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Note

From methyl mannosides to methyl octosides by a stepwise homologation with Grignard C_1 reagents

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Abstract

A four-step procedure for homologation of methyl α-D-*manno*furanoside and α-D-*manno*pyranoside was examined. The reactions consisted in (i) oxidation of the terminal hydroxymethyl group in a protected sugar derivative to an aldehyde; (ii) reaction with allyloxymethylmagnesium chloride (or (phenyldimethyl)silylmethyl–magnesium chloride); (iii) protection of the newly formed secondary alcohol group; (iv) deprotection of the terminal CH_2OR (or oxidation of the CH_2SiMe_2Ph) group. From methyl α-D-mannosides, stereoisomeric DαD and LαD methyl heptosides and from them, methyl octosides of D-*threo*- and L-*erythro*-α-D-*manno* configuration were obtained.

Keywords: Methyl 5-*O*-benzyl-2,3-*O*-isopropylidene-α-D-*manno*-hexodialdo-1,4-furanoside; Methyl 4-*O*-benzyl-2,3-*O*-isopropylidene-α-D-*manno*-hexodialdo-1,5-pyranoside; Methyl LαD- and DαD-*manno*-heptosides; Methyl octosides

Chain elongation of monosaccharide terminal aldehydes (protected pentodialdo-1,4-furanoses or hexodialdo-1,5-pyranoses) with alkoxymethylmagnesium chlorides has proved to be a practical method for homologation reactions.[1–5] We became interested in homologation of methyl mannosides in furanose and pyranose forms protected with the same groups: 2,3-*O*-isopropylidene and 5 (or 4)-*O*-benzyl. The question was posed on how far the homologation method can be continued using a simple sequence of reactions consisting of oxidation of the primary hydroxyl group to aldehyde, reaction with C_1 Grignard, separation of stereoisomers, protection of the new OH group, liberation of the primary OH group, etc. The problems to be answered concerned the yields, stereoselectivity, separation of stereoisomers, and protection of newly formed secondary alcohol groups. Homologation of methyl 2,3,4-tri-*O*-benzyl-α-D-*manno*-hexodialdo-1,5-pyranoside using the Dondoni 2-trimethylsilyl-thiazole approach[6,7] was performed by Aspinall.[8] The homologation of sugar chain from the aldehyde group (C-1, ascending synthesis) is well known.[9]

Methyl 5-*O*-benzyl-2,3-*O*-isopropylidene-α-D-mannofuranoside (**1**) was oxidized to the 6-aldehyde (**2**) and reacted with allyloxymethylmagnesium chloride to afford 78% of methyl 7-*O*-allyl-5-*O*-benzyl-2,3-*O*-isopropylidene-heptofuranosides of D- and L-*glycero*-α-D-*manno* configuration (**3** and **4**) in ca. 3.3:1 ratio. This result differs from an analogous chain elongation reaction of **2** with

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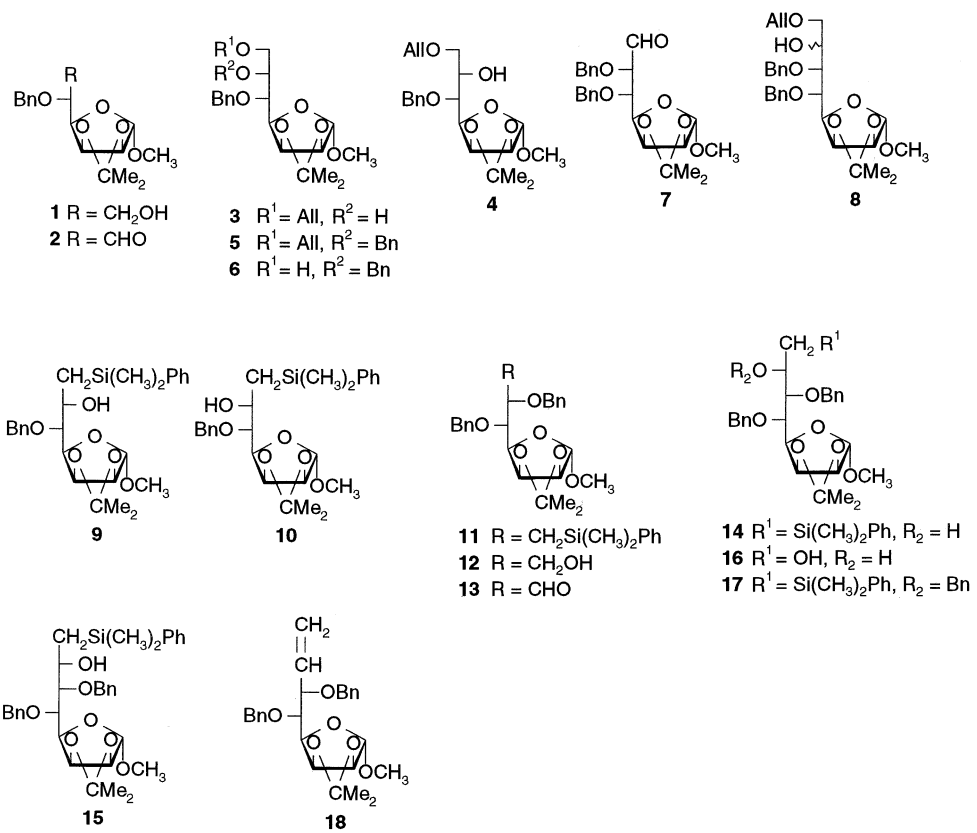
benzyloxymethylmagnesium chloride where two stereoisomeric heptofuranosides obtained were of the D-*glycero*-α-D-*manno* and of the unexpected L-*glycero*-β-L-*gulo* configuration.[10] Stereoisomers **3** and **4** were separated and the major product **3** was benzylated to yield methyl 7-*O*-allyl-5,6-di-*O*-benzyl-2,3-*O*-isopropylidene-D-*glycero*-α-D-*manno*-heptofuranoside (**5**). De-allylation of **5** with the Wilkinson's catalyst proceeded smoothly and yielded alcohol **6** for the Swern oxidation. In turn, reaction of the aldehyde **7** with allyloxymethylmagnesium chloride yielded 71% of an inseparable mixture of stereoisomeric methyl octofuranosides (**8**) of supposed D-*erythro*-α-D-*manno* and L-*threo*-α-D-*manno* configuration.

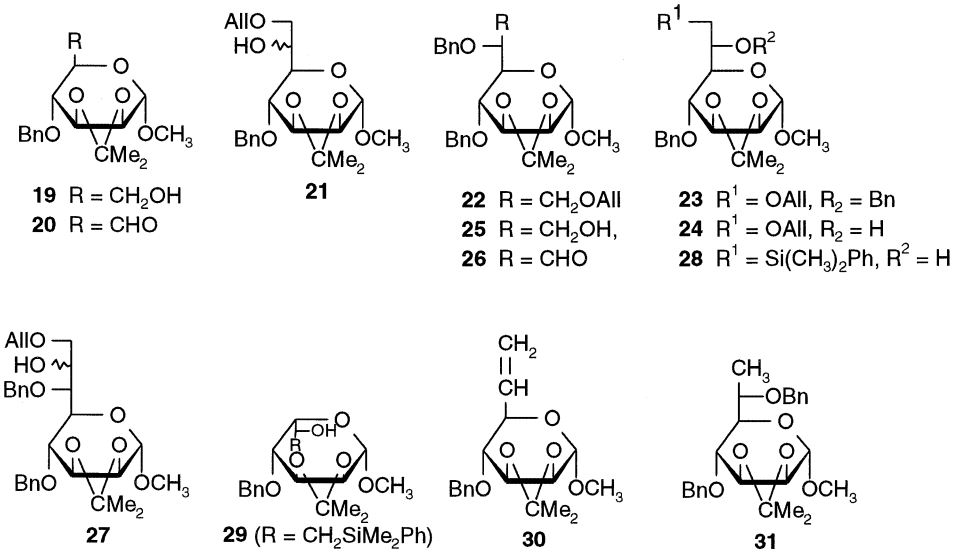
An analogous series of reactions was performed next starting with aldehyde **2** and (phenyldimethyl)silylmethylmagnesium chloride.[11] Two stereoisomeric methyl 5-*O*-benzyl-7-deoxy-2,3-*O*-isopropylidene-7-(phenyldimethyl)silyl-L- and D-*glycero*-α-*manno*-heptofuranosides (**9** and **10**) were obtained (83%, 4:1). After separation, the major stereoisomer **9** was benzylated at C-6 to yield **11**, and **11** was oxidized at C-7 to heptoside **12**, oxidized in turn to aldehyde **13**. Chain elongation was achieved with the silyl Grignard reagent to furnish methyl 5,6-di-*O*-benzyl-8-deoxy-2,3-*O*-isopropylidene-8-(phenyldimethyl)silyl-octofuranosides of D-*threo*- and L-*erythro*-α-D-*manno* configuration (**14** and **15**, 74.5%, 4.5:1). Successful oxidation of the silyl group in **14** yielded a derivative of the corresponding methyl octofuranoside (**16**) (Scheme 1).

Repetition of the benzylation procedure on the octoside **14** afforded the 7-*O*-benzyl derivative **17** in a low yield (18%). The main product was an olefin (**18**, 78%) stemming from the Peterson elimination. A number of modifications of the benzylation procedure was examined (cf. Section 1), however no improvement was achieved.

Homologation in the pyranoside series started with methyl 4-*O*-benzyl-2,3-*O*-isopropylidene-α-D-mannopyranoside (**19**), which was oxidized to methyl 4-*O*-benzyl-2,3-*O*-isopropylidene-α-D-*manno*-hexodialdo-1,5-pyranoside (**20**). Its reaction with



Scheme 1.



Scheme 2.

allyloxymethylmagnesium chloride afforded 71% of an inseparable mixture of methyl 7-*O*-allyl-4-*O*-benzyl-2,3-*O*-isopropylidene-heptopyranosides of L- and D-*glycero*-α-D-*manno* configuration (**21**) in ca. 2:1 ratio. Benzylation of this mixture led to three products isolated by chromatography: two stereoisomeric 6-O-benzylated products of D- and L-*glycero*-α-D-*manno* configuration (**22** and **23**) and a non-benzylated substrate which proved to be pure LαD stereoisomer (**24**). The major stereoisomer was de-allylated and the primary alcohol **25** was oxidized to aldehyde **26**. Unexpectedly, Grignard reaction of **26** with $AllOCH_2MgCl$ was very inefficient and yielded — besides the unreacted aldehyde — only negligible amounts of the octosides **27** which were identified only by the ^1H NMR spectrum.

Elongation of the aldehyde **20** with silyl Grignard led, as expected, to 77% of methyl 4-*O*-benzyl-7-deoxy-2,3-*O*-isopropylidene-7-(phenyldimethyl)silyl-L-*glycero*-α-D-*manno*-heptopyranoside (**28**) and a slight amount (9%) of inverted product **29** of D-*glycero*-β-L-*gulo* configuration. It must be added that formation of an inverted product was observed also earlier;[4] silyl Grignard usually furnishes normal products, without inversion of α configuration to the aldehyde group.

As in the previous case in the furanoside series, benzylation (BnBr, NaH, DMF, with and without Bu_4NBr) of **28** led only to the Peterson olefin **30** (78%), and under two-phase conditions (BnBr, Bu_4NBr, 50% NaOH) to the 7-deoxy-heptoside **31**.

The configuration of the new secondary alcohol grouping in: **9**, **14**, **15**, **24**, **28** and **29** was unequivocally determined by the CD spectra with rhodium[12] and in **16** with molybdenum complexes.[13] Configuration of **5** could be established by comparison of its NMR spectral data with the data of an analogous compound.[10] Also configurations of **21** were assigned similarly[2] (Scheme 2).

Stepwise homologation of hexosides to higher sugars is based on a four-step procedure: reaction of allyloxymethyl Grignard with terminal aldehyde, protection of the new secondary alcohol group, deprotection at the primary alcohol position, Swern oxidation to the aldehyde and the next Grignard reaction. Although experimentally not complicated, it experiences difficulties in separation of the stereoisomeric homologs formed. In the reactions performed, a preference for the formation of the D configuration at the new secondary alcohol center is noted. This remains in accord with our earlier observations on domination of the Felkin–Anh pathway in reactions of alkoxymethyl Grignard reagents with sugar aldehydes.[4,5] A single exception is the chain-elongation of the aldehyde **20** where LαD heptopyranoside dominated over the DαD stereoisomer.

For the stepwise homologation, (phenyldimethyl)silylmethylmagnesium chloride may also be conveniently used. This reagent displays a preference for the formation of L-configurated secondary alcohol when reacting with protected methyl α-D-*manno*-hexodialdo-1,4-furanoside or -1,5-pyranoside. The stereoisomeric homologs can be readily separated but successful protection of the new secondary alcohol group strongly depends on reaction conditions employed. The usual benzylation may fail due to Peterson elimination. It is remarkable that on passing from heptose to octose system (**13** → **14** + **15**) a preference for the D configuration at C-7 was noted.

Aspinall[8] obtained derivatives of L- and D-*glycero*-α-D-*manno*-heptopyranosides in ca. 55:37 ratio. Allyloxymethyl Grignard route leads to the corresponding derivatives of heptopyranosides in a ratio of 47:24 and to a reverse proportion (3:10) of heptofuranosides. The best stereoselectivity leading to the most desired L-*glycero*-D-*manno*-heptoside can be obtained with the silyl Grignard introduced by van Boom.[11] This is also confirmed in the experiments described here.

1. Experimental

Reactions were performed under strictly anhydrous conditions under Ar. For TLC, plates covered with Silica Gel $60F_{254}$, E. Merck were used. Tetrahydrofuran was distilled from potassium–benzophenone ketyl. Products were separated and purified by column chromatography (E. Merck Silica Gel 60, 230–400 mesh ASTM). Solvents used for elution were of technical grade and were distilled over CaH_2 before use. ^1H NMR spectra were recorded with a Varian AC-200 (200 MHz) or Bruker AM-500 (500 MHz) spectrometers using $CDCl_3$ as solvent and Me_4Si as internal standard. ^{13}C NMR spectra were recorded in the DEPT mode. High-resolution mass spectra (HR-MS) were measured in the LSIMS mode with an AMD-604 mass spectrometer. Optical rotation were measured with a JASCO DIP-360 automatic polarimeter at 24 ± 2 °C for solutions in $CHCl_3$. CD spectra were recorded between 280 and 750 nm at rt with a JASCO J715 spectropolarimeter using hexane or $CHCl_3$ solution in cells of 0.1 or 0.2 path length (spectral band width 1 nm, sensitivity $10 \times 10^{-6}\Delta A$ unit/nm). CD spectra of heptose and octose derivatives having free hydroxyl group at C-6 or C-7 (6–8 mg) with $(CF_3COO)_4Rh_2$ complex (3–4 mg) were measured in chloroform (10 mL, Spectrograde). A positive E band at 342–358 nm indicated the D configuration.[12] The shift of the E band to 401–413 nm in the CD spectra of **9** and **14** is due to the presence of the dimethylphenylsilyl group next to the secondary alcohol grouping.[14] The configuration of **16** was determined with $Mo(AcO)_4$ complex in Me_2SO solution; a positive band at 312.5 nm indicated a D configuration.[13] Substrates were obtained according to published methods: methyl 5-*O*-benzyl-2,3-*O*-isopropylidene-α-D-*manno*-hexodialdo-1,4-furanoside (**2**)[15] and methyl 4-*O*-benzyl-2,3-*O*-isopropylidene-α-D-*manno*-hexodialdo-1,5-pyranoside (**20**)[16] were obtained from the corresponding primary alcohols **1** and **19** by Swern oxidation.

*Methyl 7-*O*-allyl-5-*O*-benzyl-2,3-*O*-isopropylidene*-D- *and* L-glycero-α-D-manno-*heptofuranosides* (**3** and **4**).—To the Grignard reagent $AllOCH_2MgCl$, prepared at −30 °C according to Ref. 4 from magnesium (0.86 g, 36.8 mmol) and freshly distilled allyloxymethyl chloride (3.91g, 36.8 mmol) in abs THF (8 mL), was added dropwise a solution of **2** (2.96 g, 9.2 mmol) in abs THF (8 mL) and stirring at −30 °C was continued for 2 h. Afterwards, the reaction mixture was allowed to attain rt and was additionally stirred for 12 h. The mixture was cooled to 0 °C, poured into cold aq ammonium chloride (50 mL) and extracted with Et_2O. The extract was dried over $MgSO_4$ and concentrated in vacuo to dryness. The residue was separated on a silicagel column with 8:3 → 4:1 hexane–EtOAc as eluent. First eluted was **3** (2.16 g, 59.7%), followed by **4** (0.66 g, 18.4%)

In a similar manner were synthesized the 7-*O*-allyl derivatives of methyl DαD and LαD heptopyranosides and 8-*O*-allyl derivatives of octofuranosides and -pyranosides. The phenyldimethylsilylmethyl Grignard reagent was obtained according to Fleming et al.[17] using the procedure of van Boom et al.[18] Its

reactions with aldehydes **2**, **7**, **13**, and **20** were performed at −30 °C according to prescription for **2**→**3**+**4**. Unmasking of the silyl group from compounds **11** and **14** was accomplished with HOOAc–NaBr–NaOAc[19] to furnish heptofuranosides **12** and **16**.

Methyl 7-O-allyl-5-O-benzyl-2,3-O-isopropylidene-D-glycero-α-D-manno-heptofuranoside (**3**).—Colorless oil, 2.16 g, (59.7%); $[\alpha]_D$ +39.7° (*c* 1.9, $CHCl_3$); CD: 355 nm ($\Delta e'$ 0.0087, *c* 0.00106 M); ^{1}H NMR: δ 7.35–7.31 (m, 5 H, Ph), 5.93 (m, 1 H, CH=), 5.28, 518 (2 q, 2 H, CH_2=), 4.88 (s, 1 H, H-1) 4.79 (dt, 1 H, $J_{3,4}$ 2.8 Hz, H-3) 4.52 (d, 1 H, $J_{2,3}$ 5.9 Hz, H-2), 4.15 (m, 1 H, $J_{5,6}$ 1.6 Hz, H-5), 4.05 (dt, 1 H, $J_{4,5}$ 9.3 Hz, H-4), 3.98 (m, 1 H, $J_{6,7}$ 7.00 Hz, H-6), 3.64 (bs, 2 H, OCH_2), 3.32 (AB, 1 H, 2 H, $J_{7a,7b}$ 10.0 Hz), 3.29 (s, 3 H, OCH_3), 2.82 (bs, 1 H, OH), 1.47, 1.33 [2 s, 6 H, $(CH_3)_2C$]. ^{13}C NMR ($CDCl_3$): δ 134.7 (CH=), 128.2–127.5 (Ph), 117.1 (CH_2=), 107.5 (C-1), 84.3 (C-2), 80.0, 79.2, 76.9 (C-3,4,5), 74.1 (CH_2Ph), 72.3 (OCH_2), 72.2 (C-6), 70.5 (C-7), 54.6 (OCH_3), 26.2, 24.9 [$(CH_3)_2C$]. LSIMS (HRMS): *m*/*z* 417.1899 $[M+Na]^+$. Calcd for $C_{21}H_{30}NaO_7$: 417.1889. Anal. Calcd for $C_{21}H_{30}O_7 \cdot 1/2\ H_2O$: C, 62.52; H, 7.74. Found: C, 62.57; H, 7.67.

Methyl 7-O-allyl-5-O-benzyl-2,3-O-isopropylidene-L-glycero-α-D-manno-heptofuranoside (**4**).—Colorless oil, 0.66 g (18.4%); $[\alpha]_D$ +31.6° (*c* 1.6, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 7.48–7.36 (m, 5 H, Ph), 5.89 (m, 1 H, CH=), 5.32, 5.18 (2 q, 2 H, CH_2=), 4.89 (s, 1 H, H-1), 4.81 (dd, 1 H, $J_{3,4}$ 2.9 Hz, H-3), 4.74 (d, 2 H, CH_2Ph), 4.56 (d, 1 H, $J_{2,3}$ 5.9 Hz, H-2), 4.13 (dd, 1 H, $J_{4,5}$ 9.8 Hz, H-4), 4.01 (dd, 1 H, $J_{5,6}$ 2.8 Hz, H-5), 3.98 (m, 2 H, OCH_2), 3.52 (AB, 2 H, $J_{7a,7b}$ 10 Hz, H-7a, H-7b), 3.30 (s, 3 H, OCH_3), 1.45, 1.34 [2 s, 6 H, $(CH_3)_2C$]. ^{13}C NMR ($CDCl_3$): δ 134.6 (CH=), 128.4–127.6 (Ph), 116.9 (CH_2=), 107.2 (C-1), 84.9 (C-2), 79.9, 78.3, 75.6 (C-3,4,5), 74.1 (CH_2Ph), 72.2 (OCH_2), 71.5 (C-7), 70.2 (C-6), 54.5 (OCH_3), 26.2, 25.0 [$(CH_3)_2C$]. LSIMS (HRMS): *m*/*z* 417.1899 $[M+Na]^+$. Calcd for $C_{21}H_{30}NaO_7$: 417.1891.

Methyl 7-O-allyl-5,6-di-O-benzyl-2,3-O-isopropylidene-D-glycero-α-D-manno-heptofuranoside (**5**).—To a solution of **3** (1.75 g, 4.44 mmol) in DMF (15 mL) cooled to −10 °C, sodium hydride (50% suspension, 0.317 g, 6.63 mmol) was added and the mixture was stirred for 30 min. Benzyl bromide (1.13 g, 6.63 mmol) was added dropwise. After 15 min the mixture was allowed to attain rt and stirring was continued for 3 h. Water (25 mL) was slowly added and the product was extracted with ether (3 × 30 mL). The combined organic extracts were washed with water (25 mL), dried over Na_2SO_4 and concentrated to dryness. Column chromatography of the residue with 4:1 hexane–EtOAc gave **5** (1.73 g, 80.5%) as a colorless oil, $[\alpha]_D$ +26.6° (*c* 3.1, $CHCl_3$); ^{1}H NMR ($CDCl_3$); δ 7.37–7.28 (m, 5 H, Ph), 5.90 (m, 1 H, CH=), 5,25, 5.15 (2 q, 2 H, CH_2=), 4.86 (s, 1 H, H-1), 4.78 (dd, 1 H, $J_{3,4}$ 3.8 Hz, H-3), 4.82, 4.65 (2 d, 4 H, CH_2Ph), 4.51 (d, 1 H, $J_{2,3}$ 5.8 Hz, H-2), 4.13 (dd, 1 H, $J_{5,6}$ 1.4 Hz, H-5), 4.05 (dd, 1 H, $J_{4,5}$ 9.5 Hz, H-4), 4.01 (m, 1 H, $J_{6,7a}$ 1.8, $J_{6,7b}$ 5.2 Hz, H-6), 3.94 (m, 2 H, H-7a, H-7b), 3.27 (s, 3 H, OCH_3), 1.44, 1.32 [2 s, 6 H, $(CH_3)_2C$]. ^{13}C NMR ($CDCl_3$): δ 134.9 (CH=), 128.1–127.2 (2 × Ph), 116.5 (CH_2=), 107.2 (C-1), 84.5 (C-2), 80.0, 79.7, 78.2 (C-3,4,5), 77.4 (C-6), 74.0, 72.5 (2 × CH_2Ph), 72.1 (OCH_2), 70.4 (C-7), 54.4 (OCH_3), 26.2, 25.1 ($CH_3)_2C$]. LSIMS (HRMS): *m*/*z* 507.2360 $[M+Na]^+$. Calcd for $C_{28}H_{36}NaO_7$ 507.2358. Anal. Calcd for $C_{28}H_{36}O_7$: C, 69.40; H, 7.49. Found: C, 69.27; H, 7.51.

Methyl 5,6-di-O-benzyl-2,3-O-isopropylidene-D-glycero-α-D-manno-heptofuranoside (**6**).—To a solution of **5** (1.64 g, 3.38 mmol) in 9:3:1 EtOH–benzene–water (26 mL) were added the Wilkinson's catalyst (0.148 g) and 1,4-diazabicyclo[2.2.2]octane (52 mg) and the mixture was refluxed until the reaction was complete (4 h). The mixture was filtered and the solvents were evaporated under diminished pressure. The residue was dissolved in 10:1 acetone–water (22 mL), $HgCl_2$ (0.75 g) and HgO (0.59 g) were added and the mixture was stirred for 1 h. Then, it was filtered through a Celite layer, washed with aq 50% KI, aq 1% $NaHSO_3$ and 1% $NaHCO_3$, dried and concentrated. The residue was purified by chromatography with 4:1 hexane–EtOAc to give **6** (1.02 g, 67.8%), oil, $[\alpha]_D$ +36.3° (*c* 1.7, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 7.36–7.25 (m,

2 × Ph), 4,87 (s, 1 H, H-1), 4.81 (dd, 1 H, $J_{3,4}$ 3.5 Hz, H-3), 4.53 (d, 1 H, $J_{2,3}$ 5.9 Hz, H-2), 4.20 (dd, 1 H, $J_{5,6}$ 1.9 Hz, H-5), 4.78, 4.68 (2 × AB, 4 H, 2 × CH_2Ph), 4.02 (dd, 1 H, $J_{4,5}$ 9.5 Hz, H-4), 3.92–3.80 (m, 3 H, H-6, H-7a, H-7b), 3.28 (s, 3 H, OCH_3), 2.62 (d, 1 H, OH), 1.46, 1.39 [2 s, 6 H, $(CH_3)_2C$]. ^{13}C NMR ($CDCl_3$): δ 128.4–127.6 (2 × Ph), 107.4 (C-1), 84.5 (C-2), 79.91, 79.90, 78.3 (C-3,4,5), 77.6 (C-6), 74.5, 71.9 (2 × CH_2Ph), 61.5 (C-7), 54.6 (OCH_3), 26.2, 25.0 [$(CH_3)_2C$]. Anal. Calcd for $C_{25}H_{32}O_7$: C, 67.56; H, 7.20. Found: C, 67.31; H, 7.23.

*Methyl 8-*O*-allyl-5,6-di-*O*-benzyl-2,3-*O*-isopropylidene-*D*-erythro-α-*D*-manno-octofuranosides* (**8**).—Colorless syrup, 0.226 g (70.8%), obtained from **7** [0.28 g, obtained from **6** (0.37 g, 76.5%) by Swern oxidation]. NMR data were taken from the spectra of a 6:1 mixture stereoisomeric octosides. The *D-erythro*-α-*D-manno* configuration was assigned to the dominating stereoisomer on the basis of similarity of the NMR data with those of methyl 5,7-di-*O*-benzyl-2,3-*O*-isopropylidene-*D-glycero*-α-*D-manno*-heptofuranoside.[10] ^1H NMR ($CDCl_3$): δ 7.31–7.25 (m, 2 × Ph), 5.85 (m, 1 H, CH=), 5.26, 5.15 (2g, 2 H, CH_2=), 4.85 (s, 1 H, H-1), 4.78, 4.58 (2 × AB, 4 H, 2 × CH_2Ph), 4.81 (dd, 1 H, $J_{3,4}$ 3.0 Hz, H-3), 4.52 (d, 1 H, $J_{2,3}$ 5.8 Hz, H-2), 4.27 (dd, 1 H, $J_{5,6}$ 2.9 Hz, H-5), 4.20 (dd, 1 H, $J_{4,5}$ 9.5 Hz, H-4), 4.14–4.06 (m, 3 H, H-6, OCH_2), 4.01–3.95 (m, 1 H, $J_{7,8a}$ 7.8, $J_{7,8b}$ 1.1 Hz, H-7), 3.88, 3.54 (AB, 2 H, H-8a, H-8b), 3.27 (s, 3 H, OCH_3), 2.82 (d, 1 H, OH), 1.45, 1.33 [2 s, 6 H, $(CH_3)_2C$]. ^{13}C NMR ($CDCl_3$): δ 134.7 (CH=), 128.3–127.4 (2 × Ph), 117.0 (CH_2=), 107.3 (C-1), 84.4 (C-2), 80.3, 79.4, 78.0 (C-3,4,5), 77.6 (C-6), 70.5 (C-7), 71.0 (C-8), 73.7, 71.7 (2 × CH_2Ph), 72.2 (OCH_2), 54.5 (OCH_3), 26.3, 25.1 [$(CH_3)_2C$]. LSIMS (HRMS): m/z 537.2467 $[M + Na]^+$. Calcd for $C_{29}H_{38}NaO_8$ 537.2464.

*Methyl 5-*O*-benzyl-7-deoxy-2,3-*O*-isopropylidene-7-(phenyldimethyl)silyl-*L*-glycero-α-*D*-manno-heptofuranoside* (**9**).—From **2** (1.95 g) and (phenyldimethyl)silylmethylmagnesium chloride, white foam, 1.89 g (66.4%); $[\alpha]_D$ + 42.5° (*c* 1.6, $CHCl_3$); CD: 413 nm ($\Delta e'$ − 0.0367, *c* 0.0011 M); ^1H NMR ($CDCl_3$): δ 7.36–7.24 (m, 2 × Ph), 4.86 (s, 1 H, H-1), 4.76 (dd, 1 H, $J_{3,4}$ 3.3 Hz, H-3), 4.72, 4.54 (AB, 4 H, 2 × CH_2Ph), 4.58 (d, 1 H, $J_{2,3}$ 5.8 Hz, H-2), 4.20 (m, 1 H, $J_{6,7}$ 7.1 Hz, H-6), 4.08 (dd, 1 H, $J_{4,5}$ 9.2 Hz, H-4), 3.78 (dd, 1 H, $J_{5,6}$ 2.3 Hz, H-5), 3.28 (s, 3 H, OCH_3), 2.38 (d, 1 H, OH), 1.46, 1.31 [2 s, 6 H, $(CH_3)_2C$], 1.20 (m, 2 H, H-7a, H-7b), 0.36, 0.35 [2 s, 6 H, $(CH_3)_2Si$]. ^{13}C NMR ($CDCl_3$): δ 128.5–127.2 (2 × Ph), 107.3 (C-1), 84.6 (C-2), 79.9, 79.1, 78.7 (C-3,4,5), 74.1 (CH_2Ph), 69.3 (C-6), 54.6 (OCH_3), 26.2, 24.9 [$(CH_3)_2C$], 20.9 (C-7), − 1.9, − 2.5 [$(CH_3)_2Si$]. LSIMS (HRMS): m/z 459.2177 $[M + Na]^+$. Calcd for $C_{26}H_{36}NaO_6Si$ 495.2179.

*Methyl 5-*O*-benzyl-7-deoxy-2,3-*O*-isopropylidene-7-(phenyldimethyl)silyl-*D*-glycero-α-*D*-manno-heptofuranoside* (**10**).—White foam, 0.474 g (16.6%); $[\alpha]_D$ + 47.8° (*c*, 1.1, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 7.55–7.35 (m, 2 × Ph), 4.91 (s, 1 H, H-1), 4.70 (dd, 1 H, $J_{3,4}$ 3.5 Hz, H-3), 4.87, 4.65 (AB, 2 H, CH_2Ph), 4.52 (d, 1 H, $J_{2,3}$ 5.8 Hz, H-2), 4.22 (dd, 1 H, $J_{4,5}$ 9.0 Hz, H-4), 3.98 (dd, 1 H, $J_{5,6}$ 3.0 Hz, H-5), 3.76 (m, 1 H, $J_{6,7a}$ 8.4, $J_{6,7b}$ 2.8 Hz, H-6), 3.29 (s, 3 H, OCH_3), 1.27–1.19 (m, 2 H, H-7a, H-7b), 1.95 (d, 1 H, OH), 1.28, 1.16 [2 s, 6 H, $(CH_3)_2C$], 0.31, 0.29 [2 s, 6 H, $[(CH_3)_2Si]$. ^{13}C NMR ($CDCl_3$): δ 133.8–127.6 (2 × Ph), 107.1 (C-1), 84.7 (C-2), 82.4, 81.2, 79.9 (C-3,4,5), 74.0 [(CH_2Ph), 69.5 (C-6), 54.3 (OCH_3), 23.0 (C-7), 26.0, 24.7 [$(CH_3)_2C$], − 2.1, − 2.8 [$(CH_3)_2Si$]. Anal. Calcd for $C_{26}H_{36}O_6Si$: C, 66.10; H, 7.62. Found: C, 65.92; H, 7.71.

*Methyl 5-*O*-benzyl-7-deoxy-2,3-*O*-isopropylidene-7-(phenyldimethyl)silyl-*D*-glycero-α-*D*-manno-heptofuranoside* (**11**).—Obtained from **9** (1.7 g), colorless oil, 1.46 g (72.2%); $[\alpha]_D$ + 22.1° (*c* 2.4, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 7.38–7.27 (m, 3 × Ph), 4.86 (s, 1 H, H-1), 4.76 (dd, 1 H, $J_{3,4}$ 3.2 Hz, H-3), 4.54 (d, 1 H, $J_{2,3}$ 5.9 Hz, H-2), 4.65, 4.52 (AB, 4 H, 2 × CH_2Ph), 4.18 (dd, 1 H, $J_{4,5}$ 9.2 Hz, H-4), 3.88 (m, 1 H, $J_{6,7a}$ 7.6 Hz, H-6), 3.77 (dd, 1 H, $J_{5,6}$ 2.6 Hz, H-5), 3,21 (s, 3 H, OCH_3), 1.47, 1.31 [2 s, 6 H, $(CH_3)_2C$], 1.41 (dd, 1 H, $J_{7a,7b}$ 14.7 Hz, H-7a), 1.14 (dd, 1 H, $J_{7b,6}$ 6.3 Hz, H-7b), 0.29, 0.28 [2 s, 6 H, $(CH_3)_2Si$]. ^{13}C NMR ($CDCl_3$): δ 133.6–127.4 (3 × Ph), 107.4 (C-1), 84.9 (C-2), 80.2, 78.9, 78.8 (C-3,4,5), 77.1 (C-6), 73.8, 71.6 (2 × CH_2Ph), 54.7 (OCH_3), 26.4, 25.1 [$(CH_3)_2C$], 18.1 (C-7), − 1.9, − 2.3 [$(CH_3)_2Si$]. LSIMS (HRMS): m/z 585.2646 $[M + Na]^+$ Calcd for $C_{33}H_{42}NaO_6Si$ 585.2648.

*Methyl 5,6-di-*O*-benzyl-2,3-*O*-isopropylidene-*L*-glycero-α-*D*-manno-heptofuranoside* (**12**).—Obtained from **11** (1.1 g), colourless oil, 0.558 g (64.2%); $[\alpha]_D$ +27.5° (*c* 2.5, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 7.38–7.24 (2 × Ph), 4.91 (s, 1 H, H-1), 4.86 (dd, 1 H, $J_{3,4}$ 3.2 Hz, H-3), 4.58 (d, 1 H, $J_{2,3}$ 5.8 Hz, H-2), 4.23 (dd, 1 H, $J_{4,5}$ 9.4 Hz, H-4), 4.82, 4.56 (AB, 4 H, 2 × CH_2Ph), 3.98 (dd, 1 H, $J_{5,6}$ 3.6 Hz, H-5), 3.87 (m, 1 H, $J_{6,7a}$ 9.3, $J_{6,7b}$ 5.1 Hz, H-6), 3.74 (m, 2 H, H-7a, H-7b), 3.20 (s, 3 H, OCH_3), 2.40 (bs, 1 H, OH), 1.50, 1.36 [$(CH_3)_2$C]. ^{13}C NMR ($CDCl_3$): δ 128.8–127.4 (2 × Ph), 107.9 (C-1), 84.7 (C-2), 80.8, 80.0, 78.7 (C-3,4,5), 76.5 (C-6), 74.1, 73.3 (2 × CH_2Ph), 61.8 (C-7), 55.1 (OCH_3), 26.2, 25.0 [$(CH_3)_2$C]. LSIMS (HRMS): *m*/*z* 467.2048 $[M + Na]^+$. Calcd for $C_{25}H_{32}NaO_7$ 467.2046.

*Methyl 5,6-di-*O*-benzyl-8-deoxy-2,3-*O*-isopropylidene-8-(phenyldimethyl)silyl-*D*-threo-α-*D*-manno-octofuranoside* (**14**).—Obtained from **13** (0.7 g), colorless oil, 0.572 g (60.9%); $[\alpha]_D$ +21.9° (*c* 1.1, $CHCl_3$); CD: 401 nm (Δ*e*′ 0.0208, *c* 0.00105 M); ^{1}H NMR ($CDCl_3$): δ 7.38–7.27 (m, 3 × Ph), 4.87 (s, 1 H, H-1), 4.82 (dd, 1 H, $J_{3,4}$ 3.1 Hz, H-3), 4.55 (d, 1 H, $J_{2,3}$ 5.8 Hz, H-2), 4.75, 4.62 (AB, 4 H, 2 × CH_2Ph), 4.16 (dd, 1 H, $J_{4,5}$ 9.4 Hz, H-4), 4.02 (dd, 1 H, $J_{5,6}$ 3.9 Hz, H-5), 3.49 (m, 1 H, $J_{6,7a}$ 5.4, $J_{6,7b}$ 8.3 Hz, H-6), 3.20 (s, 3 H, OCH_3), 1.49, 1.33 [2 s, 6 H, $(CH_3)_2$C], 1.16–0.89 (m, 2 H, H-7a, H-7b), 0.34, 0.32 [2 s, 6 H, $(CH_3)_2$Si]. ^{13}C NMR ($CDCl_3$): δ 136.8–127.2 (3 × Ph), 108.2 (C-1), 86.2 (C-2), 84.7, 80.1, 79.3 (C-3,4,5), 76.7 (C-6), 75.2, 74.2 (2 × CH_2Ph), 69.2 (C-7), 55.2 (OCH_3), 26.3, 25.0 [$(CH_3)_2$C], 20.8 (C-8), −1.6, −2.3 [$(CH_3)_2$Si]. LSIMS (HRMS): *m*/*z* 615.2748 $[M + Na]^+$. Calcd for $C_{34}H_{44}NaO_7Si$ 615.2752.

*Methyl 5,6-di-*O*-benzyl-8-deoxy-2,3-*O*-isopropylidene-8-(phenyldimethyl)silyl-*L*-erythro-α-*D*-manno-octofuranoside* (**15**).—Colorless oil 0.127 g (13.6%); $[\alpha]_D$ +34.2° (*c* 0.9, $CHCl_3$); CD: 353.5 nm (Δ*e*′ −0.1386, *c* 0.00107 M); ^{1}H NMR ($CDCl_3$): δ 7.49–7.24 (m, 3 × Ph), 4.84 (s, 1 H, H-1), 4.86 (dd, 1 H, $J_{3,4}$ 3.0 Hz, H-3), 4.73, 4.66 (AB, 4 H, 2 × CH_2Ph), 4.59 (d, 1 H, $J_{2,3}$ 5.9 Hz, H-2), 4.25 (dd, 1 H, $J_{5,6}$ 2.9 Hz, H-5), 4.20 (dd, 1 H, $J_{4,5}$ 9.1 Hz, H-4), 4.02 (m, 1 H, H-7), 3.48 (dd, 1 H, $J_{6,7}$ 5.8 Hz, H-6), 3.23 (s, 3 H, OCH_3), 1.49, 1.35 [2 s, 6 H, $(CH_3)_2$C], 1.18 (dd, 1 H, $J_{8a,7}$ 5.6, $J_{8a,8b}$ 10.8 Hz, H-8a), 0.98 (dd, 1 H, $J_{8b,7}$ 3.8 Hz, H-8b), 0.31, 0.30 [2 s, 6 H, $(CH_3)_2$Si]; ^{13}C NMR ($CDCl_3$): δ 128.8–127.5 (3 × Ph), 107.9 (C-1), 85.0 (C-2), 84.0, 80.0, 78.7 (C-3,4,5), 75.2 (C-6), 74.0, 73.4 (2 × CH_2Ph), 68.7 (C-7), 55.1 (OCH_3), 26.2, 25.1 [$(CH_3)_2$C], 20.8 (C-8), −2.0, −2.2 [$(CH_3)_2$Si]. Anal. Calcd for $C_{34}H_{44}O_7Si$: C 68.91, H 7.43. Found C 68.72, H 7.56.

*Methyl 5,6-di-*O*-benzyl-2,3-*O*-isopropylidene-*D*-threo-α-*D*-manno-octofuranoside* (**16**).—Obtained from **14** (0.13 g), colorless oil, 0.076 g (72.7%); $[\alpha]_D$ +28.6° (*c* 1.0, $CHCl_3$); CD: 355 nm (Δ*e*′ 0.0087, *c* 0.00106 M); ^{1}H NMR: δ 7.33–7.28 (m, 10H, Ph), 4.92 (s, 1 H, H-1), 4.86 (dd, 1 H, $J_{3,4}$ 3.6 Hz, H-3), 4.82, 4.68 (AB, 4 H, 2 × CH_2Ph), 4.58 (d, 1 H, $J_{2,3}$ 5.9, H-2), 4.21 (dd, 1 H, $J_{4,3}$ 3.4, $J_{4,5}$ 9.3 Hz, H-4), 4.05 (dd, 1 H, $J_{5,6}$ 3.9 Hz, H-5), 3.93 (dd, 1 H, $J_{7,8a}$ 10.0 Hz, H-7), 3.73 (dd, 1 H, $J_{6,7}$ 4.8 Hz, H-6), 3.54 (d, 2 H, $J_{7,8b}$ 5.2 Hz, H-8a, H-8b), 3.31 (s, 3 H, OCH_3), 2.85, 1.98 (2 × bs, 2 H, OH), 1.50, 1.35 [2 s, 6 H, $(CH_3)_2$C]. ^{13}C NMR ($CDCl_3$): δ 128.5–127.8 (2 × Ph), 108.2 (C-1), 84.7 (C-2), 80.0, 79.9, 79.3, 76.4 (C-3,4,5,6), 74.7, 74.0 (2 × CH_2Ph), 71.7 (C-7), 63.9 (C-8), 55.3 (OCH_3), 26.3, 25.1 [$(CH_3)_2$C]. LSIMS (HRMS): *m*/*z* 497.2167 $[M + Na]^+$. Calcd for $C_{26}H_{34}NaO_8$ 497.2154. Anal. Calcd for $C_{26}H_{34}O_8 \cdot H_2O$: C, 63.40; H, 7.37. Found: C, 63.50; H, 7.31.

*Methyl 5,6,7-tri-*O*-benzyl-8-deoxy-2,3-*O*-isopropylidene-8-(phenyldimethyl)silyl-*D*-threo-α-*D*-manno-octofuranoside* (**17**).—Obtained from **14** (0.5 g), colorless oil, 0.106 g (18.4%); $[\alpha]_D$ +21° (*c* 1.4, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 7.31–7.20 (m, 3 × Ph), 4.86 (s, 1 H, H-1), 4.82 (dd, 1 H, $J_{3,4}$ 3.2 Hz, H-3), 4.76, 4.64, 4.56 (AB, 6 H, 3 × CH_2Ph), 4.58 (d, 1 H, $J_{2,3}$ 5.8 Hz, H-2), 4.34 (dd, 1 H, $J_{4,5}$ 9.3 Hz, H-4), 4.09 (dd, 1 H, $J_{5,6}$ 2.3 Hz, H-5), 3.91 (m, 1 H, $J_{7,8a}$ 8.2, $J_{7,8b}$ 5.1 Hz, H-7), 3.21 (s, 3 H, OCH_3), 1.50 (dd, 1 H, $J_{8a,8b}$ 10.1 Hz, H-8a), 1.49, 1.33 [2 s, 6 H, $(CH_3)_2$C], 1.15 (dd, 1 H, H-8a), 0.27, 0.25 [2 s, 6 H, $(CH_3)_s$Si]. ^{13}C NMR ($CDCl_3$): δ 128.7–127.0 (3 × Ph), 107.9 (C-1), 85.2 (C-2), 83.7, 80.0, 78.9, 77.5 (C-3,4,5,6), 75.9 (C-7), 74.9, 73.4, 72.8 (3 × CH_2Ph), 55.2 (OCH_3), 26.3, 25.1 [$(CH_3)_2$C], 19.1 (C-8), −1.2, −2.0 [$(CH_3)_2$Si]. LSIMS

(HRMS) m/z 705.3225 $[M + Na]^+$. Calcd for $C_{41}H_{50}NaO_7Si$ 705.3223.

Methyl 5,6-di-O-benzyl-7,8-dideoxy-2,3-O-isopropylidene-L-glycero-α-D-manno-oct-7-enofuranoside (**18**).—Colorless oil, 0.291 g (78.3%); $[\alpha]_D$ +41.6° (*c* 1.1, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 7.31–7.24 (m, 2 × Ph), 6.01 (m, 1 H, $J_{7,6}$ 7.8, $J_{7,8a}$ 2.5, $J_{7,8b}$ 0.7 Hz, H-7), 5.35 (dq, 1 H, $J_{8a,8b}$ 14.6 Hz, H-8a), 5.26 (dq, 1 H, H-8b), 4.85 (s, 1 H, H-1), 4.82 (dd, 1 H, $J_{3,4}$ 3.3 Hz, H-3), 4.55 (d, 1 H, $J_{2,3}$ 5.8 Hz, H-2), 4.68, 4.52 (AB, 4 H, 2 × CH_2Ph), 4.30 (dd, 1 H, $J_{4,5}$ 9.5 Hz, H-4), 4.09 (dd, 1 H, $J_{6,7}$ 7.8 Hz, H-6), 3.83 (dd, 1 H, $J_{5,6}$ 2.6 Hz, H-5), 3.18 (s, 3 H, OCH_3), 1.48, 1.32 [2 s, 6 H, $(CH_3)_2C$]. ^{13}C NMR ($CDCl_3$): δ 128.8–127.3 (2 × Ph), 136.3 (C-7), 117.9 (C-8), 107.5 (C-1), 84.8 (C-2), 81.2, 80.0, 79.5 (C-3,4,5), 78.0 (C-6), 74.7, 70.9 (2 × CH_2Ph), 54.5 (OCH_3), 26.2, 24.9 [$(CH_3)_2C$]. LSIMS (HRMS) m/z 463.2079 $[M + Na]^+$. Calcd for $C_{26}H_{32}NaO_6$ 463.2096.

*Methyl 7-O-allyl-4-O-benzyl-2,3-O-isopropylidene-*L-glycero *and* D-glycero-α-D-manno-*heptopyranosides* (**21**).—Obtained from **20** (1.7 g) and allyloxymethylmagnesium chloride, following the procedure for **3** and **4**, as an inseparable mixture of stereoisomeric LαD- and DαD-*manno*-heptopyranosides (1.48 g, 71%, approx. 2:1). The proportion and configuration of stereoisomers could be deduced after the benzylation experiment and isolation of the pure LαD stereoisomer **24** (see below).

*Methyl 7-O-allyl-4-O-benzyl-2,3-O-isopropylidene-*L-glycero-α-D-manno-*heptopyranoside* (**24**).—Obtained from **21** (1.36 g), colorless oil, 0.462 g (47.3%); $[\alpha]_D$ +46.3° (*c* 1.4, $CHCl_3$); CD: 352.5 nm ($\Delta e'$ −0.0135, *c* 0.00107 M); CD: 355 nm ($\Delta e'$ 0.0087, *c* 0.00106 M); ^1H NMR ($CDCl_3$): δ 7.37–7.28 (m, Ph), 5.90 (m, 1 H, CH=), 5.26, 5.18 (dq, 2 H, CH_2=), 4.93 (s, 1 H, H-1), 4.82, 4.65 (AB, 2 H, CH_2Ph), 4.32 (t, 1 H, $J_{3,4}$ 6.0 Hz, H-3), 4.18 (dd, 1 H, $J_{4,5}$ 7.3 Hz, H-4), 4.11 (d, 1 H, $J_{2,3}$ 5.7 Hz, H-2), 4.02 (m, 2 H, OCH_2), 3.72 (dd, 1 H, $J_{5,6}$ 6.8 Hz), 3.64–3.59 (m, 1 H, H-6), 3.58–3.40 (m, 2 H, H-7a, H-7b), 3.34 (s, 3 H, OCH_3), 2.20 (bs, 1 H, OH), 1.50, 1.36 [2 s, 6 H, $(CH_3)_2C$]. ^{13}C NMR ($CDCl_3$): δ 134.4 (CH=), 128.2–127.6 (Ph), 117.2 (CH_2=), 98.4 (C-1), 78.8, 77.9, 75.5, 74.9 (C-2,3,4,6), 73.1 (CH_2Ph), 71.3 (OCH_2), 70.4 (C-7), 67.3 (C-5), 54.9 (OCH_3), 27.9, 26.3 [$(CH_3)_2C$]. LSIMS (HRMS): m/z 417.1893 $[M + Na]^+$. Calcd for $C_{21}H_{30}NaO_7$ 417.1889. Anal. Calcd for $C_{21}H_{30}O_7 \cdot H_2O$: C, 61.15; H, 7.82. Found: C, 61.41; H, 7.49.

*Methyl 7-O-allyl-4,6-di-O-benzyl-2,3-O-isopropylidene-*D-glycero-α-D-manno-*heptopyranoside* (**22**).—Colorless oil, 0.482 g (64.6%); $[\alpha]_D$ +56.2° (*c* 1.4, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 7.29–7.23 (m, 2 × Ph), 5.89 (m, 1 H, CH=), 5.26, 5.18 (dg, 2 H, CH_2=), 4.97 (s, 1 H, H-1), 4.82, 4.60 (AB, 4 H, 2 × CH_2Ph), 4.24 (t, 1 H, $J_{3,4}$ 6.0 Hz, H-3), 4.12 (dd, 1 H, $J_{2,3}$ 5.9 Hz, H-2) 4.08–3.98 (m, 3 H, OCH_2, H-6), 3.84–3.62 (m, 4 H, H-4, H-5, H-7a, H-7b), 3.35 (s, 3 H, OCH_3), 1.54, 1.37 [2 s, 6 H, $[(CH_3)_2C]$. ^{13}C NMR ($CDCl_3$): δ 134.5 (CH=), 128.1–127.4 (2 × Ph), 116.8 (CH=), 98.5 (C-1), 79.1, 75.6, 75.0, 74.9 (C-2,3,4,6), 73.4, 72.2 (2 × CH_2Ph), 72.0 (OCH_2), 69.7 (C-7), 67.8 (C-5), 54.9 (OCH_3), 27.9, 26.3 [$(CH_3)_2C$]. LSIMS (HRMS): m/z 507.2356 $[M + Na]^+$. Calcd for $C_{28}H_{36}NaO_7$ 507.2358.

*Methyl 7-O-allyl-4,6-di-O-benzyl-2,3-O-isopropylidene-*L-glycero-α-D-manno-*heptopyranoside* (**23**).—Colorless oil, 0.263 g (35.3%); $[\alpha]_D$ +51.1° (*c* 1.9, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 7.35–7.27 (m, 2 × Ph), 5.88 (m, 1 H, CH=), 5.22, 5.14 (dq, 2 H, CH_2=), 4.85 (s, 1 H, H-1), 4.78, 4.58 (AB, 4 H, 2 × CH_2Ph), 4.31 (t, 1 H, $J_{3,4}$ 6.2 Hz, H-3), 4.10 (d, 1 H, $J_{2,3}$ 5.8 Hz, H-2), 4.02 (dd, 1 H, $J_{4,5}$ 7.6 Hz, H-4), 3.98–3.80 (m, 4 H, H-5, H-6, OCH_2), 3.67–3.59 (m, 2 H, H-7a, H-7b), 3.37 (s, 3 H, OCH_3), 1.49, 1.36 [2 s, 6 H, $(CH_3)_2C$]. ^{13}C NMR ($CDCl_3$): δ 134.8 (CH=), 128.3–127.3 (2 × Ph), 116.5 (CH_2=), 98.0 (C-1), 79.2, 77.7, 75.6, 75.5 (C-2,3,4,5), 72.6, 72.4 (2 × CH_2Ph), 72.1 (OCH_2), 70.2 (C-7), 68.7 (C-6), 54.7 (OCH_3), 27.9, 26.3 [$(CH_3)_2C$]. LSIMS (HRMS): m/z 507.2360 $[M + Na]^+$. Calcd for $C_{28}H_{36}NaO_7$ 507.2358.

Methyl 4,6-di-O-benzyl-2,3-O-isopropylidene-D-glycero-α-D-manno-heptopyranoside (**25**).—Obtained from **22** (0.39 g), colorless oil, 0.289 g (80.4%); $[\alpha]_D$ +61.5° (*c* 1.8, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 7.32–7.35 (m, 2 × Ph), 4.98 (s, 1 H, H-1), 4.82, 4.50 (AB, 4 H, 2 × CH_2Ph), 4.34 (t, 1 H, $J_{3,4}$ 6.3 Hz, H-3), 4.14 (d, 1 H, $J_{2,3}$ 5.9 Hz, H-2), 3.96–3.30 (m, 3 H, $J_{4,5}$ 10.3, $J_{5,6}$ 3.0 Hz, H-4, H-5, H-6),

3.78–3.73 (m, 2 H, H-7a, H-7b), 3.39 (s, 3 H, OCH_3), 1.55, 1.37 [2 s, 6 H, $(CH_3)_2C$]. ^{13}C NMR ($CDCl_3$): δ 128.4–127.7 (2 × Ph), 98.6 (C-1), 78.9, 76.4, 75.5, 75.2 (C-2,3,4,5), 73.0, 72.2 (2 × CH_2Ph), 69.6 (C-6), 62.6 (C-7), 55.3 (OCH_3), 27.9, 26.3 [$(CH_3)_2C$]. LSIMS (HRMS): m/z 467.2038 $[M + Na]^+$. Calcd for $C_{25}H_{32}NaO_7$ 467.2045

*Methyl 8-*O*-allyl-4,6-di-*O*-benzyl-2,3-*O*-isopropylidene-*D*-erythro- and* L*-threo-α-*D*-manno-octopyranosides* (**27**).—Obtained from **26** (0.124 g) and allyloxymethylmagnesium chloride, following the procedure for **3** and **4**, as an inseparable mixture of stereoisomeric D-*erythro*- and L-*threo*-α-D-*manno*-octopyranosides and together with some unreacted aldehyde (11 mg). ^1H NMR ($CDCl_3$): inter alia δ 9.41 (d, J 1.0 Hz, CHO), 5.85 (m, allyl –CH=), 3.17, 3.15, 3.13 (3 s, 3 × OCH_3).

*Methyl 4-*O*-benzyl-7-deoxy-2,3-*O*-isopropylidene-7-(phenyldimethyl)silyl-*L*-glycero-α-D-manno-heptofuranoside* (**28**).—Obtained from **20** (2.2 g), colorless oil, 2.49 g (77.3%); $[\alpha]_D$ + 37.9° (*c* 1.7, $CHCl_3$); CD: 360.5 nm ($\Delta e'$ − 0.0238, *c* 0.00105 M); CD: 355 nm ($\Delta e'$ 0.0087, *c* 0.00106 M); ^1H NMR ($CDCl_3$): δ 7.47–7.24 (m, 2 × Ph), 4.93 (s, 1 H, H-1), 4.58, 4.52 (AB, 4 H, 2 × CH_2Ph), 4.28 (dd, 1 H, $J_{3,4}$ 6.8 Hz, H-3), 4.16–4.02 (m, 1 H, H-6), 4.09 (d, 1 H, $J_{2,3}$ 5.7 Hz, H-2), 3.62 (dd, 1 H, $J_{4,5}$ 10.0 Hz, H-4), 3.34 (dd, 1 H, $J_{5,6}$ 3.8 Hz, H-5), 3.25 (s, 3 H, OCH_3), 1.60 (dd, 1 H, $J_{7a,6}$ 3.8, $J_{7a,7b}$ 14.7 Hz, H-7a), 1.50, 1.36 [2 s, 6 H, $(CH_3)_2C$], 0.92 (dd, 1 H, $J_{7b,6}$ 11.0 Hz, H-7b), 0.36, 0.35 [2 s, 6 H, $(CH_3)_2Si$]. ^{13}C NMR ($CDCl_3$): δ 128.3–127.6 (2 × Ph), 98.4 (C-1), 78.9 (C-2), 75.9, 75.5, 71.7 (C-3,4,5), 73.2 (CH_2Ph), 67.3 (C-6), 55.1 (OCH_3), 27.9, 26.3 [$(CH_3)_2C$], 21.5 (C-7), − 2.1, − 2.4 [$(CH_3)_2Si$]. LSIMS (HRMS): m/z 495.2177 $[M + Na]^+$. Calcd for $C_{26}H_{36}NaO_6Si$ 495.2178.

*Methyl 4-*O*-benzyl-7-deoxy-2,3-*O*-isopropylidene-7-(phenyldimethyl)silyl-*D*-glycero-β-L-gulo-heptopyranoside* (**29**).—Colorless oil, 0.277 g (8.6%); $[\alpha]_D$ + 79.1° (*c* 3.1, $CHCl_3$); CD: 352 nm ($\Delta e'$ 0.0462, *c* 0.00105 M); ^1H NMR ($CDCl_3$): δ 7.47–7.24 (m, 2 × Ph), 4.58 (AB, 2 H, CH_2Ph), 4.38 (dd, 1 H, $J_{3,4}$ 2.3 Hz, H-3), 4.28 (d, 1 H, $J_{1,2}$ 7.0 Hz, H-1), 4.05 (m, 1 H, $J_{6,7a}$ 10.9, $J_{6,7b}$ 2.2 Hz, H-6), 3.97 (dd, 1 H, $J_{2,3}$ 5.8 Hz, H-2), 3.76 (t, 1 H, $J_{4,5}$ 1.9 Hz, H-4), 3.51 (s, 6 H, OCH_3), 3.35 (dt, $J_{5,6}$ 7.6 Hz, H-5), 2.70 (bs, 1 H, OH), 1.47, 1.36 [2 s, 6 H, $(CH_3)_2C$], 0.87 (dd, 1 H, $J_{7a,7b}$ 14.3 Hz, H-7a), 0.60 (dd, 1 H, H-7b), 0.31, 0.30 [2 s, 6 H, $(CH_3)_2Si$]. ^{13}C NMR ($CDCl_3$): δ 128.6–127.4 (Ph), 104.0 (C-1), 79.2 (C-2), 74.6, 73.7, 72.2 (C-3,4,5), 72.3 (CH_2Ph), 68.1 (C-6), 56.8 (OCH_3), 27.9, 26.0 [$(CH_3)_2C$, 19.1 (C-7), − 1.6, − 2.5 [$(CH_3)_2Si$]. LSIMS (HRMS): m/z 495.2180 $[M + Na]^+$. Calcd for $C_{26}H_{36}NaO_6Si$ 495.2178. Anal. Calcd for $C_{26}H_{36}O_6Si \cdot 1/2H_2O$: C, 64.86; H, 7.69. Found: C, 64.88; H, 7.43

*Methyl 4-*O*-benzyl-6,7-dideoxy-2,3-*O*-isopropylidene-α-D-manno-hept-6-enopyranoside* (**30**).—Obtained (BnBr, NaH, DMF) from **28** (3.81 g), 0.953 g (78.1%), white foam; $[\alpha]_D$ + 34.4° (*c* 1.3, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 7.35–7.27 (m, Ph), 5.98 (ddd, 1 H, $J_{6,7a}$ 17.3, $J_{6,7b}$ 10.4 Hz, H-6), 5.44 (dq, 1 H, $J_{7a,7b}$ 17.5 Hz, H-7a), 5.26 (dq, 1 H, H-7b), 4.92 (s, 1 H, H-1), 4.82, 4.61 (AB, 2 H, CH_2Ph), 4.29 (t, 1 H, $J_{3,4}$ 7.0 Hz, H-3), 4.14 (d, 1 H, $J_{2,3}$ 5.8 Hz, H-2), 4.01 (dd, 1 H, $J_{5,6}$ 5.7 Hz, H-5), 3.36 (dd, 1 H, $J_{4,5}$ 10.1 Hz, H-4), 3.32 (s, 3 H, OCH_3), 1.47, 1.36 [2 s, 6 H, $(CH_3)_2C$]. ^{13}C NMR ($CDCl_3$): δ 134.9 (C-6), 128.1–127.5 (Ph), 117.3 (C-7), 98.0 (C-1), 79.4, 78.6, 75.7, 68.8 (C-2,3,4,5), 72.9 (CH_2Ph), 54.8 (OCH_3), 27.8, 26.2 [$(CH_3)_2C$]. LSIMS (HRMS): m/z 343.1524 $[M + Na]^+$. Calcd for $C_{18}H_{24}NaO_5$ 343.1521.

*Methyl 4,6-di-*O*-benzyl-7-deoxy-2,3-*O*-isopropylidene-*L*-glycero-α-D-manno-heptofuranoside* (**31**).—To methyl 4-*O*-benzyl-7-deoxy-2,3-*O*-isopropylidene-7-(phenyldimethyl)silyl-L-*glycero*-α-D-*manno*-heptofuranoside (**28**) (0.35 g, 0.74 mmol) was added 5 mL of aq 50% NaOH and the mixture was stirred at rt for a few minutes. Benzyl bromide (1.5 mL) and tetrabutylammonium bromide (30 mg) were added, and vigorous stirring was continued for 1 h. The product was extracted with Et_2O (3 × 20 mL). Combined organic extracts were washed with water (20 mL), dried over Na_2SO_4 and concentrated to dryness. Column chromatography of the residue with 6:1 hexane–EtOAc gave **31** (0.267 g, 84.2%) as a colorless oil; $[\alpha]_D$ + 72.5° (*c* 1.2, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 7.36–7.27 (m, Ph), 5.01 (s, 1 H, H-1), 4.83, 4.64 (AB, 4 H,

$2 \times CH_2Ph$), 4.36 (dd, 1 H, $J_{3,4}$ 6.3 Hz, H-3), 4.30 (dd, 1 H, $J_{5,6}$ 1.2 Hz, H-5), 4.12 (d, 1 H, $J_{2,3}$ 5.9 Hz, H-2), 4.00 (dg, 1 H, $J_{6,7}$ 6.6 Hz, H-6), 3.81 (dd, 1 H, $J_{4,5}$ 10.0 Hz, H-4), 3.38 (s, 3 H, OCH_3), 1.54, 1.37 [2 s, 6 H, $(CH_3)_2C$], 1.32 (d, 3 H_7, CH_3). ^{13}C NMR ($CDCl_3$): δ 128.4–127.7 ($2 \times Ph$), 98.6 (C-1), 79.2 (C-2), 75.6, 75.5, 71.4, 71.3 (C-3,4,5,6), 72.4, 71.1 ($2 \times CH_2Ph$), 54.9 (OCH_3), 27.9, 26.3 [$(CH_3)_2C$], 15.8 (C-7). LSIMS (HRMS): m/z 451.2091 $[M + Na]^+$. Calcd for $C_{25}H_{32}NaO_6$ 451.2096. Anal. Calcd for $C_{25}H_{32}O_6 \cdot H_2O$: C, 67.24; H, 7.67. Found: C, 67.13; H, 7.23.

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