3,4,6-Tri-*O*-benzyl-α-D-*arabino*-hexopyranos-2-ulosyl Bromide: A Versatile Glycosyl Donor for the Efficient Generation of β-D-Mannopyranosidic Linkages

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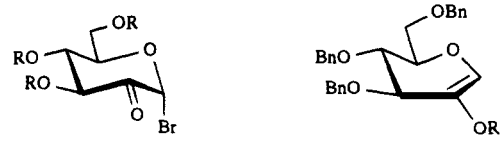
An expedient four-step sequence is described for the conversion of acetobromoglucose into the title 2-oxohexosyl ("ulosyl") bromide **4**. Due to its *O*-benzyl protection, **4** is considerably more reactive than its acylated analogs **1**–**3**: Ag_2CO_3-promoted glycosidations with 2-propanol, diacetonegalactose, and methyl 2,3-*O*-isopropylidene-α-L-rhamnoside are complete within minutes and, in addition, are endowed with β-specificity. This renders ulosyl bromide **4** a most propitious, indirect β-D-mannosyl donor, inasmuch as the borohydride reduction of the β-D-glycosiduloses formed (**14**–**16** → **19**, **21**, and **22**) proceeds with *manno* selectivities of >20:1. Comparative evaluation of the *manno/gluco* ratios obtained in all 21 β-D-*arabino* hexosidulose reductions (Table 1) reveals the 3-*O*-blocking group to have a pronounced effect on the outcome: >20:1 in cases with a 3-*O*-benzyl group versus only 2:1 to 3:1 in the presence of 3-*O*-acyl functions.

Introduction

Despite the recent explosive growth of oligosaccharide synthesis, the construction of β-D-mannosidic linkages remains a crucial step, far from being adequately solved in preparative terms. The various β-D-mannosyl donors available are accessible either by multistage synthesis only or lack appreciable β-selectivity in glycosylations or both.[1] Recent strategies for intramolecular aglycon delivery[2,3] solve the β-selectivity problem, yet their practical utility for the synthesis of biologically relevant β-D-mannosides remains to be demonstrated. The same applies to the different methodologies developed for C-2-epimerization of β-D-glucosides[3] and for the β-D-mannosidase-promoted mannosyl transfer,[4] which, although promising, has not attained the practicality stage.

The presently most relevant method for the construction of β-D-mannosidic linkages appears to be an "indirect" one, involving β-D-glycosid-2-uloses (2-oxoglycosides) as the key intermediates. These are generated from suitably protected β-D-glucosides in which the 2-OH can selectively be liberated, oxidized, and reduced—an approach that has been used extensively[5–13] despite of the fact that the stereoselectivity of the reduction is rarely very high. The alternate protocol to β-D-glycosiduloses, the direct glycosidation of 2-oxoglycosyl (ulosyl) bromides of types **1**–**3**, is endowed with lesser steps and, hence, substantially higher yields:[1,14] the Koenigs–Knorr-type glycosidations are essentially β-specific;[14–17] thus, only the reduction step, with selectivities of about 3:1 in favor of the β-D-mannoside, needs to be improved.

The comparatively low anomeric reactivity of ulosyl bromides may be enhanced by replacing the bromine with alkylthio or alkylsulfoxy residues[14] or with iodine—the ulosyl iodides are about 10 times more reactive. Another relevant possibility would be to replace the acyl blocking groups in **1**–**3** by suitable alkyl functionalities, such as, e.g., the benzyl group. A suitable precursor for the benzylated analog, title compound **4**, was deemed to be a 3,4,6-tri-*O*-benzyl-2-(acyloxy)glucal **5** or **6**, in which the benzyl groups were anticipated to survive the comparatively mild NBS/alcohol treatment[14] required for the one-



	R
1	Ac
2	Bz
3	Piv
4	Bn

	R
5	Bz
6	Ac

(Bz = benzoyl, Piv = pivaloyl, Bn = benzyl)

step conversion into the respective ulosyl bromide. Since the benzoate **5** is accessible from D-glucose in a lengthly nine-step sequence with only 19% overall yield,[5] a more expeditious route was required and eventually found in the three-step generation of the acetate **6** from acetobro-

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moglucose. The procedure for the acquisition of **6** and its conversion into ulosyl bromide **4** is detailed in this paper, as well as its utility for β-specific glycosidations and essentially stereospecific carbonyl reductions to a variety of β-D-mannosides.[18]

Results and Discussion

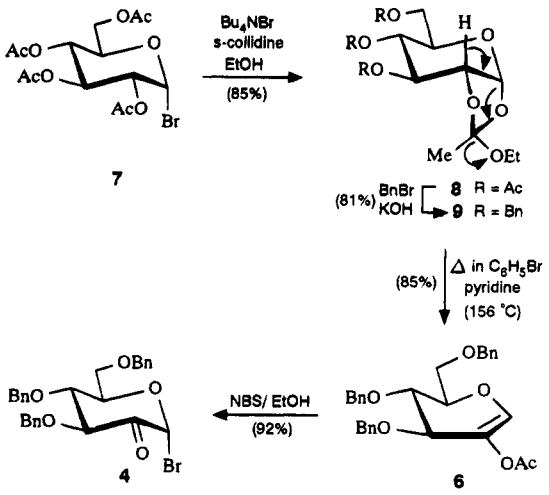
Generation of Ulosyl Bromide 4. The benzylated 2-acetoxyglucal **6** was prepared from acetobromoglucose **7** via orthoester **8**, smoothly generated[19] on exposure to ethanol/*s*-collidine in the presence of tetrabutylammonium bromide (85%). Subsequent exchange of acetyl against benzyl blocking groups, i.e., **8** → **9**, was effected in a one-pot procedure with benzyl bromide/KOH in THF (81%) (Scheme 1). The conversion of orthoester **9** into the 2-acetoxyglucal **6** could be readily accomplished by provoking the excision of ethanol through refluxing in bromobenzene (156 °C) in the presence of pyridine,[20] which was complete within 1.5 h and allowed the isolation of **6** in 85% yield. This surprisingly efficient thermolysis is thought to proceed as indicated by the arrows in **9**, under the likely assumption that an antiperiplanar arrangement exists for such a generally base-catalyzed fragmentation pathway. Alternately, an oxonium intermediate may be formed involving specific base catalysis.

The concluding transformation of **6** into ulosyl bromide **4** was effected by brief exposure to NBS/ethanol in dichloromethane (90 s, 25 °C),[14] the unusually short reaction time already reflecting the higher anomeric reactivity of **4** over its acylated analogs **1**–**3**. The conversion **6** → **4** was quantitative (isolated yield: 92%). Thus, the benzyl-protected ulosyl bromide **4**, constituting a most versatile indirect β-D-mannosyl donor, is now accessible from acetobromoglucose **7** in a simple four-step sequence with an overall yield of 54%.

Originally, the orthoester **9** was first converted into the known[7] 2-*O*-acetyl-3,4,6-tri-*O*-benzyl-α-D-glucosyl bromide by dioxolane ring opening with HBr/acetic acid in dichloromethane. Many attempts to eliminate HBr therefrom, under standard (NaI in acetone, then diethylamine,[21]) or various other conditions, invariably resulted in mixtures of several products, from which in one case (DBU as base) **6** was isolated by chromatography in only 31% yield.

Anomeric Modifications and Glycosidations of 4. The ulosyl chloride **10** provides one possibility for an anomerically modified glycosulosyl donor and, indeed, was readily obtained (87%) on treatment of **4** with AgCl in acetonitrile for 1 h at −20 °C. That **10** has an α-configuration entails a double inversion at the anomeric center; i.e., the β-chloride formed initially is reactive

Scheme 1



enough to undergo a second S_N2 displacement by chloride. The fluoride **11**, however, correspondingly generated on exposure to AgF (15 min, −20 °C), has a β-configuration, indicating that the anomeric fluorine is stable toward further displacement under the reaction conditions.

Other anomerically modified ulosyl donors are the β-thioglycosiduloses **12** and **13**, which are generated smoothly on applying thiation conditions used previously,[22] i.e., RSH in dichloromethane with tetramethyl urea as an acid scavenger (Scheme 2). Toward alcohols, ulosyl bromide **4** exhibits a considerably higher anomeric reactivity than its acylated analogs **2** and **3**. It undergoes spontaneous methanolysis on dissolution in methanol, whereas **2** and **3** are quantitatively recovered from this solvent. Under standard Koenigs–Knorr conditions (Ag_2CO_3/dichloromethande at room temperature), β-specific alcoholysis is a matter of minutes with 2-propanol (→ **14**, 91%) with the primary 6-OH of diacetonegalactose (→ **15**, 85%) or with the 4-OH of methyl 2,3-isopropylidene-α-L-rhamnopyranoside (→ **16**, 84%). In contrast to the isopropyl uloside **14**, which crystallized as such in well-formed needles, the disaccharide analogs **15** and **16** accumulated as syrupy mixtures of the 2-keto and 2,2-dihydroxy (monohydrate) forms, as evidenced by two sets of signals in their ^1H and ^{13}C NMR spectra. This behavior is characteristic for acylated and benzylated 2-uloses and has repeatedly been observed.[14,15]

The anomeric configuration of the glycosiduloses **12**–**16** followed from the following pieces of evidence: *first* the rotations for **12** (−93°), **13** (−117°), and **14** (−49°) are distinctly negative and in line with the equally negative values observed[14] for their benzoylated analogs; this is contrasted by strongly positive rotations for the α-ulosyl halides **4** (+172°) and **10** (+110°); *second*, NOE experiments with **12**–**16** invariably showed the signal enhancements indicated in formula **23**;*third*, the high-yield reductions of **14**–**16** to the respective β-D-mannosides **17**–**22**, which were easily characterized by their

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(17) The apparent reasons for alcoholysis of **1**–**3** proceeding in an exclusive S_N2 fashion have been discussed: ref 1, p 132 ff.
(18) Major portions of this work were included in a review[1] and have been presented at the VIIth European Carbohydrate Symposium, Cracow, Poland, Aug 22–27, 1993, Abstract A 142, and at the 207th American Chemical Society Meeting, San Diego, March 13–17, 1994, Abstract CARB 100.
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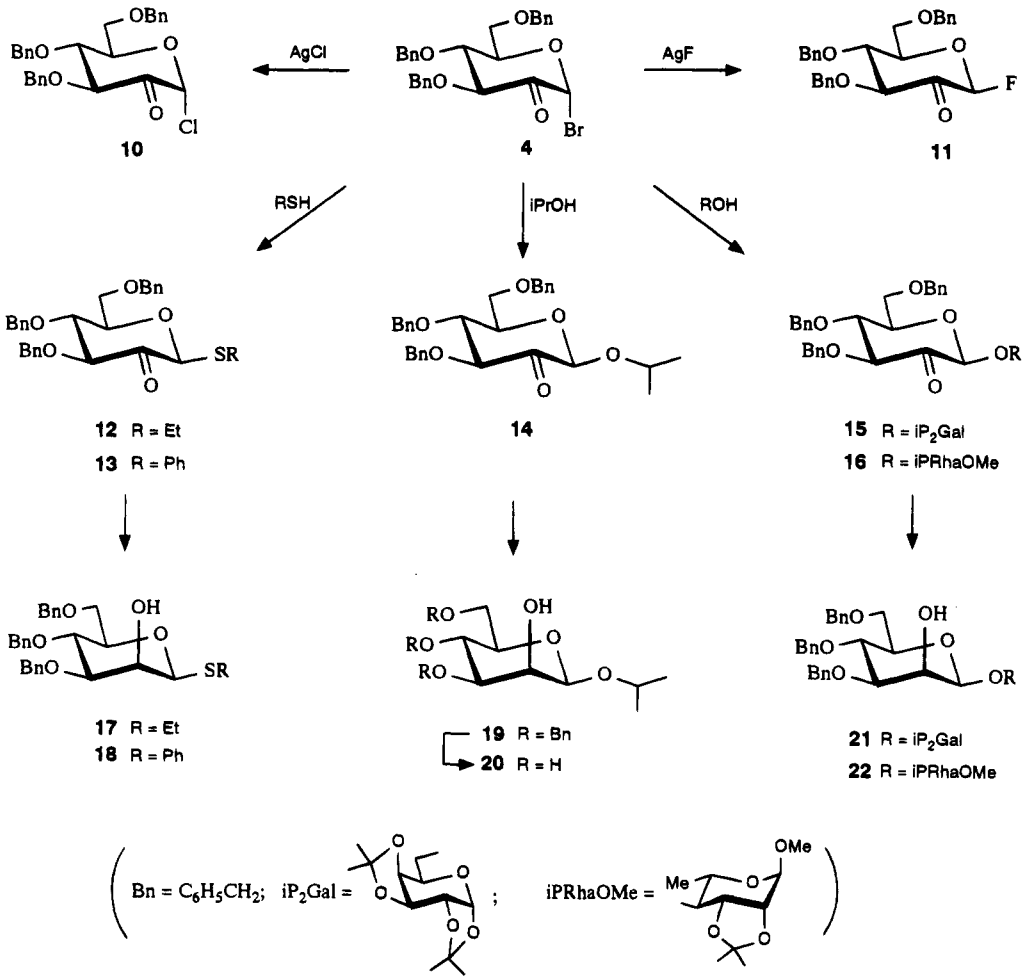
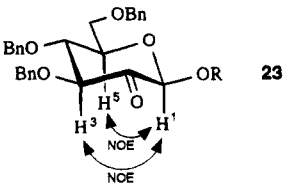
Scheme 2





^{1}H-coupling patterns (cf. below), unequivocally proved the presence of β-D-glucosiduloses in each case.

Carbonyl Reductions of Glycosid-2-uloses 12–16. Once the generation of benzylated β-D-glucosiduloses from ulosyl bromide **4** was solved—glycosidations of **4** are fast, β-specific, and allow isolation of the products in yields of 80–90%—their carbonyl reductions had to be addressed next, since the *manno/gluco*-stereoselectivies attainable determine the practical utility of the ulosyl bromide approach to β-D-mannosides.

On exposure of the isopropyl uloside **14** or either one of the *S*-glycosiduloses **12** or **13** to sodium borohydride in 1:1 dichloromethane/methanol (2–3 h, O °C → room temperature), an essentially stereospecific course of the reduction is observed, no D-*gluco* isomer being detectable in the reaction mixtures by TLC or ^{1}H NMR. Accordingly, the β-D-mannosides **12–14** are each isolable in a crystalline form and in over 90% yields. In the disaccharide–uloside cases **15** and **16**, a faint spot attributable to the 2-epimeric glucoside was detectable by TLC in the reduction mixtures, simple workup providing the respective galactosyl (**21**, 79%) and rhamnosyl β-D-mannosides (**22**, 90%).

The essential β-D-*manno* specificity in the borohydride reductions of glycosiduloses **12–16** is surprising, inasmuch as there are instances where such reductions resulted in *manno/gluco* mixtures with ratios far from being preparatively satisfactory. In order to get a notion of the factors governing the stereoselectivities of such reductions, the presently available 21 β-D-glucosidulose examples—12 from the literature, five from this paper, four from unpublished data[27,28]—are listed in Table 1. Under the premise that the varying conditions employed for the sodium borohydride treatment are of minor importance in determining stereoselectivities, the following picture emerges: the steric outcome of the carbonyl reduction is not only dependent on the anomeric configuration—the hydride ion preferentially attacks from the side opposite to the anomeric substituent, i.e., from the α-face in β-D-glycosiduloses—but also on the nature of the 3-*O*-blocking group. As evidenced by compounds **28** (3-*O*-tosyl group) and **30–34** (benzoyl or pivaloyl residues at O–3), the presence of a sulfonyloxy or an acyloxy function vicinal to the C-2-carbonyl invariably results in low stereoselectivities, *manno/gluco* ratios being in the 2:1 to 5:1 range only. The same seems to be the case for a 3-*O*-allyl group, as **39** gives a 7:3 mixture of the two epimers. On the other hand, 3-*O*-alkyl-

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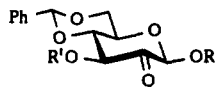
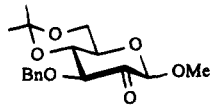
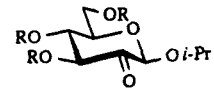
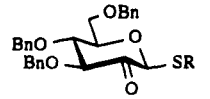
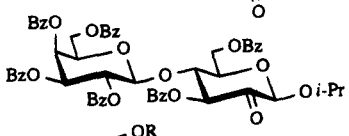
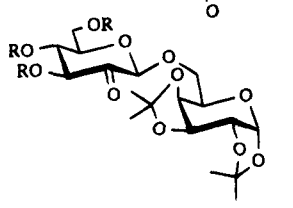
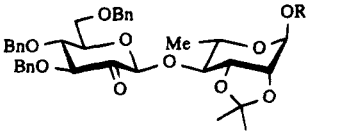
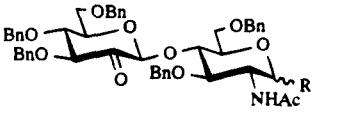
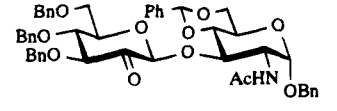
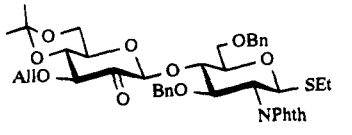
Table 1. Stereoselectivities in $NaBH_4$ Reductions of β-D-Glycosid-2-uloses

β-D-glycosidulose			$NaBH_4$ reduction conditions solvents	temp.	*manno/gluco* ratio	β-D-mannoside isol. yield (%)	ref.
	**24**	R = Bn, R' = Bn	MeOH/DMF (8:1)	rt	~10:1	65	24
	25	R = Bn, R' = Me	MeOH/DMF (8:1)	rt	~10:1	73	24
	26	R = Me, R' = Me	MeOH	rt	19:1	82	25
	27	R = Me, R' = Bn	MeOH/DMF (8:1)	rt	~10:1	57	24
	28	R = Me, R' = Ts	MeOH/DMF (15:1)	rt	2:1	63	26
	**29**		MeOH/CH_2Cl_2 (1:1)	0 °C	>10:1	83	11
	**14**	R = Bn	MeOH/CH_2Cl_2 (1:1)	0 °C→ rt	>50:1[a]	91	b
	30	R = Bz	CH_2Cl_2	rt	5:2[c]	[d]	27
	31	R = Piv	dioxane/H_2O (10:1)	0 °C→ rt	3:1[c]	[d]	28
	**12**	R = Et	MeOH/CH_2Cl_2 (1:1)	0 °C→ rt	50:1[a]	94	b
	13	R = Ph	MeOH/CH_2Cl_2 (1:1)	0 °C→ rt	50:1[a]	94	b
	**32**		dioxane/H_2O (10:1)	rt	5:1	72	14
	**15**	R = Bn	MeOH/CH_2Cl_2 (1:1)	0 °C→ rt	>20:1[c]	79	b
	33	R = Bz	dioxane/H_2O (10:1)	0 °C→ rt	3:1	56	27
	34	R = Piv	dioxane/H_2O (10:1)	0 °C→ rt	3:2[c]	[d]	28
	**16**	R = Me	MeOH/CH_2Cl_2 (1:1)	0 °C→ rt	>20:1[e]	90	b
	35	R = Bn	EtOH/water (3:1)	60 °C	15:1	88	6
	**36**	R = α-OBn	MeOH/CH_2Cl_2 (1:1)	rt	>20:1[f]	64	9
	37	R = β-OBn	MeOH/CH_2Cl_2 (1:1)	rt	>20:1[g]	69	8
	**38**		MeOH/CH_2Cl_2 (1:1)	rt	>20:1[g]	82	7
	**39**		*i*-PrOH/CH_2Cl_2 (2:1)	0 °C	7:3	53	12

[a] No *gluco* isomer detectable by ^1H NMR or TLC. [b] This paper. [c] Based on ^1H NMR of reaction mixture. [d] Mixture of *manno* and *gluco* isomers not separated. [e] A faint spot of the *gluco* derivative was detectable by TLC. [f] A very slight contamination by the *gluco* isomer was revealed by TLC. [g] Reduction claimed to be stereospecific.

substituted β-D-glucosiduloses provide distinctly higher stereoselectivities: the 3-*O*-methyl derivatives **25** and **26** lie in the 10:1 to 20:1 range, while the glycosiduloses with benzyl protection at O-3 give the respective β-D-mannosides either stereospecifically (**12**–**14**) or nearly exclusively (>20:1 for **15**, **16**, and **35**–**38**).

Although the reasons for the improvement of *manno/gluco* selectivities by 3-*O*-acyl groups are not clearly apparent—they are more likely to be electronic in nature than steric only—the data of Table 1 suffice to point toward the avoidance of ester functions at O-3 of β-D-glycosiduloses in order to foster a uniform course of their hydride reductions. Rather, 3-*O*-benzyl groups appear to be most propitious for achieving high or essentially exclusive *manno*-selectivities and, hence, satisfactory yields.

By way of summation, a preparatively expedient protocol has been elaborated for the conversion of acetobromoglucose into the benzyl-protected α-D-*arabino*-hexosulosyl bromide **4** (54% over four steps). It proved to be a most favorable indirect β-D-mannosyl donor, since each of the two following key steps—β-glycosidation and carbonyl reduction—proceed either stereospecifically or with stereoselectivities of at least 20:1. Accordingly, this methodology constitutes a short and efficient approach with which to construct β-D-mannopyranosidic linkages. In order to adapt it to the straightforward synthesis of

antennary oligosaccharides, branched at the center β-D-mannose unit, differentiation of the blocking group pattern in **4** is deemed important—studies that are soon to be implemented.

Experimental Section

General Methods. Melting points were determined with a hot stage microscope and are not corrected. Mass spectra (MS) were taken in EI and FAB modes. ^{1}H NMR spectra were recorded at 300 MHz, ^{13}C NMR at 75.5 MHz. All reactions were monitored by thin layer chromatography (TLC) performed on Kieselgel 60 F_{254} plastic sheets. Developers employed: A, toluene/EtOAc (8:1); B, toluene/EtOAc (20:1); C, CCl_4/EtOAc (2:1). The spots were visualized by UV light or by spraying with 50% sulfuric acid and charring at 120 °C for 5 min. Column chromatography was performed on silica gel 60 (63–200 μm).

3,4,6-Tri-*O*-benzyl-α-D-*arabino*-hexopyranos-2-ulosyl Bromide (4). To a solution of 2-acetoxyglucal **6** (3.3 g, 7 mmol) in CH_2Cl_2 (60 mL) were added 2 g of molecular sieves (3 Å) and absolute ethanol (0.58 mL, 10 mmol), and the mixture was cooled (0 °C) and stirred for 10 min. *N*-Bromosuccinimide (1.23 g, 7 mmol), freshly recrystallized, was then added in one batch, whereafter the solution turned red-brown after 1–2 min and was then worked up immediately by dilution with cold dichloromethane (100 mL) and successive washings with cold 10% $Na_2S_2O_3$ solution (50 mL) and ice–water (50 mL). Drying (Na_2SO_4), filtration, and concentration in vacuo gave a syrup, which was dried at 0.01 Torr: 3.35 g (92%) of **4** as a colorless syrup; $[\alpha]^{20}_D$ +172° (*c* 1.1, $CHCl_3$). The product is sufficiently pure for glycosidations: ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.70 (dd, 1H, *J* = 2.0, 11.1 Hz), 3.83 (dd, 1H, *J* = 3.3, 11.1 Hz), 4.02 (dd, 1H, *J* = 9.8, 9.9 Hz), 4.23 (m, 1H), 4.47, 4.54, 4.56, 4.64, 4.84, 4.84, 5.01 (6 d, 1H each, *J* = 10.7, 11.2, 12.1 Hz); ^{13}C NMR (75.5 MHz $CDCl_3$) δ 67.2, 73.5, 74.2, 75.4, 75.6, 76.9, 81.4, 85.7, 127.8–128.4, 137.1, 137.4, 137.5, 194.5; MS (FD) *m/e* 511 (M^+).

2-*O*-Acetyl-1,5-anhydro-3,4,6-tri-*O*-benzyl-D-*arabino*-hex-1-enitol (2-Acetoxy-3,4,6-tri-*O*-benzyl-D-glucal) (6). (a) By Thermal Fragmentation of Orthoester 9. A solution of 7.8 g (15 mmol) of **9** in 150 mL of bromobenzene containing 0.7 mL of pyridine was refluxed for 1.5 h, and the solvent was removed in vacuo. The resulting brown syrup was purified by elution from a silica gel column (3 × 35 cm) with toluene/ethyl acetate (20:1). Concentration of the eluates with R_f = 0.28 (in B) gave 6.05 g (85%) of **6** as a colorless syrup, homogeneous by TLC and suitable for the next step (→ **4**). Trituration with diisopropyl ether resulted in crystallization: mp 49–50 °C; $[\alpha]^{20}_D$ +24° (*c* = 1.6, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.05 (s, 3H), 3.72 (dd, 1H, *J* = 3.6, 10.8 Hz), 3.81 (dd, 1H, *J* = 5.4, 10.8 Hz), 3.96 (dd, 1H, *J* = 5.1, 7.1 Hz), 4.21 (m, 1H), 4.43 (dd, 1H, *J* = 0.7, 5.1 Hz), 4.49, 4.59, 4.60, 4.73 (4 d, 1H, each, *J* = 11.5, 11.6 Hz), 4.55 (s, 2H), 6.60 (s, 1H), 7.22–7.35 (m, 15H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 20.6, 67.9, 71.8, 73.0, 73.4, 73.8, 75.0, 127.6–129.7, 129.8, 137.7, 137.8, 138.0, 138.2, 169.6; MS (FD) *m/e* 474 (M^+). Anal. Calcd for $C_{29}H_{30}O_6$ (474.3): C, 73.41; H, 6.32. Found: C, 73.38; H, 6.41.

(b) By Dehydrobromination of 2-*O*-Acetyl-3,4,6-tri-*O*-benzyl-α-D-glucopyranosyl Bromide. A solution of this compound (1.6 g, 2.9 mmol), prepared by HBr/HOAc treatment of **9** (see below), and sodium iodide (500 mg, 3.3 mmol) in 10 mL of dry acetone was stirred for 15 min at ambient temperature. After addition of DBU (1.5 mL, 10 mmol) the mixture was stirred for another 45 min and was subsequently diluted with CH_2Cl_2 (50 mL), washed with 2 N HCl (2 × 30 mL) and water, dried (Na_2SO_4), and evaporated to dryness in vacuo. Purification of the syrupy residue by elution from a short silica gel column with toluene–ethyl acetate (8:1), removal of the solvents from the eluates, and crystallization from diisopropyl ether afforded 430 mg (31%) of **4**, identical with the product described above.

2-*O*-Acetyl-3,4,6-tri-*O*-benzyl-α-D-glucopyranosyl Bromide. To a cooled (0 °C) solution of 1.70 g (3.27 mmol) of **9** in CH_2Cl_2 (50 mL) was added 5 mL of a 33% solution of HBr in acetic acid, and the mixture was stirred for 30 min followed by dilution with CH_2Cl_2 (250 mL). Washing with ice–water (2 × 100 mL), saturated $NaHCO_3$ solution (2 × 100 mL), and again water gave, upon drying (Na_2SO_4) and removal of the solvent in vacuo, a chromatographically uniform syrup (1.61 g, 89%): $[\alpha]^{20}_D$ +139° (*c* 1, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.66, 3.80 (2 m, 1H each), 3.85 (dd, 1H, *J* = 9.5 Hz), 4.08 (dd, 1H, *J* = 9.8, 9.5 Hz), 4.48, 4.55, 4.60, 4.70, 4.78, 4.81 (6 d, 1H each, *J* = 11.0, 11.3, 12.1 Hz), 4.76 (dd, 1H, *J* = 3.8, 9.8 Hz), 6.65 (d, 1H, *J* = 3.8 Hz), 7.20–7.40 (m, 15H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 20.7, 67.5, 73.2, 73.3, 75.2, 75.4, 75.5, 76.2, 80.3, 89.3, 127.5–128.9, 137.6–138.2, 169.9.

The compound has been prepared previously,[7] yet was not purified, and hence, no physical data were advanced.

3,4,6-Tri-*O*-acetyl-1,2-*O*-(*exo*-ethoxyethylidene)-α-D-glucopyranose (8). To a solution of 20.5 g (50 mmol) of tetra-*O*-acetyl-α-D-glucopyranosyl bromide (**7**) in *s*-collidine (70 mL) was added dry ethanol (5 mL) and Bu_4NBr (5.0 g, 15.5 mmol), and the mixture was stirred at 50 °C for 12 h. From the homogeneous solution initially obtained, crystals of *s*-collidinium bromide began to separate gradually, resulting in an almost solid reaction mixture after 12 h. Chloroform (150 mL) was then added, and the clear solution was washed with 2 N HCl (70 mL), a saturated aqueous $NaHCO_3$ solution (70 mL), and finally water. Drying (Na_2SO_4) and removal of the $CHCl_3$ in vacuo left a semicrystalline mass, which was recrystallized from hot ethanol: 15.8 g (85%) of **8** as sturdy crystals; mp 95–96 °C; $[\alpha]^{20}_D$ +34° (*c* 1.0, $CHCl_3$) (lit.[19] mp 95–96 °C; $[\alpha]^{20}_D$ +35° (*c* 1.5, $CHCl_3$)); ^{1}H NMR (300 MHz, $CHCl_3$) δ 1.18 (t, 3H), 1.72 (s, 3H), 2.09, 2.10, 2.11 (3 s, 3H each), 3.54 (q, 2H), 3.94 (ddd, 1H, *J* = 9.6, 3.5, 4.7 Hz), 4.19–4.21 (m, 2H), 4.32 (dd, 1H, *J* = 5.2, 3.0 Hz), 4.91 (dd, 1H, *J* = 2.7, 9.6 Hz), 5.18 (dd, 1H, *J* = 3.0, 2.7 Hz), 5.71 (d, 1H, *J* = 5.2 Hz).

3,4,6-Tri-*O*-benzyl-1,2-*O*-(*exo*-ethoxyethylidene)-α-D-glucopyranose (9). To a solution of orthoester **8** (15.1 g, 40 mmol) and benzyl bromide (15 mL, 3.2 molar equiv) in dry THF (100 mL) was added powdered KOH (26 g, 0.45 mol), and the mixture was refluxed for 3 h with stirring. After the mixture was cooled to room temperature, CH_2Cl_2 (300 mL) was added, and the solution was successively washed with water (5 × 150 mL), a saturated $NaHCO_3$ solution (2 × 100 mL), and water (2 × 100 mL), followed by drying (Na_2SO_4) and evaporation to dryness in vacuo. The yellowish oil remaining was purified by elution from a silica gel column (3 × 20 cm) with toluene/EtOAc (8:1) containing 0.1% of triethylamine[29] to give 16.9 g (81%) of **9** as a colorless syrup: R_f = 0.4 (in solvent B); $[\alpha]^{20}_D$ +34.8° (*c*, 1.1, $CHCl_3$) (lit.[7] $[\alpha]^{25}_D$ +35 (*c* 1.5, $CHCl_3$)); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.19 (t, 3H), 1.66 (s, 3H), 3.47–3.59 (m, 2H), 3.65 (m, 2H), 3.71 (dd, 1H, *J* = 4.2, 9.5 Hz), 3.79 (m, 1H), 3.87 (dd, 1H, *J* = 3.8, 4.2 Hz), 4.34, 4.50, 4.51, 4.60, 4.66 (6 d, 6H, *J* = 11.5, 12.0, 12.2 Hz), 4.41 (dd, 1H, *J* = 5.2, 3.8 Hz), 5.76 (d, 1H, *J* = 5.2 Hz), 7.10–7.40 (m, 15H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 15.3, 21.8, 58.7, 69.1, 70.4, 71.9, 72.9, 73.4, 74.8, 75.7, 78.7, 97.8, 120.9, 125.3–129.0, 137.7–138.0; MS (FD) *m/e* 491 ($M^+ - C_2H_5$).

3,4,6-Tri-*O*-benzyl-α-D-*arabino*-hexopyranos-2-ulosyl Chloride (10). Silver chloride (200 mg, 1.4 mmol) was added to a cooled (−20 °C) solution of ulosyl bromide **4** (415 mg, 0.8 mmol) in 10 mL of acetonitrile, the mixture was stirred for 1 h and then filtered through Celite, and the filtrate was taken to dryness in vacuo. The resulting syrup was dissolved in CH_2Cl_2, and the solution was washed with aqueous $Na_2S_2O_3$ and water (30 mL each), dried (Na_2SO_4), and evaporated to dryness: 326 mg (87%) of **10** as a colorless syrup: $[a]^{20}_D$ +110° (*c* 1.6, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.72 (dd, 1 H, *J* = 1.9, 11.1 Hz), 3.83 (dd, 1H, *J* = 3.4, 11.1 Hz), 4.01 (ddd, 1H, *J* = 1.9, 3.4, 9.8 Hz), 4.48, 4.53, 4.57, 4.62 (4 d, 1H each, *J* = 10.7, 11.3, 12.0, 12.1 Hz), 4.77 (d, 1H, *J* = 9.7 Hz), 4.85 (d, 1H, *J* = 10.7 Hz), 4.99 (d, 1H, *J* = 11.3 Hz), 5.96 (s, 1H0, 7.20–7.40 (m, 15H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 67.3, 73.5, 74.1, 74.1, 75.4, 77.5, 81.9, 90.2, 127.7–137.4, 194.9; MS (FD) *m/e*

(29) As observed previously,[7] orthoester **8**, as well as **9**, are exceedingly acid sensitive and can be chromatographed on silica gel without hydrolysis only by the addition of 0.1% triethylamine to the solvent B.

466 (M^+). Anal. Calcd for $C_{27}H_{27}O_5Cl$ (467.0): C, 69.45; H, 5.83; Cl, 7.59. Found: C, 69.36; H, 5.75; Cl, 7.48.

3,4,6-Tri-*O*-Benyl-β-D-*arabino*-hexopyranos-2-ulosyl Fluoride (11). A solution of ulosyl bromide **4** (445 mg, 0.86 mmol) in acetonitrile (25 mL) was cooled to −20 °C and, after the addition of AgF (320 mg, 2.5 mmol), stirred at this temperature for 15 min. Workup as described for the chloride **10** (cf. above) and crystallization of the syrup, initially obtained, from ether/hexane gave **11** (298 mg, 77%) as colorless needles: mp 89 °C; $[\alpha]^{20}_D$ +19° (*c* 1.6, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$ δ 3.62 (dd, 1H, *J* = 4.0, 10.7 Hz), 3.69 (dd, 1H, *J* = 5.3, 10.7 Hz), 3.69 (dd, 1H, *J* = 5.3, 10.7 Hz), 3.97 (dd, 1H, *J* = 8.3, 7.3 Hz), 4.12 (m, 1H), 4.30 (dd, 1H, *J* = 2.3, 8.3 Hz), 4.49, 4.53, 4.55, 4.61, 4.77, 4.94 (6 d, 1H, each. *J* = 11.2, 11.5, 12.0 Hz), 5.46 (d, ^1H, *J* = 52.3 Hz), 7.13−7.39 (m, 15H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 69.4, 73.5, 73.6, 74.2, 77.0, 78.0, 83.2, 103.3 (d, *J* = 233.7), 127.7−137.8, 197.4 (d, *J* = 21.1 Hz); MS (FD) *m/e* 450 (M^+). Anal. Calcd for $C_{27}H_{27}FO_5$ (450.5): C, 71.98; H, 6.04. Found: C, 71.79; H, 6.00.

Ethyl 3,4,6-Tri-*O*-benzyl-1-thio-β-D-*arabino*-hexopyranosid-2-ulose (12). A solution of ulosyl bromide **4** (950 mg, 1.86 mmol), EtSH (0.19 mL, 3 mmol), and 1,1,3,3-tetramethylurea (0.29 mL, 2.5 mmol) in dry CH_2Cl_2 (15 mL) was stirred at room temperature for 1.5 h. Subsequently, the mixture was diluted with dichloromethane (20 mL) and successively washed with 2 N HCl (30 mL), saturated $NaHCO_3$ solution (30 mL), and water (30 mL). The organic phase was dried (Na_2SO_4) and freed from the solvent in vacuo; the resulting syrup crystallized from methanol: 715 mg (80%) of **12** as colorless crystals; mp 68−69 °C; $[\alpha]^{20}_D$ −93° (*c* 1, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 1.29 (t, 3H), 2.72 (q, 2H), 3.70 (dd, 1H, *J* = 1.9, 11.0 Hz), 3.77 (dd, 1H, *J* = 4.9, 11.0 Hz), 3.83 (m, 1H), 3.90 (dd, 1H, *J* = 8.4, 9.4 Hz), 4.20 (d, 1H, *J* = 8.4 Hz), 4.55 (m, 4H), 4.83, 4.97 (2 d, 1 H each, *J* = 10.9, 12.3 Hz), 5.06 (s, 1H), 7.15−7.40 (m, 15H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 14.9, 23.9, 68.9, 73.4, 73.6, 74.8, 79.5, 79.8, 86.1, 86.1, 127.6−137.9, 197.7; MS (FD) *m/e* = 492 (M^+), 493 (M^+ + H), 402 (M^+ − $CH_2C_6H_5$). Anal. Calcd for $C_{29}H_{32}O_5S$ (492.6): C, 70.70; H, 6.54. Found: C, 70.50; H, 6.43.

Phenyl 3,4,6-Tri-*O*-benzyl-1-β-D-*arabino*-hexopyranosid-2-ulose (13). To a stirred solution of ulosyl bromide **4** (970 mg, 1.9 mmol) in CH_2Cl_2 (15 mL) was added tetramethylurea (0.3 mL) and thiophenol (0.27 mL, 2.4 mmol), and the mixture was stirred for 1.5 h at ambient temperature. Dilution with CH_2Cl_2 (230 mL), washing with 2 N HCl and water (30 mL each), drying (Na_2SO_4), and removal of the solvent in vacuo gave a residue which crystallized from diisopropyl ether: 820 mg (81%) of **13** as colorless crystals; mp 94−96 °C; $[\alpha]^{20}_D$ −117° (*c* = 1.6, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 3.71 (dd, 1H, *J* = 4.9, 10.7 Hz), 3.83 (m, 1H), 3.86 (m, 1H), 3.90 (dd, 1H, *J* = 8.0, 9.3 Hz), 4.24 (d, 1H, *J* = 8.0 Hz), 4.54 (m, 4H), 4.84 (d, 1H, *J* = 11.5 Hz), 4.96 (d, 1H, *J* = 11.0 Hz), 5.27 (s, 1H), 7.23−7.60 (m, 20H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 69.0, 73.4, 73.6, 74.9, 79.5, 80.1, 86.2, 89.0, 127.6−137.9, 197.0; MS (FD) *m/e* 540 (M^+). Anal. Calcd for $C_{33}H_{32}O_5S$ (540.7): C, 73.30; H, 5.96. Found: C, 73.43; H, 5.88.

Isopropyl 3,4,6-Tri-*O*-benzyl-β-D-*arabino*-hexopyranosid-2-ulose (14). A suspension of 2-propanol (1 mL, 13 mmol), Ag_2CO_3 (5.0 g, 18 mmol), and molecular sieves (3 Å, 2 g) in CH_2Cl_2 (30 mL) was stirred for 15 min at ambient temperature, and a solution of ulosyl bromide **4** (2.76 g, 5.4 mmol) in CH_2Cl_2 (5 mL) was added. After 30 s the mixture was filtered through Kieselgel and freed from the solvent in vacuo. The resulting amorphous residue was crystallized from diisopropyl ether: 2.38 g (91%) of **14** as matted needles: mp 84−86 °C; $[\alpha]^{20}_D$ −49 (*c* 1.1, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 1.22, 1.30 (2 d, 3H each), 3.73 (m, 2H), 3.83 (m, 1H), 3.83 (dd, 1H, *J* = 7.9, 9.2 Hz), 4.05 (spt, 1H), 4.22 (dd, 1H, *J* = 0.5, 7.9 Hz), 4.50−4.60 (m, 4H), 4.84 (d, 1H, *J* = 10.9 Hz), 4.85 (s, 1H), 4.97 (d, 1H, *J* = 11.4 Hz), 7.16−7.41 (m, 15H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 21.9, 23.5, 69.5, 72.3, 73.6, 75.1, 75.8, 80.5, 85.9, 98.0, 127.6−128.4, 137.6, 137.9, 138.2, 197.4; MS (FD) *m/e* 490 (M − $CH_2C_6H_5$). Anal. Calcd for $C_{30}H_{34}O_6$ (490.9): C, 73.44; H, 6.93. Found: C, 73.38; H, 6.86.

Methyl 4-*O*-(3,4,6-Tri-*O*-benzyl-β-D-*arabino*-hexopyranos-2-ulosyl)-2,3-*O*-isopropylidene-α-L-rhamnopyranoside (16). A mixture of methyl 2,3-*O*-isopropylidene-α-L-rhamnoside[30] (260 mg, 1.2 mmol), Ag_2CO_3 (1.4 g, 5 mmol), molecular sieves (4 Å, 0.5 g), and CH_2Cl_2 (3 mL) was stirred for 15 min at room temperature with the exclusion of moisture. A CH_2Cl_2 solution of ulosyl bromide **4** (0.51 g, 1 mmol, in 2 mL) was then injected, and stirring was continued for 3 min, followed by filtration through Celite with extensive washing of the filter cake with CH_2Cl_2. The combined filtrate and washings were taken to dryness in vacuo, and the residue was purified by elution from a silica gel column (3 × 20 cm) with CCl_4/EtOAc (2:1). Evaporation of the fractions with R_f = 0.6 (in solvent system C) gave 585 mg (90%) of **16** as a colorless syrup, containing (^1H NMR) about 10% of the hydrate form: ^1H NMR (300 MHz, $CDCl_3$), *ulosyl-H* δ 3.73 (m, 3H), 3.91 (dd, 1H, *J* = 8.8, 9.1 Hz), 4.26 (d, 1H, *J* = 8.8 Hz), 4.56 (m, 4H), 4.85 (d, 1H, *J* = 11.4 Hz), 4.86 (s, 1H), 4.97 (d, 1H, *J* = 11.0 Hz), 7.16−7.44 (m, 15H); *rhamnosyl-H* δ 1.30 (d, 3H), 1.31 (s, 3H), 1.46 (s, 3H), 3.35 (s, 3H), 3.73 (m, 2H), 4.09 (d, 1H, *J* = 5.7 Hz), 4.30 (dd, 1H, *J* = 5.7 Hz), 5.35 (d, 1H, *J* = 0.5 Hz); ^{13}C NMR (75.5 MHz, $CDCl_3$), *ulosyl-C* δ 68.5, 73.6, 75.1, 78.6, 80.7, 86.1, 97.8, 127.0−138.0, 196.5; *rhamnosyl-C* δ 17.6, 26.4, 27.9, 54.8, 63.8, 78.4, 75.8, 76.2, 97.8, 109.5; MS (FD) *m/e* 648 (M^+).

Ethyl 3,4,6-Tri-*O*-benzyl-1-thio-β-D-mannopyranoside (17). $NaBH_4$ (200 mg) was added to a stirred, cooled (0 °C) solution of **12** (200 mg, 0.4 mmol) in 10 mL of CH_2Cl_2/MeOH (1:1), and stirring was continued for 2 h, allowing the mixture to warm to room temperature. Dilution with CH_2Cl_2 (20 mL), successive washing with water (15 mL), a 1% citric acid solution (2 × 15 mL), and again water (2 × 15 mL), drying (Na_2SO_4), removal of the solvent in vacuo, and crystallization of the residue from diisopropyl ether gave 185 mg (92%) of **17** as colorless needles: mp 84−86 °C; $[\alpha]^{20}_D$ −38 (*c* 0.8, $CHCl_3$); ^1H NMR (300 MH, $CDCl_3$) δ 1.30 (t, 3H), 2.54 (d, 1H), 2.73 (q, 2H), 3.45 (m, 1H), 3.60 (dd, 1H, *J* = 3.3, 9.1 Hz), 3.68 (dd, 1H, *J* = 1.7, 11.0 Hz), 3.76 (dd, 1H, *J* = 5.4, 11.0 Hz), 3.79 (dd, 1H, *J* = 9.1, 9.3 Hz), 4.12 (m, 1H), 4.58 (bs, 1H, *J* = 1.0 Hz), 4.54, 4.58, 4.60, 4.65, 4.73, 4.86 (6 d, 1H each, *J* = 10.9, 11.6, 11.7 Hz), 7.19−7.34 (m, 15H); MS (FD) *m/e* 494 (M^+). Anal. Calcd for $C_{29}H_{34}O_5S$ (494.8): C, 70.33; H, 6.87. Found: C, 70.40; H, 6.79.

Phenyl 3,4,6-Tri-*O*-benzyl-1-thio-β-D-mannopyranoside (18). Subjection of **13** (450 mg) to reduction with $NaBH_4$ (300 mg) in CH_2Cl_2/MeOH (1:1, 15 mL) and processing of the mixture (as described above for **12** → **17**) yielded 430 mg (94%) of **18** as colorless needles: mp 109−110 °C; $[\alpha]^{20}_D$ −52° (*c* 1.5, $CHCl_3$); ^1H NMR (300 Hz, $CDCl_3$) δ 2.75 (d, 1H0, 3.49 (ddd, 1H, *J* = 9.6, 1.9, 5.8 Hz), 3.60 (dd, 1H, *J* = 3.2, 9.1 Hz), 3.69 (dd, 1H, *J* = 1.9, 10.8 Hz), 3.81 (m, 1H), 4.27 (m, 1H), 4.52, 4.56, 4.58, 4.64, 4.71, 4.85 (6d, 1H, each, *J* = 10.9, 11.6, 11.9 Hz), 4.78 (bs, 1H, *J* < 1.0 Hz), 7.18−7.55 (m, 20H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 69.4, 69.9, 71.8, 73.4, 74.2, 75.2, 79.6, 82.6, 86.6, 127.7−128.9, 130.7, 135.0, 137.4, 138.0, 138.3; MS (FD) *m/z* 542 (M^+). Anal. Calcd for $C_{33}H_{34}O_5S$ (542.7): C, 73.06; H, 6.27. Found: C, 73.11; H, 6.30.

Isopropyl 3,4,6-Tri-*O*-benzyl-β-D-mannopyranoside (19). To a cooled (0 °C), stirred solution of uloside **14** in 80 mL of CH_2Cl_2/MeOH (1:1) was added $NaBH_4$ (900 mg), and stirring was continued for 2 h whereupon the mixture was allowed to warm to ambient temperature. Dilution with CH_2Cl_2 (70 mL), successive washing with water (70 mL), a 1% aqueous citric acid solution (2 × 70 mL), and water (70 mL), followed by drying (Na_2SO_4) and evaporation to dryness in vacuo, gave a syrup, which was filtered through a silica gel column (3 × 15 cm) with CCl_4/EtOAc (4:1). Removal of the solvents from the filtrate and crystallization of the residue from methanol afforded 1.40 g (93%) of **19** as colorless crystals: mp 51−53 °C; $[\alpha]^{20}_D$ −25.1° (*c* 1.2, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 1.16, 1.27 (two 3H-d), 2.46 (s, 1H), 3.41 (m, 1H), 3.56 (dd, 1H, *J* = 3.1, 9.4 Hz), 3.68 (dd, 1H, *J* = 2.0, 10.8 Hz), 3.77 (dd, 1H, *J* = 5.4, 10.8 Hz), 3.83 (dd, 1H, *J* = 9.4 Hz), 4.0 (m, 2H), 4.49

(30) Bebault, G. M.; Dutton, G. G. S. *Can. J. Chem.* **1972**, *50*, 3373−3378.

(bs, 1H, J < 1.0 Hz), 4.50, 4.56, 4.65, 4.76, 4.89 (5 d, 6 H, J = 10.8, 12.0, 12.2 Hz), 4.57 (s, 1H), 7.15–7.35 (m, 15H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 21.8, 23.3, 69.0, 69.5, 71.2, 71.4, 73.6, 75.3, 74.5, 75.4, 81.9, 97.8, 126.8–128.6, 138.1, 138.4, 138.5; MS (FD) *m/e* 492 (M^+), 401 ($M^+ - CH_2C_6H_5$). Anal. Calcd for $C_{30}H_{36}O_6$ (492.6): C, 73.14; H, 7.36. Found: C, 72.98; H, 7.34.

Isopropyl β-D-Mannopyranoside (20). A mixture of mannoside **19** (335 mg, 0.68 mmol), 200 mg of 10% Pd/C, and ethanol (20 mL) was hydrogenated for 5 h, followed by removal of the catalyst by filtration and evaporation to dryness in vacuo: 150 mg (98%) of **20** as a colorless syrup: $[\alpha]^{20}_D$ −60 °C (*c* 0.9, chloroform); ^{1}H NMR (300 MHz, DMSO-d_6) δ 1.09, 1.13 (two 3H-*d*), 3.03 (bs, 1H), 3.27 (m, 2H), 3.45 (m, 1H), 3.56 (bs, 1H), 3.68 (dd, 1H, J = 6.1, 11.4 Hz), 3.94 (m, 1H), 4.22 (d, 1H), 4.44 (bs, 1H), 4.54 (d, 1H; J = 4.8 Hz), 4.73 (d, 1H, J = 5.7 Hz); ^{13}C NMR (75.5 MHz, DMSO-d_6 δ 20.9, 23.5, 61.4, 67.2, 69.3, 71.2, 73.9, 77.4, 98.1; MS (FD) *m/e* 222 (M^+). Anal. Calcd for $C_9H_{18}O_6$ (222.2): C, 43.23; H, 8.09. Found: C, 43.18; H, 8.15.

1,2:3,4-Di-*O*-isopropylidene-6-*O*-(3,4,6-tri-*O*-benzyl-β-D-mannopyranosyl)-α-D-galactopyranose (21). A suspension of 1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose[31] (624 mg, 2.4 mmol), Ag_2CO_3 (2.7 g, 10 mmol), and molecular sieves (4 Å, 500 mg) in CH_2Cl_2 (5 mL) was stirred for 15 min at room temperature with the exclusion of light and moisture. A CH_2Cl_2 solution of ulosyl bromide **4** (1.02 g, 2 mmol, in 5 mL) was added dropwise in the course of 2 min, and after being stirred for another minute the mixture was filtered through Celite, followed by washing of the filter cake with CH_2Cl_2, and evaporation of the combined filtrates in vacuo. The syrupy residue was purified by elution from a silica gel column (3 × 20 cm) with CCl_4/EtOAc (4:1) to give 1.19 g (85%) of a colorless syrup, consisting (^{1}H and ^{13}C NMR) of an approximate 1:1 mixture of **15** and its monohydrate. The product was dissolved in 15 mL of CH_2Cl_2/MeOH (1:1) and exposed to reduction with $NaBH_4$ (250 mg) for 2.5 h, first at 0 °C and then at ambient temperature. Dilution with CH_2Cl_2 (20 mL), successive washings with water (20 mL), a 1% aqueous citric acid solution (2 × 20 mL), and water (20 mL), drying (Na_2SO_4), and removal of the solvent in vacuo left a syrup which was purified by elution from the silica gel column (3 × 20 cm) with CCl_4/EtOAc (4:1): 930 mg of **21** (79% based on uloside **15**, 67% based on ulosyl bromide **4**); colorless syrup; R_f 0.22 in solvent system C; $[\alpha]^{20}_D$ −49.1° (*c* 0.8, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) *mannosyl-H* δ 2.51 (s, 1H), 3.41 (m, 1H), 3.54 (dd, 1H, J = 3.1, 9.1 Hz), 3.72 (m, 2H), 3.90 (dd, 1H, J = 9.1, 9.4 Hz), 4.03 (m, 1H), 4.50 ("s", 1H), 4.52–4.65 (m, 4H), 4.76 (d, 1H, J = 10.8 Hz), 4.89 (d, 1H, J = 11.8 Hz), 7.16–7.38 (m, 15H); *galactosyl-H* δ 1.30, 1.32, 1.43, 1.52 (4 s, 12H), 3.76 (m, 1H), 4.11 (dd, 1H, J = 2.8, 11.2 Hz), 4.19 (dd, 1H, J = 1.9 Hz), 4.21 (m, 1H), 4.31 (dd, 1H, J = 2.4 Hz), 4.57 (dd, 1H, J = 2.4 Hz), 5.54 (d, 1H); ^{13}C NMR (75.5 MHz, $CDCl_3$) *mannosyl-C* δ 68.2, 69.4, 71.3, 73.7, 74.4, 75.4, 75.5, 81.3, 100.5, 128.7–128.9, 138.1, 138.5, 138.6, *galactosyl-C* δ 24.6, 25.2, 26.2, 26.3, 68.1, 69.3, 70.6, 70.9, 71.6, 96.5, 108.9, 109.6; MS (FD) *m/e* 692 (M^+). Anal. Calcd for $C_{39}H_{48}O_{11}$ (692.8): C, 67.61; H, 6.76. Found: C, 67.51; H, 6.83.

Methyl 4-*O*-(3,4,6-Tri-*O*-benzyl-β-D-mannopyranosyl)-2,3-*O*-isopropylidene-α-L-rhamnopyranoside (22). A mixture of methyl 2,3-*O*-isopropylidene-α-L-rhamnopyranoside[30] (525 mg, 2.4 mmol), silver carbonate (2.7 g, 10 mmol), molecular sieves (4 Å, 1.0 g), and CH_2Cl_2 (5 mL) was stirred for 15 min at ambient temperature in the dark with careful exclusion of moisture. A solution of ulosyl bromide **4** (1.02 g, 2 mmol) in CH_2Cl_2 (5 mL) was injected with a syringe, and after being stirred for 3 min, the mixture was filtered through Celite and washed with CH_2Cl_2. The filtrate and washings were evaporated to dryness to yield 1.09 g (84%) of a syrup, consisting of an approximately 6:1 mixture (^{1}H NMR) of uloside **16** and its monohydrate. It was dissolved in 40 mL of CH_2Cl_2/MeOH (1:1) cooled (0 °C), and stirred for 2 h with 350 mg of $NaBH_4$, thereby allowing the mixture to warm to room temperature. Workup by dilution with CH_2Cl_2, successive washing with 1% aqueous citric acid (2 × 30 mL) and water (2 × 30 mL), drying (Na_2SO_4), and removal of the solvent in vacuo left a syrup which was purified by elution from a silica gel column (2 × 20 cm) with CCl_4/EtOAc (3:1): 995 mg of **22** as a colorless syrup (90% based on uloside **16**, 76% for the two steps from **4**); $[\alpha]^{20}_D$ −41 (*c* 1, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$), *mannosyl-H* δ 2.37 (s, 1H), 3.41 (m, 1H), 3.59 (dd, 1H, J = 3.0, 9.4 Hz), 3.72 (m, 2H), 3.90 (dd, 1H, J = 9.4, 9.6 Hz), 4.13 (d, 1H, J = 1.0, 3.0 Hz), 4.53, 4.57, 4.62, 4.65, 4.77, 4.89 (6d, 1H each, J = 10.3, 11.9, 12.2 Hz), 4.86 (d, 1H, J = 1.0 Hz), 7.20–7.39 (m, 15H); *rhamnosyl-H* δ 1.33 (m, 3H), 1.32 (s, 3H), 1.45 (s, 3H), 3.36 (s, 3H), 3.72 (m, 2H), 4.08 (d, 1H, J = 5.5 Hz), 4.19 (dd, 1H, J = 5.5, 6.2 Hz), 4.91 (s, 1H); ^{13}C NMR (75.5 MHz, $CDCl_3$), *mannosyl-C* δ 68.3, 69.0, 71.3, 73.5, 74.3, 75.1, 75.5, 81.8, 97.8, 127.5–138.3; *rhamnosyl-C* δ 17.6, 26.4, 27.8, 54.8, 64.1, 76.1, 78.0, 78.4, 98.4, 109.4; MS (FD) *m/e* 650 (M^+). Anal. Calcd for $C_{37}H_{46}O_{10}$ (650.8): C, 68.28; H, 7.12. Found: C, 68.18; H, 7.03.

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