Form</th>
<th>C-1</th>
<th>C-2</th>
<th>C-3</th>
<th>C-4</th>
<th>C-5</th>
<th>C-6</th>
<th>C-7</th>
<th>C-8</th>
<th>C-9</th>
<th>CH$_3$CON</th>
<th>CH$_3$CON</th>
</tr>
</thead>
<tbody>
<tr>
<td>49α</td>
<td>H</td>
<td>173.1</td>
<td>97.3</td>
<td>41.2</td>
<td>68.9</td>
<td>53.7</td>
<td>75.2</td>
<td>54.4</td>
<td>69.4</td>
<td>19.8</td>
<td></td>
</tr>
<tr>
<td>49α</td>
<td>Na</td>
<td>176.7</td>
<td>98.2</td>
<td>41.7</td>
<td>69.7</td>
<td>54.2</td>
<td>75.2</td>
<td>54.4</td>
<td>70.1</td>
<td>19.8</td>
<td></td>
</tr>
<tr>
<td>49β</td>
<td>H</td>
<td>174.3</td>
<td>96.5</td>
<td>40.4</td>
<td>68.3</td>
<td>54.1</td>
<td>72.9</td>
<td>54.4</td>
<td>69.3</td>
<td>19.8</td>
<td></td>
</tr>
<tr>
<td>49β</td>
<td>Na</td>
<td>177.3</td>
<td>97.5</td>
<td>40.8</td>
<td>68.6</td>
<td>54.2</td>
<td>72.9</td>
<td>54.4</td>
<td>69.7</td>
<td>19.8</td>
<td></td>
</tr>
<tr>
<td>50α</td>
<td>H</td>
<td>176.1</td>
<td>96.5</td>
<td>38.9</td>
<td>66.7</td>
<td>50.4</td>
<td>72.2</td>
<td>54.9</td>
<td>19.9</td>
<td></td>
<td></td>
</tr>
<tr>
<td>50α</td>
<td>Na</td>
<td>176.1</td>
<td>96.5</td>
<td>38.9</td>
<td>66.7</td>
<td>50.4</td>
<td>72.2</td>
<td>54.9</td>
<td>19.9</td>
<td></td>
<td></td>
</tr>
<tr>
<td>50β</td>
<td>H</td>
<td>174.5</td>
<td>96.1</td>
<td>37.7</td>
<td>66.9</td>
<td>50.0</td>
<td>68.5</td>
<td>54.9</td>
<td>69.2</td>
<td>19.9</td>
<td></td>
</tr>
<tr>
<td>50β</td>
<td>Na</td>
<td>177.3</td>
<td>97.1</td>
<td>37.8</td>
<td>67.4</td>
<td>50.1</td>
<td>68.7</td>
<td>54.7</td>
<td>69.7</td>
<td>19.9</td>
<td></td>
</tr>
<tr>
<td>51α</td>
<td>H</td>
<td>172.9</td>
<td>97.2</td>
<td>41.1</td>
<td>68.7</td>
<td>54.7</td>
<td>77.3</td>
<td>54.3</td>
<td>66.5</td>
<td>20.0</td>
<td></td>
</tr>
<tr>
<td>51α</td>
<td>Na</td>
<td>175.6</td>
<td>97.4</td>
<td>41.7</td>
<td>69.5</td>
<td>55.4</td>
<td>76.0</td>
<td>54.9</td>
<td>66.5</td>
<td>20.2</td>
<td></td>
</tr>
<tr>
<td>51β</td>
<td>H</td>
<td>173.7</td>
<td>96.1</td>
<td>39.9</td>
<td>67.6</td>
<td>54.7</td>
<td>75.7</td>
<td>53.9</td>
<td>66.6</td>
<td>20.2</td>
<td></td>
</tr>
<tr>
<td>51β</td>
<td>Na</td>
<td>177.1</td>
<td>97.2</td>
<td>40.4</td>
<td>68.1</td>
<td>54.9</td>
<td>75.9</td>
<td>53.5</td>
<td>66.5</td>
<td>20.3</td>
<td></td>
</tr>
<tr>
<td>52α</td>
<td>H</td>
<td>173.9</td>
<td>96.0</td>
<td>36.8</td>
<td>68.0</td>
<td>49.1</td>
<td>73.0</td>
<td>54.4</td>
<td>67.4</td>
<td>20.0</td>
<td></td>
</tr>
<tr>
<td>52α</td>
<td>Na</td>
<td>174.7</td>
<td>96.8</td>
<td>35.5</td>
<td>66.1</td>
<td>49.9</td>
<td>70.3</td>
<td>54.4</td>
<td>66.0</td>
<td>20.0</td>
<td></td>
</tr>
<tr>
<td>52β</td>
<td>H</td>
<td>177.6</td>
<td>97.8</td>
<td>36.0</td>
<td>66.7</td>
<td>50.1</td>
<td>70.2</td>
<td>54.6</td>
<td>66.0</td>
<td>20.0</td>
<td></td>
</tr>
<tr>
<td>52β</td>
<td>Na</td>
<td>176.6</td>
<td>98.6</td>
<td>41.9</td>
<td>70.1</td>
<td>53.4</td>
<td>72.8</td>
<td>54.8</td>
<td>68.2</td>
<td>20.4</td>
<td></td>
</tr>
<tr>
<td>53α</td>
<td>H</td>
<td>173.7</td>
<td>96.1</td>
<td>39.9</td>
<td>68.2</td>
<td>53.4</td>
<td>73.2</td>
<td>54.4</td>
<td>68.0</td>
<td>20.4</td>
<td></td>
</tr>
<tr>
<td>53α</td>
<td>Na</td>
<td>177.6</td>
<td>97.6</td>
<td>40.6</td>
<td>68.4</td>
<td>53.9</td>
<td>70.9</td>
<td>54.4</td>
<td>67.5</td>
<td>20.4</td>
<td></td>
</tr>
<tr>
<td>53β</td>
<td>H</td>
<td>174.4</td>
<td>96.6</td>
<td>40.3</td>
<td>68.4</td>
<td>53.9</td>
<td>70.9</td>
<td>54.4</td>
<td>67.5</td>
<td>20.4</td>
<td></td>
</tr>
<tr>
<td>53β</td>
<td>Na</td>
<td>177.6</td>
<td>97.6</td>
<td>40.8</td>
<td>68.8</td>
<td>54.0</td>
<td>70.7</td>
<td>54.5</td>
<td>67.7</td>
<td>20.4</td>
<td></td>
</tr>
<tr>
<td>54α</td>
<td>H</td>
<td>177.0</td>
<td>96.7</td>
<td>39.5</td>
<td>67.1</td>
<td>50.1</td>
<td>69.9</td>
<td>55.0</td>
<td>68.2</td>
<td>19.8</td>
<td></td>
</tr>
<tr>
<td>54α</td>
<td>Na</td>
<td>177.0</td>
<td>96.7</td>
<td>39.5</td>
<td>67.1</td>
<td>50.1</td>
<td>69.9</td>
<td>55.0</td>
<td>68.2</td>
<td>19.8</td>
<td></td>
</tr>
<tr>
<td>54β</td>
<td>H</td>
<td>174.7</td>
<td>96.3</td>
<td>37.6</td>
<td>67.1</td>
<td>49.7</td>
<td>66.5</td>
<td>54.7</td>
<td>67.2</td>
<td>20.4</td>
<td></td>
</tr>
<tr>
<td>54β</td>
<td>Na</td>
<td>176.7</td>
<td>97.3</td>
<td>37.8</td>
<td>67.6</td>
<td>49.9</td>
<td>66.2</td>
<td>54.8</td>
<td>67.4</td>
<td>20.4</td>
<td></td>
</tr>
<tr>
<td>55α</td>
<td>H</td>
<td>173.0</td>
<td>97.0</td>
<td>41.2</td>
<td>69.1</td>
<td>54.9</td>
<td>76.0</td>
<td>55.8</td>
<td>67.8</td>
<td>19.7</td>
<td></td>
</tr>
<tr>
<td>55α</td>
<td>Na</td>
<td>175.4</td>
<td>98.0</td>
<td>41.7</td>
<td>69.8</td>
<td>55.2</td>
<td>75.8</td>
<td>55.9</td>
<td>67.8</td>
<td>19.8</td>
<td></td>
</tr>
<tr>
<td>55β</td>
<td>H</td>
<td>173.7</td>
<td>96.1</td>
<td>39.9</td>
<td>68.2</td>
<td>55.3</td>
<td>73.7</td>
<td>55.5</td>
<td>67.6</td>
<td>19.7</td>
<td></td>
</tr>
<tr>
<td>55β</td>
<td>Na</td>
<td>177.1</td>
<td>97.1</td>
<td>40.4</td>
<td>68.9</td>
<td>55.7</td>
<td>73.8</td>
<td>55.2</td>
<td>67.6</td>
<td>19.8</td>
<td></td>
</tr>
<tr>
<td>56α</td>
<td>H</td>
<td>35.0</td>
<td>67.3</td>
<td>49.9</td>
<td>72.1</td>
<td>53.8</td>
<td>68.2</td>
<td>16.7</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>56α</td>
<td>Na</td>
<td>35.0</td>
<td>67.3</td>
<td>49.9</td>
<td>72.1</td>
<td>53.8</td>
<td>68.2</td>
<td>16.7</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>56β</td>
<td>H</td>
<td>174.9</td>
<td>97.0</td>
<td>35.6</td>
<td>66.1</td>
<td>49.9</td>
<td>71.4</td>
<td>54.0</td>
<td>68.1</td>
<td>16.7</td>
<td></td>
</tr>
<tr>
<td>56β</td>
<td>Na</td>
<td>177.4</td>
<td>97.7</td>
<td>36.0</td>
<td>66.5</td>
<td>50.1</td>
<td>71.4</td>
<td>54.2</td>
<td>68.1</td>
<td>16.6</td>
<td></td>
</tr>
<tr>
<td>57α</td>
<td>H</td>
<td>93.5</td>
<td>35.7</td>
<td>67.4</td>
<td>48.5</td>
<td>71.8</td>
<td>54.4</td>
<td>68.6</td>
<td>17.0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>57α</td>
<td>Na</td>
<td>34.8</td>
<td>67.6</td>
<td>49.5</td>
<td>71.5</td>
<td>53.8</td>
<td>68.6</td>
<td>17.0</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>57β</td>
<td>H</td>
<td>174.6</td>
<td>96.4</td>
<td>33.3</td>
<td>67.1</td>
<td>48.9</td>
<td>67.1</td>
<td>53.8</td>
<td>67.9</td>
<td>16.7</td>
<td></td>
</tr>
<tr>
<td>57β</td>
<td>Na</td>
<td>174.9</td>
<td>97.3</td>
<td>33.5</td>
<td>67.6</td>
<td>49.0</td>
<td>67.0</td>
<td>54.1</td>
<td>68.1</td>
<td>16.7</td>
<td></td>
</tr>
</tbody>
</table>

* Assignment could be interchanged.
Table 4

<table>
<thead>
<tr>
<th>Configuration (compound)</th>
<th>H-3eq</th>
<th>H-3ax</th>
<th>H-4</th>
<th>H-5</th>
<th>H-6</th>
<th>H-7</th>
<th>H-8</th>
<th>H-9</th>
<th>NH-5</th>
<th>NH-9</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(J_{\text{seq,ax}})</td>
<td>(J_{\text{ax,ax}})</td>
<td>(J_{\text{seq,ax}})</td>
<td>(J_{\text{ax,ax}})</td>
<td>(J_{\text{seq,ax}})</td>
<td>(J_{\text{ax,ax}})</td>
<td>(J_{\text{seq,ax}})</td>
<td>(J_{\text{ax,ax}})</td>
<td>(J_{\text{NH,5}})</td>
<td>(J_{\text{NH,9}})</td>
</tr>
<tr>
<td>(\alpha)-d-glycero-d-galacto ((\alpha)-64)</td>
<td>2.71</td>
<td>2.11</td>
<td>5.28</td>
<td>3.85</td>
<td>4.53</td>
<td>4.38</td>
<td>4.88</td>
<td>1.23</td>
<td>5.73</td>
<td>5.83</td>
</tr>
<tr>
<td></td>
<td>(13.5)</td>
<td>(5.1)</td>
<td>(10.0)</td>
<td>(10.7)</td>
<td>(1.4)</td>
<td>(7)</td>
<td>(6.4)</td>
<td>(9.4)</td>
<td>(10.0)</td>
<td></td>
</tr>
<tr>
<td>(\beta)-d-glycero-d-galacto ((\beta)-64)</td>
<td>2.55</td>
<td>1.80</td>
<td>5.66</td>
<td>3.45</td>
<td>4.34</td>
<td>4.40</td>
<td>4.86</td>
<td>1.21</td>
<td>5.94</td>
<td>6.88</td>
</tr>
<tr>
<td></td>
<td>(13.3)</td>
<td>(11.0)</td>
<td>(5.1)</td>
<td>(10.6)</td>
<td>(10.5)</td>
<td>(1)</td>
<td>(7)</td>
<td>(6.5)</td>
<td>(8.4)</td>
<td>(10.0)</td>
</tr>
<tr>
<td>(\alpha)-l-glycero-d-galacto ((\alpha)-62)</td>
<td>2.72</td>
<td>2.07</td>
<td>5.44</td>
<td>3.59</td>
<td>4.61</td>
<td>4.23</td>
<td>5.14</td>
<td>1.31</td>
<td>5.81</td>
<td>5.87</td>
</tr>
<tr>
<td></td>
<td>(13.6)</td>
<td>(5.1)</td>
<td>(9.5)</td>
<td>(10.0)</td>
<td>(1)</td>
<td>(7.2)</td>
<td>(6.4)</td>
<td>(9.3)</td>
<td>(9.9)</td>
<td></td>
</tr>
<tr>
<td>(\beta)-l-glycero-d-galacto ((\beta)-62)</td>
<td>2.61</td>
<td>1.77</td>
<td>5.82</td>
<td>3.21</td>
<td>4.53</td>
<td>4.29</td>
<td>5.10</td>
<td>1.17</td>
<td>5.99</td>
<td>6.73</td>
</tr>
<tr>
<td></td>
<td>(13.2)</td>
<td>(11.2)</td>
<td>(5.0)</td>
<td>(10.2)</td>
<td>(10.3)</td>
<td>(1)</td>
<td>(7.0)</td>
<td>(6.4)</td>
<td>(7.6)</td>
<td>(9.7)</td>
</tr>
<tr>
<td>(\alpha)-d-glycero-l-altro ((\alpha)-63)</td>
<td>2.39</td>
<td>1.94</td>
<td>5.18</td>
<td>4.42</td>
<td>3.69</td>
<td>4.06</td>
<td>5.81</td>
<td>1.19</td>
<td>5.86</td>
<td>6.38</td>
</tr>
<tr>
<td></td>
<td>(13.2)</td>
<td>(12.7)</td>
<td>(5.0)</td>
<td>(10.3)</td>
<td>(10.9)</td>
<td>(1)</td>
<td>(7)</td>
<td>(6.4)</td>
<td>(9.0)</td>
<td>(9.2)</td>
</tr>
<tr>
<td>(\alpha)-l-glycero-l-altro ((\alpha)-65)</td>
<td>2.48</td>
<td>1.95</td>
<td>5.21</td>
<td>4.14</td>
<td>3.83</td>
<td>4.59</td>
<td>5.01</td>
<td>1.29</td>
<td>6.11</td>
<td>6.40</td>
</tr>
<tr>
<td></td>
<td>(13.3)</td>
<td>(4.9)</td>
<td>(10.4)</td>
<td>(11.0)</td>
<td>(1)</td>
<td>(7.0)</td>
<td>(6.4)</td>
<td>(9.4)</td>
<td>(9.7)</td>
<td></td>
</tr>
<tr>
<td>(\beta)-l-glycero-l-altro ((\beta)-65)</td>
<td>2.65</td>
<td>2.03</td>
<td>5.05</td>
<td>4.07</td>
<td>4.15</td>
<td>4.53</td>
<td>4.89</td>
<td>1.19</td>
<td>6.25</td>
<td>6.77</td>
</tr>
<tr>
<td></td>
<td>(13.4)</td>
<td>(4.8)</td>
<td>(10.5)</td>
<td>(9.7)</td>
<td>(2)</td>
<td>(6.8)</td>
<td>(6.3)</td>
<td>(8.8)</td>
<td>(9.8)</td>
<td></td>
</tr>
</tbody>
</table>

\(\alpha\)-d-glycero-d-galacto (\(\alpha\)-64)
\(\beta\)-d-glycero-d-galacto (\(\beta\)-64)
\(\alpha\)-l-glycero-d-galacto (\(\alpha\)-62)
\(\beta\)-l-glycero-d-galacto (\(\beta\)-62)
\(\alpha\)-d-glycero-l-altro (\(\alpha\)-63)
\(\alpha\)-l-glycero-l-altro (\(\alpha\)-65)
\(\beta\)-l-glycero-l-altro (\(\beta\)-65)

Fig. 1. NOE correlations and conformation of the side chain in methyl (5,7-diacetamido-2,4,8-tri-O-acetyl-3,5,7,9-tetradeoxynon-2-ulopyranosonates (62-65). Only correlations designated in Table 5 as strong are shown.

Small \(3J_{H-6,H-7}\) coupling constant values (1–2.5 Hz) were observed for all O-acetylated compounds, thus indicating the gauche orientation of H-6 and H-7 (Fig. 1). Relatively large \(3J_{H-7,H-8}\) values of \(\sim 7\) Hz for 62 (l-glycero-d-galacto) and 64 (d-glycero-d-galacto) showed the trans-like orientation of H-7 and H-8 in the predominant conformer. Almost
the same large value (5–7 Hz, depending on the anomeric configuration) was observed for 65 (l-glycero-l-altro), whereas in 63 (d-glycero-l-altro) it was significantly smaller (~ 1 Hz).

Correlations between H-7 and both H-6 and NH-5 in the l- and d-glycero-d-galacto isomers (62 and 64) that were revealed by a NOESY experiment defined the predominant rotamer around the C-6–C-7 bond (Table 5, Fig. 1(a) and (b)). This conformation was in agreement with a small $J_{H-6,H-7}$ value (1.4–7 Hz). The NOESY spectra of both 62 and 64 showed only a weak H-8,H-7 correlation that, together with a relatively large $J_{H-7,H-8}$ value (~ 7 Hz), indicated the trans-like orientation of H-7 and H-8. Strong H-9,H-7 and medium H-9,NH-7 correlations for 64 showed a spatial proximity of H-9 and H-7, and a strong H-8,H-6 correlation demonstrated that these protons are close to each other (Fig. 1(b)). In 62, H-9 is more close to H-6 than to H-7 as followed from a stronger H-9,H-6 correlation compared to a H-9,H-7 correlation (Fig. 1(a)). Therefore, in 62 and 64, predominant are the trans,trans and trans,cis side-chain (C-7–C-8–C-9) conformers, respectively.

An HMBC experiment optimized for a coupling constant of 8 Hz revealed a strong H-6,C-8 correlation for the d- and l-glycero-l-altro isomers (63 and 65), which corresponded to a $J_{H-6,C-8}$ coupling constant of > 5 Hz. This finding showed the trans-like orientation of H-6 and C-8 in the predominant rotamer around the C-6–C-7 bond, which was confirmed by a strong H-7,H-6 correlation with no H-8,H-6 and H-9,H-6 correlations in the NOESY spectra of 63 and 65. The most populated rotamers around the C-7–C-8 bond are characterized by strong H-9,H-7 and H-8,H-5 correlations for 63 and strong H-8,H-5 and weak H-9,H-5 correlations for 65 (Table 5, Fig. 1(c) and (d)). The presence of an intense H-7,H-8 correlation peak in the NOESY spectrum of 65 seems to be inconsistent with a relatively large $J_{H-7,H-8}$ value (5–7 Hz). This contradiction could be accounted for by a significant contribution of rotamers with a small H-7–C-7–C-8–H-8 dihedral angle. The predominant conformers of 63 and 64 have cis,trans and cis,cis side-chain orientation, respectively.

3. Experimental

NMR spectra were recorded on Bruker DRX-500 and Bruker AM-300 instruments. Spectra of hexose derivatives were measured for solutions in CDCl$_3$ unless otherwise stated, and $^1$H NMR chemical shifts were referenced to a residual solvent signal. Spectra of 5,7-diacetamido-3,5,7,9-tetradexoxyron-2-ulosonic acids were measured for solutions in D$_2$O using acetone ($\delta_H$ 2.225, $\delta_C$ 31.45) as internal standard. Sodium salts were obtained by passing aqueous solutions of the acids through a short column of Amberlite IR-420 (Na$^+$ form). A mixing time of 300 or 900 ms was used in NOESY experiments with methyl (5,7-diacetamido-2,4,8-tri-O-acetyl-3,5,7,9-tetradexoxyron-2-ulospyranos)onates.

Melting points were determined with a Kofler apparatus and are uncorrected. Optical
rotation values were measured on a JASCO DIP-360 polarimeter at 22 ± 2°C. TLC was performed on Kieselgel 60 F254 plates (E. Merck), and visualization was accomplished using UV light or by charring with 10% H2SO4. Column chromatography was carried out on Silpearl silica gel (Chemapol) in a medium pressure mode. Preparative reversed-phase C18 HPLC was performed on a column (250 × 24 mm) of 7.5 μm Silasorb C18 (Czech Republic) in 0.05% aq CF3CO2H at 10 mL/min using a Knauer 98.00 refractometer for monitoring. ESIMS data were recorded with a Micromass Quattro system. All reactions involving air- or moisture-sensitive reagents were carried out in dry solvents under dry argon.

Benzyl 3,4-di-O-benzoyl-β-L-rhamnopyranoside (2), benzyl 2,4-di-O-benzoyl-β-L-rhamnopyranoside (3), and benzyl 2,3-di-O-benzoyl-β-L-rhamnopyranoside (4).—A mixture of 1 (7.8 g, 21 mmol) and Bu3SnO (5.49 g, 22 mmol) in benzene (150 mL) was boiled with azeotropic removal of water for 2 h, whereupon a crystalline precipitate of the stannylene derivative formed. Tetra-butilammonium bromide (7.08 g, 22 mmol) and benzyl bromide (5 mL, 42 mmol) were added, and the mixture was boiled under reflux for 4 h. After cooling, the solution was washed thoroughly with water and concentrated. Column chromatography of the residue (95:5 toluene–EtOAc) gave a mixture of 2–4 (8.95 g, 92%) in ratios of 4:3:1, which was used in the next step without separation.

A small portion of the above mixture was subjected to column chromatography (85:15 light petroleum–EtOAc) to give, in order of elution, pure compounds 2, 3, and 4.

3,4-Dibenzozoate 2: mp 172–174°C (EtOAc–hexane); [α]D + 129° (c 2). 1H NMR: δ, 1.42 (d, 3 H, J5,6 6.2 Hz, H-6), 2.53 (br. s, 1 H, OH), 3.73 (dq, 1 H, H-5), 4.37 (dd, 1 H, J2,3 3.2 Hz, H-2), 4.74, 4.99 (2 d, 2 H, Jgem 11.9 Hz, PhCH2), 4.75 (d, 1 H, J1,2 1.1 Hz, H-1), 5.28 (dd, 1 H, J4,9 10.8 Hz, H-3), 5.67 (t, 1 H, J4,9 9.7 Hz, H-4), 7.30–8.04 (m, 15 H, 3 Ph). Anal. Calcd for C27H26O7: C, 70.12; H, 5.67.

2,4-Dibenzoate 3: mp 123–125°C (EtOAc–hexane); [α]D + 91° (c 2). 1H NMR: δ, 1.44 (d, 3 H, J5,6 6.1, H-6), 3.71 (dq, 1 H, H-5), 4.02 (dd, 1 H, J3,4 9.8 Hz, H-3), 4.70, 4.93 (2 d, 2 H, Jgem 12.4 Hz, PhCH2), 4.73 (s, 1 H, H-1), 5.23 (t, 1 H, J4,9 9.6 Hz, H-4), 5.72 (d, 1 H, J2,3 3.6 Hz, H-2), 7.28–8.21 (m, 15 H, 3 Ph). Anal. Calcd for C27H26O7: C, 70.12; H, 5.67. Found: C, 70.13; H, 5.61.

2,3-Dibenzoate 4 had mp 135–137°C (EtOAc–hexane), [α]D + 82° (c 1.7). 1H NMR: δ, 1.54 (d, 3 H, J3,4 6.1, H-6), 2.43 (d, 1 H, J4,OH 4.6 Hz, OH), 3.52 (dq, 1 H, H-5), 3.92 (dt, 1 H, J4,9 9.2 Hz, H-4), 4.71, 4.92 (2 d, 2 H, Jgem 12.3 Hz, PhCH2), 4.78 (s, 1 H, H-1), 5.17 (dd, 1 H, J3,4 9.7 Hz, H-3), 5.83 (d, 1 H, J2,3 3.1 Hz, H-2), 7.29–8.15 (m, 15 H, 3 Ph). Anal. Calcd for C27H26O7: C, 70.12; H, 5.67. Found: C, 69.71; H, 5.65.

Benzyl β-L-rhamnopyranoside (5).—A solution of the above mixture of 2–4 (9.44 g, 20.4 mmol) in MeOH (50 mL) was treated with 2 M CH3ONa (1 mL) for 5 h at 40°C. The mixture was neutralized with Amberlite IR-120 (H+), filtered, and the filtrate was concentrated. The residue was chromatographed (1:1 toluene–acetone) to yield 5 (4.40 g, 85%): mp 107–108°C (EtOAc–hexane); [α]D + 103° (c 1.7). 1H NMR (CDCl3 + D2O): δ, 1.33 (d, 3 H, J5,6 6.0 Hz, H-6), 3.16 (dq, 1 H, H-5), 3.34 (dd, 1 H, J3,4 9.5 Hz, H-3), 3.42 (t, 1 H, J4,9 8.9 Hz, H-4), 3.89 (d, 1 H, J2,3 3.0 Hz, H-2), 4.36 (s, 1 H, H-1), 4.55, 4.84 (2 d, 2 H, Jgem 11.9 Hz, PhCH2), 7.23–7.34 (m, 5 H, Ph). Anal. Calcd for C27H26O7: C, 61.40; H, 7.04. Found: C, 61.43; H, 7.04.

Benzyl 2,4-di-O-acetyl-β-L-rhamnopyranoside (6).—p-Toluenesulfonic acid monohydrate (190 mg, 1 mmol) was added to a solution of 5 (8.86 g, 34.9 mmol) and trimethyl orthoacetate (13.2 mL, 105 mmol) in CH3CN (100 mL), and the mixture was stirred for 30 min. Py (5 mL) was added, and the solvent was evaporated. The residue was dissolved in py (60 mL) and treated with Ac2O (20 mL) overnight. The excess of Ac2O was destroyed by adding water at 0°C, the resulting mixture was diluted with CH2Cl2, washed successively with water, M HCl, satd aq NaHCO3, and water. The solvent was evaporated, and the residue was treated with 80%
Conventional acetylation of 8 with Ac₂O in py afforded 2-acetate 9. ¹H NMR: δ 1.50 (d, 3 H, J₃,₄ 7.5 Hz, H-6), 2.17 (s, 3 H, CH₃CO), 3.07 (d, 1 H, J₃,₄ 4.0 Hz, H-3), 4.10 (q, 1 H, H-5), 4.57, 4.86 (2 d, 2 H, J₃,₄ 13.2 Hz, PhCH₂), 4.64 (d, 1 H, J₁,₂ 2.1 Hz, H-1), 5.25 (t, 1 H, J₂,₃ 1.8 Hz, H-2), 7.25-7.38 (m, 5 H, Ph).

Conventional acetylation of 8 with Ac₂O in py gave 3-acetate 10. ¹H NMR: δ 1.38 (d, 3 H, J₃,₄ 6.5 Hz, H-6), 2.05 (s, 3 H, CH₃CO), 3.48 (dd, 1 H, J₃,₄ 1.7 Hz, H-4), 3.69 (dd, 1 H, J₂,₃ 3.4 Hz, H-2), 4.03 (dq, 1 H, H-5), 4.69, 4.96 (2 d, 2 H, J₃,₄ 11.8 Hz, PhCH₂), 4.79 (d, 1 H, J₁,₂ 8.1 Hz, H-1), 5.33 (t, 1 H, J₂,₃ 3.5 Hz, H-3), 7.30-7.42 (m, 5 H, Ph).

Benzyl 3,4-anhydro-2-azido-2,6-dideoxy-β-L-allopyranoside (11).—Compound 8 (5.66 g, 24 mmol) was treated with Tf₂O (6.71 mL, 40 mmol) in the presence of py (5.82 mL, 72 mmol) in CH₂Cl₂ (75 mL) as described in the preparation of 7. The crude triolate 10 obtained was dissolved in DMF (50 mL), sodium azide (7.8 g, 120 mmol) was added, and the mixture was stirred for 1 h at rt. The mixture was diluted with EtOAc, washed thoroughly with water, dried with MgSO₄ and concentrated. Column chromatography of the residue (85:15 light petroleum–EtOAc) gave 11 (5.22 g, 83%): mp 52-54 °C (hexane); [α]D +78° (c 1.1). ¹H NMR: δ 1.44 (d, 3 H, J₃,₄ 6.8 Hz, H-6), 3.17 (t, 1 H, H-4), 3.45 (dd, 1 H, J₂,₃ 4.2 Hz, H-3), 3.69 (dd, 1 H, J₁,₂ 2.2 Hz, H-2), 4.09 (q, 1 H, H-5), 4.58 (d, 1 H, J₁,₂ 7.6 Hz, H-1), 4.62, 4.87 (2 d, 2 H, J₃,₄ 11.4 Hz, PhCH₂), 7.29-7.41 (m, 5 H, Ph). Anal. Caled for C₁₃H₁₆N₄O₃: C, 59.76; H, 5.79; N, 27.62. Found: C, 59.64; H, 5.80; N, 16.08.

Conventional acetylation of 12 with Ac₂O in py gave 3-acetate 13. ¹H NMR: δ 1.38 (d, 3 H, J₃,₄ 6.5 Hz, H-6), 2.05 (s, 3 H, CH₃CO), 3.48 (dd, 1 H, J₃,₄ 1.7 Hz, H-4), 3.69 (dd, 1 H, J₂,₃ 3.4 Hz, H-2), 4.03 (dq, 1 H, H-5), 4.69, 4.96 (2 d, 2 H, J₃,₄ 11.8 Hz, PhCH₂), 4.79 (d, 1 H, J₁,₂ 8.1 Hz, H-1), 5.33 (t, 1 H, J₂,₃ 3.5 Hz, H-3), 7.30-7.42 (m, 5 H, Ph).
Benzyl 2,4-diacetamido-2,4,6-trideoxy-β-L-gulopyranoside (14).—20% Pd(OH)₂/C (950 mg) was added to a solution of 12 (3.77 g, 12.4 mmol) in MeOH (60 mL), and the mixture was stirred vigorously in a hydrogen atmosphere for 2.5 h at 30–32°C. The catalyst was filtered through Celite, washed with MeOH, and the combined filtrate and washings were concentrated to a volume of ~20 mL. Ac₂O (6 mL) was added, and the solution was kept for 1 h and evaporated. Residual Ac₂O was removed by coevaporation with toluene, and the residue was chromatographed (9:5 chloroform–MeOH) to give 14 (3.48 g, 84%) as an amorphous solid: [z]D  146° (c 3). ¹H NMR (CDCl₃ + D₂O): δ 1.17 (d, 3 H, J₃,6 2.5 Hz, H-6), 1.96, 2.02 (2 s, 6 H, CH₂(C₆H₅), 3.87 (t, 1 H, J₃,4 3.7 Hz, H-3), 3.98 (dd, 1 H, J₄,5 1.5 Hz, H-4), 4.05 (dd, 1 H, J₃,5 3.4 Hz, H-2), 4.20 (dq, 1 H, H-5), 4.56, 4.86 (2 d, 2 H, J₆,7 2.5 Hz, PhCH₂), 4.58 (dd, 1 H, J₁,₂ 8.6 Hz, H-1), 7.28–7.37 (m, 5 H, Ph). Anal. Caled for C₁₇H₂₄N₂O₅.5H₂O: C, 59.11; H, 7.29; N, 8.11. Found: C, 59.28; H, 7.36; N, 8.45.

2,4-Diacetamido-2,4,6-trideoxy-β-L-gulopyranose (15).—A solution of 14 (4.45 g, 13.2 mmol) in MeOH (60 mL) was stirred with 20% Pd(OH)₂/C (1 g) under hydrogen for 4 h at 32–34°C, filtered through Celite, (Caution: Extreme fire hazard) and concentrated. Column chromatography of the residue (9:4:6 CHCl₃–MeOH) gave 15 (3.20 g, 94%): mp 146–148 °C (MeOH–ether); [z]D  +65° (c 1.6, MeOH). ¹H NMR (D₂O): 15α, δ 1.16 (d, 3 H, J₃,6 6.6 Hz, H-6), 2.06, 2.07 (2 s, 6 H, 2 CH₂CO), 3.91 (t, 1 H, J₃,4 3.8 Hz, H-3), 3.95 (dd, 1 H, J₄,5 1.7 Hz, H-4), 4.11 (t, 1 H, J₁,₂ 3.5 Hz, H-2), 4.62 (dq, 1 H, H-5), 5.15 (d, 1 H, J₁,₂ 4.0 Hz, H-1); 15β, δ 1.18 (d, 3 H, J₃,6 6.5 Hz, H-6), 2.04, 2.08 (2 s, 6 H, 2 CH₂CO), 3.85 (dd, 1 H, J₁,₂ 3.2 Hz, H-2), 3.87 (dd, 1 H, J₄,5 1.6 Hz, H-4), 3.94 (t, 1 H, J₃,₄ 3.4 Hz, H-3), 4.29 (dq, 1 H, H-5), 4.94 (d, 1 H, J₁,₂ 8.9 Hz, H-1). The ratio 15α:15β  1:5. Anal. Caled for C₁₇H₁₈N₂O₅.25 H₂O: C, 47.60; H, 7.39; N, 11.10. Found: C, 47.59; H, 7.50; N, 11.49.

Benzyl 2-azido-3-O-benzyl-2-deoxy-β-D-mannopyranoside (17).—Pyridinium perchlorate (1.14 g, 6.34 mmol) was added to a solution of 16 (3.00 g, 6.34 mmol) in 90% aq CH₃CN (30 mL), and the mixture was heated at 80 °C for 4 h. Py (0.5 mL) was added, and the solvent was evaporated. The residue was distributed between water (50 mL) and CHCl₃ (50 mL), the organic layer was separated, and the water layer was extracted with CHCl₃ (3 × 50 mL). The combined extract was concentrated, and the residue was subjected to column chromatography (3:2 toluene–EtOAc) to give 17 (2.37 g, 97%) as a syrup: [z]D  +106° (c 1, CHCl₃). ¹H NMR: δ 3.26 (ddd, 1 H, H-5), 3.46 (dd, 1 H, J₃,4 9.2 Hz, H-3), 3.82 (dd, 1 H, J₅,₆a 4.9 Hz, J₆a,₆b 12.1 Hz, H-6a), 3.87 (t, 1 H, J₄,₅ 9.5 Hz, H-4), 3.92 (dd, 1 H, J₅,₆b 3.7 Hz, H-6b), 3.95 (d, 1 H, J₂,₃ 3.6 Hz, H-2), 4.56 (br. s, 1 H, H-1), 4.61, 4.74 (2 d, 2 H, J₆,₇ 11.7 Hz, PhCH₂), 4.64, 4.94 (2 d, 2 H, J₆,₇ 12.2 Hz, PhCH₂), 7.30–7.42 (m, 10 H, 2 Ph). Anal. Caled for C₂₅H₂₃N₃O₇: C, 62.32; H, 6.02; N, 10.90. Found: C, 62.46; H, 5.92; N, 10.85.

Benzyl 2-azido-3-O-benzyl-2-deoxy-6-O-tosyl-β-D-mannopyranoside (18).—p-Toluene-sulfonyl chloride (1.72 g, 9.04 mmol) was added at 0°C to a solution of 17 (2.32 g, 6.02 mmol) in py (15 mL). The stirred mixture was allowed to warm to rt for 1.5 h, and stirring was continued for the next 2 h. The reaction was quenched by adding water, the resulting mixture was diluted with CHCl₃, washed successively with water, M HCl, and water, and concentrated. Column chromatography of the residue (9:1 toluene–EtOAc) yielded 18 (2.86 g, 88%) as a syrup: [z]D  79.6° (c 2, CHCl₃). ¹H NMR: δ 2.41 (s, 3 H, CH₃C₆H₅), 2.47 (br. s, 1 H, OH), 3.39 (dd, 1 H, J₃,₄ 9.1 Hz, H-3), 3.42 (ddd, 1 H, H-5), 3.70 (t, 1 H, J₄,₅ 9.8 Hz, H-4), 3.94 (d, 1 H, J₂,₃ 3.4 Hz, H-2), 4.23 (dd, 1 H, J₅,₆a 6.6 Hz, J₆a,₆b 10.9 Hz, H-6a), 4.43 (dd, 1 H, J₅,₆b 1.7 Hz, H-6b), 4.48 (s, 1 H, H-1), 4.56 (d, 2 H, J₆,₇ 11.8 Hz, PhCH₂), 4.73 (d, 1 H, J₆,₇ 11.7 Hz, PhCH₂), 4.86 (d, 1 H, J₇,₈ 12.0 Hz, PhCH₂), 7.30–7.84 (m, 14 H, 2 Ph, CH₃C₆H₅). Anal. Caled for C₂₇H₂₅N₃O₇: C, 60.10; H, 5.42; N, 7.79. Found: C, 59.89; H, 5.57; N, 8.03.

Integral intensities of signals for the compounds 15, 32, and 48 are given within anomeric series.
Benzyl 2-azido-3-O-benzyl-2,6-dideoxy-6-ido-β-D-mannopyranoside (19).—A solution of 18 (2.76 g, 5.12 mmol) and sodium iodide (3.84 g, 25.6 mmol) in CH$_2$CN (30 mL) was heated with stirring at 80–85 °C for 7 h. The solvent was evaporated, and a suspension of the residue in CHCl$_3$ was washed successively with water, M Na$_2$S$_2$O$_5$, and water, and then concentrated. The residue was chromatographed (95:5 toluene–EtOAc) to give 19 (2.42 g, 96%) as a syrup: [α]$_D$ = −77.3° (c 2, CHCl$_3$). $^1$H NMR: δ 3.22 (dt, 1 H, H-5), 2.46 (d, 1 H, $J_{\text{4,OH}}$ 1.5 Hz, OH), 3.30 (t, 1 H, $J_{\text{5,6a}}$ 9.1 Hz, $J_{\text{6a,6b}}$ 10.4 Hz, H-6a), 3.39 (dd, 1 H, $J_{\text{3,4}}$ 9.0 Hz, H-3), 3.64 (dt, 1 H, $J_{\text{4,5}}$ 8.9 Hz, H-4), 3.65 (dd, 1 H, $J_{\text{5,6b}}$ 1.8 Hz, H-6b), 3.97 (d, 1 H, $J_{\text{2,3}}$ 3.4 Hz, H-2), 4.53 (d, 2 H, $J_{\text{gem}}$ 11.6 Hz, PhCH$_2$), 4.54 (s, 1 H, H-1), 4.75, 5.02 (2 d, 2 H, $J_{\text{gem}}$ 12.1 Hz, PhCH$_2$), 7.33–7.45 (m, 10 H, 2 Ph). Anal. Calcd for C$_{20}$H$_{22}$I$_3$N$_3$O$_4$: C, 48.50; H, 4.48; N, 8.48. Found: C, 68.65; H, 7.11; N, 3.52.

Benzyl 2-acetamido-3-O-benzyl-2,6-dideoxy-β-D-lyxo-hexopyranoside-4-oxide, oxime (22).—A solution of DMSO (0.97 mL, 13.6 mmol) in CH$_2$Cl$_2$ (4 mL) was added at −60 °C to a solution of oxalyl chloride (0.54 mL, 6.19 mmol) in CH$_2$Cl$_2$ (15 mL), and the mixture was stirred for 0.5 h while the temperature gradually increased to −30 °C. After cooling to −60 °C, a solution of 20 (1.59 g, 4.13 mmol) in CH$_2$Cl$_2$ (15 mL) was added dropwise, the mixture was stirred at −60 °C for 45 min, and then N,N-diisopropylethylamine (5.3 mL) was added. The mixture was allowed to warm to −20 °C, diluted with CHCl$_3$, washed with M HCl, water, and concentrated. The residue was passed through a short column with silica gel in (85:15) toluene–acetone, and the eluate was concentrated. The residue was subjected to column chromatography (95:5 toluene–EtOAc) to give 21 (2.42 g, 96%) as a syrup: [α]$_D$ = −77.3° (c 2, CHCl$_3$). 1H NMR: δ 1.64 (d, 3 H, $J_{\text{5,6}}$ 7.1 Hz, H-6), 2.00 (s, 3 H, CH$_3$CO), 4.28 (d, 1 H, $J_{\text{5,6b}}$ 4.9 Hz, H-5), 4.47 (dd, 1 H, $J_{\text{2,3}}$ 4.3 Hz, H-2), 4.30, 5.01 (2 d, 2 H, $J_{\text{gem}}$ 12.0 Hz, PhCH$_2$), 4.51, 4.67 (2 d, 2 H, $J_{\text{gem}}$ 11.9 Hz, PhCH$_2$), 4.92 (d, 1 H, H-3), 5.29 (q, 1 H, $J_{\text{gem}}$ 4.0 Hz, H-2), 5.92 (q, 1 H, $J_{\text{gem}}$ 4.0 Hz, H-2), 6.19 mmol) in CH$_2$Cl$_2$ (15 mL), and the mixture was stirred at the same temperature for 45 min, and then N,N-diisopropylethylamine (5.3 mL) was added. The mixture was allowed to warm to −20 °C, diluted with CHCl$_3$, washed with M HCl, water, and concentrated. The residue was passed through a short column with silica gel in (85:15) toluene–acetone, and the eluate was concentrated. The residue was subjected to column chromatography (85:15 toluene–acetone) to give 22 (1.59 g, 97%) as a mixture of isomers in a ratio of ~ 8:1. Crystallization from ether–light petroleum gave the major isomer: mp 127–129 °C, [α]$_D$ = −35° (c 1, CHCl$_3$). $^1$H NMR: δ 1.64 (d, 3 H, $J_{\text{5,6}}$ 7.1 Hz, H-6), 2.00 (s, 3 H, CH$_3$CO), 4.28 (d, 1 H, $J_{\text{5,6b}}$ 4.9 Hz, H-5), 4.47 (dd, 1 H, $J_{\text{2,3}}$ 4.3 Hz, H-2), 4.30, 5.01 (2 d, 2 H, $J_{\text{gem}}$ 12.0 Hz, PhCH$_2$), 4.51, 4.67 (2 d, 2 H, $J_{\text{gem}}$ 11.9 Hz, PhCH$_2$), 4.92 (d, 1 H, H-3), 5.29 (q, 1 H, $J_{\text{gem}}$ 4.0 Hz, H-2), 6.19 mmol) in CH$_2$Cl$_2$ (15 mL), and the mixture was stirred at the same temperature for 45 min, and then N,N-diisopropylethylamine (5.3 mL) was added. The mixture was allowed to warm to −20 °C, diluted with CHCl$_3$, washed with M HCl, water, and concentrated. The residue was passed through a short column with silica gel in (85:15) toluene–acetone, and the eluate was concentrated. The residue was subjected to column chromatography (85:15 toluene–acetone) to give 20 (1.63 g, 84%) as a foam: [α]$_D$ = −116° (c 1, CHCl$_3$). $^1$H NMR: δ 1.49 (d, 3 H, $J_{\text{5,6}}$ 6.3 Hz, H-6), 2.08 (s, 3 H, CH$_3$CO), 3.27 (t, 1 H, $J_{\text{4,5}}$ 9.1 Hz, H-4), 3.32 (dq, 1 H, H-5), 3.35 (dd, 1 H, $J_{\text{1,4}}$ 9.1 Hz, H-3), 4.39, 4.93 (2 d, 2 H, $J_{\text{gem}}$ 10.9 Hz, PhCH$_2$), 4.54 (s, 1 H, H-1), 4.63, 4.86 (2 d, 2 H, $J_{\text{gem}}$ 12.2 Hz, PhCH$_2$), 4.84 (dd, 1 H, $J_{\text{2,3}}$ 4.0 Hz, H-2), 5.74 (d, 1 H, $J_{\text{NH,2}}$ 9.5 Hz, NH), 7.27–7.39 (m, 10 H, 2 Ph). Anal. Calcd for C$_{22}$H$_{27}$NO$_5$: C, 68.55; H, 7.06; N, 3.63. Found: C, 68.65; H, 7.11; N, 3.52.

Benzyl 2,4-diacetamido-3-O-benzyl-2,4,6-trideoxy-β-D-talopyranoside (23) and benzyl 2,4-diacetamido-3-O-benzyl-2,4,6-trideoxy-β-D-mannopyranoside (24).—Sodium borohydride (1.55 g, 40.7 mmol) was added portionwise to a solution of 22 (1.62 g, 4.07 mmol) and NiCl$_2$-6H$_2$O (1.94 g, 8.14 mmol) in MeOH (50 mL) at −35 °C over 0.5 h. The mixture was stirred at the same temperature for 0.5 h and quenched by adding satd aq...
NaHCO₃ (50 mL). The bulk of the MeOH was evaporated, and the remaining aqueous solution was extracted with CH₂Cl₂ (3 × 50 mL). The combined extract was concentrated, and the residue was acetylated with Ac₂O (1.5 mL) in MeOH (20 mL) overnight. The solvent was evaporated, the Ac₂O was coevaporated with toluene, and the residue was subjected to column chromatography (95:5 CHCl₃–MeOH) to yield a mixture of 23 and 24.

Individual 23 (1.39 g, 80%) and 24 (130 mg, 8%) were isolated by preparative HPLC on a Zorbax SIL (250 × 21 mm) column (DuPont) in 97:3 EtOAc–MeOH.

Compound 23: mp 158–159 °C (MeOH–Et₂O), [x]D − 49.4° (c 1, CHCl₃). ¹H NMR (toluene-δ₉, 333 K): δ 1.50 (d, 3 H, J₆,₇ 6.3 Hz, H-6), 1.98, 2.00 (2 s, 6 H, 2 CH₃CO), 3.53 (poorly resolved q, 1 H, H-5), 3.61 (poorly resolved t, 1 H, J₂,₃ 2 Hz, H-2), 4.60 (s, 1 H, H-1), 4.62 (unresolved, 1 H, H-4), 4.69, 4.98 (2 d, 2 H, J₆,₇ 12.0 Hz, PhCH₂), 4.79 (unresolved, 1 H, H-2), 4.81 (s, 2 H PhCH₃), 6.18 (unresolved, 1 H, NH), 6.44 (unresolved, 1 H, NH), 7.33–7.73 (m, 10 H, 2 Ph). Anal. Calcd for C₁₇H₁₈N₂O₅: C, 67.58; H, 7.09; N, 6.57. Found: C, 67.44; H, 7.07; N, 6.56.

Compound 24 was obtained as a foam: [x]D − 109.5° (c 1, CHCl₃). ¹H NMR (C₆D₆): δ 1.37 (d, 3 H, J₅,₆ 6.2 Hz, H-6), 1.68, 1.70 (2 s, 6 H, 2 CH₂CO), 3.02 (dq, 1 H, H-5), 3.15 (dd, 1 H, J₃,₄ 10.3 Hz, H-3), 3.94 (q, 1 H, J₄,₅ 9.8 Hz, H-4), 4.35 (s, 1 H, H-1), 4.43, 4.84 (2 d, 2 H, J₆,₇ 12.2 Hz, PhCH₂), 4.57, 4.94 (2 d, 2 H, J₆,₇ 12.2 Hz, PhCH₂), 4.86 (d, 1 H, J₇,₈ 8.9 Hz, NH-4), 5.09 (dd, 1 H, J₂,₃ 4.2 Hz, H-2), 6.29 (d, 1 H, J₇,₈ 9.7 Hz, NH-2), 7.08–7.39 (m, 10 H, 2 Ph). Anal. Calcd for C₂₉H₃₀N₂O₅: C, 67.58; H, 7.09; N, 6.57. Found: C, 66.86; H, 6.96; N, 6.69.

2,4-Diacetamido-2,4,6-trideoxy-β-D-talose (25).—A solution of 23 (1.24 g, 2.91 mmol) in MeOH (20 mL) and water (10 mL) was stirred with 20% Pd(OH)₂/C (500 mg) under hydrogen for 6 h at rt. The catalyst was filtered through Celite, and washed with MeOH, (Caution: Extreme fire hazard), the combined filtrate and washings were concentrated, and the residue was subjected to column chromatography (85:15 CHCl₃–MeOH) to give 25 (630 mg, 88%) as an amorphous solid: [x]D + 23.6° → + 15.3° (c 1, water). For ¹H and ¹³C NMR data see Table 1. Anal. Calcd for C₁₀H₁₈N₂O₅: C, 48.77; H, 7.37; N, 11.38. Found: C, 48.98; H, 7.57; N, 11.42.

Benzyl 3-O-benzoyl-β-D- fucopyranoside (27).—A mixture of 26 (2.22 g, 8.74 mmol) and Bu₃SnO (2.29 g, 9.18 mmol) in benzene (40 mL) was boiled with stirring and azeotropic removal of water for 5 h, then 15 mL benzene was distilled off from the mixture. The remaining solution was cooled to 0 °C and benzoyl chloride (1.12 mL, 9.61 mmol) was added. After stirring at 0–5 °C for 2 h, MeOH (0.5 mL) and py (0.5 mL) were added to destroy the excess benzoyl chloride. After being stirred for 0.5 h at rt, the mixture was concentrated, and the residue was subjected to column chromatography (9:1 toluene–EtOAc) to give 27 (1.90 g, 61%): mp 97–98 °C (EtOAc–light petroleum); [x]D + 12.5° (c 1, CHCl₃). ¹H NMR: δ 1.38 (d, 3 H, J₅,₆ 6.4 Hz, H-6), 2.11, 2.34 (2 br. s, 2 H, 2 OH), 3.76 (q, 1 H, H-5), 3.96 (d, 1 H, H-4), 4.03 (dd, 1 H, J₂,₃ 10.1 Hz, H-2), 4.47 (d, 1 H, J₁,₂ 7.7 Hz, H-1), 4.65, 4.99 (2 d, 2 H, J₆,₇ 11.7 Hz, PhCH₂), 5.07 (dd, 1 H, J₃,₄ 3.0 Hz, H-3), 7.32–8.11 (m, 10 H, 2 Ph). Anal. Calcd for C₃₀H₃₂N₂O₅: C, 67.02; H, 6.19. Found: C, 66.92; H, 6.29.

Benzyl 2,4-diazido-3-O-benzoyl-2,4,6-trideoxy-β-D-mannopyranoside (29).—Ti(O) (3.10 mL, 18.5 mmol) was added dropwise at 0 °C to a solution of 27 (2.20 g, 6.14 mmol) and py (2.98 mL, 36.8 mmol) in CH₂Cl₂ (40 mL). The mixture was stirred at 0 °C for 1 h, diluted with CHCl₃, washed successively with water, M HCl, and water, and concentrated. The crude di triflate 28 obtained was dissolved in toluene (40 mL) and tetrabutylammonium azide (10.45 g, 36.8 mmol) was added. The mixture was stirred for 1 h at 65–70 °C and then for 1.5 h at 100–105 °C, cooled, diluted with toluene, washed twice with water, and concentrated. Column chromatography of the residue (7.3 toluene–light petroleum) gave 29 (2.12 g, 85%) as a syrup, [x]D − 46.1° (c 1, CHCl₃). ¹H NMR: δ 1.59 (d, 3 H, J₅,₆ 6.1 Hz, H-6), 3.40 (dq, 1 H, H-5), 3.77 (t, 1 H, J₄,₅ 9.7 Hz, H-4), 4.36 (d, 1 H, J₂,₃ 3.6 Hz, H-2), 4.77, 5.09 (2 d, 2 H, J₆,₇ 12.1 Hz, PhCH₂), 4.77 (s,
1 H, H-1), 5.14 (dd, 1 H, J_{3,4} 10.1 Hz, H-3), 7.40–8.23 (m, 10 H, 2 Ph). Anal. Calcd for 
C_{35}H_{30}N_{10}O_{10}: C, 58.81; H, 4.94; N, 20.58. Found: C, 59.18; H, 5.05; N, 20.61.

**Benzyl 2,4-di-acetamido-2,4,6-trideoxy-β-D-mannopyranoside (31).—** A solution of 29
(2.12 g, 5.20 mmol) in MeOH (20 mL) was treated with 2 M sodium methoxide in MeOH
(1 mL) for 1 h at rt. The solution was neutralised by adding Amberlite IR-120 (H+ form) ion-exchange resin, and filtered, and the filtrate was concentrated. A solution of crude
30 in MeOH (30 mL) was stirred with 20% Pd(OH)_2/C (400 mg) at 30 °C under hydrogen
for 1.5 h. The catalyst was filtered off through Celite, washed with MeOH, and the combined
filtrate and washings were concentrated. After being kept for 1 h at rt, the mixture was evaporated to dryness, and the residue was subjected to column chromatography
(97:3 CHCl_3–MeOH) to yield 31 (1.51 g, 86%) as a foam: [α]_D + 25.2° (c 1, CHCl_3).

**1H NMR (D_2O):** 4.20 (dd, 1 H, J_{3,4} 4.07 Hz, H-3), 1.86, 1.96 (2 s, 6 H, 2 CH_3CO),
3.32 (dq, 1 H, H-5), 3.84 (dd, 1 H, J_{3,4} 10.5 Hz, H-3), 3.97 (t, 1 H, J_{3,4} 10.8 Hz, H-3), 4.30 (dd, 1 H, J_{3,4} 6.4 Hz, H-2), 7.07–7.43 (m, 5 H, Ph). Anal. Calcd for
C_{10}H_{18}N_{2}O_{5}: C, 58.29; H, 7.53. Found: C, 58.32; H, 7.48.

**2,4-Diacetamido-2,4,6-trideoxy-D-mannopyranose (32).—** A mixture of 31 (1.35 g, 4.02
mmol) and 20% Pd(OH)_2/C (400 mg) in MeOH (25 mL) was stirred at 32 °C in hydrogen
atmosphere for 2 h. The catalyst was filtered through Celite, washed with MeOH, (Caution: Extreme fire hazard), and the combined filtrate and washings were concentrated.

The residue was chromatographed (85:15 CHCl_3–MeOH) to give 32 (840 mg, 85%) as an
amorphous solid: [α]_D + 38.1° (c 1, water).

**1H NMR (D_2O):** 32α, δ 1.19 (d, 3 H, J_{5,6} 6.3 Hz, H-6), 2.04, 2.08 (2 s, 6 H, 2 CH_3CO), 3.78
(t, 1 H, J_{5,6} 10.2 Hz, H-4), 3.97 (dq, 1 H, H-5), 4.07 (dd, 1 H, J_{5,6} 10.8 Hz, H-3), 4.30 (dd, 1 H, J_{2,3} 4.6 Hz, H-2), 5.11 (d, 1 H, J_{1,2} 1.3 Hz, H-1). 32β, δ 1.23 (d, 3 H, J_{5,6} 6.2 Hz, H-6),
2.03, 2.12 (2 s, 6 H, 2 CH_3CO), 3.51 (dq, 1 H, H-5), 3.67 (t, 1 H, J_{4,5} 10.0 Hz, H-4), 3.84 (dd,
concentrated. Column chromatography of the residue (85:15 toluene–EtOAc) afforded 35 (5.44 g, 94%), mp 69–70 °C (ether–hexane), \([\text{\text{[3]}]} \text{D} + 108.6 \text{°} (c 1, \text{CHCl}_3)\). \(1^H\) NMR: \(\delta 1.40\) (d, 3 H, \(J_{5,6} 6.4 \text{ Hz}, \text{H}-6\)), 1.42, 1.63 (2 s, 6 H, isopropylidene), 2.81 (d, 1 H, \(J_{\text{OH,4}} 9.8 \text{ Hz}, \text{OH}\)), 3.50 (q, 1 H, H-5), 3.60 (dd, 1 H, H-4), 4.16 (dd, 1 H, \(J_{3,3} 6.3 \text{ Hz}, \text{H}-2\)), 4.21 (t, 1 H, \(J_{3,4} 5.6 \text{ Hz}, \text{H}-3\)), 4.72 (d, 1 H, \(J_{\text{gem}} 2.4 \text{ Hz}, \text{H}-1\)), 4.77, 4.97 (2 d, 2 H, \(J_{\text{gem}} 12.3 \text{ Hz}, \text{PhCH}_2\)), 7.30–7.43 (m, 5 H, Ph). Anal. Calcd for \(\text{C}_{18}\text{H}_{22}\text{O}_5\): C, 65.29; H, 6.75. Found: C, 65.35; H, 7.47.

**Benzyl 6-deoxy-\(\beta\)-L-talopyranoside (36).**—A solution of 35 (925 mg, 3.15 mmol) in 80% aq AcOH (10 mL) was heated at 40 °C for 1.5 h. The solvent was coevaporated several times with toluene, and the residue was subjected to column chromatography (4:1 toluene–acetone) to give 36 (795 mg, 99%); mp 86–88 °C (EtOAc–light petroleum); \([\text{\text{[3]}]} \text{D} + 89.4 \text{°} (c 1, \text{CHCl}_3)\). \(1^H\) NMR: \(\delta 1.40\) (d, 3 H, \(J_{5,6} 6.5 \text{ Hz}, \text{H}-6\)), 3.45 (q, 1 H, H-5), 3.48 (t, 1 H, \(J_{3,4} 3.4 \text{ Hz}, \text{H}-3\)), 3.53 (d, 1 H, H-4), 3.95 (d, 1 H, \(J_{3,3} 3.2 \text{ Hz}, \text{H}-2\)), 4.38 (s, 1 H, H-1), 4.68, 4.96 (2 d, 2 H, \(J_{\text{gem}} 11.9 \text{ Hz}, \text{PhCH}_2\)), 7.30–7.38 (m, 5 H, Ph). Anal. Calcd for \(\text{C}_{13}\text{H}_{18}\text{O}_5\): C, 61.40; H, 7.14. Found: C, 61.34; H, 7.04.

**Benzyl 3-O-benzoyl-6-deoxy-\(\beta\)-L-talopyranoside (37).**—A mixture of 36 (302 mg, 1.19 mmol) and \(\text{Bu}_2\text{SnO}\) (311 mg, 1.25 mmol) in benzene (20 mL) was boiled with stirring and azeotropic removal of water for 2.5 h, then 10 mL benzene was distilled from the mixture. The remaining solution was cooled to 0 °C, and benzoyl chloride (152 µl, 1.31 mmol) was added. After stirring at 0–5 °C for 45 min, MeOH (0.1 mL) and py (0.1 mL) were added to destroy the excess of benzoyl chloride. After being stirred for 0.5 h at rt, the mixture was concentrated, and the residue was subjected to column chromatography (85:15 toluene–EtOAc) to give 37 (334 mg, 78%); mp 100–102 °C (ether–light petroleum); \([\text{\text{[3]}]} \text{D} + 27.1 \text{°} (c 1, \text{CHCl}_3)\). \(1^H\) NMR: \(\delta 1.43\) (d, 3 H, \(J_{5,6} 6.1 \text{ Hz}, \text{H}-6\)), 2.71 (br s, 1 H, OH-2), 2.80 (d, 1 H, \(J_{3,OH} 8.4 \text{ Hz}, \text{OH-3}\)), 3.15 (dq, 1 H, H-5), 3.29 (t, 1 H, \(J_{4,5} 9.8 \text{ Hz}, \text{H}-4\)), 3.54 (m, 1 H, \(J_{3,4} 9.6 \text{ Hz}, \text{H}-3\)), 3.97 (d, 1 H, \(J_{2,3} 3.0 \text{ Hz}, \text{H}-2\)), 4.44 (s, 1 H, H-1), 4.64, 4.92 (2 d, 2 H, \(J_{\text{gem}} 11.8 \text{ Hz}, \text{PhCH}_2\)), 7.33–7.39 (m, 5 H, Ph). Anal. Calcd for \(\text{C}_{16}\text{H}_{21}\text{N}_3\text{O}_4\): C, 60.17; H, 6.63; N, 15.16. Found: C, 59.92; H, 6.60; N, 13.30.

**Benzyl 4-azido-4,6-dideoxy-\(\beta\)-L-mannopyranoside (42).**—A solution of 41 (3.37 g, 10.56 mmol) in 80% aq AcOH (30 mL) was heated at 40 °C for 5 h. The solvent was evaporated and coevaporated several times with toluene. Column chromatography of the residue (7:3 toluene–EtOAc) gave 42 (2.79 g, 95%); mp 89–91 °C (Et,O–light petroleum); \([\text{\text{[3]}]} \text{D} + 85.3 \text{°} (c 1, \text{CHCl}_3)\). \(1^H\) NMR: \(\delta 1.41\) (d, 3 H, \(J_{5,6} 6.1 \text{ Hz}, \text{H}-6\)), 2.71 (br s, 1 H, OH-2), 2.80 (d, 1 H, \(J_{3,OH} 8.4 \text{ Hz}, \text{OH-3}\)), 3.15 (dq, 1 H, H-5), 3.29 (t, 1 H, \(J_{4,5} 9.8 \text{ Hz}, \text{H}-4\)), 3.54 (m, 1 H, \(J_{3,4} 9.6 \text{ Hz}, \text{H}-3\)), 3.97 (d, 1 H, \(J_{2,3} 3.0 \text{ Hz}, \text{H}-2\)), 4.44 (s, 1 H, H-1), 4.64, 4.92 (2 d, 2 H, \(J_{\text{gem}} 11.8 \text{ Hz}, \text{PhCH}_2\)), 7.33–7.39 (m, 5 H, Ph). Anal. Calcd for \(\text{C}_{18}\text{H}_{17}\text{N}_3\text{O}_4\): C, 55.90; H, 6.14; N, 15.05. Found: C, 56.02; H, 6.38; N, 15.24.

**Benzyl 4-azido-3-O-benzoyl-4,6-dideoxy-\(\beta\)-L-mannopyranoside (43).**—Diol 42 (3.25 g, 11.65 mmol) was subjected to \(\text{Bu}_2\text{SnO-medi-}
ated benzylation as described for 37. After column chromatography of the reaction mixture (95:5 toluene–EtOAc), the monobenzoate 43 (3.98 g, 89%) was obtained as a syrup: [α]_D + 126° (c 1, CHCl_3). ^1H NMR: δ 1.50 (d, 3 H, J_5,6 6.1 Hz, H-6), 2.52 (broad s, 1 H, OH), 3.34 (dq, 1 H, H-5), 3.82 (t, 1 H, J_{3,4} 9.7 Hz, H-4), 4.31 (broad s, 1 H, H-2), 4.59 (s, 1 H, H-1), 4.69, 4.94 (2 d, 2 H, J_{gem} 11.9 Hz, PhCH_2), 5.00 (dd, 1 H, J_{gem} 10.2 Hz, J_{2,3} 2.6 Hz, H-3), 7.32–8.16 (m, 10 H, 2 Ph). Anal. Calcd for C_20H_{21}N_3O_5: C, 62.65; H, 11.00. 

**Benzyl 2,4-di diazido-3-O-benzoyl-2,4,6-trideoxy-β-L-glucopyranoside (39).**—Tf_2O (3.36 mM, 20 mmol) was added at 0 °C to a solution of 43 (3.84 g, 10.03 mmol) and py (4.04 mL, 40 mmol) in CH_2Cl_2 (40 mL), and the mixture was stirred at 0–5 °C for 1 h. The solution was diluted with CHCl_3, washed successively with water, M HCl, and water, and then concentrated. Crude triflate 44 was dissolved in DMF (30 mL), sodium azide (3.25 g, 50 mmol) was added, and the resulting mixture was stirred at rt overnight. The mixture was diluted with EtOAc, washed thoroughly with water, satd NaCl solution, dried with MgSO_4 and concentrated. Column chromatography of the residue (9:1 light petroleum–EtOAc) gave 39 (3.82 g, 93%): mp 91–92 °C (Et_2O–light petroleum); [α]_D + 1.3° (c 1, CHCl_3). ^1H NMR: δ 1.47 (d, 3 H, J_{5,6} 6.1 Hz, H-6), 3.35 (t, 1 H, J_{4,5} 9.7 Hz, H-4), 3.44 (dq, 1 H, H-5), 3.63 (dd, 1 H, J_{2,3} 10.3 Hz, H-2), 4.51 (d, 1 H, J_{1,2} 8.0 Hz, H-1), 4.73, 4.97 (2 d, 2 H, J_{gem} 11.8 Hz, PhCH_2), 5.18 (t, 1 H, J_{3,4} 9.8 Hz, H-3), 7.33–8.15 (m, 10 H, 2 Ph). Anal. Calcd for C_{17}H_{24}N_2O_5: C, 60.70; H, 7.19; N, 8.33. Found: C, 60.60; H, 7.21; N, 8.37.

**Benzyl 2,4-di diacetamido-2,4,6-trIDEOXY-3-O-mesyL-β-L-glucopyranoside (46).**—Methanesulfonyl chloride (1.68 mL, 21.7 mmol) was added at 0 °C to a suspension of 45 (1.82 g, 5.42 mmol) in CH_2Cl_2 (30 mL) and py (10 mL), and the mixture was stirred for 2 h at 0 °C, then overnight at rt. Water (100 mL) was added, and the two-phase solution was stirred for 2 h at rt. The organic layer was separated, the aqueous layer was extracted twice with CHCl_3, and the combined organic solution was concentrated to give 0.72 g of crude 46. The aqueous solution was concentrated to a volume of ~30 mL and left at 5 °C overnight. The crystalline precipitate was filtered off and dried to give the second portion of 46. Both portions of 46 were combined and subjected to column chromatography (95:5 CHCl_3–MeOH) to yield pure 46 (2.16 g, 96%): mp 187–189 °C (MeOH); [α]_D + 43° (c 1, DMF). ^1H NMR (CDCl_3 + CD_3OD): δ 1.15 (d, 3 H, J_{5,6} 5.7 Hz, H-6), 1.78, 1.83 (2 s, 6 H, 2 CH_3CO), 2.84 (s, 3 H, CH_3SO_2), 3.46–3.59 (m, 3 H, H-2,4,5), 4.45, 4.73 (2 d, 2 H, J_{gem} 12.1 Hz, PhCH_2), 4.64 (d, 1 H, J_{1,2} 8.3 Hz, H-1), 4.85 (t, 1 H, J_{2,3} ~J_{3,4} ~9.8 Hz, H-3), 7.13–7.21 (m, 5 H, Ph). Anal. Calcd for C_{17}H_{26}N_2O_5S: C, 52.16; H, 6.32; N, 6.76. Found: C, 52.13; H, 6.46; N, 6.47.

**Benzyl 2,4-di diacetamido-2,4,6-trIDEOXY-β-L-allpyranoside (47).**—A mixture of 46 (2.10 g,
5.07 mmol) and AcONa (2.08 g, 25.4 mmol) in 95% aq 2-methoxyethanol (50 mL) was boiled under reflux for 2.5 h. The solvent was evaporated and a suspension of the residue in 85:15 CHCl₃-MeOH was filtered through a layer of silica gel. The filtrate was concentrated, and the residue was chromatographed (92:8 CHCl₃-MeOH) to give 47 (1.62 g, 95%): mp 235°C (EtOH-Et₂O); [α]d₂₅ +47.6° (c 1, DMF). ¹H NMR (CDCl₃): δ 1.28 (d, 3 H, J₅,₆ 5.8 Hz, H-6), 1.83, 1.84 (2 s, 6 H, 2 CH₂CO), 3.92 (dq, 1 H, H-5), 3.97 (dd, 1 H, J₄,₅ 10.2 Hz, H-4), 4.02 (t, 1 H, J₃,₄ 2.3 Hz, H-3), 4.16 (dd, 1 H, J₂,₃ 2.8 Hz, H-2), 4.51, 4.82 (2 d, 2 H, J₆₇ 12.0 Hz, PhCH₂), 4.87 (d, 1 H, J₁,₂ 8.6 Hz, H-1), 7.08–7.28 (m, 5 H, Ph). Anal. Calcd for C₁₀H₁₈N₂O₅: C, 48.77; H, 7.37; N, 8.33. Found: C, 60.53; H, 7.19; N, 8.33. After being stirred for 72 h, the mixture was neutralized with Amberlite 420 (H⁺), and filtered, and the filtrate was concentrated to a volume of 3–4 mL. The solution was applied to a column of Dowex 1 × 8 (HCOO⁻), and the column was washed first with water to elute neutral products, then with 0.3 M formic acid. The appropriate fractions were pooled and concentrated, and the residue was subjected to preparative reversed-phase C₁₈ HPLC to give 49 (75 mg, 18%), tR 9.2 min, and 50 (84 mg, 20%), tR 10.5 min, as amorphous solids. Acid 49 had [α]d₂₅ +15.4° (c 1.6, water). ESIMS (+): Calcd for [M+Na]⁺ 357.1. Found 356.8. Compound 50 had [α]d₂₅ −19.2° (c 1.6, water). ESIMS (+): Calcd for [M+Na]⁺ 357.1. Found 356.8. For ¹H and ¹³C NMR data for 49 and 50, see Tables 2 and 3.

3,4-Diacetamido-2,4,6-trideoxy-L-allopyranose (48). — 20% Pd(OH)₂/C (500 mg) was added to a solution of 47 (1.40 g, 4.17 mmol) in MeOH (50 mL), (Caution: Extreme fire hazard), and the mixture was stirred under hydrogen at 35°C for 1 h. Water (10 mL) was added until complete dissolution of a white precipitate and formation of a clear solution over the catalyst, then hydrogenolysis was continued for another 1 h. The catalyst was filtered off through Celite, and washed with 80% aq MeOH, and the combined filtrate and washings were concentrated. Crystallization from water-EtOH-Et₂O gave 48 (890 mg, 87%): mp 235–242°C; [α]d₂₅ −3.5° → −15.7° (c 1, water). ¹H NMR (D₂O): 48α: δ 1.20 (d, 3 H, J₅,₆ 6.2 Hz, H-6), 2.04, 2.06 (2 s, 6 H, 2 CH₂CO), 3.79 (dd, 1 H, J₄,₅ 10.6 Hz, H-4), 3.96 (t, 1 H, J₃,₄ 2.8 Hz, H-3), 4.05 (t, 1 H, J₁,₂ 3.3 Hz, H-2), 4.18 (dq, 1 H, H-5), 5.15 (d, 1 H, J₁,₂ 3.8 Hz, H-1). 48β: δ 1.20 (d, 3 H, J₅,₆ 6.2 Hz, H-6), 2.03, 2.04 (2 s, 6 H, 2 CH₂CO), 3.76 (dd, 1 H, J₃,₄ 10.4 Hz, H-4), 3.81 (dd, 1 H, J₁,₂ 2.9 Hz, H-2), 3.92 (dq, 1 H, H-5), 3.97 (t, 1 H, J₃,₄ 2.9 Hz, H-3), 4.94 (d, 1 H, J₁,₂ 8.8 Hz, H-1). The ratio 48α:48β ≈ 1:3.3. Anal. Calcd for C₁₆H₁₈N₂O₅: C, 48.77; H, 7.37; N, 11.38. Found: C, 48.76; H, 7.41; N, 11.40.

3,4,5,7,9-Pentadecanamido-2,4,6-trideoxy-D-glycero-D-galacto- and D-glycero-D-talo-non-2-ulosonic acids (49 and 50). — Oxalacetic acid (165 mg, 1.25 mmol) was dissolved in water (4 mL), and the pH of the solution was adjusted to 10.5 by adding 5 M NaOH solution. Sodium tetraborate decahydrate (190 mg, 0.5 mmol) was added, and the pH was adjusted to 10.5 again. Then solid 15 (308 mg, 1.25 mmol) was added, and the resulting mixture was stirred at rt while the pH was maintained at 10.5 as above. More oxalacetic acid (42 mg, 0.31 mmol) was added after 6, 24, and 48 h. After being stirred for 72 h, the mixture was neutralized with Amberlite 420 (H⁺), and filtered, and the filtrate was concentrated to a volume of 3–4 mL. The solution was applied to a column of Dowex 1 × 8 (HCOO⁻), and the column was washed first with water to elute neutral products, then with 0.3 M formic acid. The appropriate fractions were pooled and concentrated, and the residue was subjected to preparative reversed-phase C₁₈ HPLC to give 49 (75 mg, 18%), tR 9.2 min, and 50 (84 mg, 20%), tR 10.5 min, as amorphous solids. Acid 49 had [α]d₂₅ +15.4° (c 1.6, water). ESIMS (+): Calcd for [M+Na]⁺ 357.1. Found 356.8. Compound 50 had [α]d₂₅ −19.2° (c 1.6, water). ESIMS (+): Calcd for [M+Na]⁺ 357.1. Found 356.8. For ¹H and ¹³C NMR data for 49 and 50, see Tables 2 and 3.
[M − H]− 333.1. Found 332.9 for 53 and 333.1 for 54. For 1H and 13C NMR data, see Tables 2 and 3.

5,7-Diacetamido-3,5,7,9-tetraedoxy-L-glucero-L-altro-, L-glycero-L-manno-, and L-glycero-L-gluco-non-2-ulosonic acids (55, 56, and 57). — Reaction of 48 (308 mg, 1.25 mmol) with oxalacetic acid, followed by anion-exchange chromatography and reversed-phase HPLC, afforded 56 (12 mg, 3%), tR 8.5 min, [α]d 56.9° (c 1, water), 57 (5 mg, 1%), tR 12.5 min, [α]d −76.0° (c 0.5, water), and 55 (34 mg, 8%), tR 13.3 min, [α]d −48.2° (c 1, water). ESIMS (−): Caled for [M − H]− 333.1. Found 333.4 for 56 and 333.5 for both 56 and 57. For 1H and 13C NMR data see Tables 2 and 3.

Methyl (5,7-diacetamido-2,4,8-tri-O-acetyl-3,5,7,9 - tetroedoxymon - 2 - ulopyranosonates (62–65). — Etheral diazomethane was added to solutions of acids 49, 51, 53, and 55 (15–20 mg of each) in MeOH (0.5–0.7 mL) until a yellow colour in the solutions persisted. A drop of AcOH was added, and the mixtures were taken to dryness. The residues were subjected to reversed-phase C18 HPLC in aq MeOH (6–8%) to give esters 58–61 as amorphous solids.

Compound 58: yield 52%; [α]d +26.0° (c 1, water). 1H NMR: δ 1.15 (d, 3 H, J3ax,4 6.3 Hz, H-9), 1.89 (dd, 1 H, J3ax,4 11.5 Hz, H-3ax), 1.98, 2.00 (2 s, 6 H, 2 CH3CO), 2.30 (dd, 1 H, J3eq,4 4.9 Hz, J3ax,3eq 13.1 Hz, H-3eq), 3.71 (t, 1 H, J6,7 10.5 Hz, H-5), 3.83 (dq, 1 H, H-8), 3.86 (s, 3 H, CH3O), 3.91 (dd, 1 H, J4,5 10.4 Hz, H-4), 4.32 (dd, 1 H, J6,7 2.1 Hz, H-6).

Compound 59: yield 35%; [α]d −27.7° (c 0.4, water). 1H NMR: δ 1.09 (d, 3 H, J3ax,4 6.4 Hz, H-9), 1.93 (dd, 1 H, J3ax,4 11.6 Hz, H-3ax), 2.05, 2.06 (2 s, 6 H, 2 CH3CO), 2.34 (dd, 1 H, J3eq,4 4.7 Hz, J3ax,3ax 13.2 Hz, H-3eq), 3.84 (s, 3 H, CH3O), 3.85 (t, 1 H, J5,6 10.3 Hz, H-5), 3.92 (dd, 1 H, J6,7 3.0 Hz, H-6), 3.93 (d, 1 H, H-7), 3.99 (dd, 1 H, J4,5 11.3 Hz, H-4), 4.39 (q, 1 H, H-8).

Compound 60: yield 57%; [α]d +33.5° (c 1, water). 1H NMR: δ 1.15 (d, 3 H, J3ax,4 6.3 Hz, H-9), 1.89 (dd, 1 H, J3ax,4 11.5 Hz, H-3ax), 1.98, 2.00 (2 s, 6 H, 2 CH3CO), 2.30 (dd, 1 H, J3eq,4 4.9 Hz, J3ax,3ax 13.1 Hz, H-3eq), 3.71 (t, 1 H, J5,6 10.5 Hz, H-5), 3.83 (dq, 1 H, H-8), 3.86 (s, 3 H, CH3O), 3.91 (dd, 1 H, J4,5 8.8 Hz, H-7), 3.97 (ddd, 1 H, J4,5 10.2 Hz, H-4), 4.32 (dd, 1 H, J6,7 2.1 Hz, H-6).

Compound 61: yield 49%; [α]d −55.1° (c 1, water). 1H NMR: δ 1.18 (d, 3 H, J3ax,4 6.4 Hz, H-9), 1.94 (dd, 1 H, J3ax,4 11.2 Hz, H-3ax), 2.03, 2.07 (2 s, 6 H, 2 CH3CO), 2.30 (dd, 1 H, J3eq,4 4.6 Hz, J3ax,3ax 13.2 Hz, H-3eq), 3.84 (s, 3 H, CH3O), 3.88 (t, 1 H, J4,5 10.4 Hz, H-5), 3.94 (ddd, 1 H, J4,5 11.1 Hz, H-4), 3.95 (dd, 1 H, J6,7 3.2 Hz, H-6), 4.04 (quintet, 1 H, H-8), 4.15 (dd, 1 H, J6,7 5.7 Hz, H-7).

Esters 58–61 (5–10 mg of each) were acetylated with Ac2O (0.2 mL) in py (0.4 mL) for 48 h at rt. After concentration and removal of residual Ac2O and py by coevaporation with toluene, the residues were passed through a Sep Pak Silica cartridge in 96:4 CHCl3–MeOH and the eluates were concentrated to give acetates 62–65, respectively. For 1H and 13C NMR data see Table 4.

Acknowledgements

This work was supported by grant 436 RUS 113/314/0 of the Deutsche Forschungsgemeinschaft and grants 99-03-32955 and 00-04-04009 of the Russian Foundation for Basic Research. The authors thank Prof. L.V. Backinowsky for critical reading of the manuscript.

References