ELSEVIER

www.elsevier.nl/locate/carres

Carbohydrate Research 327 (2000) 367–375

CARBOHYDRATE RESEARCH

Synthesis of α-galactosylated fragments related to the core-structure of the GPI anchor of *Trypanosoma brucei*

Thomas Ziegler [a,*], Ralf Dettmann [a], Michael Duszenko [b]

[a] *Institute of Organic Chemistry, University of Cologne, Greinstraße 4, D-50939 Cologne, Germany*
[b] *Institute of Physiological Chemistry, University Tübingen, Hoppe-Seyler-Straße 4, D-72076 Tübingen, Germany*

Received 24 September 1999; accepted 24 February 2000

Abstract

A series of octyl glycosides di- to tetrasaccharides related to the GPI anchor of *Trypanosoma brucei* was prepared. Treatment of octyl 2-*O*-benzoyl-4,6-*O*-(1,1,3,3-tetraisopropyl-1,3-disiloxane-1,3-diyl)-α-D-mannopyranoside with ethyl 2,3,4,6-tetra-*O*-benzyl-1-thio-β-D-galactopyranoside under activation with bromine and silver trifluoromethanesulfonate afforded the α-linked disaccharide octyl 2-*O*-benzoyl-3-*O*-(2,3,4,6-tetra-*O*-benzyl-α-D-galactopyranosyl)-4,6-*O*-(1,1,3,3-tetraisopropyl-1,3-disiloxane-1,3-diyl)-α-D-mannospyranoside, the siloxane ring of which was regioselectively opened with a HF–pyridine complex to give the disaccharide acceptor octyl 3-*O*-(2,3,4,6-tetra-*O*-benzyl-α-D-galactopyranosyl)-2-*O*-benzoyl-4-*O*-(3-fluoro-1,1,3,3-tetraisopropyl-1,3-disiloxane-3-yl)-α-D-mannopyranoside (**4**). Mannosylation of **4** with benzobromomannose (**7**), followed by fluoride catalyzed desilylation gave the trisaccharide octyl 2-*O*-benzoyl-6-*O*-(2,3,4,6-tetra-*O*-benzoyl-α-D-mannopyranosyl)-3-*O*-(2,3,4,6-tetra-*O*-benzyl-α-D-galactopyranosyl)-α-D-mannospyranoside, which was deblocked via the deacylated intermediate octyl 3-*O*-(2,3,4,6-tetra-*O*-benzyl-α-D-galactopyranosyl)-6-*O*-(α-D-mannopyranosyl)-α-D-mannospyranoside to afford the octyl glycoside trisaccharide octyl 3-*O*-(α-D-galactopyranosyl)-6-*O*-(α-D-mannopyranosyl)-α-D-mannospyranoside. Glycosylation of **4** with 3,4,6-tri-*O*-acetyl-2-*O*-(2,3,4,6-tetra-*O*-benzoyl-α-D-mannopyranosyl)-α-D-mannopyranosyl trichloroacetimidate resulted in the tetrasaccharide octyl 2-*O*-benzoyl-4-*O*-(1-fluoro-1,1,3,3-tetraisopropyl-1,3-disiloxane-3-yl)-3-*O*-(2,3,4,6-tetra-*O*-benzyl-α-D-galactopyranosyl)-6-*O*-[2-*O*-(2,3,4,6-tetra-*O*-benzoyl-α-D-mannopyranosyl)-3,4,6-tri-*O*-acetyl-α-D-mannopyranosyl]-α-D-mannospyranoside, sequential desilylation, deacylation and debenzylation, respectively, of which via the intermediate octyl 2-*O*-benzoyl-3-*O*-(2,3,4,6-tetra-*O*-benzyl-α-D-galactopyranosyl)-6-*O*-[2-*O*-(2,3,4,6-tetra-*O*-benzoyl-α-D-mannopyranosyl)-3,4,6-tri-*O*-acetyl-α-D-mannopyranosyl]-α-D-mannospyranoside afforded the octyl glycoside tetrasaccharide octyl 3-*O*-(α-D-galactopyranosyl)-6-*O*-[2-*O*-(α-D-mannopyranosyl)-α-D-mannopyranosyl]-α-D-mannospyranoside.

Keywords: GPI anchor; *Trypanosoma brucei*; Glycodesilylation

1. Introduction

Eukaryotic membrane proteins are attached to the membrane either by membrane-spanning hydrophobic peptide domains or by a glycosyl-phosphatidylinositol (GPI) anchor, which is covalently linked to the C-terminus of the protein. The latter is a membrane anchor motif of variant surface glycoprotein (VSG), a surface protein, which forms a protective barrier around the bloodstream forms of the protozoan parasite *Trypanosoma brucei* and accounts for about 10% of the total trypanosomal proteins [1]. Furthermore, GPI-

* Corresponding author. Tel.: +49-221-4703078; fax: +49-221-4705057.
E-mail address: aco10@rrz.uni-koeln.de (T. Ziegler).

0008-6215/00/$ - see front matter
PII: S0008-6215(00)00071-9

anchored proteins are found in virtually all classes of eukaryotes [2] and VSG was the first protein of which the GPI structure was completely determined. However, a clear and defined biological function of the GPI anchor has still to be elucidated, but it is noteworthy that GPI-anchored proteins are involved in important processes of cell–cell interaction, cell adhesion, and immunoresponse [3].

Studies of GPI structures obtained from several sources [2–8] revealed that all GPI anchors contain a highly conserved pentasaccharide core structure **ABCDE** (Fig. 1). In the case of the trypanosomal VSG GPI anchor, this core structure is differently galactosylated. These variable galactose side-chains may be important for the integrity of the VSG coat in order to serve as a molecular diffusion barrier and could perform space-filling functions in order to compensate for differences in the three-dimensional VSG structures [9]. For example, in *T. brucei* variant MITat 1.4 strain 427 [10], the core structure of the GPI anchor is modified by a diantennary galactan tetrasaccharide, which is α-(1→3)-linked to the mannosyl residue **C** (Fig. 1). Although the distinct enzymes involved in the biosynthetic pathway of trypanosomal GPI anchors are still unknown, it was reported recently that octyl glycosides and octyl 1-thio-glycosides may serve as substrates for trypanosomal α-galactosyltransferases [11–13]. Since trypanosomes can cause severe infections in animals and man, the respective galactosyltransferases are of fundamental interest as possible targets for a new anti-trypanosomal strategy. Thus, synthetic fragments related to trypanosomal GPI anchors can serve as probes for revealing the biosynthesis and biological properties of these structures and several chemical syntheses of GPI anchors and fragments thereof are described already in the literature [12–19].

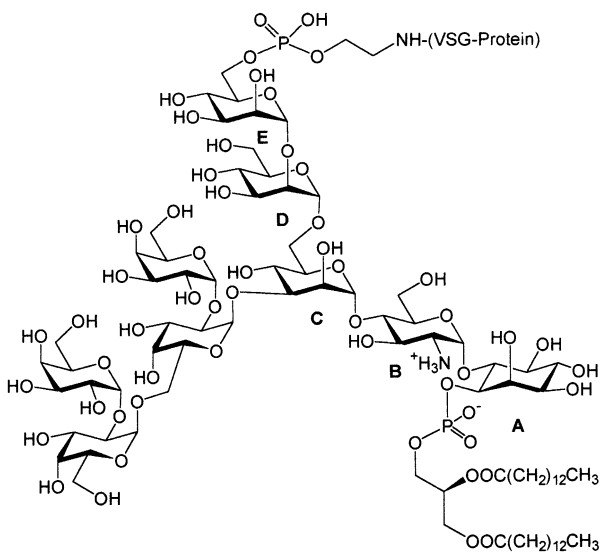


Fig. 1.

In continuation of our previous study on synthetic substrates for trypanosomal UDP-gal:glycosylphosphatidylinositol anchor α-(1→3)-galactosyltransferases [12], we describe the chemical synthesis of α-galactosylated fragments related to the GPI anchor of *T. brucei*. In particular, syntheses of α-galactosylated mono- to trisaccharide octyl glycopyranosides of the core region **CDE** (Fig. 1) are described that are planned to serve as substrates for trypanosomal α-galactosyltransferases.

2. Results and discussion

Originally, it was planned to construct the α-(1→3)-galactosylated key fragment **C** (Fig. 1) by intramolecular glycosylation [20] of a 4,6-tetraisopropyl-1,3-disiloxane-1,3-diyl protected mannopyranoside related to compound **1**. However, preliminary studies revealed that problems arose with this approach since rearrangement of the siloxane protecting group resulted in exclusive α-(1→6)-galactosylation of that mannosyl acceptor [21]. Therefore, a classical approach using siloxane protected mannoside **1** [12] as the acceptor was chosen here. Previously, Kovac and Edgar [22] showed for α-(1→3)-selective galactosylations of a series of 4,6-*O*-protected glucosamine derivatives with tetra-*O*-benzyl-α-D-galactopyranosyl chloride that 4,6-siloxane blocked acceptors reacted rather sluggishly or with low diastereoselectivity. Therefore, we chose ethyl 2,3,4,6-tetra-*O*-benzyl-1-thio-α-D-galactopyranoside (**2**) [23] as the donor in combination with Bundles [24] activation procedure. Thus, under optimized reaction conditions (see Section 3), the α-(1→3)-linked disaccharide **3** was obtained in 48% yield and no β-galactosylated

disaccharide could be detected in the crude reaction mixture. Other activation procedures of **2** gave lower yields or anomeric mixtures of the corresponding (1→3)-linked disaccharide. The α-configuration of the galactosyl residue in compound **3** was evident from the NMR spectra, which showed characteristic coupling constants of $J_{1,2} = 3.4$ Hz and $J_{C\text{-}1,H\text{-}1} = 165$ Hz [25]. The siloxane ring of compound **3** was regioselectively opened with HF–pyridine complex [26] to afford first octyl disaccharide **4** (90%). The regioselective ring opening of compound **3** instead of a direct glycodesilylation methodology with mannosyl fluorides, as previously described for similar siloxane protected monosaccharide octyl glycosides [12], was chosen here because compound **4** was planned to be condensed with bromide **7** and imidate **11** (see below). Although compound **4** was only obtained in medium overall yield, its preparation from easily accessible intermediates **1** and **2** appears to be straightforward since it can be used in a flexible strategy for the construction of various GPI anchor fragments as follows. Conventional sequential deblocking of the siloxane moiety (Bu_4NF) afforded first **5** debenzoylation and debenzylation of which gave disaccharide **6** in 70% overall yield. Also, disaccharide **4** served as the glycosyl acceptor for further elongation of the sugar chain. First, silver trifluoromethanesulfonate promoted condensation of **4** with benzobromomannose **7**, followed by fluoride catalyzed removal of the siloxane moiety, gave partially blocked trisaccharide **8** (78%). Next, conventional removal of the benzoyl groups (Zemplen) resulted in intermediate **9** (69%), which was finally debenzylated to give octyl glycoside trisaccharide **10** in 64% yield. Recently, compound **10** has also been prepared by a classical approach via galactosylation of a partially benzoylated octyl mannodisaccharide and has been used as substrate for enzymatic glycosylations with trypanosomal membrane preparations [27]. For the construction of the tetrasaccharide compound, disaccharide **4** was coupled with disaccharide imidate **11**, which has been previously used for the preparation of GPI anchor-related fragments [12]. However, TMSOTf promoted reaction of **4** and **11** resulted in incomplete glycosylation. Thus, tetrasaccharide **12** could be isolated in 52% yield besides unreacted **4** (45%). This may be due to a steric hindrance of the substituents at the 3- and 4-position of **4** since previously, similar (1→6)-selective condensations of **11** with octyl 2-*O*-benzoyl-4-*O*-(1-fluoro-1,1,3,3-tetraisopropyl-1,3-disiloxane-1-yl)-α-D-mannopyranoside proceeded in high yield [12]. Final sequential deblocking of **12** via saccharide **13** (89%) afforded tetrasaccharide octyl glycoside **14**.

Previously, enzymatic α-galactosylations of the trisaccharide α-D-Man*p*-(1→2)-α-D-Man*p*-(1→6)-α-D-Man*p*-1-*O*-$(CH_2)_7CH_3$ using trypanosomal membrane fractions and radiolabelled UDP-Gal have been shown to result in the formation of three different tetrasaccharides in which the α-linked galactosyl residues were shown by glycosidase digestion to be attached to mannose residues 1, 2, and 3, respectively [12]. No conclusion, however, could be deduced from these galactosylation experiments to which position of the respective mannosyl residues the galactosyl residues were linked. Preliminary enzymatic galactosylations of compounds **6**, **10**, and **14**, respectively, with radiolabeled UDP-galactose and trypanosomal membrane fractions, as previously described [12], revealed that saccharides **10** and **14** were significantly galactosylated at a faster rate than the corresponding non-galactosylated counterparts. For example, tetrasaccharide **14** reacted about 1000-fold faster than the aforementioned mannosyl trisaccharide octyl glycoside, as was judged from the relative rate of incorporation of radiolabeled galactose. Similarly, compound **10** was recently described to be most probably α-galactosylated at position 2 of the galactosyl residue [27]. Thus, it must be concluded that the three tetrasaccharides obtained previously by enzymatic galactosylation of α-D-Man*p*-(1→2)-α-D-Man*p*-(1→6)-α-D-Man*p*-1-*O*-$(CH_2)_7CH_3$ do not contain tetrasaccharide **14**. This finding could be the result of the presence of different α-galactosyltransferases in the trypanosomal membrane fraction used here. Alternatively, significantly different substrate selectivities of a single galactosyltransferase could account for this finding. Therefore, further investigations toward enzymatic galacto-

sylations of synthetic GPI anchor fragments are now under investigation.

3. Experimental

Mps were determined with a Büchi apparatus and are uncorrected. Optical rotations were measured with a Perkin–Elmer 241 polarimeter at 20 °C. ^{1}H and ^{13}C NMR spectra were recorded with a Bruker AC 300F spectrometer at 300 and 75.46 MHz, respectively. For trisaccharides **8**–**10** and tetrasaccharides **12**–**14**, protons and carbons of the 1st, 2nd and 3rd mannosyl residue, where the 1st residue is that one bearing the aglycone, was assigned with non-acentuated, single acentuated and double acentuated numbers. Thin-layer chromatography (TLC) was performed on precoated silica gel plates (E. Merck, $60F_{254}$) using appropriately adjusted mixtures of toluene–acetone or CCl_4–acetone. Detection of the products was achieved by charring with 5% H_2SO_4 in EtOH. Column chromatography was carried out on silica gel using columns of different length. Solvents were destilled prior to use. Solutions in organic solvents were dried with anhyd Na_2SO_4, and concentrated at 2 kPa, <40 °C. Compounds **1** [12], **2** [23], **7** [28] and **11** [12] were prepared as described in the literature.

*Octyl 2-*O*-benzoyl-3-*O*-(2,3,4,6-tetra-*O*-benzyl-α-*D*-galactopyranosyl)-4,6-*O*-(1,1,3,3-tetraisopropyl-1,3-disiloxane-1,3-diyl)-α-*D*-mannospyranoside* (**3**).—Tetramethyl urea (580 μL, 4.84 mmol) and silver trifluoromethanesulfonate (1.26 g, 4.88 mmol) were added to a stirred solution of **1** (1.55 g, 2.43 mmol), **2** (1.72 g, 2.94 mmol) and 3 Å molecular sieves in toluene (30 mL). After 20 min, bromine (195 μL, 3.7 mmol) was added and the mixture was stirred until TLC indicated complete conversion of **1** and **2** (4.5 h). The reaction was quenched with triethylamine (1.9 mL) and diluted with toluene. The mixture was filtered through a layer of Celite washed with water, aq $Na_2S_2O_3$ solution, water, aq $NaHCO_3$ solution, dried and concentrated. Chromatography (1:3 *n*-hexane–CH_2Cl_2) of the residue afforded **3** (1.36 g, 48%) as a colorless oil; $[\alpha]_D \pm 0°$ (*c* 1.5, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 8.05–7.00 (m, 25 H, ArH), 5.40 (dd, 1 H, $J_{1,2}$ 1.6, $J_{2,3}$ 2.7 Hz, H-2_{Man}), 5.02 (d, 1 H, H-1_{Man}), 4.97 (d, 1 H, $J_{1,2}$ 3.4 Hz, H-1_{Gal}), 4.83 (d, 1 H, J −11.3 Hz, $PhCH_2$), 4.79–4.57 (m, 5 H, $PhCH_2$), 4.44 (d, 1 H, J −11.3 Hz, $PhCH_2$), 4.17 (dd, 1 H, $J_{5,6a}$ 1.2 Hz, $J_{6a,6b}$ −12.5 Hz, H-$6a_{Man}$), 4.08–3.84 (m, 8 H, $PhCH_2$, H-2_{Gal}, H-3_{Man}, H-4_{Man}, H-4_{Gal}, H-5_{Man}, H-5_{Gal}), 3.68–3.39 (m, 5 H, OCH_2, H-3_{Gal}, H-$6b_{Man}$, H-$6a_{Gal}$), 3.18 (dd, 1 H, $J_{5,6b}$ 4.7 Hz, $J_{6a,6b}$ -8.5 Hz, H-$6b_{Gal}$), 1.50–0.81 (m, 45 H, CH, CH_2, CH_3); ^{13}C NMR ($CDCl_3$): δ 166.0 (CO), 139.1, 139.0, 138.9, 137.9, 133.2, 129.9, 129.7, 128.4, 128.3, 128.1, 128.0, 127.9, 127.6, 127.5, 127.3, 127.2 (ArC), 100.9 ($J_{C\text{-}1,H\text{-}1}$ 165 Hz, C-1_{Gal}), 97.2 ($J_{C\text{-}1,H\text{-}1}$ 171 Hz, C-1_{Man}), 80.6, 78.9, 76.7, 74.8 ($PhCH_2$), 74.7, 73.7 (C-5_{Man}), 73.6 (C-3_{Man}), 73.1 (2 C, $PhCH_2$), 72.9 ($PhCH_2$), 69.7 (C-4_{Man}), 68.2 (C-6_{Gal}), 67.6 (OCH_2), 65.9 (C-2_{Man}), 61.0 (C-6_{Man}), 31.9, 29.4, 29.3, 26.1, 22.7 (CH_2), 17.9, 17.8, 17.5, 17.4, 17.3, 17.1, 14.1, 13.3, 13.0, 12.7 (CH, CH_3).

*Octyl 2-*O*-benzoyl-4-*O*-(1-fluoro-1,1,3,3-tetraisopropyl-1,3-disiloxane-3-yl)-3-*O*-(2,3,4,6-tetra-*O*-benzyl-α-*D*-galactopyranosyl)-α-*D*-mannospyranoside* (**4**).—HF-pyridine (70%, 0.4 mL) was added to a stirred solution of **3** (1.7 g, 1.46 mmol) in CH_2Cl_2 at room temperature (rt). After 45 min, the solution was washed with an aq $NaHCO_3$ solution, dried, and concentrated. Chromatography (30:1 CCl_4–acetone) of the residue afforded **4** (1.54 g, 90%) as a colorless oil; $[\alpha]_D$ +9.2° (*c* 0.9, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 8.06–6.99 (m, 25 H, ArH), 5.36 (t, 1 H, $J_{1,2}$ 2.95 Hz, H-2_{Man}), 5.02 (d, 1 H, H-1_{Man}), 4.89 (d, 1 H, $J_{1,2}$ 3.4 Hz, H-1_{Gal}), 4.83–4.64 (m, 5 H, $PhCH_2$), 4.47 (d, 1 H, J 7.8 Hz, OH), 4.40 (dd, 1 H, J −11.3 Hz, $PhCH_2$), 4.73 (dd, 1 H, $J_{5,6a}$ 2.6 Hz, $J_{6a,6b}$ −8.1 Hz, H-$6a_{Man}$), 4.00 (dd, 1 H, $J_{2,3}$ 3.2, $J_{3,4}$ 10.8 Hz, H-3_{Man}), 3.92–3.67 (m, 9 H, H-2_{Gal}, H-3_{Gal}, H-4_{Man}, H-4_{Gal}, H-5_{Man}, H-5_{Gal}, H-$6b_{Man}$, H-$6a_{Gal}$, $PhCH_2$), 3.49–3.40 (m, 2 H, OCH_2), 2.98 (dd, 1 H, $J_{5,6b}$ 4.4, $J_{6a,6b}$ 7.9 Hz, H-$6b_{Gal}$), 1.63–0.85 (m, 45 H, CH, CH_2, CH_3); ^{13}C NMR ($CDCl_3$): δ 165.6 (CO), 138.9, 138.8, 138.6, 137.9, 133.2, 130.0, 129.6, 128.6, 128.3, 128.26, 128.2, 128.0, 127.8, 127.7, 127.6, 127.5, 127.4, 127.3, 127.2 (ArC), 99.8 (C-1_{Gal}), 96.3 (C-1_{Man}), 79.4, 79.0, 75.9 (C-2_{Gal},

C-3_{Gal}, C-4_{Gal}, C-5_{Gal}), 74.8 (2 C, C-3_{Man}, CH_2), 73.6, 73.0, 72.9 (CH_2), 72.5 (C-5_{Man}), 69.8 (C-4_{Man}), 68.5 (C-6_{Gal}), 67.7, 67.6 (OCH_2), 61.9 (C-6_{Man}), 31.8, 29.5, 29.4, 29.3, 26.1, 22.7 (CH_2), 17.6, 17.3, 17.1, 16.8, 16.7, 14.1, 12.8, 12.5, 12.4 (CH, CH_3); Anal. Calcd for $C_{67}H_{93}FO_{13}Si_2$: C, 68.21; H, 7.98. Found: C, 68.10; H, 7.93.

*Octyl 2-*O*-benzoyl-3-*O*-(2,3,4,6-tetra-*O*-benzyl-α-*D*-galactopyranosyl)-α-*D*-mannospyranoside* (**5**).—A solution of **4** (500 mg, 0.42 mmol) in THF (10 mL) was treated with a catalytic amount of Bu_4NF at rt for 1 h. The mixture was concentrated, the residue dissolved in CH_2Cl_2, washed with aq $NaHCO_3$ solution, dried and concentrated. Chromatography (7:1 CCl_4–acetone) afforded **5** (317 mg, 82%) as a colorless oil; $[\alpha]_D$ +21.7° (*c* 1.2, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 8.05–7.17 (m, 25 H, PhH), 5.42 (dd, 1 H, $J_{1,2}$ 1.6, $J_{2,3}$ 3.1 Hz, H-2_{Man}), 5.03 (d, 1 H, $J_{1,2}$ 3.8 Hz, H-1_{Gal}), 4.88 (d, 1 H, H-1_{Man}), 4.85 (d, 1 H, J −11.5 Hz, $PhCH_2$), 4.82 (d, 1 H, J −11.3 Hz, $PhCH_2$), 4.68 (d, 1 H, J −11.6 Hz, $PhCH_2$), 4.61 (d, 1 H, J −11.8 Hz, $PhCH_2$), 4.58 (d, 1 H, J −11.7 Hz, $PhCH_2$), 4.49 (d, 1 H, J −11.4 Hz, $PhCH_2$), 4.38 (d, 1 H, J −11.8 Hz, $PhCH_2$), 4.31 (d, 1 H, J −11.8 Hz, $PhCH_2$), 4.11 (t, 1 H, $J_{3,4} = J_{4,5}$ 9.5 Hz, H-4_{Man}), 4.04 (dd, 1 H, $J_{2,3}$ 10 Hz, H-2_{Gal}), 3.97 (dd, 1 H, H-3_{Man}), 3.92–3.64 (m, 8 H, H-3_{Gal}, H-4_{Man}, H-5_{Man}, H-5_{Gal}, H-$6a_{Man}$, H-$6b_{Man}$, H-$6a_{Gal}$, H-$6b_{Gal}$), 3.53 (t, 1 H, $J_{3,4} = J_{4,5}$ 8.7 Hz, H-4_{Gal}), 3.46–3.37 (m, 2 H, OCH_2), 2.21 (brs, 1 H, OH), 1.77 (brs, 1 H, OH), 1.62–1.55 (m, 2 H, CH_2), 1.37–1.04 (m, 10 H, CH_2), 0.91–0.87 (m, 3 H, CH_3); ^{13}C NMR (CDCl3): δ 166.1 (PhCO), 139.1, 138.8, 138.5, 138.1, 133.7, 130.2, 128.9, 128.8, 128.7, 128.6, 128.4, 128.1, 127.9, 127.8 (PhC), 101.6 (C-1_{Gal}), 97.8 (C-1_{Man}), 81.0 (C-3_{Man}), 79.5 (C-5_{Gal}), 76.4 (C-2_{Gal}), 74.7, 74.4 ($PhCH_2$), 74.3 (C-3_{Gal}), 73.2, 72.4 ($PhCH_2$), 72.2 (C-4_{Gal}), 71.7 (C-5_{Man}), 69.7 (C-2_{Man}), 68.3 (C-6_{Gal}), 68.0 (OCH_2), 68.0 (C-4_{Man}), 62.9 (C-6_{Man}), 31.8, 29.4, 29.2, 26.1, 22.7 (CH_2), 14.1 (CH_3); Anal. Calcd for $C_{55}H_{66}O_{12}$: C, 71.87; H, 7.24. Found: C, 71.67; H, 7.26.

*Octyl 3-*O*-(α-*D*-galactopyranosyl)-α-*D*-mannospyranoside* (**6**).—A solution of **5** (299 mg, 0.33 mmol) in MeOH (20 mL) was treated with a catalytic amount of 1 M NaOMe in MeOH for 4 days. The solution was neutralized with ion-exchange resin (Dowex 1X8, H^+) and concentrated. Chromatography (3:1 CCl_4–acetone) of the residue afforded a colorless oil, which was dissolved in aq 90% MeOH (8 mL) and AcOH (0.5 mL) and hydrogenolyzed with H_2 (1 atm) over a catalytic amount of Pd–C. The mixture was stirred until TLC (9:4:2 EtOAc–*i*-propanol–water) indicated the end of the reaction. Filtration and concentration of the mixture, followed by chromatography of the residue with water on Bio-Gel P2 afforded **6** (118 mg, 85%); $[\alpha]_D$ +68.4° (*c* 0.3, H_2O); ^{13}C NMR (D_2O): δ 101.9 (C-1_{Gal}), 101.1 (C-1_{Man}), 80.8 (C-3_{Man}), 73.2 (C-5_{Man}), 72.2 (C-2_{Man}), 71.0 (C-2_{Gal}), 70.6 (C-5_{Gal}), 70.2 (C-3_{Gal}), 70.0 (C-4_{Gal}), 68.9 (OCH_2), 66.5 (C-4_{Man}), 62.1 (C-6_{Gal}), 61.7 (C-6_{Man}), 32.9, 30.5, 30.3 (2 C), 27.1, 23.7 (CH_2), 15.0 (CH_3); Anal. Calcd for $C_{20}H_{38}NaO_{11}$: 477.23118 $[M + Na]^+$. Found: *m/z* 477.23123 $[M + Na]^+$ (HRFABMS).

*Octyl 2-*O*-benzoyl-6-*O*-(2,3,4,6-tetra-*O*-benzoyl-α-*D*-mannopyranosyl)-3-*O*-(2,3,4,6-tetra-*O*-benzyl-α-*D*-galactopyranosyl)-α-*D*-mannospyranoside* (**8**).—Silver triflate (121 mg, 0.47 mmol) was added at −10 °C under Ar to a stirred mixture of **4** (0.5 g, 0.42 mmol) and 3 Å molecular sieves (0.5 g) in CH_2Cl_2 (3 mL). After 0.5 h, a solution of **7** (307 mg, 0.47 mmol) and *sym*-collidine (45 μL, 0.34 mmol) in CH_2Cl_2 (1 mL) was added dropwise and the mixture was stirred for 1 h, filtered through a layer of Celite, washed with an aq $Na_2S_2O_3$ solution, 1 M HCl, an aq $NaHCO_3$ solution, dried and concentrated. Chromatography (30:1 CCl_4–acetone) of the residue afforded an oil, which was dissolved in THF (5 mL) and treated with a catalytic amount of Bu_4NF, as described for the preparation of **5**. Chromatography (30:1 CCl_4–acetone) of the residue afforded **8** (483 mg, 78%); $[\alpha]_D$ +2.1° (*c* 1.0, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 8.01–7.07 (m, 25 H, PhH), 6.07 (t, 1 H, $J_{3,4} = J_{4,5}$ 10.0 Hz, H-4′), 5.89 (dd, 1 H, $J_{2,3}$ 3.1 Hz, H-3′), 5.71 (dd, 1 H, $J_{1,2}$ 1.8 Hz, H-2′), 5.42 (dd, 1 H, $J_{1,2}$ 1.5 Hz, $J_{2,3}$ 3.0 Hz, H-2), 5.15 (d, 1 H, H-1′), 4.95 (d, 1 H, $J_{1,2}$ 3.8 Hz, H-1_{Gal}), 4.85 (d, 1 H, H-1), 4.79 (d, 1 H, J −11.4 Hz, $PhCH_2$), 4.75 (d 1 H, J −11.2 Hz, $PhCH_2$),

4.63 (d, 1 H, J −11.7 Hz, $PhCH_2$), 4.60–4.34 (m, 4 H, H-5′, $PhCH_2$), 4.33 (d, 1 H, J −11.7 Hz, $PhCH_2$), 4.25 (d, 1 H, J 11.8 Hz, $PhCH_2$), 4.10 (t, 1 H, $J_{3,4} = J_{4,5}$ 9.6 Hz, H-4), 4.08–3.65 (m, 11 H, H-2_{Gal}, H-3, H-3_{Gal}, H-5, H-5_{Gal}, H-6a,b, H-6a,b′,H-6a,b_{Gal}), 3.51 (t, 1 H, $J_{3,4} = J_{4,5}$ 8.7 Hz, H-4_{Gal}), 3.44–3.36 (m, 2 H, OCH_2), 1.67–1.53 (m, 3 H, OH, CH_2), 1.32–1.16 (m, 10 H, CH_2), 0.79–0.74 (m, 3 H, CH_3); ^{13}C NMR ($CDCl_3$): δ 166.3, 165.9, 165.5, 165.4, 165.2 (Ph–CO), 138.8, 138.5, 138.3, 137.8, 133.4, 133.3, 133.2, 133.1, 130.1, 129.9 (2 C), 129.5, 129.4, 129.2, 128.7, 128.6, 128.5, 128.4, 128.3 (2 C), 128.1 (2 C), 127.8, 127.6, 127.4 (ArC), 102.0 (C-1_{Gal}), 98.0 (C-1′), 97.6 (C-1), 81.8 (C-3), 79.6 (C-5_{Gal}), 76.5 (C-2_{Gal}), 74.9, 74.5 ($PhCH_2$), 74.4 (C-3_{Gal}), 73.3, 72.5 ($PhCH_2$), 72.2 (C-4_{Gal}), 71.5 (C-5), 70.5 (C-5′), 70.3 (C-3′), 69.8 (C-2), 68.9 (C-2′), 68.4 (C-6_{Gal}), 67.0 (C-4), 66.9 (C-4′), 66.6 (C-6), 62.8 (C-6′), 31.9, 29.6 (2C), 29.4, 26.3, 22.6 (CH_2), 14.2 (CH_3); Anal. Calcd for $C_{89}H_{92}O_{21}$: 1496.6. Found: m/z 1496.4 $[M]^+$ (FABMS).

Octyl3-O-*(2,3,4,6-tetra*-O-*benzyl*-α-D-*galactopyranosyl)-6*-O-*(*α-D-*mannopyranosyl)*-α-D-*mannospyranoside* (**9**).—A catalytic amount of NaOMe was added to a solution of **8** (462 mg, 0.31 mmol) in MeOH (30 mL). After 5 days, the mixture was neutralized with ion-exchange resin (Dowex 5w80) and filtered. Chromatography (10:1 CH_2Cl_2–MeOH) of the residue afforded **9** (209 mg, 69%) as a white foam; $[\alpha]_D$ +64.6° (*c* 1.0, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 7.40–7.19 (m, 20 H, PhH), 4.95 (d, 1 H, $J_{1',2'}$ 2.3 Hz, H-1′), 4.90–4.79 (m, 4 H, $PhCH_2$), 4.75 (d, 1 H, $J_{1,2}$ 4.0 Hz, H-1_{Gal}), 4.48 (d, 1 H, J −11.8 Hz, $PhCH_2$), 4.42 (d, 1 H, J −12.0 Hz, $PhCH_2$), 4.40 (d, 1 H, $J_{1,2}$ 2.2 Hz, H-1), 4.20 (dd, 1 H, $J_{2,3}$ 3.5, $J_{3,4}$ 7.6 Hz, H-3), 4.08–3.11 (m, 28 H, H-2, 2′, 2_{Gal}, H-3′, 3_{Gal}, H-4, 4′, 4_{Gal}, H-5, 5′, 5_{Gal}, H-6a,b, 6a,b′, 6a,b_{Gal}, OH, $PhCH_2$, OCH_2), 1.47 (brs, 2 H, CH_2), 1.27 (brs, 10 H, CH_2), 0.88 (brt, 3 H, CH_3); ^{13}C NMR ($CDCl_3$): δ 138.7, 138.5, 137.8, 137.3, 128.9, 128.8, 128.6, 128.5, 128.4 (2C), 128.3, 128.0, 127.9 (ArC), 100.8 (C-1_{Gal}), 100.5 (C-1′), 100.2 (C-1), 83.5 (C-3), 79.6 (C-5_{Gal}), 76.9 (C-2_{Gal}), 75.3 (C-3_{Gal}), 74.8, 74.1 (2C), 73.4 ($PhCH_2$), 72.6 (C-5), 72.0 (C-4_{Gal}), 71.62 (C-5′), 71.1 (C-3), 70.8 (OCH_2), 70.7 (C-2), 70.13 (C-2′), 68.1 (C-6_{Gal}), 67.1 (C-4′), 66.1 (C-6), 65.4 (C-4), 61.7 (C-6′), 32.3, 29.9 (2C), 29.7, 26.6, 23.1 (CH_2), 14.5 (CH_3); Anal. Calcd for $C_{54}H_{72}O_{16}$: 976.5. Found m/z 999.4 $[M + Na]^+$ (FABMS).

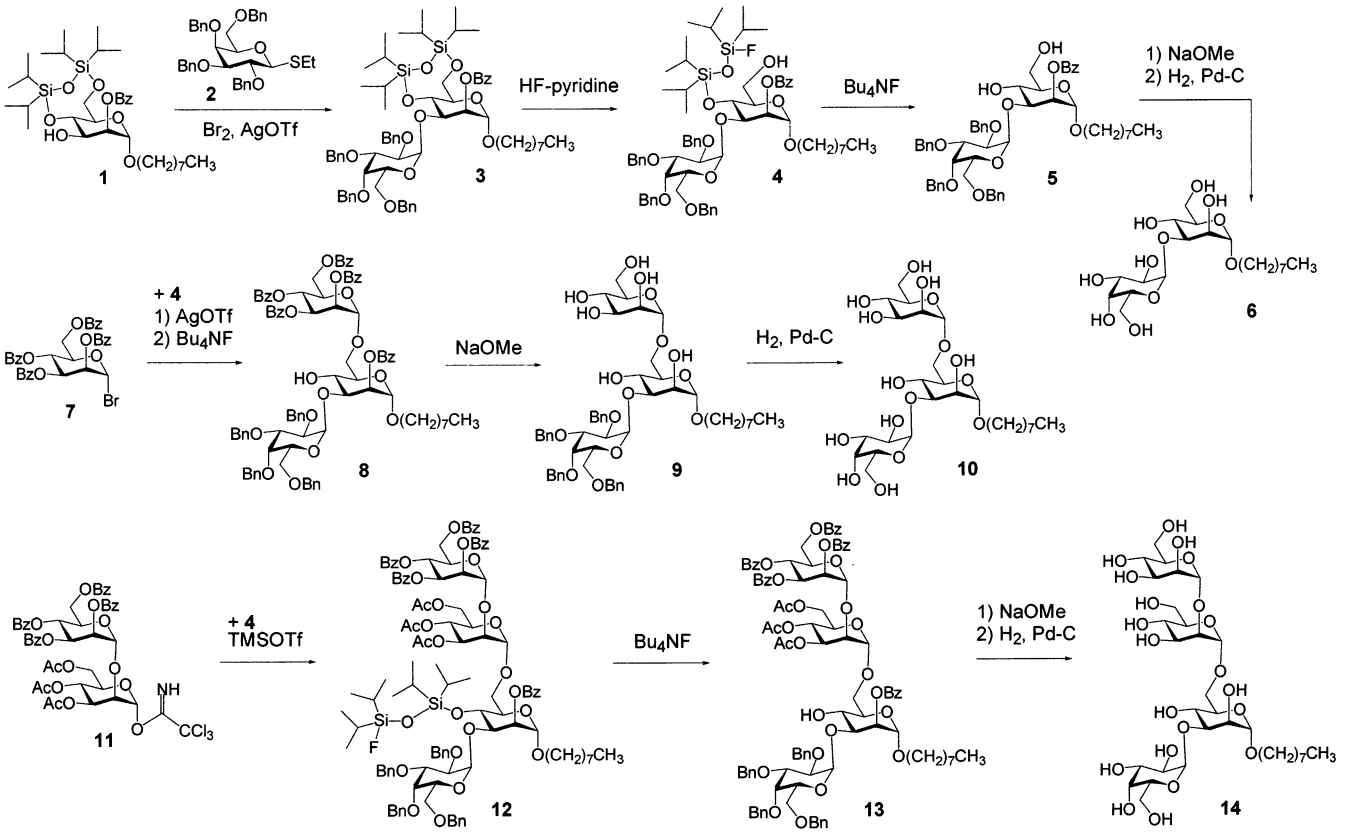
Octyl 3-O-*(*α-D-*galactopyranosyl)-6*-O-*(*α-D-*mannopyranosyl)*-α-D-*mannospyranoside* (**10**).—Compound **9** (184 mg, 0.19 mmol) was dissolved in 90% aq MeOH (8 mL) and AcOH (0.5 mL) and treated with H_2 (1 atm) and a catalytical amount of Pd–C until all starting material was consumed and the mixture was filtered and concentrated. Chromatography of the residue with water on Bio-Gel P2 afforded **10** (73 mg, 64%); $[\alpha]_D$ +70.5° (*c* 0.2, water); ^{13}C NMR (D_2O): δ 102.1 (C-1_{Gal}), 101.2 (C-1), 100.7 (C-1′), 81.3 (C-3), 73.8 (C-5), 72.4 (C-2), 72.2 (C-3′), 71.9 (C-2′), 71.2 (C-5′), 71.0 (C-2_{Gal}), 70.6 (C-5_{Gal}), 70.2(C-3_{Gal}), 70.0 (C-4_{Gal}), 69.2 (OCH_2), 67.7 (C-4′), 66.3 (C-4,6), 62.2 (C-6_{Gal}), 61.9 (C-6′), 32.7, 30.0 (2C), 26.9 and 23.5 (CH_2), 14.9 (CH_3); Anal. Calcd for $C_{26}H_{48}O_{16}Na^+$: 639.2840. Found: m/z 639.28332 $[M + Na]^+$ (HRFABMS).

Octyl 2-O-*benzoyl-4*-O-*(1-fluoro-1,1,3,3-tetraisopropyl-1,3-disiloxane-3-yl)-3*-O-*(2,3,4,6-tetra*-O-*benzyl*-α-D-*galactopyranosyl)-6*-O-*[2*-O-*(2,3,4,6-tetra*-O-*benzoyl*-α-D-*mannopyranosyl)-3,4,6-tri*-O-*acetyl*-α-D-*mannopyranosyl]*-α-D-*mannospyranoside* (**12**).—A catalytic amount of Me_3SiOTf (10 μL, 0.05 mmol) was added at −30 °C to a stirred solution of **4** (420 mg, 0.355 mmol) and 4 Å molecular sieves (0.5 g) in CH_2Cl_2 (4.5 mL), followed by dropwise addition of a solution of **11** (468 mg, 0.455 mmol) in CH_2Cl_2 (4.5 mL). After 20 min an additional amount of **11** (192 mg, 0.187 mmol) was added, the mixture was stirred for 0.5 h, and the reaction was quenched with pyridine. Concentration of the mixture and chromatography (10:1 CCl_4–acetone) of the residue afforded first unchanged **4** (197 mg, 47%). Eluted next was **12** (375 mg, 52%); $[\alpha]_D$ −5° (*c* 0.8, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 8.15–6.89 (m, 5 H, ArH), 6.15 (t, 1 H, $J_{3'',4''} = J_{4'',5''}$ 10.3 Hz, H-4″), 5.89 (dd, 1 H, $J_{2'',3''}$ 3.1 Hz, H-3″), 5.53 (dd, 1 H, $J_{1,2}$ 1.9 Hz, H-2), 5.44 (t, 1 H, $J_{3',4'} = J_{4',5'}$ 9.8 Hz, H-4′), 5.33 (dd, 1 H, $J_{2',3'}$ 3.7 Hz, H-3′), 5.32 (dd, 1 H,

$J_{1'',2''}$ 1.6 Hz, H-2″), 5.21 (s, 1 H, H-1′), 5.11 (d, 1 H, H-1″), 4.89 (d, 1 H, $J_{1,2}$ 2.8 Hz, H-1_{Gal}), 4.82–4.64 (m, 6 H, H-1′, $PhCH_2$), 4.58 (t, 1 H, $J_{3,4} = J_{4,5}$ 9.2 Hz, H-4), 4.48–4.19 (m, 6 H, H-2′, H-2_{Gal}, H-6a″, $PhCH_2$), 4.13–3.89 (m, 9 H, H-3, H-3_{Gal}, H-5, H-5′, H-5″, H-5_{Gal}, H-6b″, H-6a,b′), 3.78–3.68 (m, 4 H, H-6a,b, H-$6a_{Gal}$, OCH_2), 3.55–3.49 (m, 2 H, 1 H, OCH_2), 3.42 (t, 1 H, $J_{3,4l} = J_{4,5}$ 9.0 Hz, H-4_{Gal}), 3.82 (dd, 1 H, $J_{5,6b}$ 4.6, $J_{6a,6b}$ 8.3 Hz, H-$6b_{Gal}$), 2.23, 2.11, 2.08 (s, 3 H, CH_3), 1.75–1.63 (m, 2 H, CH_2), 1.55–0.88 (m, 41 H, CH, CH_2, CH_3); ^{13}C NMR ($CDCl_3$): δ 171.1, 170.3, 169.6 (CO), 166.0, 165.5, 165.3, 165.1, 165.0 (PhCO), 139.0 (3 C), 138.0, 133.6, 133.4, 133.1, 132.9, 129.9, 129.8, 129.7, 128.8, 128.4, 128.3, 128.1, 127.8 (2 C), 127.6, 127.4, 127.3 (ArC), 100.1 (C-1_{Gal}), 99.5 (C-1″), 98.7 (C-1′), 96.3 (C-1), 79.7 (C-3), 79.3 (C-5_{Gal}), 77.4 (C-2′), 76.1 (C-2_{Gal}), 75.0 (C-4_{Gal}), 74.8 (2 C, C-3_{Gal}, $PhCH_2$), 73.6, 73.2 ($PhCH_2$), 73.0 (2 C, C-5, $PhCH_2$), 70.5 (C-5′), 70.4 (C-5″), 70.0 (C-2), 69.5 (C-3′), 69.2 (C-3″), 68.6 (C-2″), 68.5 (C-6_{Gal}), 67.9 (C-4), 67.6 (OCH_2), 66.8 (C-4′), 66.3 (C-4″), 65.5 (C-6), 62.4 (2 C, C-6′, C-6″), 31.9, 29.5, 29.4 (2 C), 26.3, 22.8 (CH_2), 21.0, 20.7, 17.8, 17.4, 17.3, 17.2, 16.8, 14.2, 12.5, 12.2 (CH, CH_3); Anal. Calcd for $C_{113}H_{135}FO_{30}Si_2$: C, 66.26; H, 6.64. Found: C, 66.15; H, 6.64.

Octyl 2-O-*benzoyl-3*-O-*(2,3,4,6-tetra*-O-*benzyl-α*-D-*galactopyranosyl)-6*-O-*[2*-O-*(2,3,4,6-tetra*-O-*benzoyl-α*-D-*mannopyranosyl)-3,4,6-tri*-O-*acetyl-α*-D-*mannopyranosyl]-α*-D-*mannospyranoside* (**13**).—A solution of **12** (320 mg, 0.156 mmol) in THF (5 mL) was treated with a catalytic amount of Bu_4NF as described for the preparation of compound **8**. Chromatography (7:1 CCl_4–acetone) of the residue afforded **13** (247 mg, 89%) as a white foam; $[\alpha]_D$ −2.8° (*c* 0.7, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 8.01–7.04 (m, 45 H, PhH), 6.02 (t, 1 H, $J_{3'',4''} = J_{4'',5''}$ 10.0 Hz, H-4″), 5.86 (dd, 1 H, $J_{2'',3''}$ 3.1 Hz, H-3″), 5.59 (dd, 1 H, $J_{1,2}$ 1.8, $J_{2,3}$ 2.8 Hz, H-2), 5.40, (t, 1 H, $J_{3',4'} = J_{4',5'}$ 9.6 Hz, H-4′), 5.35–5.32 (m, 2 H, H-3′, H-2″), 5.10 (d, 1 H, $J_{1',2'}$ 0.6 Hz, H-1′), 4.93 (d, 1 H, $J_{1,2}$ 3.4 Hz, H-1_{Gal}), 4.85 (d, 1 H, H-1), 4.83 (d, 1 H, $J_{1'',2''}$ 1.6 Hz, H-1″), 4.79 (d, 1 H, *J* −11.8 Hz, $PhCH_2$), 4.73 (d, 1 H, *J* −11.4 Hz, $PhCH_2$), 4.63 (d, 1 H, *J* 11.6 Hz, $PhCH_2$), 4.58–4.30 (m, 12 H, H-2′, H-5′, H-5″, H-6a,b′, H-6a,b″, $PhCH_2$), 4.27–3.57 (m, 10 H, H-2_{Gal}, H-3, H-3_{Gal}, H-4, H-5, H-5_{Gal}, H-6a,b, H-6a,b_{Gal}), 3.55 (t, 1 H, $J_{3,4} = J_{4,5}$ 8.8 Hz, H-4_{Gal}), 3.38–3.28 (m, 2 H, OCH_2), 2.11 (s, 3 H, CH_3), 2.05 (s, 3 H, CH_3), 1.96 (s, 3 H, CH_3), 1.74 (brs, 1 H, OH), 1.52–1.50 (brm, 2 H, CH_2), 1.19–1.13 (brs, 10 H, CH_2), 0.82–0.77 (brm, 3 H, CH_3); ^{13}C NMR ($CDCl_3$): δ 171.0, 170.4, 169.5 (CO), 165.9, 165.5 (2 C), 165.1, 165.0 (PhCO), 138.7, 138.4, 138.1, 137.8, 133.5, 133.4, 133.1, 133.0, 132.9, 129.8, 129.7, 129.3, 129.1, 128.9, 128.6, 128.5, 128.4, 128.3 (2 C), 128.2, 128.1, 127.9, 127.6, 127.4, 127.3 (ArC), 101.9 (C-1_{Gal}), 99.6 (C-1″), 98.4 (C1′), 97.7 (C-1), 81.6 (C-3), 79.6 (C-5_{Gal}), 77.6 (C-2′), 76.4 (C-2_{Gal}), 74.8, 74.4 ($PhCH_2$), 74.3 (C-3_{Gal}), 73.2, 72.5 ($PhCH_2$), 72.3 (C-4_{Gal}), 71.7 (C-5), 70.7 (C-5′), 70.5 (C-5″), 69.7 (C-2), 69.5 (2 C, C-3′, C-3″), 68.6 (C-2″), 68.4 (C-6_{Gal}), 68.0 (OCH_2), 67.0 (C-4), 66.6 (C-4′), 66.4 (C-4″), 65.8 (C-6), 62.8 (C-6′), 62.3 (C-6″), 31.9, 29.5 (2 C), 29.3, 26.3, 22.8 (CH_2), 21.0, 20.9 (2 C), 14.2 (CH_3); Anal. Calcd for $C_{101}H_{108}O_{29}$: C, 67.93; H, 6.10. Found: C, 67.82; H, 6.11.

Octyl 3-O-*(α*-D-*galactopyranosyl)-6*-O-*[2*-O-*(α*-D-*mannopyranosyl)-α*-D-*mannopyranosyl]-α*-D-*mannospyranoside* (**14**).—A solution of **13** (230 mg, 0.129 mmol) in MeOH (30 mL) was treated with a catalytic amount of NaOMe as described for the preparation of compound **8**. The crude deacylated intermediate was dissolved in 90% aq MeOH (90%) and hydrogenolyzed as described for the preparation of compound **10**. Chromatography of the residue with water on Bio-Gel P-2 afforded **14** (48 mg, 78%); $[\alpha]_D$ +63° (*c* 0.2, H_2O); ^{13}C NMR (D_2O): δ 103.5 (C-1″), 102.0 (C-1_{Gal}), 101.0 (C-1), 99.2 (C-1′), 80.5 (C-3), 79.9 (C-2′), 74.4 (C-5″), 73.9 (C-5), 72.5 (C-2), 72.3 (C-2″), 71.5 (C-5′), 71.4 (C-2_{Gal}), 71.1 (C-5_{Gal}), 71.0 (C-3_{Gal}), 70.5 (C-3′), 70.4 (C-3″), 69.9 (C-4_{Gal}), 69.3 (OCH_2), 68.00 (2 C, C-4′,4″), 66.74 (C-6), 66.68 (C-4), 62.4 (C-6″),62.3 (C-6_{Gal}), 62.0 (C-6′), 32.3, 29.6 (2 C), 29.53, 29.52 and 23.2 (CH_2), 14.6 (CH_3); Anal. Calcd for $C_{32}H_{58}O_{21}Na^+$: 801.336828. Found: *m/z* 801.33607 $[M + Na]^+$ (HR-FABMS) (Scheme 1).



Scheme 1.

Acknowledgements

This work was financially supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie. We thank Dr H. Schmickler, C. Schmitz for performing the NMR spectra and the elemental analyses.

References

[1] (a) M.A.J. Ferguson, K. Haldar, G.A.M. Cross, *J. Biol. Chem.*, 260 (1985) 4963–4968. (b) M.A.J. Ferguson, M. Duszenko, G.S. Lamont, P. Overath, G.A.M. Cross, *J. Biol. Chem.*, 261 (1986) 356–362. (c) M.A.J. Ferguson, S.W. Homans, R.A. Dwek, T.W. Rademacher, *Science*, 239 (1988) 753–759.
[2] M.J. McConville, M.A.J. Ferguson, *Biochem. J.*, 294 (1993) 305–324.
[3] A.J. Turner, *Essays Biochem.* (*Engl.*), 28 (1994) 113–127.
[4] J.R. Thomas, R.A. Dwek, T.W. Rademacher, *Biochemistry*, 29 (1990) 5413–5414.
[5] M.L.S. Günther, M.L. Cardoso de Almeida, N. Yoshida, M.A.J. Ferguson, *J. Biol. Chem.*, 267 (1992) 6820–6828.
[6] A. Mehlert, I. Silman, S.W. Homans, M.A.J. Ferguson, *Biochem. Soc. Trans.*, 21 (1992) 43S.
[7] S.W. Homans, M.A.J. Ferguson, A.F. Williams, *Nature*, 333 (1988) 269–272.
[8] M.A. Deeg, D.R. Humphrey, S.M. Yang, T.R. Ferguson, V.N. Reinhold, T.L. Rosenberry, *J. Biol. Chem.*, 267 (1992) 18573–18580.
[9] S.W. Homans, M.A.J. Ferguson, R.A. Dwek, T.W. Rademacher, *Biochemistry*, 28 (1989) 2881–2887.
[10] G.A.M. Cross, *Parasitology*, 71 (1975) 393–417.
[11] S. Pingel, R.A. Field, M.L.S. Günther, M. Duszenko, M.A.J. Ferguson, *Biochem. J.*, 309 (1995) 877–882.
[12] T. Ziegler, R. Dettmann, V. Duszenko, V. Kolb, *Carbohydr. Res.*, 295 (1996) 7–23.
[13] M.M. Palcic, L.D. Heerze, M. Pierce, O. Hindsgaul, *Glycoconjugate J.*, 5 (1988) 89–98.
[14] R. Verduyn, C.J.J. Elie, C.E. Dreef, G.A. van der Marel, J.H. van Boom, *Recl. Trav. Chim. Pays-Bas*, 109 (1990) 591–593.
[15] C. Murakata, T. Ogawa, *Carbohydr. Res.*, 235 (1992) 95–114.
[16] (a) D.R. Mootoo, P. Konradsson, B. Fraser-Reid, *J. Am. Chem. Soc.*, 111 (1989) 8540–8542. (b) R. Madsen, U.E. Udodong, C. Roberts, D.R. Mootoo, P. Konradsson, B. Fraser-Reid, *J. Am. Chem. Soc.*, 117 (1995) 1554–1565.
[17] (a) T.G. Mayer, B. Kratzer, R.R. Schmidt, *Angew. Chem.*, 106 (1994) 2289–2293; *Angew Chem. Int. Ed. Engl.*, 33 (1994) 2177–2181. (b) T.G. Mayer, R.R. Schmidt, *Eur. J. Org. Chem.*, (1999) 1153–1165.
[18] D.K. Baeschlin, A.R. Chaperon, V. Charbonneau, L.G. Green, S.V. Ley, U. Lücking, E. Walther, *Angew. Chem.*, 110 (1998) 3609–3614; *Angew. Chem. Int. Ed.*, 37 (1998) 3423–3428.
[19] (a) H. Dietrich, J.F. Espinosa, J.L. Chiara, J. Jimenez-Barbero, Y. Leon, I. Varela-Nieto, J.-M. Mato, F.H.

Cano, C. Foces-Foces, M. Martin-Lomas, *Chem. Eur. J.*, 5 (1999) 320–336. (b) N. Khiar, M. Martin-Lomas, in Y. Chapleur (Ed.), *Carbohydrate Mimics*, Wiley-VCH, Weinheim, 1998, pp. 443–462. (c) H. Dietrich, J.F. Espinosa, J.L. Chiara, J. Jimenez-Barbero, Y. Leon, I. Varela-Nieto, J.-M. Mato, F.H. Cano, C. Foces-Foces, M. Martin-Lomas, *Chem. Eur. J.*, 5 (1999) 320–336.

[20] (a) T. Ziegler, R. Lau, *Tetrahedron Lett.*, 36 (1995) 1417–1420. (b) R. Lau, G. Schüle, U. Schwaneberg, T. Ziegler, *Liebigs Ann.*, (1995) 1745–1754. (c) T. Ziegler, G. Lemanski, R. Rakoczy, *Tetrahedron Lett.*, 36 (1996) 8973–8976. (c) T. Ziegler, G. Lemanski, *Eur. J. Org. Chem.*, (1998) 163–170. (d) T. Ziegler, G. Lemanski, *Angew. Chem.*, 110 (1998) 3367–3369.

[21] T. Ziegler, R. Dettmann, Ariffadhillah, U. Zettl, *J. Carbohydrate Chem.* (1999), in press.

[22] P. Kovac, K.J. Edgar, *J. Org. Chem.*, 52 (1992) 2455–2467.

[23] A.K. Sarkar, A.K. Ray, N. Roy, *Carbohydr. Res.*, 190 (1989) 181–190.

[24] J.O. Kihlberg, D.A. Leigh, D.R. Bundle, *J. Org. Chem.*, 55 (1990) 2860–2863.

[25] (a) K. Bock, I. Lundt, C. Pederson, *Tetrahedron Lett.*, 13 (1973) 1037–1040. (b) K. Bock, C. Pedersen, *J. Chem. Soc., Perkin Trans. II*, (1974) 293–297. (c) K. Bock, C. Pederson, *Acta Chim. Scand. B*, 29 (1975) 258–264. (c) J.H. Bradbury, G.H. Jenkins, *Carbohydr. Res.*, 126 (1984) 125–156. (d) C.A. Podlasek, J. Wu, W.A. Stripe, P.B. Bondo, A.S. Serianni, *J. Am. Chem. Soc.*, 117 (1995) 8635–8644.

[26] (a) T. Ziegler, K. Neumann, E. Eckhardt, G. Herold, G. Pantkowski, *Synlett*, (1991) 699–701. (b) T. Ziegler, E. Eckhardt, *Tetrahedron Lett.*, 44 (1992) 6615–6618. (c) T. Ziegler, E. Eckhardt, G. Pantkowski, *J. Carbohydr. Chem.*, 13 (1993) 81–109.

[27] J.R. Brown, T.K. Smith, M.A.J. Ferguson, R.A. Field, *Bioorg. Med. Chem. Lett.*, 8 (1998) 2051–2054.

[28] R.K. Ness, H.G. Fletcher, C.S. Hudson, *J. Chem. Soc.*, 72 (1950) 2200–2205.