ELSEVIER

Carbohydrate Research 305 (1998) 293–303

CARBOHYDRATE RESEARCH

# 4,6-Di-*O*-benzoyl-3-*O*-benzyl-α-D-*arabino*-hexopyranos-2-ulosyl bromide: A conveniently accessible glycosyl donor for the expedient construction of diantennary β-D-mannosides branched at O-3 and O-6

Frieder W. Lichtenthaler [a,*], Ulrich Kläres [a], Zoltán Szurmai [b], Bernd Werner [a]

[a] *Institut für Organische Chemie, Technische Universität Darmstadt, Petersenstraße 22, D-64287 Darmstadt, Germany*

[b] *Institute of Biochemistry, L. Kossuth University, P.O.B. 55, H-4010 Debrecen, Hungary*

Received 6 May 1997; accepted 1 August 1997

**Abstract**

A concise practical, large scale-adaptable six-step sequence has been developed for the transformation of diacetone-glucose into 4,6-di-*O*-benzoyl-3-*O*-benzyl-α-D-*arabino*-hexopyranos-2-ulosyl bromide (**7**), a most useful indirect β-D-mannosyl donor as its blocking group pattern allows the construction of biologically relevant β-D-mannosides branched at O-3 and O-6. The broad utility of this new ulosyl bromide **7** resides in its high anomeric reactivity, and in the ease and uniformity with which β-stereocontrol can be achieved over both, glycosidations and carbonyl reduction of the β-ulosides formed: Koenigs–Knorr conditions exclusively provide β-glycosiduloses, hydride reduction of their carbonyl functions proceeds with high stereoselectivities (> 20:1) in favor of the β-D-mannosides. These preparatively auspicious properties are materialized in an efficient, straightforward synthesis of α-D-Man*p*-(1 → 6)-[α-D-Man*p*-(1 → 3)]-β-D-Man*p*-(1 → *O*)-Octyl, the 3,6-O-branched core-mannotrioside carrying an octyl spacer instead of the chitobiosyl unit. © 1998 Elsevier Science Ltd

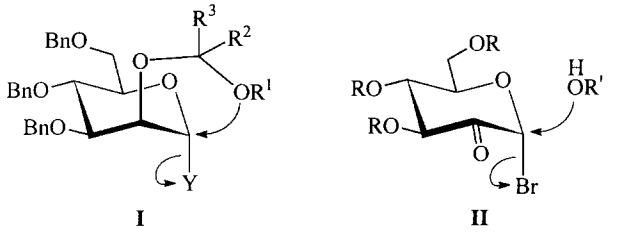
*Keywords:* β-D-Mannosides; β-D-Glycosid-2-uloses; Glycosidation; Mannotrioside; Oligosaccharide synthesis

## 1. Introduction

Of the numerous strategies developed for the construction of β-D-mannosidic linkages [1], the *intramolecular aglycon delivery* method [2–4] and the *ulosyl bromide approach* [5–11] have performed particularly well with respect to the β-selectivities attainable in the crucial glycosidation step. In both cases, the underlying reasons for the essentially complete β-stereocontrol are the same: practically full

* Corresponding author.


*PII* S0008-6215(97)00249-8



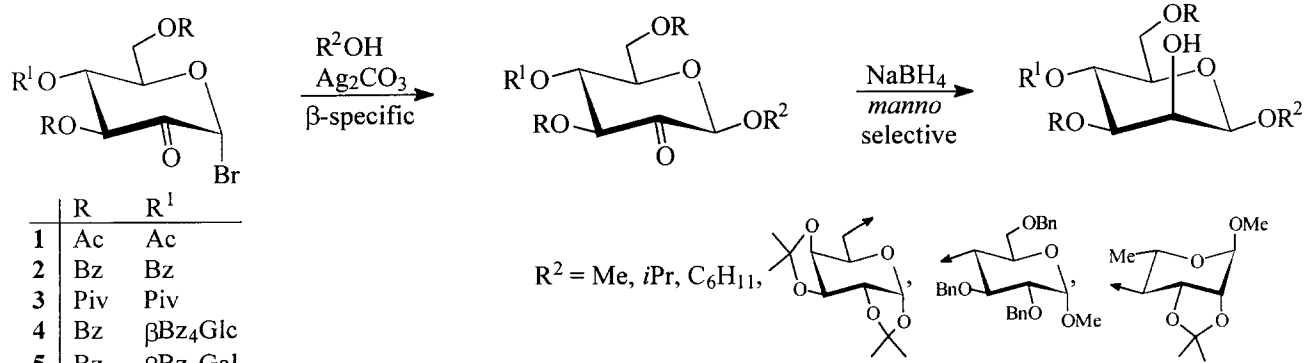

Scheme 1. Anomeric stereocontrol involved in the intramolecular aglycon delivery (**I**) [2–4] and the ulosyl bromide approach (**II**) [5–10] for the generation of β-D-mannosidic linkages.

suppression of oxocarbenium ion formation following anomeric activation of the mannosyl donor. In the intramolecular aglycon delivery protocol, this is accomplished by covalent pre-attachment of the saccharidic acceptor to O-2 of a latent mannosyl donor, which entails a concerted reaction of the type depicted in I. In the procedure involving 2-oxo-glycosyl ('ulosyl') bromides of type II as indirect β-D-mannosyl donors, the stereocontrol relies on the electron withdrawing effect of the 2-keto group which favors direct $S_N2$ displacement of the anomeric substituent by the alcohol component to such an extent that β-D-glycosiduloses are obtained exclusively (Scheme 1).

Aside from the essential β-specificity attainable in the insoluble silver salt-promoted glycosidation step, ulosyl bromides have the preparative advantage to be nearly as well accessible from glucose (→ **1–3** [5,8,9]), cellobiose (→ **4** [6]), or lactose (→ **5** [6]), as the respective glycosyl bromides. Key intermediates for the four steps required are their 2-acyloxy-glycal esters or ethers, which simply by exposure to *N*-bromosuccinimide/methanol provide the ulosyl bromides in 80–90% yields [5–9]. An alternate protocol from 2-acyloxy-glycals to ulosyl bromides comprises the three-step sequence hydroxylaminolysis [12] → deoximation → anomeric photobromination [13], a protocol that, on replacement of the deoximation step by *O*-benzoylation of the oxime, can also be utilized for the acquisition of the 2-benzoximino analogs of **1–6** [6–8,13] which have proven to be highly useful indirect β-D-mannosaminyl donors [14–17] (Scheme 2).

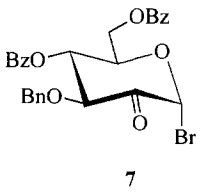
The other key parameter of this ulosyl bromide approach concerns the degree of *manno*-selectivity achievable on hydride reduction of the 2-keto group in the β-D-glucosiduloses obtained on β-specific glycosidation of **1–6**. The β-D-mannosides invariably are the major products, yet there seems to be a peculiar dependence of the *manno*/*gluco* ratio obtained on the nature of the 3-*O*-blocking group: 2:1 to 5:1 in favor of the β-D-mannosides in cases with 3-*O*-acyl moieties versus preparatively satisfactory 20:1 to 50:1 ratio, when the 3-oxygen, vicinal to the carbonyl function, is protected by a benzyl residue. Due to these favorable assets, and the fact that the β-D-mannosides accumulate with a free 2-OH group suited for introduction of other glycosyl residues, the benzylated ulosyl bromide **6** has been successfully applied to the synthesis of a fairly complex trisaccharide unit of the *Hyriopsis schlegelii* glycosphingolipid [10] and of a physiologically active fungal metabolite [11].

For broadening the scope of ulosyl bromides as indirect β-D-mannosyl donors, it appeared indispensable to provide analogs with a blocking group pattern allowing for glycosylations at O-3 and O-6 in order to address synthetically the core structure of high-mannose-type glycoproteins. These requirements are met by the 3-*O*-benzyl-4,6-di-*O*-benzoyl protected ulosyl bromide **7**, whose straightforward acquisition from diacetone-glucose is described in this paper,

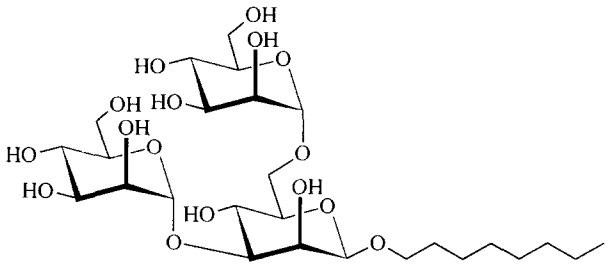



| | R | $R^1$ |
|---|---|---|
| **1** | Ac | Ac |
| **2** | Bz | Bz |
| **3** | Piv | Piv |
| **4** | Bz | βBz4Glc |
| **5** | Bz | βBz4Gal |
| **6** | Bn | Bn |

Scheme 2. The ulosyl bromide approach [5–10] for the generation of β-D-mannopyranosides. Piv: pivaloyl (*t*BuCO); β$Bz_4$Glc: 2,3,4,6-tetra-*O*-benzoyl-β-D-glucopyranosyl; β$Bz_4$Gal: 2,3,4,6-tetra-*O*-benzoyl-β-D-galactopyranosyl).



7



8

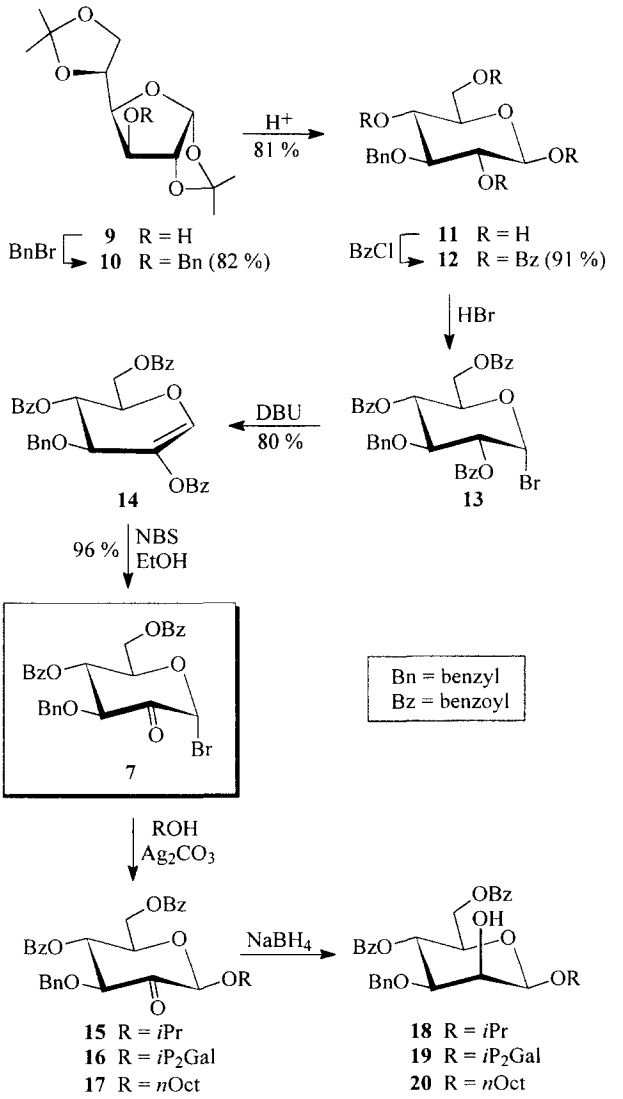
Scheme 3.

together with its utilization for the synthesis of $O^3$,$O^6$-branched β-D-mannosides, e.g. the core-trisaccharide **8** of high-mannose-type oligosaccharides carrying an octyl spacer instead of the chitobiosyl moiety (Scheme 3).

## 2. Results and discussion

For the acquisition of the title ulosyl bromide **7**, with a benzyl group at O-3 and benzoyl groups at O-4 and O-6, an expedient six-step reaction sequence was elaborated starting from diacetone-glucose, which allows for a quite satisfactory overall yield of 49%. In the first three steps it involved adaption of published procedures to the 20 g scale, i.e. 3-*O*-benzylation (**9** → **10** [18]), removal of the isopropylidene groups by treatment with a strongly acidic resin [19], and benzoylation of the resulting 3-*O*-benzyl-D-glucose (**11** → **12**) [23] (Scheme 4). The conversion of tetrabenzoate **12** into its α-bromide **13** by exposure to hydrogen bromide/acetic acid and the subsequent base-induced elimination of hydrogen bromide was readily performed in one continuous operation, to afford the 2-benzoyloxy-glucal **14** in 80% yield for the two steps. The transformation of **14** into ulosyl bromide **7** was effected by brief exposure to *N*-bromosuccinimide/ethanol in dichloromethane (10 min, 0 °C) which smoothly and nearly quantitatively generated the desired ulosyl bromide **7**; it was characterized as a uniform syrup of the expected positive rotation ($[\alpha]_D^{20}$ +103.7°), which surprisingly is only half of the rotational value obtained for its fully benzoylated analog **2** (+208° [13]).

Glycosidations of ulosyl bromide **7** under the Koenigs–Knorr-type conditions used previously [8–10], i.e. silver carbonate/dichloromethane at room temperature, proceeded in essentially β-specific manner and were completed within minutes: isopropanol gave the glycosidulose **15** in 95% yield, isolable either as an approximate 10:1 mixture of its 2-keto and 2,2-dihydroxy (monohydrate) forms, or as the pure monohydrate, depending on the mode of crystallization — a behaviour not unexpected in view of analogous previous observations [20]; reaction of **7** with 1,2:3,4-diacetone-galactose (→ **16**, 80%) and with *n*-octanol (→ **17**, 77%) proceeded as readily, again affording the β-D-glycosiduloses as crystalline mixtures of the 2-keto and monohydrate forms.

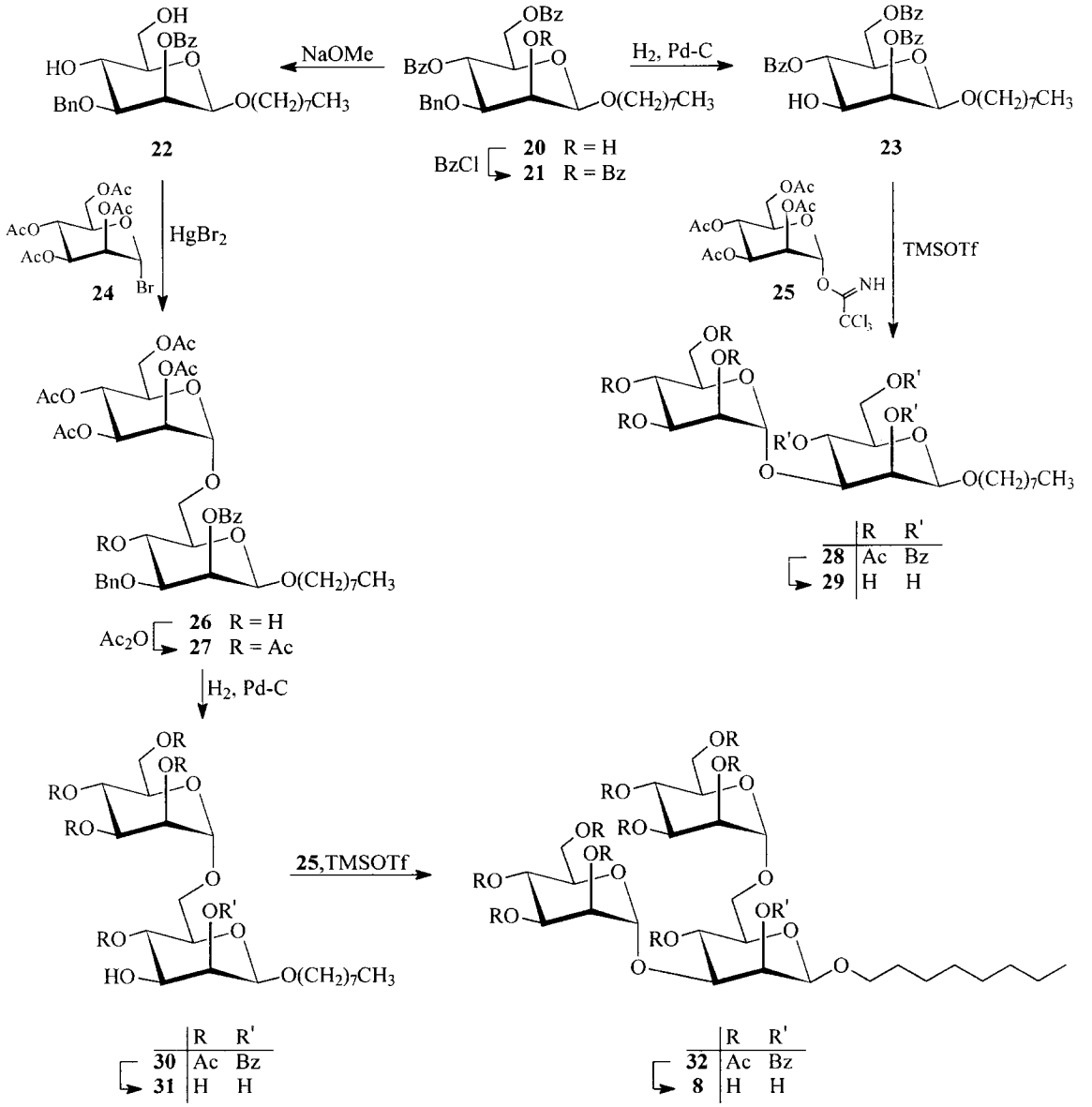



Scheme 4.

β-D-Glycosiduloses with a benzyl protecting group at O-3 have been shown to provide particularly high *manno*-selectivities on hydride reduction (20:1 to 50:1 [9]). Thus, not unexpectedly, the same degree of stereoselection was observed in the sodium borohydride reductions of ulosides **15–17** affording the respective β-D-mannosides **18–20** in average yields of 80%.

Comparing the performance of ulosyl bromide **7** as an indirect β-D-mannosyl donor with that of its perbenzylated analog **6** [9], it is apparent that the two benzoyl ester functionalities at O-4 and O-6 have little if any effect on the high anomeric reactivity of **7** as well as on the steric course of the glycosidation, as both proceed with similar ease and in β-specific fashion. That, in addition, *manno*-selectivities of > 20:1 are obtained in the uloside reduction step (**15–17** → **18–20**) renders ulosyl bromide **7** with its differentiated blocking group pattern a most versatile donor for the generation of β-D-mannosides not only ramified at O-2—a free 2-OH group already emerges from the reaction sequence—but at O-3 and O-6 as well through simple blocking group manipulations.

To probe the utility of this ulosyl bromide for the synthesis of the O-3,6-branched diantennary core-mannotrioside type, the suitably blocked octyl β-D-mannoside **20**, readily accessible from **7** in two high-yielding steps (overall yield: 74%), was subjected to α-mannosylations at O-3 and/or O-6, respectively. Accordingly, upon 2-*O*-benzoylation (**20** → **21**), the




Scheme 5.

hydroxyl functions at C-4 and C-6 were liberated by selective Zemplén de-*O*-benzoylation (**21** → **22**), or alternately O-3 was deblocked by hydrogenolysis of the 3-*O*-benzyl group (**20** → **23**)—manipulations, that were readily effected in preparatively satisfactory yields and led to nicely crystalline products (Scheme 5).

The α-mannosylation of the 3-OH-free octyl β-D-mannoside **23** was either carried out with aceto-bromo-mannose (**24**) under modified Helferich conditions (mercury(II) bromide in dichloromethane) or with 2,3,4,6-tetra-*O*-acetyl-α-D-mannopyranosyl trichloroacetimidate (**25**) by trimethylsilyl triflate promotion, to smoothly provide Man-α(1 → 3)-Man-β-*O*Oct **28** in acylated form (76%). Deblocking was smoothly achieved in one step to give the free dimannoside **29** (88%). In similar fashion, the octyl 2-*O*-benzoyl-3-*O*-benzyl-β-D-mannoside **22** could be regioselectively 6-O-mannosylated with **24** and mercury(II) bromide in dichloromethane, setting the stage — upon acetylation **26** → **27** — to liberation of the 3-OH junction in the central mannose residue by hydrogenolysis (**27** → **30**), and its trimethylsilyl triflate induced α-mannosylation with trichloroacetimidate **25**: the fully acylated mannotrioside **32** was thus obtained (73%), and was readily deblocked under Zemplén conditions to yield the desired octyl 3,6-di-*O*-(α-D-mannosyl)-β-D-mannoside **8**.

By way of summation, the easy accessibility (49% overall yield for the six steps from diacetone-glucose), the differentiated blocking group pattern, and the high anomeric reactivity render the 4,6-di-*O*-benzoyl 3-*O*-benzyl-protected ulosyl bromide **7** a most versatile indirect β-D-mannosyl donor with which O-3,6-diantennary as well as O-2,3,6-triantennary manno-oligosaccharides may advantageously be assembled.

## 3. Experimental

*General methods.*—$^1$H (300 MHz) and $^{13}$C (75 MHz) NMR spectra were recorded at 25 °C with a Bruker AC 300 spectrometer. Chemical shifts (δ) are given in ppm relative to the signal for internal $Me_4Si$ ($CDCl_3$). Column chromatography was performed on Kieselgel 60 (Merck, 230 mesh) and fractions were monitored by TLC on Kieselgel 60 $F_{254}$ (Merck) by detection with UV light and then charring with $H_2SO_4$. Optical rotations were measured for solutions in $CHCl_3$ at 20 °C with a Perkin Elmer 241 polarimeter, using a 10 cm/1 mL cell.

*3-O-Benzyl-1,2:5,6-di-O-isopropylidene-α-D-glucofuranose* (**10**).—A solution of 1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose (**9**) (18.0 g, 69 mmol) in dry tetrahydrofuran (80 mL) was added dropwise to a suspension of NaH (1.9 g, 76.5 mmol) and tetrabutylammonium iodide (200 mg, 0.5 mmol) in dry tetrahydrofuran (50 mL) at 0 °C. The mixture was allowed to warm up to room temperature then benzyl bromide (9 mL, 76 mmol) added, and the solution was at 50 °C for 2 h. MeOH (40 mL) was added and the mixture was further stirred for 2 h before cooling, filtering through Celite and concentrating. The residue was dissolved in $CH_2Cl_2$ (250 mL), the solution washed with water (2 × 100 mL), dried ($Na_2SO_4$), and concentrated to a syrup which was distilled in a Kugelrohr: 21.1 g (87%) of **10**; bp 147 °C/0.05 torr; $[\alpha]_D^{20}$ −26.4° (*c* 1.2, $CHCl_3$); lit.: bp 165–169 °C/0.02 torr [21]; $[\alpha]_D^{20}$ −29.8 °C (*c* 1.0, $CHCl_3$) [18]; $^1$H NMR (300 MHz, $CDCl_3$): δ 1.30, 1.36, 1.42, and 1.48 (4 s, each 3 H, 4 $CH_3$), 3.99 (dd, 1 H, H-6a), 4.01 (d, 1 H, H-3), 4.11 (dd, 1 H, H-6b), 4.14 (dd, 1 H, H-4), 4.36 (dt, 1 H, H-5), 4.57 (d, 1 H, H-2), 4.62 and 4.67 (2d, each 1 H, $CH_2C_6H_5$), 5.88 (d, 1 H, H-1), 7.30–7.34 (m, 5 H, $C_6H_5$); $J_{1,2}$ = 3.7, $J_{3,4}$ = 3.2, $J_{4,5}$ = 7.7, $J_{5,6}$ = 6.0, $J_{5,6b}$ = 6.1, $J_{6,6}$ = 8.6, $J_{BnCH2}$ = 11.8 Hz; $^{13}$C NMR (75.5 MHz, $CDCl_3$): δ 25.4, 26.3, 26.8, and 26.9 ($CH_3$), 67.4 (C-6), 72.4 ($CH_2C_6H_5$), 72.6 (C-5), 81.4 (C-4), 81.8 (C-3), 82.7 (C-2), 105.3 (C-1), 109.4, and 111.8 ($C(CH_3)_2$), 127.6–137.7 ($C_6H_5$).

*1,2,4,6-Tetra-O-benzoyl-3-O-benzyl-β-D-glucopyranose* (**12**).—A solution of **10** (16.2 g, 46 mmol) in water (80 mL) was stirred with Dowex 50 resin ($H^+$ form, 30 g) for 2 h at 70 °C. Thereupon, the resin was filtered off, the filtrate was taken to dryness and the syrupy residue was crystallized from EtOAc (100 mL) to yield 10.1 g (81%) of 3-*O*-benzyl-α,β-D-glucopyranose (**11**) as a 1:1 α/β-anomeric mixture ($^1$H NMR), mp 132–134 °C, lit. 132–134 °C [22]. The product (10.0 g, 37 mmol) was dissolved in pyridine/$CHCl_3$ (100 mL each) and benzoyl chloride (21.5 mL, 185 mmol) was added. After stirring for 24 h at room temperature the mixture was diluted with $CHCl_3$ (200 mL), washed with 2 M HCl (4 × 100 mL), aq $NaHCO_3$, and water (100 mL), and dried ($Na_2SO_4$). Evaporation of the solvent and dissolution of the residue in MeOH resulted in crystallization on cooling: 23.2 g (91%) of **12**; mp 210–212 °C, lit. 209–210 °C [23]; $[\alpha]_D^{20}$ +0.3° (*c* 1.1, $CHCl_3$), lit. 0° (*c* 0.8, $CHCl_3$); $^1$H NMR (300 MHz, $CDCl_3$): δ 4.21 (t, 1 H, H-3), 4.25-4.30 (m, 1 H, H-5), 4.45 (dd, 1 H, H-6a), 4.61-4.65 (m, 1 H, H-6b), 4.65 (bs, 2 H,

$CH_2C_6H_5$), 5.72 (dd, 1 H, H-4), 5.74 (dd, 1 H, H-2), 6.19 (d, 1 H, H-1), 6.98–8.03 (m, 25 H, 5 $C_6H_5$); $J_{1,2} = 7.7$, $J_{2,3} = J_{3,4} = 8.6$, $J_{4,5} \approx 9.3$, $J_{5,6a} \approx 5.1$, $J_{5,6b} = 3.2$, $J_{6a,b} = 12.2$ Hz; $^{13}C$ NMR (75.5 MHz, $CDCl_3$): δ 63.0 (C-6), 70.4 (C-4), 72.1 (C-2), 73.1 (C-5), 74.2 ($CH_2C_6H_5$), 79.2 (C-3), 92.6 (C-1), 127.8–133.7 (5 $C_6H_5$), 164.8, 165.0, and 166.2 ($COC_6H_5$).

*1,5-anhydro-2,4,6-tri-*O*-benzoyl-3-*O*-benzyl-*D*-arabino-hex-1-enitol* (**14**).—A solution of **12** (5.0 g, 7.3 mmol) in $CH_2Cl_2$ (50 mL) was treated with hydrogen bromide in HOAC (33%, 25 mL, 141 mmol) at 0 °C. The mixture was stirred for 10 min, diluted with ice-cold $CH_2Cl_2$ (150 mL), washed with ice water, ice-cold aqueous $NaHCO_3$ (3 × 50 mL), water (50 mL), then dried ($Na_2SO_4$). The solvent was evaporated, the residue consisting of crude **13**, was dissolved in $CH_2Cl_2$ (60 mL), and DBU (1.4 mL, 9.5 mmol) was added. After 1.5 h stirring at room temperature the solution was washed with 2 M HCl (3 × 50 mL) and water (50 mL), dried ($Na_2SO_4$) and concentrated. The residual syrup was purified by elution from a short column of silica gel with $CH_2Cl_2$, to yield on evaporation of the respective eluate 3.28 g of **14** (80%) as a hard foam; $[\alpha]_D^{20}$ −4.4° (*c* 1, $CHCl_3$); $^1H$ NMR (300 MHz, $CDCl_3$): δ 4.41 (dd, 1 H, H-6a), 4.72 (bs, 2 H, $BnCH_2$), 4.77 (ddd, 1 H, H-5), 4.85 (dd, 1 H, H-6b), 5.69 (t, 1 H, H-4), 6.83 (s, 1 H, H-1), 7.06–8.11 (m, 20 H, 4 $C_6H_5$); $J_{3,4} = J_{4,5} = 3.5$, $J_{5,6a} = 3.4$, $J_{5,6b} = 7.6$, $J_{6a,b} = 11.4$ Hz; $^{13}C$ NMR (75.5 MHz, $CDCl_3$): δ 62.0 (C-6), 68.4 (C-4), 70.8 (C-3), 71.7 ($CH_2C_6H_5$), 74.3 (C-5), 127.8–133.7 (4 $C_6H_5$), 129.7 (C-2), 138.0 (C-1), 165.4, 165.6, and 166.3 ($COC_6H_5$). MS (FD/20 mA): *m/z* 564 [$M^+$], 565 [$M^+ + 1$]. Anal. Calcd for $C_{34}H_{28}O_8$ (564.56): C, 72.33; H, 5.00. Found: C, 72.19; H, 4.93.

*4,6-Di-*O*-benzoyl-3-*O*-benzyl-α-D-arabino-hexopyranos-2-ulosyl bromide* (**7**).—To a cooled (0 °C) solution of 2-benzoyloxy-glucal **14** (1.1 g, 1.93 mmol) in $CH_2Cl_2$ (8 mL) was added EtOH (169 μL, 2.9 mmol) and powdered molecular sieves (4 Å, 500 mg). After 10 min the mixture was treated with NBS (390 mg, 2.2 mmol) stirred for 30 min, then diluted with ice-cold $CH_2Cl_2$ (100 mL), successively washed with ice-cold ag 10% $Na_2S_2O_3$ solution (30 mL) and ice water (30 mL), dried ($Na_2SO_4$) and concentrated to give sirupy ulosyl bromide **7** (1.0 g, 96%); $[\alpha]_D^{20}$ + 103.7° (*c* 1, $CHCl_3$); $^1H$ NMR (300 MHz, $CDCl_3$): δ 4.42 (dd, 1 H, H-6a), 4.61 and 4.96 ($BnCH_2$), 4.64–4.69 (m, 1 H, H-5), 4.66 (dd, 1 H, H-6b), 4.94 (d, 1 H, H-3), 5.78 (t, 1 H, H-4), 6.41 (s, 1 H, H-1), 7.05–8.10 (m, 15 H, 3 $C_6H_5$); $J_{3,4} = J_{4,5} = 10.1$, $J_{5,6a} = 5.1$, $J_{5,6b} = 2.6$, $J_{6,6} = 13.1$ Hz; $^{13}C$ NMR (75.5 MHz, $CDCl_3$): δ 61.8 (C-6), 69.6 (C-4), 73.1 (C-5), 73.7 ($CH_2C_6H_5$), 76.8 (C-3), 84.5 (C-1), 128.3-136.5 (3 $C_6H_5$), 164.6, and 166.1 ($COC_6H_5$), 193.7 (C-2). MS (FD/20 mA): *m/z* 538, 540 [$M^+$]. Anal. Calcd for $C_{27}H_{23}O_7Br$ (539.39): C, 60.12; H, 4.30; Br, 14.81. Found: C, 59.80; H, 4.20; Br, 14.70.

*Isopropyl 4,6-di-*O*-benzoyl-3-*O*-benzyl-β-D-arabino-hexopyranosid-2-ulose* (**15**).—A suspension of isopropanol (300 μL, 3.9 mmol), $Ag_2CO_3$ (1.1 g, 4 mmol), molecular sieves (4 Å, 500 mg) and $CH_2Cl_2$ (10 mL) was stirred for 15 min at room temperature with the exclusion of moisture. Ulosyl bromide **7** (950 mg, 1.76 mmol) was added and stirring was continued for 5 min, followed by filtration through Celite with extensive washing of the filter cake with $CH_2Cl_2$. The combined filtrate and washings were concentrated, the resulting residue was crystallized from $Et_2O$: 870 mg (95%) of an approximate 10:1 mixture ($^1H$ NMR) of **15** and its monohydrate (**15** · $H_2O$); mp 130–135 °C; $[\alpha]_D^{20}$ −69.9° (*c* 0.96, $CHCl_3$); $^1H$ NMR (300 MHz, $CDCl_3$): δ 1.24 (d, 3 H, $CH_3$), 1.29 (d, 3 H, $CH_3$), 4.06 (qq, 1 H, $CHMe_2$), 4.29 (ddd, 1 H, H-5), 4.31 (d, 1 H, H-3), 4.51 (dd, 1 H, H-6a), 4.59 and 4.93 ($BnCH_2$), 4.63 (dd, 1 H, H-6b), 4.98 (s, 1 H, H-1), 5.67 (dd, 1 H, H-4), 7.14–7.98 (m, 15 H, 3 $C_6H_5$); $J_{3,4} = 9.3$, $J_{4,5} = 9.0$, $J_{5,6a} = 6.1$, $J_{5,6b} = 3.8$, $J_{6a,b} = 12.1$, $J_{CHMe2} = 6.2$, $J_{BnCH2} = 12.3$ Hz; $^{13}C$ NMR (75.5 MHz, $CDCl_3$): δ 22.0, and 23.4 ($CH_3$), 64.2 (C-6), 81.1 (C-3), 98.3 (C-1), 128.2–137.1 (3 $C_6H_5$), 165.0, and 166.3 ($COC_6H_5$), 197.0 (C-2); $J_{C\text{-}1,H\text{-}1} = 159$ Hz. Anal. Calcd for $C_{30}H_{30}O_8$ (518.6): C, 69.49; H, 5.83. Found: C, 69.33; H, 5.93.

Several recrystallisations from $Et_2O$/EtOAc yielded colorless crystals of the monohydrate (**15** · $H_2O$): mp 145–147 °C; $[\alpha]_D^{20}$ −58.8° (*c* 1.05, $CHCl_3$); $^1H$ NMR (300 MHz, $CDCl_3$): δ 1.24 (d, 3 H, $CH_3$), 1.31 (d, 3 H, $CH_3$), 3.11, and 3.92 (2 bs, 2 H, 2 OH), 3.79 (d, 1 H, H-3), 3.88–3.95 (m, 1 H, H-5), 4.03 (qq, 1 H, $CHMe_2$), 4.39 (dd, 1 H, H-6a), 4.52 (s, 1 H, H-1), 4.53 (dd, 1 H, H-6b), 4.77 and 4.88 (2d, each 1 H, $BnCH_2$), 5.42 (t, 1 H, H-4), 7.05–7.96 (m, 15 H, 3 $C_6H_5$); $J_{3,4} = J_{4,5} = 9.7$, $J_{5,6a} = 6.1$, $J_{5,6b} = 3.4$, $J_{6a,b} = 11.9$, $J_{CHMe2} = 6.2$, $J_{BnCH2} = 11.7$ Hz; $^{13}C$ NMR (75.5 MHz, $CDCl_3$): δ 21.8 and 23.3 ($CH_3$), 63.9 (C-6), 70.7 (C-4), 71.9 (C-5), 75.2 ($CH_2C_6H_5$), 80.6 (C-3), 93.8 (C-2), 100.4 (C-1), 128.0–137.3 (3 $C_6H_5$), 165.3, 166.2 ($COC_6H_5$); $J_{C\text{-}1,H\text{-}1} = 159.3$ Hz.

*Octyl 4,6-di-*O*-benzoyl-3-*O*-benzyl-β-D-*arabino-

*hexopyranosid-2-ulose* (**17**).—Glycal **14** (6.0 g, 10.6 mmol) was treated like above to give ulosyl bromide **7**, which was dissolved in $CH_2Cl_2$ (50 mL). Molecular sieves (4 Å, 2 g), silver carbonate (5.8 g, 21.2 mmol) and *n*-octanol (3.4 mL, 21.2 mmol) were added. The suspension was stirred for 15 min, filtered through Celite and concentrated to give an amorphous residue, which crystallized from *t*-butyl methyl ether: 5.4 g (87%) of **17** and its monohydrate **17** · $H_2O$ as an approximate 7:1 mixture ($^1$H NMR); mp 112–112.5 °C; $[\alpha]_D^{20}$ −49.4° (*c* 1.1, $CHCl_3$); $^1$H NMR (300 MHz, $CDCl_3$): δ 0.86 (t, 3 H, $CH_3$), 1.24–1.36 (m, 10 H, 5 octyl-$CH_2$), 1.61–1.68 (m, 2 H, $OCH_2CH_2$), 3.61 (dt, 1 H, $OCH_2$), 3.88 (dt, 1 H, $OCH_2$), 4.30 (ddd, 1 H, H-5), 4.32 (d, 1 H, H-3), 4.51 (dd, 1 H, H-6a), 4.59 and 4.93 (2 d, each 1 H, B*n*$CH_2$), 4.63 (dd, 1 H, H-6a), 4.98 (s, 1 H, H-1), 5.68 (dd, 1 H, H-4), 7.14–7.99 (m, 15 H, 3 $C_6H_5$); $J_{3,4}$ = 9.3, $J_{4,5}$ = 9.1, $J_{5,6a}$ = 5.9, $J_{5,6b}$ = 3.8, $J_{6a,b}$ = 12.0, $J_{CH2,CH3}$ = 6.6, $J_{OCH2,CH3}$ = 6.8, $J_{OCH2}$ = 9.4, $J_{BnCH2}$ = 12. Hz; $^{13}$C NMR (75.5 MHz, $CDCl_3$): δ 14.5 ($CH_3$), 23.0, 26.2, 29.6, 29.7, 29.8, and 32.2 ($CH_2$), 64.3 (C-6), 70.6 ($OCH_2$), 72.9 (C-4), 73.2 ($CH_2C_6H_5$), 73.4 (C-5), 81.3 (C-3), 98.5 (C-1), 124.5–135.9 (3 $C_6H_5$), 165.0, and 166.3 ($COC_6H_5$), 197.0 (C-2); $J_{C\text{-}1,H\text{-}1}$ = 159.9 Hz. Anal. Calcd for $C_{35}H_{40}O_8$ (588.7): C, 71.41; H, 6.85. Found: C, 71.23; H, 6.96.

The monohydrate portion of **17** exhibited substantially different chemical shifts for H-1 (s at δ 4.46) and H-3 (d at 3.79), and, less pronounced, for H-4 (dd at 5.45). $^{13}$C NMR (75.5 MHz, $CDCl_3$): δ 70.5 (C-5), 71.1 (C-6), 71.8 (C-4), 75.1 ($CH_2C_6H_5$), 80.3 (C-3), 93.7 (C-2), 101.7 (C-1).

*Isopropyl 4,6-di-O-benzoyl-3-O-benzyl-β-D-mannopyranoside* (**18**).—$NaBH_4$ was added to a stirred, cooled (0 °C) solution of **15** (1.0 g, 1.93 mmol) in 33 mL of 10:1 dioxane/water and stirring was continued for 20 min, allowing the mixture to warm up to room temperature; HOAc (0.5 mL) was added and the solution was diluted with acetone, filtered through a silical gel short bed and concentrated *in vacuo*. Crystallization from $Et_2O$/*n*-hexane gave 840 mg (84%) of mannoside **18**; mp 127–129 °C; $[\alpha]_D^{20}$ −45.4° (*c* 1.1, $CHCl_3$); $^1$H NMR (300 MHz, $CDCl_3$): δ 1.19, and 1.27 (2 d, each 3 H, 2 $CH_3$), 2.60 (d, 1 H, OH), 3.71 (d, 1 H, H-3), 3.85 (ddd, 1 H, H-5), 4.05 (qq, 1 H, $CHMe_2$), 4.15 (bs, 1 H, H-2), 4.44 (dd, 1 H, H-6a), 4.57 and 2.72 (2d, each 1 H B*n*$CH_2$), 4.58 (dd, 1 H, H-6b), 4.65 (d, 1 H, H-1), 5.66 (t, 1 H, H-4), 7.17–8.05 (m, 15 H, 3 $C_6H_5$); $J_{1,2}$ ≈ 1.0, $J_{2,OH}$ = 2.1, $J_{2,3}$ = 3.2, $J_{3,4}$ = $J_{4,5}$ = 9.3, $J_{5,6a}$ = 6.2, $J_{5,6b}$ = 3.7, $J_{6a,b}$ = 11.8, $J_{CHMe2}$ = 6.2, $J_{BnCH2}$ = 12.4 Hz; $^{13}$C NMR (75.5 MHz, $CDCl_3$): δ 21.8, and 23.5 ($CH_3$), 64.2 (C-6), 68.4 (C-2), 69.0 (C-4), 71.2 ($CH_2C_6H_5$), 71.8 ($CHMe_2$), 72.1 (C-5), 77.9 (C-3), 98.1 (C-1), 127.9–137.4 (3 $C_6H_5$), 165.5, and 166.3 ($COC_6H_5$). Anal. Calcd for $C_{30}H_{32}O_8$ (520.6): C, 69.22; H, 6.20. Found: C, 69.24; H, 6.13.

*1,2:3,4-Di-O-isopropylidene-6-O-(4,6-di-O-benzoyl-3-O-benzyl-β-D-mannopyranosyl)-α-D-galactopyranose* (**19**).—A suspension of 1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose (440 mg, 1.70 mmol), silver carbonate (980 mg, 3.50 mmol), and molecular sieves (3 Å, 500 mg) in $CH_2Cl_2$ (5 mL) was stirred for 10 min at room temperature. A solution of ulosyl bromide **7** (955 mg, 1.77 mmol, in $CH_2Cl_2$ (15 mL) was added dropwise with stirring, and after 20 min the mixture was filtered through Celite and concentrated. The syrupy residue consisted ($^1$H NMR) of β-uloside **16** and its monohydrate in an approximate 5:1 ratio, and was directly subjected to reduction: dissolution in 10:1 dioxane–water (33 mL), cooling at 0 °C and stirring with $NaBH_4$ (68 mg, 1.8 mmol) for 20 min. The mixture was then allowed to warm up to room temperature, and HOAc (0.5 mL) was added followed by dilution with acetone and concentration. Purification of the residue by elution from a silica gel column with 1:1 toluene–EtOAc afforded **19** (945 mg, 77%, based on **7**) as a colorless syrup; $[\alpha]_D^{20}$ −58.3° (*c* 1.0, $CHCl_3$); $^1$H NMR (300 MHz, $CDCl_3$): *mannosyl-H*: δ 2.79 (bs, 1 H, OH), 3.69 (dd, 1 H, H-3), 3.85 (ddd, 1 H, H-5), 4.30 (m, 1 H, H-2), 4.45 (dd, 1 H, H-6a), 4.55 and 4.71 (2 d, each 1 H, B*n*$CH_2$), 4.58 (dd, 1 H, H-6b), 4.71 (d, 1 H, H-1), 5.71 (t, 1 H, H-4), 7.15–8.00 (m, 15 H, 3 $C_6H_5$); $J_{1,2}$ ≈ 1.0, $J_{2,3}$ = 3.1, $J_{3,4}$ = $J_{4,5}$ = 9.2, $J_{5,6a}$ = 5.6, $J_{5,6b}$ = 3.7, $J_{6a,b}$ = 11.9, $J_{BnCH2}$ = 12.4 Hz; *galactosyl-H*: δ 1.29, 1.33, 1.41, and 1.53 (4 s, each 3 H, 4 $CH_3$), 3.77 (dd, 1 H, H-6a), 4.04–4.07 (m, 1 H, H-5), 4.10 (dd, 1 H, H-6b), 4.15 (dd, 1 H, H-4), 4.30 (dd, 1 H, H-2), 4.53–4.61 (m, 1 H, H-3), 5.55 (d, 1 H, H-1); $J_{2,3}$ = 2.5, $J_{3,4}$ = 7.9, $J_{4,5}$ = 1.6, $J_{5,6a}$ = 7.7, $J_{5,6b}$ = 2.6, $J_{6a,b}$ = 11.1 Hz; $^{13}$C NMR (75.5 MHz, $CDCl_3$): *mannosyl-C*: δ 64.2 (C-6), 67.8 (C-2), 68.4 (C-4), 71.3 ($CH_2C_6H_5$), 72.5 (C-5), 77.9 (C-3), 100.7 (C-1), 128.1–133.4 (3 $C_6H_5$), 165.6, and 166.4 ($COC_6H_5$); *galactosyl-C*: δ 24.6, 25.2, 26.2, 26.3 ($CH_3$), 69.0 (C-5), 69.6 (C-6), 70.7 (C-2), 70.9 (C-3), 71.6 (C-4), 96.5 (C-1). Anal. Calcd for $C_{39}H_{44}O_{13}$ (720.8): C, 64.99; H, 6.15. Found: C, 65.09; H, 6.04.

*Octyl 4,6-di-O-benzoyl-3-O-benzyl-β-D-mannopyranoside* (**20**).—Subjection of **17** (950 mg,

1.6 mmol) to reduction with $NaBH_4$ (64 mg, 1.7 mmol) in 10:1 dioxane-water (33 mL), and processing of the mixture as described for **15** → **18** yielded 805 mg (85%) of **20** as colorless needles; mp 111–113 °C; $[\alpha]_D^{20}$ −32.4° (*c* 1, $CHCl_3$); $^1H$ NMR (300 MHz, $CDCl_3$): δ 0.87 (t, 3 H, $CH_3$), 1.26–1.76 (m, 12 H, 6 $CH_2$), 2.58 (d, 1 H, OH), 3.52 (dt, 1 H, $OCH_2$), 3.72 (dd, 1 H, H-3), 3.83–3.96 (m, 2 H, H-5, and $OCH_2$), 4.19 (s, 1 H, H-2), 4.47 (dd, 1 H, H-6a), 4.57 (s, 1 H, H-1), 4.58 and 4.71 (2 d, each 1 H, $BnCH_2$), 4.59 (dd, 1 H, H-6b), 5.68 (t, 1 H, H-4), 7.14–8.00 (m, 15 H, 3 $C_6H_5$); $J_{2,OH}$ = 2.3, $J_{2,3}$ = 3.1, $J_{3,4}$ = $J_{4,5}$ = 9.1, $J_{5,6a}$ = 5.9, $J_{5,6b}$ = 3.8, $J_{6a,b}$ = 11.8, $J_{CH2,CH3}$ = 6.8, $J_{OCH2,CH2}$ = 6.9, $J_{OCH2}$ = 9.3, $J_{BnCH2}$ = 12.4 Hz; $^{13}C$ NMR (75.5 MHz, $CDCl_3$): δ 14.1 ($CH_3$), 22.6, 26.0, 29.2, 29.3, 29.5, and 31.8 ($CH_2$), 64.0 (C-6), 67.9 (C-2), 68.9 (C-4), 70.1 ($OCH_2$), 71.3 ($CH_2C_6H_5$), 72.1 (C-5), 77.8 (C-3), 99.9 (C-1), 127.8–137.3 (3 $C_6H_5$), 165.4, and 166.2 ($COC_6H_5$). Anal. Calcd for $C_{35}H_{42}O_8$ (590.7): C, 71.17; H, 7.17. Found: C, 71.03; H, 6.97.

*Octyl 2,4,6-tri-O-benzoyl-3-O-benzyl-β-D-mannopyranoside* (**21**).—Benzoyl chloride (380 μL, 3.3 mmol) was added to a stirred solution of **20** (1.3 g, 2.2 mmol) in pyridine (30 mL). After 1 h the mixture was diluted with $CH_2Cl_2$ (100 mL), and was washed successively with 2 M HCl (2 × 30 mL). After drying ($Na_2SO_4$), the solvent was evaporated, and the residue was crystallized from EtOH: 1.36 g (89%) of **21**; mp 101–102 °C; $[\alpha]_D^{20}$ −110° (*c* 1, $CHCl_3$); $^1H$ NMR (300 MHz, $CDCl_3$): δ 0.84 (t, 3 H, $CH_3$), 1.17–1.56 (m, 12 H, 6 $CH_2$), 3.51 (dt, 1 H, $OCH_2$), 3.82–3.86 (m, 1 H, $OCH_2$), 3.84 (dd, 1 H, H-3), 3.89–3.94 (m, 1 H, H-5), 4.44 (dd, 1 H, H-6a), 4.53 and 4.73 (2 d, each 1 H, $BnCH_2$), 4.66–4.71 (m, 1 H, H-6b), 4.71 (s, 1 H, H-1), 5.78 (dd, 1 H, H-4), 5.90 (d, 1 H, H-2), 7.07–8.14 (m, 20 H, 4 $C_6H_5$); $J_{2,3}$ = 3.3, $J_{3,4}$ = 9.7, $J_{4,5}$ = 9.8, $J_{5,6a}$ = 5.1, $J_{5,6b}$ = 2.9, $J_{6a,b}$ = 12.0, $J_{CH2,CH3}$ = 6.5, $J_{OCH2,CH2}$ = 6.8, $J_{OCH2}$ = 9.2, $J_{BnCH2}$ = 12 Hz; $^{13}C$ NMR (75.5 MHz, $CDCl_3$): δ 14.2 ($CH_3$), 22.8, 25.9, 29.3, 29.4, 29.5, and 31.8 ($CH_2$), 63.6 (C-6), 68.1 (C-2), 68.7 (C-4), 70.1 ($OCH_2$), 70.5 ($CH_2C_6H_5$), 72.4 (C-5), 76.1 (C-3), 99.3 (C-1), 127.9–137.3 (4 $C_6H_5$), 165.4, 166.3, and 166.4 ($COC_6H_5$). Anal. Calcd for $C_{42}H_{46}O_9$ (694.8): C, 72.60; H, 6.67. Found: C, 72.52; H, 6.75.

*Octyl 3-O-benzyl-β-D-mannopyranoside* (**22** with Hinstead of Bz).—A solution of tribenzoate **21** (410 mg, 0.59 mmol) in MeOH (20 mL) was treated with NaOMe (25 mg, 0.46 mmol) and stirred for 2 h at room temperature. The resulting mixture was neutralized with an acidic resin (Dowex 50 WX 4, $H^+$-form) followed by filtration, concentration of the filtrate and elution of the residue from a short silica gel column with 10:1 $CHCl_3$–MeOH. The major fraction was taken to a syrup that was chromatographically uniform: 205 mg (91%) of octyl 3-*O*-benzyl-β-D-mannoside, $[\alpha]_D^{20}$ −61.1° (*c* 1, $CHCl_3$); $^1H$ NMR (300 MHz, $CDCl_3$): δ 0.81 (t, 3 H, $CH_3$), 1.20–1.56 (m, 12 H, 6 $CH_2$), 2.75 (bs, 2 H, 2 OH), 3.02 (bs, 1 H, 1 OH), 3.19 (ddd, 1 H, H-5), 3.30 (dd, 1 H, H-3), 3.42 (dt, 1 H, $OCH_2$), 3.74–3.86 (m, 2 H, H-6a,b), 3.82 (dt, 1 H, $OCH_2$), 3.91 (dd, 1 H, H-4), 4.02 (bd, 1 H, H-2), 4.36 (d, 1 H, H-1), 4.52 and 4.71 (2 d, each 1 H, $BnCH_2$), 7.23–7.32 (m, 5 H, $C_6H_5$); $J_{1,2}$ = 0.4, $J_{2,3}$ = 3.0, $J_{3,4}$ = 9.3, $J_{4,5}$ = 9.5, $J_{CH2CH3}$ = 6.5, $J_{OCH2,CH2}$ = 6.9, $J_{OCH2}$ = 9.5 Hz; $^{13}C$ NMR (75.5 MHz, $CDCl_3$): δ 14.2 ($CH_3$), 22.8, 26.1, 29.3, 29.5, 29.6, and 31.9 ($CH_2$), 62.4 (C-6), 66.6 (C-4), 68.0 (C-2), 70.2 ($OCH_2$), 71.3 ($CH_2C_6H_5$), 75.6 (C-5), 81.0 (C-3), 100.1 (C-1), 128.1–137.7 ($C_6H_5$). MS (FD/15 mA): *m/z* 382 [$M^+$], 383 [$M^+$ + 1], 384 [$M^+$ + 2]. Anal. Calcd for $C_{21}H_{34}O_6$ (382.5): C, 65.94; H, 8.96. Found: C, 65.86; H, 8.87.

*Octyl 2-O-benzoyl-3-O-benzyl-β-D-mannopyranoside* (**22**).—A solution of tribenzoate **21** (1.1 g, 1.6 mmol) in MeOH (20 mL) and $CH_2Cl_2$ (5 mL) was cooled (0 °C) and NaOMe (85 mg, 1.6 mmol) was added. The reaction was monitored by TLC (1:1 toluene–EtOAc ) being complete in terms of selective 4,6-di-debenzoylation after about 4.5 h. Subsequent neutralization with HOAc (3 mL), evaporation of the solution in vacuo to dryness and elution of the residue from a short silica gel column with $CHCl_3$-acetone gave 740 mg (96%) of **22** as a chromatographically uniform, colorless syrup; $[\alpha]_D^{20}$ − 80.1° (*c* 1, $CHCl_3$); $^1H$ NMR (300 MHz, $CDCl_3$): δ 0.85 (t, 3 H, $CH_3$), 1.20–1.26 (m, 10 H, 5 $CH_2$), 1.53 (m, 2 H, $OCH_2$), 2.35 and 2.80 (2 bs, each 1 H, 2 OH), 3.41 (ddd, 1 H, H-5), 3.49 and 3.82 (2 dt, each 1 H, octyl-$OCH_2$), 3.55 (dd, 1 H, H-3), 3.88 (dd, 1 H, H-6a), 3.96 (dd, 1 H, H-6b), 3.97 (dd, 1 H, H-4), 4.45 and 4.84 (2 d, each 1 H, $BnCH_2$), 4.64 (bs, 1 H, H-1), 5.82 (bs, 1 H, H-2), 7.13–8.10 (m, 10 H, 2 $C_6H_5$), $J_{1,2}$ = 0.8, $J_{,2,3}$ = 3.0, $J_{3,4}$ = $J_{4,5}$ = 9.3, $J_{5,6a}$ = 5.0, $J_{5,6b}$ = 3.3, $J_{6,6}$ = 11.9 Hz; $^{13}C$ NMR (75.5 MHz, $CDCl_3$): δ 14.1 ($CH_3$), 22.6, 25.9, 29.2, 29.3, 29.5, and 31.7 ($CH_2$), 62.7 (C-6), 67.4 (C-4), 68.0 (C-2), 70.1 ($OCH_2$), 71.2 ($CH_2C_6H_5$), 75.7 (C-5), 79.8 (C-3), 99.3 (C-1), 128.1–137.3 (2 $C_6H_5$), 166.1 ($COC_6H_5$). MS (FD/20 mA): *m/z* 486 [$M^+$], 487 [$M^+$ + 1], 488 [$M^+$ + 2]. Anal. Calcd for $C_{28}H_{38}O_7$ (486.6): C, 69.11; H, 7.87. Found: C, 68.98; H, 7.81.

*Octyl 2,4,6-tri-O-benzoyl-β-D-mannopyranoside* (**23**).—A solution of mannoside **21** (350 mg, 0.5 mmol) in MeOH (20 mL) was hydrogenated in the presence of 10% palladium–carbon. After six days the suspension was filtered and concentrated in vacuo, followed by fast elution of the residue from a short silica gel column with (5:1) toluene–EtOAc [1]. The eluate containing **23** was concentrated to give 248 mg (82%) of a syrup; $[\alpha]_D^{20}$ −55.1° (*c* 1.1, $CHCl_3$); $^1H$ NMR (300 MHz, $CDCl_3$): δ 0.84 (t, 3 H, $CH_3$), 1.15–1.55 (m, 12 H, 6 $CH_2$), 2.92 (d, 1 H, 1 OH), 3.53 (dt, 1 H, $OCH_2$), 3.85 (dt, 1 H, $OCH_2$), 4.04 (ddd, 1 H, H-5), 4.14–4.20 (m, 1 H, H-3), 4.52 (dd, 1 H, H-6a), 4.73 (dd, 1 H, H-6b), 4.82 (d, 1 H, H-1), 5.60 (t, 1 H, H-4), 5.69 (dd, 1 H, H-2), 7.35–8.11 (m, 15 H, 3 $C_6H_5$); $J_{1,2}$ = 1.1, $J_{3,OH}$ = 6.8, $J_{2,3}$ = 3.3, $J_{3,4} = J_{4,5}$ = 8.9, $J_{5,6a}$ = 5.4, $J_{5,6b}$ = 3.3, $J_{6a,b}$ = 11.9, $J_{CH2,CH3}$ = 6.7, $J_{OCH2,CH2}$ = 6.7, $J_{OCH2}$ = 9.4 Hz; $^{13}C$ NMR (75.5 MHz, $CDCl_3$): δ 14.1 ($CH_3$), 22.6, 25.8, 29.2, 29.3, 29.4, and 31.7 ($CH_2$), 63.7 (C-6), 70.0 ($OCH_2$), 70.9 (C-4), 71.4 (C-3), 71.7 (C-2), 72.3 (C-5), 99.0 (C-1), 128.4–133.6 (3 $C_6H_5$), 166.2, 166.3, and 166.5 ($COC_6H_5$). MS (FD/15 mA): *m/z* 604 [$M^+$], 606 [$M^+ + 2$]. Anal. Calcd for $C_{35}H_{40}O_9$ (604.7): C, 69.52; H, 6.69. Found: C, 69.39; H, 6.60.

*Octyl 2-O-benzoyl-3-O-benzyl-6-O-(2,3,4,6-tetra-O-acetyl-α-D-mannopyranosyl)-β-D-mannopyranoside* (**26**).—A suspension of mannoside **22** (487 mg, 1 mmol), 2,3,4,6-tetra-*O*-acetyl-α-D-mannopyranosyl bromide **24** (1.23 g, 3 mmol), and powdered molecular sieves (4 Å, 500 mg) in $CH_2Cl_2$ (15 mL) was stirred under an atmosphere of argon for 15 min; mercury(II) bromide (360 mg, 1 mmol) was added, following by stirring at room temperature for 24 h. The mixture was then diluted with $CH_2Cl_2$, filtered and successively washed with aq 5% potassium iodide solution (2 × 20 mL) and water (2 × 25 mL), dried ($Na_2SO_4$) and concentrated to a syrup, which consisted of an approximate 10:1 mixture ($^1H$ NMR) of **26** and the α-(1 → 4)-linked disaccharide. Elution of this syrup from a silica gel column with $CH_2Cl_2$–EtOAc (9:1 → 3:1 gradient) gave on concentration of the major fraction 700 mg (86%) of **26**; $^1H$ NMR (300 MHz, $CDCl_3$): *β-mannosyl-H*: δ 0.85 (t, 3 H, $CH_3$), 1.19–1.28 (m, 10 H, 5 $CH_2$), 1.52–1.56 (m, 2 H, $OCH_2CH_2$), 3.51 and 3.85 (2 dt, each 1 H, $OCH_2C_7H_{15}$), 3.48–3.57 (m, 2 H, H-3,5), 3.88 (bm, 1 H, H-6a), 3.92 (dd, 1 H, H-4), 4.01 (dd, 1 H, H-6b), 4.46 and 4.86 (2 d, each 1 H, $BnCH_2$), 4.64 (bs, 1 H, H-1), 5.85 (bd, 1 H, H-2), 7.2–8.1 (m, 10 H, 2 $C_6H_5$); $J_{1,2} > 0.5$, $J_{2,3}$ = 2.6, $J_{3,4}$ = 9.4, $J_{4,5}$ = 9.9, $J_{5,6a}$ = 3.8, $J_{5,6b}$ = 5.7, $J_{6a,b}$ = 10.7 Hz; *α-mannosyl-H*: δ 2.00, 2.01, 2.07, and 2.16 (4 s, each 3 H, 4 Ac), 4.15 (dd, 1 H, H-6a), 4.14 (m, 1 H, H-5), 4.27 (dd, 1 H, H-6b), 4.91 (d, 1 H, H-1), 5.30 (dd, 1 H, H-4), 5.27–5.38 (m, 2 H, H-2,3), $J_{1,2}$ = 1.1, $J_{5,6a}$ = 2.2, $J_{5,6b}$ = 5.6, $J_{6a,b}$ = 12.6 Hz; $^{13}C$ NMR (75.5 MHz, $CDCl_3$): *β-mannosyl-C*: δ 14.0 ($CH_3$), 22.6, 25.8, 29.1, 29.3, 29.4, and 31.7 ($OCH_2(CH_2)_6CH_3$), 66.6 (C-6), 67.7 (C-2), 69.9 ($CH_2C_7H_{15}$), 71.1 ($CH_2C_6H_5$), 74.7 (C-3), 80.0 (C-5), 99.1 (C-1), 128.1–137.1 (2 $C_6H_5$), 166.1 ($COC_6H_5$); *α-mannosyl-C*: δ 20.6, 20.7, and 20.8 (4 $COCH_3$), 62.3 (C-6), 66.0 (C-4), 68.4 (C-5), 69.1, and 69.4 (C-2, 3), 97.4 (C-1), 169.6, 169.7, 169.9, and 170.7 (4 $COCH_3$).

*Octyl 4-O-acetyl-2-O-benzoyl-3-O-benzyl-6-O-(2,3,4,6-tetra-O-acetyl-α-D-mannopyranosyl)-β-D-mannopyranoside* (**27**).—$Ac_2O$ (10 mL) was added to a solution of disaccharide **26** (700 mg) in pyridine (10 mL), and the mixture was stirred for 8 h at room temperature. The solution was taken to dryness in vacuo and the residue was purified by elution from silica gel column with 2:1 $CH_2Cl_2$–EtOAc. Concentration of the major fraction gave amorphous **27** (460 mg, 53%). Crystallization of an analytical sample from EtOH afforded fine needles; mp 118–119 °C; $[\alpha]_D^{20}$ −35° (*c* 1, $CHCl_3$). $^1H$ NMR (300 MHz, $CDCl_3$): *β-mannosyl-H*: δ 0.85 (t, 3 H, Ac), 1.19–1.27 (m, 10 H, 5 $CH_2$), 1.52–1.56 (m, 2 H, $OCH_2CH_2$), 2.15 (s, 3 H, $COCH_3$), 3.53 and 3.84 (2 dt, each 1 H, $OCH_2C_7H_{15}$), 3.56 and 3.86 (2 dd, 1 H, H-6a), 3.58 (bm, 1 H, H-5), 3.72 (dd, 1 H, H-3), 4.49 and 4.74 (2 d, each 1 H, $BnCH_2$), 4.66 (bs, 1 H, H-1), 5.16 (dd, 1 H, H-4), 5.84 (dd, 1 H, H-2), 7.23–8.10 (m, 10 H, 2 $C_6H_5$); $J_{1,2} > 0.5$, $J_{2,3}$ = 3.1, $J_{3,4} = J_{4,5}$ = 9.7, $J_{5,6a}$ = 2.8, $J_{5,6b}$ = 3.6, $J_{6,6}$ = 9.6 Hz; *α-mannosyl-H*: δ 1.99, 2.01, 2.05, and 2.07 (4 s, each 3 H, 4 Ac), 4.11 (ddd, 1 H, H-5), 4.12 and 4.29 (2d, 1 H, H-6a), 4.83 (d, 1 H, H-1), 5.27 (dd, 1 H, H-2), 5.31 (dd, 1 H, H-3), 5.33 (bm, 1 H, H-4); $J_{1,2}$ = 1.6, $J_{2,3}$ = 2.9, $J_{3,4} = J_{4,5}$ = 9.7, $J_{5,6}$ = 2.2 and 5.6, $J_{6a,b}$ = 12.5 Hz; $^{13}C$ NMR (75.5 MHz, $CDCl_3$): *β*-mannosyl-C: δ 14.1 ($CH_3$), 21.2 ($COCH_3$), 23.6, 25.9, 29.2, 29.3, 29.4, and 31.7 ($OCH_2(CH_2)_6CH_3$), 67.4 (C-6), 68.2 (C-2), 68.6 (C-4), 69.9 ($CH_2C_7H_{15}$), 70.9 ($CH_2C_6H_5$), 72.9 (C-5), 76.6 (C-3), 98.9 (C-1),

[1] Exposure of **23** to silica gel should be kept at a minimum, as longer column chromatography (i.e. overnight) leads to substantial 2-*O* → 3-*O*-benzoyl migration to give an approximate 1:1 mixture ($^1H$ NMR) of **23** and octyl 3,4,6-tri-*O*-benzoyl-β-D-mannopyranoside.

127.8–137.5 (2 $C_6H_5$), 166.1 ($COC_6H_5$), 166.5 ($COCH_3$); *α-mannosyl-C*: δ 20.7, 20.7, 20.9, and 20.9 (4 $COCH_3$), 62.3 (C-6), 66.0 (C-4), 68.7 (C-5), 69.1 (C-2), 69.4 (C-3), 97.2 (C-1), 169.7, 169.8, 170.0, and 170.0 (4 $COCH_3$). MS (FD/20 mA): *m/z* 859 [$M^+ + 1$], 858 [$M^+$], 857 [$M^+$-1], 856 [$M^+$-2], 43 [$CH_3CO^+$]. Anal. Calcd for $C_{44}H_{58}O_{17}$ (858.9): C, 61.53; H, 6.81. Found: C, 61.48; H, 6.73.

*Octyl 2,4,6-tri-O-benzoyl-3-O-(2,3,4,6-tetra-O-acetyl-α-D-mannopyranosyl)-β-D-mannopyranoside* (**28**).—A solution of 3-OH-free tribenzoate **23** (605 mg, 1 mmol) in $CH_2Cl_2$ (10 mL) was stirred with 2,3,4,6-tetra-*O*-acetyl-α-D-mannopyranosyl trichloroacetimidate (**25**) [21] and powdered molecular sieves (4 Å, 1 g) in $CH_2Cl_2$ (10 mL) under argon for 30 min at room temperature, whereupon trimethylsilyl triflate (38.7 μL, 1.15 mmol) was added dropwise. The mixture was stirred for 45 min at room temperature and quenched by the addition of pyridine (5 mL). Dilution with $CH_2Cl_2$ (40 mL), filtration through Celite, and successive washing with saturated aq $NaHCO_3$ (2 × 10 mL), and water (2 × 10 mL) gave upon drying ($Na_2SO_4$) and removal of the solvent in vacuo a syrup which was purified by elution from a silica gel column with $CH_2Cl_2$–EtOAc (97:3 → 95:5). Concentration of the eluate-containing product afforded 690 mg (76%) of **28** as an amorphous foam; $[\alpha]_D^{20}$ −47.9° (*c* 0.18, $CHCl_3$); $^1$H NMR (300 MHz, $CDCl_3$): δ 0.84 (t, 3 H, $CH_3$), 1.11–1.57 (m, 12 H, 6 $CH_2$), 1.82, 1.83, 2.00, and 2.11 (4 s, each 3 H, 4 Ac), 4.79 (bs, 1 H, H-1), 4.91 (d, 1 H, H-2′), 4.97 (bs, 1 H, H-1′), 5.10 (dd, 1 H, H-3′), 5.18 (dd, 1 H, H-4′), 5.75 (d, 1 H, H-2), 5.80 (dd, 1 H, H-4), 7.35–8.20 (m, 15 H, 3 $C_6H_5$); $J_{4,5} = 9.5$, $J_{4',5'} = 9.0$ Hz. Anal. Calcd for $C_{49}H_{58}O_{18}$ (934.95): C, 62.94; H, 6.25. Found: C, 62.88; H, 6.20.

*Octyl 3-O-(α-D-mannopyranosyl)-β-D-mannopyranoside* (**29**).—To a solution of disaccharide **28** (46.7 mg; 50 μmol) in dry MeOH (10 mL) was added NaOMe (16 mg, 0.3 mmol) and the mixture was boiled under reflux for 48 h. After cooling, the solution was neutralized with dry acidic resin (Amberlite IR 120, $H^+$-form), filtered, and concentrated. Column chromatography of the crude product with $CH_2Cl_2$–MeOH gave 20.1 mg (88%) of **29** as an amorphous foam; $[\alpha]_D^{20}$ + 6° (*c* 1.45, MeOH); $^{13}$C NMR (75.5 MHz, $CD_3OD$): δ 14.4 ($CH_3$), 23.7, 27.1, 30.4, 30.5, 30.7, and 33.0 ($OCH_2(CH_2)_6CH_3$), 62.8, and 63.1 (C-6,6′), 67.6 ($OCH_2$), 82.7 (C-3), 101.5 (C-1), 103.8 (C-1′). MS (FAB, Xe, 8 kV): *m/z* 455 [$M^+ + 1$], 477 [$M + Na^+$].

*Octyl 4-O-acetyl-2-O-benzoyl-6-O-(2,3,4,6-tetra-O-acetyl-α-D-mannopyranosyl)-β-D-mannopyranoside* (**30**).—A solution of disaccharide **27** (313 mg, 0.36 mmol) in EtOH (60 mL) and HOAc (10 mL) was hydrogenated over 10% palladium–carbon at room temperature for 2 h. The mixture was filtered, and the filtrate was concentrated to dryness to afford a residue which was eluted from a silica gel column with 7:3 $CH_2Cl_2$–EtOAc. The eluate containing **30**, upon evaporation gave 238 mg (86%) of a syrup; $[\alpha]_D^{20}$ − 5.5° (*c* 1, $CHCl_3$); $^1$H NMR (300 MHz, $CDCl_3$): δ 0.84 (t, 3 H, $CH_3$), 1.17–1.55 (m, 12 H, 6 $CH_2$), 2.00, 2.02, 2.08, 2.15, and 2.17 (5 s, each 3 H, 5 Ac), 2.51 (bs, 1 H, OH), 3.53 (dt, 1 H, $OCH_2$), 3.64–4.32 (m, 7 H, H-5,6a,6b,5′,6′a,6′b, and $OCH_2$), 3.72 (dd, 1 H, H-3), 4.72 (d, 1 H, H-1), 4.86 (d, 1 H, H-1′), 5.08 (t, 1 H, H-4), 5.27–5.38 (m, 3 H, H-2′,3′,4′), 5.63 (dd, 1 H, H-2), 7.45–8.10 (m, 5 H, $C_6H_5$); $J_{1,2} = 1.0$, $J_{2,3} \approx 2.9$, $J_{3,4} = J_{4,5} = 9.3$, $J_{1',2'} = 1.3$ Hz. MS (FD/15 mA): *m/z* 768 [$M^+$], 769 [$M^+ + 1$].

*Octyl 6-O-(α-D-mannopyranosyl)-β-D-mannopyranoside* (**31**).—To a solution of **30** (127 mg, 0.17 mmol) in dry MeOH (13 mL) was added a catalytic amount of sodium methoxide (pH 8). The mixture was kept at room temperature overnight, neutralized with dry acidic resin (Amberlite IR 120, $H^+$-form), filtered and concentrated. Column chromatography of the residue with 7:3 $CH_2Cl_2$-MeOH gave 71 mg (95%) of **31** as a white foam; $[\alpha]_D^{20}$ + 4.5° (*c* 0.19, MeOH); $^{13}$C NMR (75.5 MHz, $CD_3OD$): δ 14.4 ($CH_3$), 23.6, 27.1, 30.7, 30.5, 30.7, and 32.9 (6 $CH_2$), 62.8 (C-6′), 67.3 ($OCH_2$), 70.7 (C-6), 101.3 (C-1′), 101.8 (C-1). MS (FAB, Xe, 8 kV): *m/z* 455 [$M^+ + 1$], 477 [$M + Na^+$].

*Octyl 4-O-acetyl-2-O-benzoyl-3,6-di-O-(2,3,4,6-tetra-O-acetyl-α-D-mannopyranosyl)-β-D-mannopyranoside* (**32**).—A solution of **30** (140 mg, 0.18 mmol) and 2,3,4,6-tetra-*O*-acetyl-α-D-mannopyranosyl trichloroacetimidate [24] (**25**; 220 mg, 0.45 mmol) in $CH_2Cl_2$ (5 mL), containing molecular sieves (4 Å, 1 g) was stirred under argon for 30 min at room temperature whereupon trimethylsilyl triflate (80 μL, 0.45 mmol) was added dropwise. The mixture was stirred for 45 min at room temperature and quenched by the addition of pyridine (3 mL). Dilution with $CH_2Cl_2$ (20 mL), filtration through Celite, and successive washing with saturated aq $NaHCO_3$ (2 × 5 mL), and water (2 × 5 mL) gave upon drying ($Na_2SO_4$) and removal of the solvent in vacuo a syrup which was purified by elution from a silica gel column with 7:3 $CH_2Cl_2$-EtOAc. The eluate containing **32** upon evaporation in vacuo, afforded 145 mg (73%) as a colorless syrup; $[\alpha]_D^{20}$ − 2.1° (*c* 1.1,

$CHCl_3$); $^1H$ NMR (300 MHz, $CDCl_3$): $\delta$ 0.84 (t, 3 H, $CH_3$), 1.17–1.52 (m, 12 H, 6 $CH_2$), 1.94, 1.99, 2.01, 2.02, 2.08, 2.11, 2.14, 2.16, and 2.17 (9 s, each 3 H, 9 Ac), 4.00 (dd, 1 H, H-3), 4.70 (s, 1 H, H-1), 4.83 (d, 1 H, H-1′), 5.01 (d, 1 H, H-1″), 5.11 (dd, 1 H, H-3′), 5.21 (dd, 1 H, H-4), 5.70 (d, 1 H, H-2), 7.43–8.07 (m, 5 H, $C_6H_5$); $J_{2,3} = 3.0$, $J_{3,4} = 9.4$, $J_{4,5} = 9.6$, $J_{1',2'} = 1.5$, $J_{2',3'} = 2.9$, $J_{3',4'} = 10.1$, $J_{1'',2''} = 2.1$ Hz; $^{13}C$ NMR (75.5 MHz, $CDCl_3$): $\delta$ 14.2 ($CH_3$), 20.7–21.0 ($COCH_3$), 22.7, 26.0, 29.3, 29.4, 29.5, and 31.8 ($CH_2$), 70.0 ($OCH_2$), 70.9 (C-2), 77.7 (C-3), 97.3 (C-1′), 98.8 (C-1), 99.4 (C-1″), 128.6–133.3 ($C_6H_5$), 166.2 ($COC_6H_5$), 169.4, 169.8, 169.9, 170.2, 170.3, 170.7, 170.8 (9 $COCH_3$); $J_{C\text{-}1',\ H\text{-}1'} = 173.4$, $J_{C\text{-}1'',H\text{-}1''} = 173.0$, $J_{C\text{-}1,\ H\text{-}1} = 157.0$ Hz. MS (FD/20 mA): *m/z* 1099 [$M^+$], 1100 [$M^+ + 1$].

*Octyl 3,6-di-O-(α-D-mannopyranosyl)-β-D-mannopyranoside* (**8**).—To a solution of **32** (110 mg, 1 mmol) in dry MeOH (15 mL) was added NaOMe (20 mg, 0.37 mmol) and the mixture was boiled under reflux for 48 h. After cooling the solution was neutralized with acidic resin (Amberlite IR 120, $H^+$-form), filtered and concentrated. The residue was purified by means of column chromatography with 2:1:1 1-butanol–MeOH–water, giving 52 mg (84%) of amorphous **8**; $[\alpha]_D^{20} + 23.7°$ (*c* 1.74, $CHCl_3$); $^{13}C$ NMR (75.5 MHz, $CD_3OD$): $\delta$ 14.4 ($CH_3$), 23.7, 27.1, 30.4, 30.6, 30.7, and 33.0 (6 $CH_2$), 62.8, and 63.0 (C-6′,6″), 67.2 ($OCH_2$), 70.8 (C-6), 82.8 (C-3), 101.3 (C-1″), 101.6 (C-1), 103.9 (C-1′). MS (FAB, Xe, 8 kV): *m/z* 617 [$M^+ + 1$], 639 [$M + Na^+$].

## Acknowledgements

Support of this work by the Volkswagen–Stiftung, Hannover (fellowship to Z.S.) and the Fonds der Chemischen Industrie is gratefully acknowledged.

## References

[1] Reviews: (a) E. Kaji and F.W. Lichtenthaler, *Trends Glycosci. Glycotechnol.*, 5 (1993) 121–142; (b) F. Barresi and O. Hindsgaul, in S.H. Khan, R.A. O'Neill (Eds.), *Modern Methods in Carbohydrate Synthesis*, Harwood Acad. Publ., Amsterdam, 1996, pp. 251–276.

[2] F. Barresi and O. Hindsgaul, *J. Am. Chem. Soc.*, 113 (1991) 9376–9377; *Synlett*, (1992) 759–761; *Can. J. Chem.*, 72 (1994) 1447–1465.

[3] G. Stork and G. Kim, *J. Am. Chem. Soc.*, 114 (1992) 1087–1088; G. Stork, J.J. La Clair, *ibid.*, 118 (1996) 247–248.

[4] Y. Ito and T. Ogawa, *Angew. Chem.*, 106 (1994) 1843–1845; *Angew. Chem., Int. Ed. Engl.*, 33 (1994) 1765–1767; A. Dan, Y. Ito, and T. Ogawa, *J. Org. Chem.*, 60 (1995) 4680–4681.

[5] F.W. Lichtenthaler, E. Cuny, and S. Weprek, *Angew. Chem.*, 95 (1983) 906–907; *Angew. Chem. Int. Ed. Engl.*, 22 (1983) 891–892.

[6] F.W. Lichtenthaler, E. Kaji, and S. Weprek, *J. Org. Chem.*, 50 (1985) 3505–3515.

[7] F.W. Lichtenthaler and E. Kaji, *Liebigs Ann. Chem.*, (1985) 1659–1668.

[8] F.W. Lichtenthaler, U. Kläres, M. Lergenmüller, and S. Schwidetzky, *Synthesis*, (1992), 179–184.

[9] F.W. Lichtenthaler and T. Schneider-Adams, *J. Org. Chem.*, 59 (1994) 6728–6734.

[10] F.W. Lichtenthaler, T. Schneider-Adams, and S. Immel, *J. Org. Chem.*, 59 (1994) 6735–6738.

[11] A. Fürstner and I. Konetzki, *Tetrahedron*, 52 (1996) 15071–15078.

[12] P. Jarglis and F.W. Lichtenthaler, *Tetrahedron Lett.*, 21 (1980) 1425–1428; *Angew. Chem.*, 94 (1982) 140–141; *Angew. Chem., Int. Ed. Engl.*, 21 (1982) 141–142; *Angew. Chem. Suppl.*, (1982) 175–183.

[13] F.W. Lichtenthaler and P. Jarglis, *Angew. Chem.*, 94 (1982) 643; *Angew. Chem., Int. Ed. Engl.*, 21 (1982) 625; *Angew. Chem. Suppl.*, (1982) 1449–1459; F.W. Lichtenthaler, P. Jarglis, and W. Hempe, *Liebigs Ann. Chem.*, (1983) 1959–1972.

[14] E. Kaji, F.W. Lichtenthaler, T. Nishino, Y. Yamane, and S. Zen, *Bull. Chem. Soc. Jpn.*, 61 (1988) 1291–1297.

[15] E. Kaji, F.W. Lichtenthaler, Y. Osa, K. Takahashi, and S. Zen, *Chem. Lett.*, (1992) 707–710; *Bull. Chem. Soc. Jpn.*, 68 (1995) 2401–2408.

[16] E. Kaji and F.W. Lichtenthaler, *J. Carbohydr. Chem.*, 14 (1995) 791–803.

[17] E. Kaji, Y. Osa, K. Takahashi, M. Hirooka, S. Zen, and F.W. Lichtenthaler, *Bull. Chem. Soc. Jpn.*, 67 (1994) 1130–1140.

[18] G.W.J. Fleet and D.R. Witty, *Tetrahedron Asymmetry*, (1990), 119–136.

[19] D. Charon and L. Szabó, *J. Chem. Soc. Perkin Trans. 1*, (1980), 1971–1977.

[20] C.D. Warren, C. Augé, M.L. Laver, S. Suzuki, D. Power, and R.W. Jeanloz, *Carbohydr. Res.*, 82 (1980) 71–83; C. Augé, D.D. Warren, R.W. Jeanloz, M. Kiso, and L. Anderson, *ibid.*, 82 (1980) 85–95.

[21] K. Freudenberg, H. von Hochstetter, and H. Engels, *Ber. Dtsch. Chem. Ges.*, 58 (1925) 666–671.

[22] B.H. Koeppen, *Carbohydr. Res.*, 24 (1972) 154–158.

[23] M. Bertolini and C.P.J. Glaudemans, *Carbohydr. Res.*, 15 (1970) 263–267.

[24] J. Kerékgyártó, J.P. Kamerling, J.B. Bouwstra, J.F.G. Vliegenthart, and A. Lipták, *Carbohydr. Res.*, 186 (1989) 51–62.