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Synthesis of ketosyl and ulosonyl phosphonates by Arbuzov-type glycosidation of thiazolylketol acetates[1]

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Abstract

Some members of two novel classes of glycosyl phosphonates (*galacto*, 2-azido-2-deoxy-*galacto*, *gluco*, *manno*) carrying a diethyl phosphonate and a hydroxymethyl (ketosyl derivatives) or carboxymethyl group (ulosonyl derivatives) at the anomeric carbon have been prepared. The synthetic route involves the trimethylsilyl triflate promoted Arbuzov-type coupling between thiazolylketol acetates and triethylphosphite to give thiazolylglycosyl phosphonates in good yields (78-93%). This glycosidation reaction was highly stereoselective giving rise to the α-D-glycosyl phosphonate as single product with the exception of the reaction with the *gluco* derivative which afforded the α- and β-D-anomer in almost equal amount. The phosphono glycosides were converted by the thiazole-to-formyl deblocking protocol (*N*-alkylation, reduction, hydrolysis) into aldehydes that in turn served as common intermediates to ketosyl and ulosonyl diethylphosphonates via reduction or oxidation of the formyl group, respectively. The configuration at the anomeric carbon of all new compounds was assigned by NMR analysis through the hydrogen-phosphorus coupling constant values and HETNOE experiments. The feasibility of access to the free ketosyl and ulosonyl phosphonic acids is demonstrated taking as an example the galactopyranosyl derivatives.

Keywords: Arbuzov reactions; Carbohydrates; Glycosidation; Phosphonic acid and derivatives.

Introduction

The discovery of carbohydrate analogs and mimics that may interfere with carbohydrate processing enzymes and consequently act as competitive inhibitors, constitutes the basis for the development of potential drugs against numerous carbohydrate-based metabolic disorders [1]. Given the widespread role that glycosyl phosphates and their nucleoside diphosphate derivatives, the biological glycosyl donors, play in glycosylation processes [2-4], much attention is currently focused on their stable analogs that may act as competitive inhibitors of glycosyltransferases. For these reasons, various stable glycosylphosphonate analogs of aldose 1-phosphates as shown by types **A** [5] and **B** [6] have been prepared (Figure 1). In the

[1] Dedicated to Professor Alan R. Katritzky on the occasion of his 70th birthday.

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phosphono isosteres **A**, the phosphorus atom is linked to the sugar through a methylene bridge that replaces the chemically and enzymatically susceptible ester linkage of phosphates. In phosphonates **B**, the phosphonic acid group is directly linked to the anomeric carbon of the sugar by a carbon-phosphorus bond. These compounds are non-isosteric but isopolar analogs of glycosyl phosphates [7]. A special type **C** (X = NHAc or OH) of isopolar phosphonic acid analogs of *N*-acetylneuraminic acid, Neu5Ac, and its deaminated derivative, KDN, have been recently reported [8,9]. These compounds are potential sialidase inhibitors since they may interfere with the enzymes that catalyze the hydrolysis of the terminal sialic acids α-D-linked to the glycoproteins, glycolipids, and oligosaccharides. The biological activity is based on the expectation that the phosphonic acid group plays the same role as the carboxylic acid group in providing the negative charge for binding.

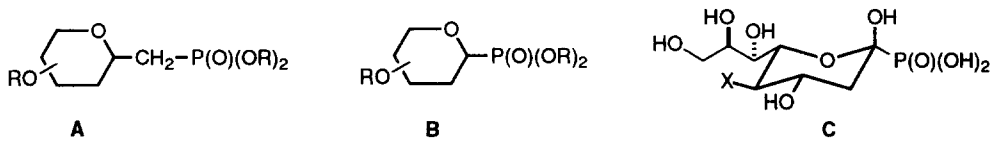
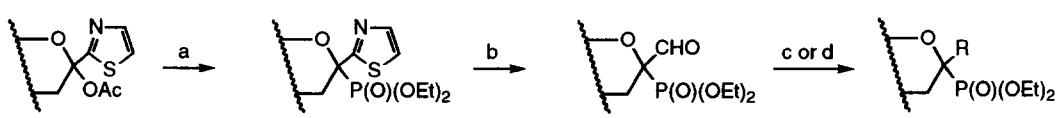


Figure 1. Glycosylphosphonate analogs of glycosylphosphates and sialic acids.

We now report an efficient and general route to the less explored classes of glycosyl phosphonates **4** and **5** (Scheme 1), *i. e.* the *P*-glycoside derivatives of ketoses (ketosyl phosphonates) and ulosonic acids (ulosonyl phosphonates), respectively. An earlier and apparently single example of a compound of type **4** is the isopolar monophosphonate analog of β-D-fructose 2,6-bisphosphate reported by Dessinges and Vasella some years ago [10]. Similarly, the synthesis of a sialyl phosphonate of type **5** has been reported very recently [11,12]. The compound has been converted into the cytidine 5'-monophospho Neu5Ac analog for sialyltransferase mechanistic studies. Our synthesis is based on two key operations. The first involves a highly stereoselective Arbuzov-type glycosidation of the ketose acetates **1** with a phosphite under the same conditions of the Vasella approach to compounds of type **B** [7]. The second consists of the efficient conversion of the thiazole ring into the formyl group (thiazole aldehyde synthesis) [13-15] by a simple and widely experienced protocol. The resulting crude aldehydes **3** were vehiculated to either the alcohols **4** or to the esters **5** by reduction or oxidation of the formyl group, respectively.

Scheme 1

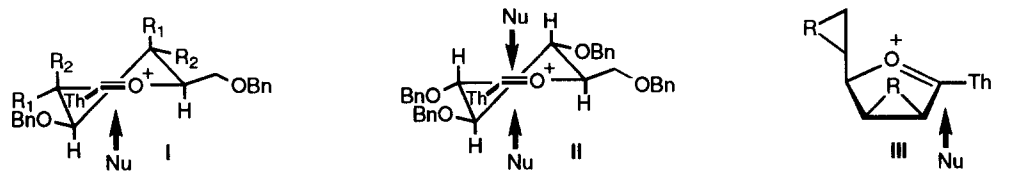


Reagents: (a) $P(OEt)_3$, TMSOTf. (b) i, MeOTf; ii, $NaBH_4$; iii, $CuCl_2$-CuO, H_2O. (c) $NaBH_4$; (d) I_2, KOH, MeOH

The main objective of this work was to probe the influence of the sugar structure on the stereochemical outcome of the glycosylation reaction and establish the scope of the whole synthetic approach to the new glycosyl phosphonates **4** and **5**. Moreover it was intended to test the role of the thiazolylketol acetates **1** as efficient ketosyl donors towards phosphorus nucleophiles such as phosphites. A remarkable high reactivity of compounds **1** under Lewis acid catalysis has been registered in our laboratory towards nitrogen [16], oxygen [17,18], and carbon nucleophiles.[2]

Results and discussion

A model *P*-glycosidation reaction was generated by treatment of the readily available [19] 1-*C*-(2-thiazolyl)-α-D-galactopyranosyl acetate **1a** (Table 1) with 2 equiv. of triethylphosphite and 1 equiv. of trimethylsilyl trifluoromethanesulfonate (TMSOTf) in CH_2Cl_2 at room temperature. The fast reaction that occurred provided after suitable work-up and chromatography of the reaction mixture, the α-linked diethylphosphonate **2a** in good yield. Under the same conditions, the 2-azido-*galacto* derivative **1b** and the α-D-mannopyranosyl isomer **1c** gave the corresponding α-configurated phosphonates **2b** and **2c**. Therefore it appears that for the *galacto* and *mannopyrano* thiazolylketol acetates the α-D-selectivity of the *P*-glycosidation reaction is highly favored. On the other hand β-D-selectivity was observed when the same reaction was performed using tetra-*O*-benzyl-mannopyranosyl acetate as glycosyl donor [7]. The above stereochemical outcome is fully consistent with the expectations based on previous reactions of the same ketol acetates with other nucleophiles [16-18] as well as their reduction with hydride releasing agents [19]. Accordingly, a similar chair-like transition state model [20] can be formulated. This transition state originates from a stereoselective axial attack of the phosphite to the less hindered face of a pyranyl oxycarbenium ion intermediate existing in a half-chair conformation **I** (Figure 2). The same type of reasoning can be applied to the reaction of the α-D-mannofuranosyl derivative **1d** which in fact afforded the α-linked phosphonate **2d** in excellent isolated yield. On the logical assumption that also in this case the substitution proceeds through an oxycarbenium ion intermediate such as **III** (Figure 2), the observed stereochemical outcome is consistent with the phosphite addition to the less hindered side opposite to the adjacent isopropylidene ring.



galacto R_1 = OBn, R_2 = H
manno R_1 = H, R_2 = OBn

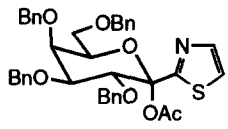
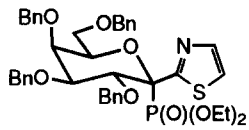
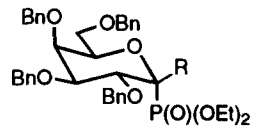
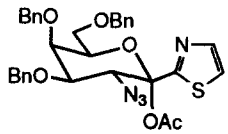
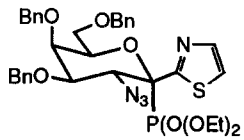
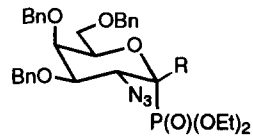
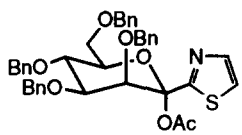
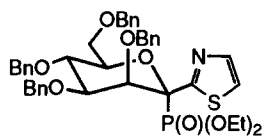
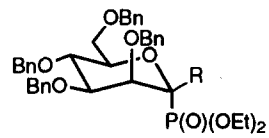
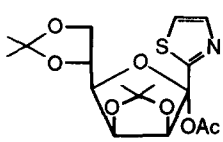
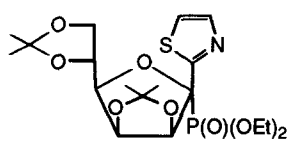
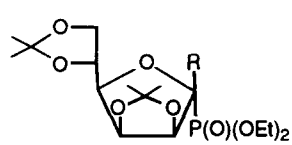
gluco

manno R = O-C(Me)$_2$-O

Figure 2. Stereochemical models for the reaction of thiazolyl ketol acetates **1** with $P(OEt)_3$.

[2] Stereoselective *C*-glycosidation of **1** has been carried out with trimethylsilyl cyanide, allyltrimethylsilane, and furan (Dondoni A, Ferrari C, Marra A, to be published).

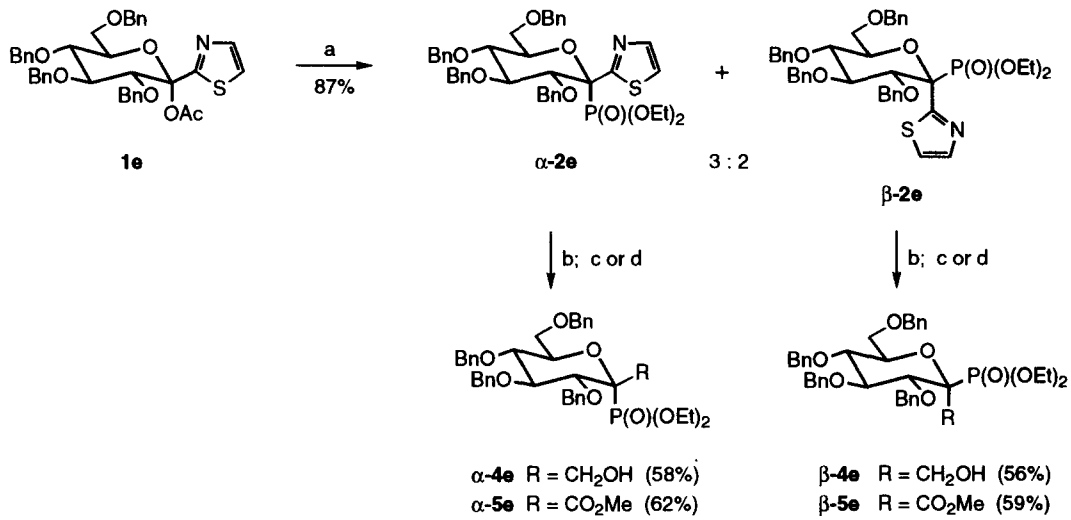
Table 1. Reaction[a] of acetates **1** with $P(OEt)_3$ and conversion[a] of phosphonates **2** into phosphonates **4** and **5**.

Acetate, 1	Phosphonate, 2	Phosphonates, 4 and 5
		
1a	**2a** (84%)	**4a** R = CH_2OH (61%) **5a** R = CO_2Me (62%)
		
1b	**2b** (78%)	**4b** R = CH_2OH (57%) **5b** R = CO_2Me (59%)
		
1c	**2c** (88%)	**4c** X = CH_2OH (50%) **5c** X = CO_2Me (51%)
		
1d	**2d** (93%)	**4d** R = CH_2OH (56%) **5d** R = CO_2Me (54%)

[a] For the reagents and conditions, see Scheme 1 and the Experimental Section. Yields in parentheses refer to isolated products.

With these results at hand, we were not surprised to observe that the *P*-glycosidation of the *gluco* thiazolylketol acetate **1e** (Scheme 2) was poorly selective since under the above reaction conditions it afforded the phosphonate **2e** as a mixture of α- and β-anomers in 3:2 ratio and 87% overall yield. Evidently in this case there are no significant steric differences around the two diastereotopic faces of the oxycarbenium ion **II** (Figure 1) to induce a selective attack of the phosphite to one of them. Attempts to increase the selectivity of this reaction by decreasing the temperature down to -20 °C gave only modest results since the observed α / β ratio was 3:1 (89%). Quite interestingly α-D-selectivity (α / β = 4:1) and high overall yield (94%) were registered by carrying out the reaction at -20 °C in the participating solvent acetonitrile [21].

Scheme 2



Reagents: (a) $P(OEt)_3$, TMSOTf, CH_2Cl_2. (b) i, MeOTf; ii, $NaBH_4$; iii, $CuCl_2$-CuO, H_2O. (c) $NaBH_4$. (d)I_2, KOH, MeOH

All thiazolylketosyl α-phosphonates **2a-d** (Table 1) as well as the individual anomers α-**2e** and β-**2e** (Scheme 2) were subjected to our improved thiazole-to-formyl deblocking protocol [22] consisting of a sequence of three reactions, *i.e. N*-alkylation with methyl triflate (MeOTf), reduction with sodium borohydride ($NaBH_4$), and $CuCl_2$-Cu_2O promoted hydrolysis. The phosphonate group was unaffected under these mild conditions as shown by the high isolated yield (65-80%) of aldosulosyl phosphonates **3a-e** (not shown) at least 90% pure by ^1H NMR analysis. The hitherto unreported unmasking of the formyl in the presence of the phosphonate group enlarges the range of application of the thiazole aldehyde synthesis. Crude compounds **3a-e** were converted without epimerization into ketosyl phosphonates **4a-e** and ulosonyl phosphonates **5a-e**. Guided by our previous work [16-18], the reduction of the formyl group was carried out by the use of NaBH4 and the oxidation-esterification by employing I_2 in methanolic KOH [23]. Compounds **4** and **5** were obtained in satisfactory isolated yields based on the corresponding thiazole derivative **2**.

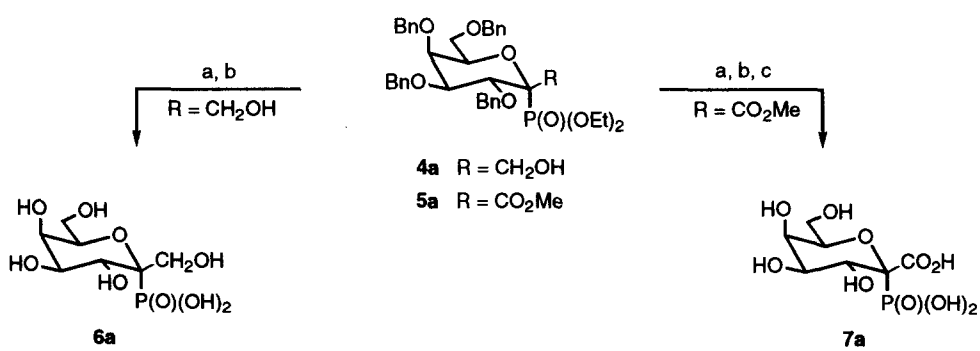
The configuration at the anomeric center of the thiazolyl *P*-glycosides **2** and the products of their functional group transformation, the aldehydes **3**, alcohols **4**, and esters **5** was proved for each set of glycoses by ^1H and ^{31}P-NMR spectroscopy. For all compounds of the *galacto* and 2-azido-*galacto* series **2a-5a** and **2b-5b**, respectively, the α-D-phosphonate linkage was easily established since they uniformly showed $^3J_{P,H\text{-}2}$ or $^3J_{P,H\text{-}3}$ coupling constant values[3] of ~30 Hz. This large value is typical [6,7,24] for a trans-diaxial relationship in pyranosyl phosphonates adopting a $^4C_1$ conformation. On the other hand, in the

[3] It is worth recalling that compounds **2** (hexose derivatives) and **3-5** (heptose derivatives) adopt a different numbering system (see the Experimental Section).

mannopyrano and *mannofurano* series the assignment was a quite difficult task because only one anomer was isolated from the *P*-glycosidation reaction and the observed small $^3J_{P,H}$ coupling constant values (1.8 and 6.8 Hz, respectively) did not allow to distinguish between α- and β-D-phosphonate linkage [7]. The problem was solved by H-P HETNOE experiments. Consistent with the α-D-configuration, irradiation of the phosphorus nucleus[4] of pyranosyl phosphonates **2c-5c** induced significant enhancement of the axial protons of the ring. The same HETNOE experiments carried out with the furanosyl phosphonates **2d-5d** showed an enhancement of the H-2 (or H-3) and H-4 (or H-5) signals.[3] Unexpectedly, also the characterization of the α- and β-anomers in the *gluco* series of phosphonates turned out to present some difficulties. The set of the β-linked isomers β-**2e**–β-**5e** showed $^3J_{P,H-2}$ or $^3J_{P,H-3}$ coupling constant values of ~10 Hz as expected for a cis equatorial-axial relationship [6,7,24]. Consistent with the assigned configuration, HETNOE experiments did not show any enhancement of the H-3 (or H-4) and H-5 (or H-6) protons. Considering the set of α-linked isomers, it was observed that only the ketosyl phosphonate α-**4e** showed the expected large coupling constant value $^3J_{P,H-3}$ (31.2 Hz). On the other hand, $^3J_{P,H-2}$ for the thiazolylketosyl phosphonate α-**2e** was 9.8 Hz and $^3J_{P,H-3}$ for the ulosonyl phosphonate α-**5e** was 8.7 Hz. This discrepancy can be simply explained by considering that α-**4e** exists in a $^4C_1$ conformation whereas compounds α-**2e** and α-**5e** adopt a $^0S_2$ conformation. According to this view, small $J_{2,3}$ and $J_{3,4}$ (or $J_{3,4}$ and $J_{4,5}$) coupling constant values (~4 Hz) were observed for the latter two compounds instead of the expected values (~10 Hz) that are typical of a trans-diaxial disposition of protons in a pyranose ring existing in a $^4C_1$ conformation.

While the protected ketosyl and ulosonyl phosphonates **4** and **5** are *per se* interesting products that may be used as precursors to more elaborated systems, we considered equally important to demonstrate a viable route to fully deprotected phosphonic acids.

Scheme 3



Reagents: (a) $BrSiMe_3$. (b) H_2, Pd/C. (c) NaOH, H_2O

[4] To the best of our knowledge, this particular application of the HETNOE technique has not been previously reported. In our case the heteronuclear NOE experiments could not be performed through irradiation of the diagnostic protons due to the partial overlap of signals in their ^1H NMR spectra. While more details will be reported elsewhere, informations are available on request to P. F.

Crucial to this operation was the hydrolysis of the quite stable diethyl phosphonate group. Following a literature procedure [7], transesterification of the model ketosyl and ulosonyl phosphonate **4a** and **5a** with excess bromotrimethylsilane gave the corresponding trimethylsilyl esters (Scheme 3). Debenzylation of these crude intermediates by hydrogenolysis over Pd-catalyst and saponification of the carboxymethyl group in one case, afforded, after purification by ion-exchange chromatography, the ketosyl phosphonic acid **6a** and the ulosonyl phosphonic acid **7a** in 81 and 85% overall yield, respectively.

Experimental

All moisture-sensitive reactions were performed under a nitrogen atmosphere using oven-dried glassware. All solvents were dried over standard drying agents [25] and freshly distilled prior to use. Commercially available powdered 4 Å molecular sieves (50 μm average particle size) were used without further activation. Flash column chromatography [26] was performed on silica gel 60 (230-400 mesh). Reactions were monitored by TLC on silica gel 60 F_{254} with detection by charring with sulfuric acid. Optical rotations were measured at 20 ± 2 °C in the stated solvent. ^1H (300 MHz), ^{13}C (75 MHz), and ^{31}P (121 MHz) NMR were recorded at r. t. for $CDCl_3$ solutions, unless otherwise specified. Assignments were aided by decoupling and/or homo- and heteronuclear two-dimensional experiments.

Diethyl (2,3,4,6-tetra-*O*-benzyl-1-*C*-(2-thiazolyl)-α-D-galactopyranosyl)phosphonate (2a). A mixture of **1a** (1.33 g, 2.0 mmol), activated 4-Å powdered molecular sieves (1.00 g), triethylphosphite (0.70 mL, 4.0 mmol), and anhydrous CH_2Cl_2 (10 mL) was stirred at room temperature for 10 min and then trimethylsilyl triflate (0.36 mL, 2.0 mmol) was added. The mixture was stirred at room temperature for 15 min, then treated with an excess of Et_3N, diluted with CH_2Cl_2, filtered through Celite, and concentrated. The residue was eluted from a column of silica gel with 5:2 cyclohexane-AcOEt to give **2a** (1.25 g, 84%) as a syrup; $[\alpha]_D$ = +41.5 (*c* 0.7, $CHCl_3$). ^1H NMR: δ 0.97 and 1.16 (2 t, 6 H, *J* = 7.2 Hz, 2 CH_2CH_3), 3.61 (dd, 1 H, $J_{5,6a}$ = 6.0, $J_{6a,6b}$ = 9.6 Hz, H-6a), 3.70 (dd, 1 H, $J_{5,6b}$= 6.3 Hz, H-6b), 3.72-3.78 (m, 1 H, CH_2CH_3), 3.89-3.99 (m, 1 H, CH_2CH_3), 4.02 (dd, 1 H, $J_{3,4}$= 2.7, $J_{4,5}$ = 0.7 Hz, H-4), 4.05-4.15 (m, 2 H, CH_2CH_3), 4.45 (dd, 1 H, $J_{2,3}$ = 9.6, $J_{2,P}$ = 28.8 Hz, H-2), 4.49 and 4.55 (2 d, 2 H, *J* = 12.0 Hz, $PhCH_2$), 4.60 and 4.94 (2 d, 2 H, *J* = 11.9 Hz, $PhCH_2$), 4.70 (dd, 1 H, $J_{2,3}$ = 9.6 Hz, H-3), 4.75 (ddd, 1 H, H-5), 4.79 and 4.84 (d, 2 H, *J* = 11.8 Hz, $PhCH_2$), 4.88 and 5.07 (2 d, 2 H, *J* = 10.7 Hz, $PhCH_2$), 7.20-7.46 (m, 21 H, 4 Ph, Th), 7.80 (d, 1 H, *J* = 3.2 Hz, Th). ^{13}C NMR: δ 16.1 (d, *J* = 5.4 Hz, CH_2CH_3), 16.3 (d, *J* = 5.5 Hz, CH_2CH_3), 63.0 (d, *J* = 7.1 Hz, CH_2CH_3), 63.5 (d, *J* = 6.3 Hz, CH_2CH_3), 69.6 (C-6), 72.7, 73.2, 74.2, and 76.1 (4 $PhCH_2$), 74.1 (C-4), 75.0 (C-5), 80.5 (C-2), 81.0 (C-3), 83.0 (d, *J* = 155.2 Hz, C-1), 119.9, 141.7, and 170.2 (Th), 127.2-128.5 and 138.1-138.8 (4 Ph). ^{31}P NMR: δ 16.7. Anal. Calcd for $C_{41}H_{46}NO_8PS$: C, 66.20; H, 6.23; N, 1.88; S, 4.31. Found: C, 66.38; H, 6.41; N, 2.03; S, 4.47.

Diethyl (2-azido-3,4,6-tri-*O*-benzyl-2-deoxy-1-*C*-(2-thiazolyl)-α-D-galacto-pyranosyl)phosphonate (2b). Ketol acetate **1b** (600 mg, 1.00 mmol) was glycosidated as described for the preparation of **2a**. Column chromatography (5:2 cyclohexane-acetone) of

the residue afforded **2b** (529 mg, 78%) as a syrup; $[\alpha]_D$ = +25.0 (*c* 0.7, $CHCl_3$). ^1H NMR: δ 1.19 and 1.21 (2 t, 6 H, *J* = 7.0 Hz, 2 CH_2CH_3), 3.54 (dd, 1 H, $J_{5,6a}$ = 6.0, $J_{6a,6b}$ = 10.0 Hz, H-6a), 3.66 (dd, 1 H, $J_{5,6b}$ = 6.5 Hz, H-6b), 3.95 (dd, 1 H, $J_{3,4}$ = 2.5, $J_{4,5}$ = 1.0 Hz, H-4), 4.04-4.20 (m, 4 H, 2 CH_2CH_3), 4.45 and 4.52 (2 d, 2 H, *J* = 12.0 Hz, $PhCH_2$), 4.48 (dd, 1 H, $J_{2,3}$ = 10.5, $J_{2,P}$ = 32.5 Hz, H-2), 4.48 (dd, 1 H, H-3), 4.55 and 4.86 (2 d, 2 H, *J* = 11.5 Hz, $PhCH_2$), 4.62 (dddd, 1 H, $J_{5,P}$ = 1.5 Hz, H-5), 4.78 and 4.88 (2 d, 2 H, *J* = 11.0 Hz, $PhCH_2$), 7.22-7.47 (m, 16 H, 3 Ph, Th), 7.80 (d, 1 H, *J* = 3.2 Hz, Th). ^{13}C NMR: δ 16.2 (d, *J* = 4.5 Hz, CH_2CH_3), 16.3 (d, *J* = 5.9 Hz, CH_2CH_3), 63.5 (d, *J* = 7.4 Hz, CH_2CH_3), 63.7 (d, *J* = 7.5 Hz, CH_2CH_3), 64.1 (d, *J* = 3.7 Hz, C-2), 69.5 (C-6), 72.8 (C-4), 73.0, 73.3, and 74.3 (3 $PhCH_2$), 75.3 (C-5), 79.2 (C-3), 82.2 (d, *J* = 156.3 Hz, C-1), 120.3, 141.9, and 169.0 (Th), 127.5-128.4, 138.0, 138.1, and 138.4 (3 Ph). ^{31}P NMR: δ 15.1. Anal. Calcd for $C_{34}H_{39}N_4O_7PS$: C, 60.16; H, 5.79; N, 8.25; S, 4.72. Found: C, 60.34; H, 5.92; N, 8.14; S, 4.38. Prolonged reaction times led to the formation of diethyl phosphoramidate derivatives [27].

Diethyl (2,3,4,6-tetra-*O*-benzyl-1-*C*-(2-thiazolyl)-α-D-mannopyranosyl)phosphonate (2c). Ketol acetate **1c** (665 mg, 1.00 mmol) was glycosidated as described for the preparation of **2a**. Column chromatography (3:1 cyclohexane-AcOEt) of the residue afforded **2c** (654 mg, 88%) as a syrup; $[\alpha]_D$ = -16.5 (*c* 1.2, $CHCl_3$). ^1H NMR ($CDCl_3$): δ 1.17 and 1.25 (2 t, 6 H, *J* = 7.0 Hz, 2 CH_2CH_3), 3.84-3.88 (m, 2 H, 2 H-6), 4.02-4.18 (m, 5 H, 2 CH_2CH_3, H-4), 4.32 and 4.76 (2 d, 2 H, *J* = 10.6 Hz, $PhCH_2$), 4.54 (dd, 1 H, $J_{2,3}$ = 2.5, $J_{3,4}$ = 9.5 Hz, H-3), 4.56 and 4.76 (2 d, 2 H, *J* = 11.5 Hz, $PhCH_2$), 4.61 and 4.92 (2 d, 2 H, *J* = 11.4 Hz, $PhCH_2$), 4.76-4.85 (m, 4 H, H-2, H-5, $PhCH_2$), 6.85-7.42 (m, 21 H, 4 Ph, Th), 7.80 (d, 1 H, *J* = 3.2 Hz, Th). ^1H NMR (C_6D_6): δ 0.97 and 1.08 (2 t, 6 H, *J* = 7.0 Hz, 2 CH_2CH_3), 3.85-4.21 (m, 6 H, 2 CH_2CH_3, 2 H-6), 4.40 (dd, 1 H, $J_{3,4}$ = 9.3, $J_{4,5}$ = 10.0 Hz, H-4), 4.51 and 4.72 (2 d, 2 H, *J* = 12.0 Hz, $PhCH_2$), 4.57 and 4.97 (2 d, 2 H, *J* = 11.5 Hz, $PhCH_2$), 4.62 and 5.01 (2 d, 2 H, *J* = 10.8 Hz, $PhCH_2$), 4.77 (s, 2 H, $PhCH_2$), 5.09 (dd, 1 H, $J_{2,3}$ = 2.6 Hz, H-3), 5.14 (dd, 1 H, $J_{2,P}$ = 1.8 Hz, H-2), 5.39 (dddd, 1 H, $J_{5,6a}$ = 2.8, $J_{5,6b}$ = 4.6, $J_{5,P}$ = 2.3 Hz, H-5), 6.70-7.39 (m, 21 H, 4 Ph, Th), 7.57 (d, 1 H, *J* = 3.2 Hz, Th). ^{13}C NMR: δ 16.2 (d, *J* = 5.2 Hz, CH_2CH_3), 16.4 (d, *J* = 4.8 Hz, CH_2CH_3), 63.6 (d, *J* = 7.9 Hz, CH_2CH_3), 63.9 (d, *J* = 7.1 Hz, CH_2CH_3), 70.3 (C-6), 72.2, 73.5, 74.6, 75.8 (4 $PhCH_2$), 73.8 (C-4), 77.9 (C-5), 78.3 (d, *J* = 18.9 Hz, C-2), 80.3 (C-3), 84.3 (d, *J* = 149.3 Hz, C-1), 119.5, 142.1, and 170.4 (Th), 127.2-128.3 and 138.4-138.7 (4 Ph). ^{31}P NMR: δ 16.5. Anal. Calcd for $C_{41}H_{46}NO_8PS$: C, 66.20; H, 6.23; N, 1.88; S, 4.31. Found: C, 66.53; H, 6.41; N, 1.83; S, 4.18.

Diethyl (2,3:5,6-di-*O*-isopropylidene-1-*C*-(2-thiazolyl)-α-D-mannofuranosyl)phosphonate (2d). A mixture of **1d** (385 mg, 1.00 mmol), activated 4-Å powdered molecular sieves (0.50 g), triethylphosphite (348 μL, 2.0 mmol), and anhydrous CH_2Cl_2 (5 mL) was stirred at room temperature for 10 min, then cooled to 0 °C and treated with trimethylsilyl triflate (181 μL, 1.0 mmol). The mixture was stirred at 0 °C for 30 min, then diluted with Et_3N (0.20 mL) and CH_2Cl_2 (20 mL), filtered through Celite, and concentrated. The residue was eluted from a column of silica gel with 1:1 cyclohexane-AcOEt to give **2d** (430 mg, 93%) as a syrup; $[\alpha]_D$ = -6.1 (*c* 1.0, $CHCl_3$). ^1H NMR: δ 1.13, 1.29, 1.42, and 1.49 (4 s, 12 H, 4 CH_3), 1.28 and 1.37 (2 t, 6 H, *J* = 7.0 Hz, 2 CH_2CH_3), 4.09-4.30 (m, 6 H, 2 CH_2CH_3, 2 H-6), 4.50 (ddd, 1 H, $J_{4,5}$ = 6.8, $J_{5,6a}$ = $J_{5,6b}$ = 5.5 Hz, H-5), 4.73 (ddd, 1 H, $J_{3,4}$ =

4.1, $J_{4,P}$ = 1.0 Hz, H-4), 5.01 (dd, 1 H, $J_{2,3}$ = 5.9 Hz, H-3), 5.44 (dd, 1 H, $J_{2,P}$ = 6.9 Hz, H-2), 7.32 and 7.87 (d, 1 H, J = 3.2 Hz, Th). ^{13}C NMR: δ 16.2 (d, J = 5.6 Hz, 2 CH_2CH_3), 23.9, 24.9, 25.3, and 26.5 (4 CH_3), 63.6 (d, J = 7.9 Hz, CH_2CH_3), 64.3 (d, J = 6.3 Hz, CH_2CH_3), 66.4 (C-6), 73.4 (C-5), 81.6 (C-3), 81.9 (C-4), 83.9 (d, J = 12.7 Hz, C-2), 88.4 (d, J = 165.5 Hz, C-1), 108.9 and 113.3 (2 OCO), 118.7, 142.9, and 166.6 (Th). ^{31}P NMR: δ 15.8. Anal. Calcd for $C_{19}H_{30}NO_8PS$: C, 49.24; H, 6.52; N, 3.02; S, 6.91. Found: C, 49.34; H, 6.71; N, 3.18; S, 6.57.

Diethyl (2,3,4,6-tetra-*O*-benzyl-1-*C*-(2-thiazolyl)-α- and -β-D-glucoyranosyl)phosphonate (α-2e and β-2e). Ketol acetate **1e** (1.33 g, 2.0 mmol) was glycosidated as described for the preparation of **2a**. Column chromatography (6:1 CH_2Cl_2-Et_2O) of the residue afforded first α-**2e** (0.79 g, 53%) as a syrup; $[\alpha]_D$ = +32.1 (*c* 1.0, $CHCl_3$). ^{1}H NMR (600 MHz, $CDCl_3$): δ 1.02 and 1.13 (2 t, 6 H, J = 7.0 Hz, 2 CH_2CH_3), 3.63-3.68 (m, 1 H, CH_2CH_3), 3.70 (dd, 1 H, $J_{3,4}$ = 3.8, $J_{4,5}$ = 9.7 Hz, H-4), 3.77 (dd, 1 H, $J_{5,6a}$ = 4.8, $J_{6a,6b}$ = 11.5 Hz, H-6a), 3.83 (dd, 1 H, $J_{5,6b}$ = 1.9 Hz, H-6b), 3.95-4.14 (m, 3 H, CH_2CH_3), 4.03 (dd, 1 H, $J_{2,3}$ = 4.9 Hz, H-3), 4.22 and 4.34 (2 d, 2 H, J = 11.4 Hz, $PhCH_2$), 4.42 and 4.54 (2 d, 2 H, J = 11.6 Hz, $PhCH_2$), 4.58 (dddd, 1 H, $J_{5,P}$ =1.5 Hz, H-5), 4.62 and 4.71 (2 d, 2 H, J = 12.1 Hz, $PhCH_2$), 4.77 (dd, 1 H, $J_{2,P}$ = 9.8 Hz, H-2), 4.78 and 5.04 (2 d, 2 H, J = 10.9 Hz, $PhCH_2$), 7.02-7.47 (m, 21 H, 4 Ph, Th), 7.78 (d, 1 H, J = 3.2 Hz, Th). ^{13}C NMR: δ 16.2 (d, J = 6.2 Hz, CH_2CH_3), 16.3 (d, J = 6.2 Hz, CH_2CH_3), 63.3 (d, J = 7.2 Hz, 2 CH_2CH_3), 69.6 (C-6), 71.9, 72.2, 73.1, and 74.5 (4 $PhCH_2$), 74.5 (C-5), 77.7 (C-4), 79.1 (C-3), 80.2 (C-2), 83.1 (d, J = 164.7 Hz, C-1), 119.9, 142.2, and 171.0 (Th), 127.3-128.4 and 137.7-138.5 (4 Ph). ^{31}P NMR: δ 16.2. Anal. Calcd for $C_{41}H_{46}NO_8PS$: C, 66.20; H, 6.23; N, 1.88; S, 4.31. Found: C, 66.41; H, 6.44; N, 1.90; S, 4.24.

Eluted second was syrupy β-**2e** (0.50 g, 34%); $[\alpha]_D$ = +112.6 (*c* 0.4, $CHCl_3$). ^{1}H NMR (600 MHz, $CDCl_3$): δ 1.05 and 1.25 (2 t, 6 H, J = 7.0 Hz, 2 CH_2CH_3), 3.76-3.97 (m, 7 H), 4.17-4.35 (m, 2 H, CH_2CH_3), 4.40 (dd, 1 H, $J_{2,3}$ = 9.8, $J_{2,P}$ = 11.0 Hz, H-2), 4.58 and 4.65 (2 d, 2 H, J = 11.9 Hz, $PhCH_2$), 4.60 and 4.81 (2 d, 2 H, J = 10.5 Hz, $PhCH_2$), 4.77 and 4.87 (2 d, 2 H, J = 10.9 Hz, $PhCH_2$), 5.00 and 5.22 (2 d, 2 H, J = 10.6 Hz, $PhCH_2$), 7.15-7.48 (m, 21 H, 4 Ph, Th), 7.87 (d, 1 H, J = 3.2 Hz, Th). ^{13}C NMR: δ 16.0 (d, J = 5.6 Hz, CH_2CH_3), 16.3 (d, J = 5.6 Hz, CH_2CH_3), 63.5 (d, J = 7.2 Hz, CH_2CH_3), 64.8 (d, J = 7.2 Hz, CH_2CH_3), 68.5 (C-6), 73.1, 75.1, 75.5, and 75.8 (4 $PhCH_2$), 74.5 (d, J = 13.5 Hz, C-5), 77.7 (C-4), 80.5 (C-2), 81.8 (d, J = 174.9 Hz, C-1), 83.2 (d, J = 13.5 Hz, C-3), 121.6, 141.7, and 162.2 (Th), 127.9-128.2 and 137.8-138.2 (4 Ph). ^{31}P NMR: δ 16.0. Anal. Calcd for $C_{41}H_{46}NO_8PS$: C, 66.20; H, 6.23; N, 1.88; S, 4.31. Found: C, 66.49; H, 6.35; N, 2.00; S, 4.02.

Diethyl (2,3,4,6-tetra-*O*-benzyl-α-D-*galacto*-heptulopyranosyl)phosphonate (4a). A mixture of **2a** (372 mg, 0.50 mmol), activated 4-Å powdered molecular sieves (0.50 g), and anhydrous CH_3CN (5 mL) was stirred at room temperature for 10 min, then methyl triflate (71 μL, 0.65 mmol) was added. The suspension was stirred at room temperature for 15 min and then concentrated to dryness. The crude *N*-methylthiazolium salt was suspended in MeOH (5 mL), cooled to 0 °C, and treated with $NaBH_4$ (38 mg, 1.00 mmol). The mixture was stirred at room temperature for an additional 10 min, diluted with acetone (5 mL), filtered through Celite, and concentrated. To a solution of the crude thiazolidine in 10:1 CH_3CN-H_2O (5 mL), was added under vigorous stirring CuO (159 mg, 2.00 mmol) and

$CuCl_2 \cdot 2H_2O$ (85 mg, 0.50 mmol). The mixture was stirred for 15 min, filtered through Celite, and concentrated (bath temperature not exceeding 40 °C) to give a brown syrup. The residue was triturated with Et_2O (4 x 5 mL) and the liquid phase was pipetted and filtered through a pad of Florisil (100-200 mesh) to afford a colorless solution. After a further washing of Florisil with AcOEt (5 mL), the organic phase was concentrated to give **3a** (280 mg) as a syrup. ^1H NMR: δ 1.03 and 1.20 (2 t, 6 H, J = 9.5 Hz, 2 CH_2CH_3), 3.56 (dd, 1 H, $J_{6,7a}$ = 6.7, $J_{7a,7b}$ = 9.5 Hz, H-7a), 3.65 (dd, 1 H, $J_{6,7b}$ = 6.1, H-7b), 3.70-3.84 (m, 1 H, CH_2CH_3), 3.94-4.24 (m, 2 H, CH_2CH_3) 3.98 (dd, 1 H, $J_{4,5}$ = 3.1, $J_{5,6}$ = 1.1 Hz, H-5), 4.12 (ddd, 1 H, H-6), 4.24 (dd, 1 H, $J_{3,4}$ = 9.5, $J_{3,P}$ = 29.7 Hz, H-3), 4.42 and 4.51 (2 d, 2 H, J = 12.0 Hz, $PhCH_2$), 4.50-4.55 (m, 2 H, H-4 and H-5), 4.54 and 4.89 (2 d, 2 H, J = 11.5 Hz, $PhCH_2$), 4.72 and 4.94 (2 d, 2 H, J = 10.8 Hz, $PhCH_2$), 7.20-7.40 (m, 20 H, 4 Ph), 9.50 (s, 1 H, H-1). To a solution of the crude aldehyde **3a** in MeOH (4 mL) was added $NaBH_4$ (30 mg, 0.80 mmol). Stirring was continued at room temperature for 10 min, then acetone (2 mL) was added and the mixture was concentrated. The residue was eluted from a column of silica gel with 5:2 cyclohexane-AcOEt to give **4a** (211 mg, 61%) as a syrup; $[\alpha]_D$ = +51.5 (*c* 0.8, $CHCl_3$). ^1H NMR: δ 1.02 and 1.19 (2 t, 6 H, J = 7.0 Hz, 2 CH_2CH_3), 2.25 (d, 1 H, $J_{1,OH}$ = 9.7 Hz, OH), 3.50 (dd, 1 H, $J_{6,7a}$ = 6.5, $J_{7a,7b}$ = 9.7 Hz, H-7a), 3.57 (dd, 1 H, $J_{6,7b}$ = 5.8 Hz, H-7b), 3.72-3.88 (m, 3 H, 2 H-1 and CH_2CH_3), 3.93-4.17 (m, 3 H, CH_2CH_3), 3.98 (d, 1 H, $J_{4,5}$ = 2.6, $J_{5,6}$ = 0.6 Hz, H-5), 4.38 (ddd, 1 H, H-6), 4.43 and 4.48 (2 d, 2 H, J = 11.7 Hz, $PhCH_2$), 4.45 (dd, 1 H, $J_{3,4}$ = 9.7, $J_{3,P}$ = 29.9 Hz, H-3), 4.55 and 4.98 (2 d, 2 H, J = 11.7 Hz, $PhCH_2$), 4.57 (dd, 1 H, H-4), 4.71 and 4.97 (2 d, 2 H, J = 11.0 Hz, $PhCH_2$), 7.20-7.40 (m, 20 H, Ph). ^{13}C NMR: δ 16.2 (d, J = 6.1 Hz, CH_2CH_3), 16.5 (d, J = 4.8 Hz, CH_2CH_3), 62.2 (d, J = 7.3 Hz, CH_2CH_3), 62.4 (d, J = 6.1 Hz, CH_2CH_3), 63.7 (d, J = 8.5 Hz, C-1), 69.3 (C-7), 72.4, 73.2, 74.4, 76.3 (4 $PhCH_2$), 74.1 (C-5), 74.6 (C-6), 75.2 (C-3), 81.8 (d, J = 152.6 Hz, C-2), 81.1 (C-4), 126.9 -128.3 and 137.9-138.8 (4 Ph). ^{31}P NMR: δ 21.6. Anal. Calcd for $C_{39}H_{47}O_9P$: C, 67.81; H, 6.86. Found: C, 67.94; H, 7.00.

Diethyl (2-azido-3,4,6-tri-*O*-benzyl-2-deoxy-α-D-*galacto*-heptulopyranosyl)-phosphonate (4b). Thiazolylketoside **2b** (339 mg, 0.50 mmol) was treated as described for the preparation of **3a** to give **3b** (250 mg) as a syrup. ^1H NMR: δ 1.23 and 1.32 (2 t, 6 H, J = 7.0 Hz, 2 CH_2CH_3), 3.49 (dd, 1 H, $J_{6,7a}$ = 6.0, $J_{7a,7b}$ = 10.0 Hz, H-7a), 3.61 (dd, 1 H, $J_{6,7b}$= 6.0 Hz, H-7b), 3.90 (dd, 1 H, $J_{4,5}$ = 2.5, $J_{5,6}$ = 0.8 Hz, H-5), 4.15-4.27 (m, 4 H, 2 CH_2CH_3), 4.18 (dd, 1 H, $J_{3,4}$ = 10.5, $J_{3,P}$ = 29.5 Hz, H-3), 4.31 (dd, 1 H, H-4), 4.42 and 4.48 (2 d, 2 H, J = 12.0 Hz, $PhCH_2$), 4.43 (dddd, 1 H, $J_{6,P}$ = 1.0 Hz, H-6), 4.50 and 4.86 (2 d, 2 H, J = 11.5 Hz, $PhCH_2$), 4.74 and 4.83 (2 d, 2 H, J = 11.0 Hz, $PhCH_2$), 7.20-7.45 (m, 15 H, 3 Ph), 9.50 (d, 1 H, $J_{1,P}$ = 1.0 Hz, H-1). Crude aldehyde **3b** was reduced as described for the preparation of **4a**. Column chromatography (5:2 cyclohexane-acetone) of the residue afforded **4b** (178 mg, 57%) as a syrup; $[\alpha]_D$ = +27.7 (*c* 0.5, $CHCl_3$). ^1H NMR: δ 1.22 and 1.32 (2 t, 6 H, J = 7.0 Hz, 2 CH_2CH_3), 3.47 (dd, 1 H, $J_{6,7a}$ = 6.5, $J_{7a,7b}$ = 9.5 Hz, H-7a), 3.54 (dd, 1 H, $J_{6,7b}$ = 6.0 Hz, H-7b), 3.76 (dd, 1 H, $J_{1a,1b}$ = 12.0, $J_{1a,P}$ = 3.5 Hz, H-1a), 3.84 (dd, 1 H, $J_{1b,P}$ = 4.2 Hz, H-1b), 3.95 (dd, 1 H, $J_{4,5}$ = 2.5, $J_{5,6}$ = 1.2 Hz, H-5), 4.02-4.24 (m, 5 H, 2 CH_2CH_3 and OH), 4.32 (dddd, 1 H, $J_{6,P}$ = 1.8 Hz, H-6), 4.42 and 4.47 (2 d, 2 H, J = 12.0 Hz, $PhCH_2$), 4.44 (dd, 1 H, $J_{3,4}$ = 10.5 Hz, H-4), 4.50 (dd, 1 H, $J_{3,P}$ = 32.0 Hz, H-3), 4.49 and 4.90 (2 d, 2 H, J = 11.5 Hz, $PhCH_2$), 4.74 and 4.79 (2 d, 2 H, J = 11.5 Hz, $PhCH_2$), 7.20-7.40 (m, 15 H, 3 Ph).

^{13}C NMR: δ 16.4 (d, J = 5.0 Hz, 2 CH_2CH_3), 58.3 (d, J = 3.9 Hz, C-3), 62.5 (d, J = 7.3 Hz, $POCH_2CH_3$), 62.8 (d, J = 7.6 Hz, CH_2CH_3), 63.7 (d, J = 7.7 Hz, C-1), 69.2 (C-7), 72.3, 73.3, and 74.5 (3 $PhCH_2$), 72.8 (C-5), 74.8 (C-6), 79.4 (C-4), 81.0 (d, J = 153.8 Hz, C-2), 127.6-128.4, 137.7, and 138.4 (3 Ph). ^{31}P NMR: δ 20.3. Anal. Calcd for $C_{32}H_{40}N_3O_8P$: C, 61.43; H, 6.44; N, 6.72. Found: C, 61.50; H, 6.64; N, 6.54.

Diethyl (2,3,4,6-tetra-*O*-benzyl-α-D-*manno*-heptulopyranosyl)phosphonate (4c). Thiazolylketoside **2c** (372 mg, 0.50 mmol) was treated as described for the preparation of **3a** to give **3c** (220 mg) as a syrup. ^{1}H NMR: δ 1.23 and 1.29 (2 t, 6 H, J = 7.0 Hz, 2 CH_2CH_3), 3.78 (d, 2 H, $J_{7a,7b}$ = 3.5 Hz, 2 H-7), 3.89-4.26 (m, 5 H, 2 CH_2CH_3, H-5), 4.32 (dd, 1 H, $J_{3,4}$ = 2.6, $J_{4,5}$ = 8.7 Hz, H-4), 4.50 (dd, 1 H, $J_{3,P}$ = 2.6 Hz, H-3), 4.52 and 4.65 (2 d, 2 H, J = 12.1 Hz, $PhCH_2$), 4.56 and 4.84 (2 d, 2 H, J = 11.2 Hz, $PhCH_2$), 4.58 (m, H-6), 4.57 and 4.92 (2 d, 2 H, J = 11.2 Hz, $PhCH_2$), 4.75 and 4.80 (2 d, 2 H, J = 12.1 Hz, $PhCH_2$), 7.20-7.40 (m, 20 H, 4 Ph), 9.30 (s, 1 H, H-1). Crude aldehyde **3c** was reduced as described for the preparation of **4a**. Column chromatography (3:1 cyclohexane-AcOEt) of the residue afforded **4c** (173 mg, 50%) as a syrup; $[\alpha]_D$ = +17.6 (*c* 0.9, $CHCl_3$). ^{1}H NMR: δ 1.24 and 1.28 (2 t, 6 H, J = 7.0 Hz, 2 CH_2CH_3), 3.20 (dd, 1 H, $J_{1a,OH}$ = 10.3, $J_{1b,OH}$ = 2.9 Hz, OH), 3.64 (dd, 1 H, $J_{6,7a}$ = 5.2, $J_{7a,7b}$ = 11.3 Hz, H-7a), 3.70 (dd, 1 H, $J_{6,7b}$ = 2.2 Hz, H-7b), 3.87 (ddd, 1 H, $J_{1a,1b}$ = $J_{1a,P}$ = 11.5 Hz, H-1a), 3.91 (dd, 1 H, $J_{4,5}$ = $J_{5,6}$ = 8.9 Hz, H-5), 3.94 (ddd, 1 H, $J_{1b,P}$ = 21.0 Hz, H-1b), 4.11-4.23 (m, 5 H, 2 CH_2CH_3 and H-6), 4.27 (dd, 1 H, $J_{3,P}$ = $J_{3,4}$ = 2.2 Hz, H-3), 4.41 (dd, 1 H, H-4), 4.48 and 4.58 (2 d, 2 H, J = 11.8 Hz, $PhCH_2$), 4.55 and 4.86 (2 d, 2 H, J = 11.1 Hz, $PhCH_2$), 4.77 and 4.95 (2 d, 2 H, J = 11.0 Hz, $PhCH_2$), 4.77 (s, 2 H, $PhCH_2$), 7.20-7.45 (m, 20 H, 4 Ph). ^{13}C NMR: δ 16.4 (d, J = 5.3 Hz, 2 CH_2CH_3), 62.9 (d, J = 6.7 Hz, CH_2CH_3), 63.3 (d, J = 6.7 Hz, CH_2CH_3), 63.8 (C-1), 70.1 (C-7), 72.6, 73.2, 74.5, and 75.5 (4 $PhCH_2$), 74.8 (C-5), 75.7 (d, J = 21.3 Hz, C-3), 77.0 (C-6), 80.8 (d, J = 144.3 Hz, C-2), 80.9 (C-4), 127.3-128.4 and 138.5 (4 Ph). ^{31}P NMR: δ 23.9. Anal. Calcd for $C_{39}H_{47}O_9P$: C, 67.81; H, 6.86. Found: C, 67.56; H, 6.89.

Diethyl (2,3:5,6-di-*O*-isopropylidene-α-D-*manno*-heptulofuranosyl)phosphonate (4d). Thiazolylketoside **2d** (232 mg, 0.50 mmol) was treated as described for the preparation of **3a** to give **3d** (150 mg) as a syrup. ^{1}H NMR selected data: δ 4.96 (dd, 1 H, $J_{3,4}$ = 5.9, $J_{4,5}$ = 3.5 Hz, H-4), 5.40 (dd, 1 H, $J_{3,P}$ = 7.6 Hz, H-3), 9.45 (s, 1 H, H-1). Crude aldehyde **3d** was reduced as described for the preparation of **4a**. Column chromatography (1:1 cyclohexane-AcOEt) of the residue afforded **4d** (115 mg, 56%) as a syrup; $[\alpha]_D$ = 15.4 (*c* 0.9, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.36, 1.37, 1.44, and 1.54 (4 s, 12 H, 4 CH_3), 1.38 (t, 6 H, J = 7.0 Hz, 2 CH_2CH_3), 2.76 (dd, 1 H, $J_{1a,OH}$ = 6.0, $J_{1b,OH}$ = 8.0 Hz, OH), 3.85-4.02 and 4.18-4.28 (2 m, 6 H, 2 H-1 and 2 CH_2CH_3), 4.33 (dd, 1 H, $J_{4,5}$ = 4.0, $J_{5,6}$ = 7.3 Hz, H-5), 4.38 (ddd, 1 H, H-6), 4.93 (dd, 1 H, $J_{3,4}$ = 6.0 Hz, H-4), 5.13 (dd, 1 H, $J_{3,P}$ = 6.0 Hz, H-3). ^{13}C NMR: δ 16.4 (d, J = 4.9 Hz, CH_2CH_3), 16.5 (d, J = 4.8 Hz, CH_2CH_3), 23.8, 25.2, 25.4, and 26.8 (4 CH_3), 62.6 (C-1 and CH_2CH_3), 63.5 (d, J = 7.3 Hz, CH_2CH_3), 66.8 (C-7), 73.3 (C-5), 81.5 (C-4), 81.7 (C-6), 83.0 (d, J = 15.8 Hz, C-3), 85.2 (d, J = 157.5 Hz, C-2), 109.2 and 113.2 (2 OCO). ^{31}P NMR: δ 22.2. Anal. Calcd for $C_{17}H_{31}O_9P$: C, 49.75; H, 7.61. Found: C, 49.53; H, 7.80

Diethyl (2,3,4,6-tetra-*O*-benzyl-α-D-*gluco*-heptulopyranosyl)phosphonate (α-4e). Thiazolylketoside **α-2e** (372 mg, 0.50 mmol) was treated as described for the

preparation of **3a** to give α-**3e** (270 mg) as a syrup. ^{1}H NMR: δ 1.15 and 1.25 (2 t, 6 H, J = 7.0 Hz, 2 CH_2CH_3), 3.54 (dd, 1 H, $J_{4,5}$ = 3.0, $J_{5,6}$ = 10.2 Hz, H-5), 3.66 (dd, 1 H, $J_{6,7a}$ = 5.4, $J_{7a,7b}$ = 11.5 Hz, H-7a), 3.76 (dd, 1 H, $J_{6,7b}$ = 2.0 Hz, H-7b), 3.88 (ddd, 1 H, $J_{3,4}$ = 4.3, $J_{4,P}$ = 3.4 Hz, H-4), 3.96-4.20 (m, 4 H, 2 CH_2CH_3), 4.25 and 4.41 (2 d, 2 H, J = 11.4 Hz, PhCH_2), 4.26 and 4.48 (2 d, 2 H, J = 12.0 Hz, PhCH_2), 4.29 (dd, 1 H, $J_{3,P}$ = 8.8 Hz, H-3), 4.56 and 4.64 (2 d, 2 H, J = 12.0 Hz, PhCH_2), 4.71 and 4.82 (2 d, 2 H, J = 11.4 Hz, PhCH_2), 7.10-7.45 (m, 20 H, 4 Ph), 9.81 (s, 1 H, H-1). Crude aldehyde α-**3e** was reduced as described for the preparation of **4a**. Column chromatography (5:2 cyclohexane-AcOEt) of the residue afforded α-**4e** (200 mg, 58%) as a syrup; $[\alpha]_D$ = +50.2 (c 0.6, $CHCl_3$). ^{1}H NMR: δ 1.10 and 1.29 (2 t, 6 H, J = 7.0 Hz, 2 CH_2CH_3), 2.47 (d, 1 H, J = 10.2 Hz, OH), 3.56 (dd, 1 H, $J_{4,5}$ = $J_{5,6}$ = 9.7 Hz, H-5), 3.69 (d, 2 H, $J_{6,7}$ = 3.0 Hz, 2 H-7), 3.78 (dd, 1 H, $J_{1a,1b}$ = 11.8, $J_{1a,P}$ = 3.8 Hz, H-1a), 3.90 (d, 1 H, $J_{1b,P}$ = 4.5 Hz, H-1b), 3.80-4.18 (m, 4 H, 2 CH_2CH_3), 4.03 (dd, 1 H, $J_{3,P}$ = 31.2, $J_{3,4}$ = 9.6 Hz, H-3), 4.22 (ddt, 1 H, $J_{6,P}$ = 1.5 Hz, H-6), 4.47 and 4.55 (2 d, 2 H, J = 12.0 Hz, PhCH_2), 4.57 and 4.93 (2 d, 2 H, J = 11.0 Hz, PhCH_2), 4.59 (dd, 1 H, H-4), 4.73 and 4.85 (2 d, 2 H, J = 10.8 Hz, PhCH_2), 4.90 and 4.95 (2 d, 2 H, J = 11.4 Hz, PhCH_2), 7.20-7.40 (m, 20 H, 4 Ph). ^{13}C NMR: δ 16.1 (d, J = 5.6 Hz, CH_2CH_3), 16.4 (d, J = 5.5 Hz, CH_2CH_3), 62.1 (d, J = 6.4 Hz, CH_2CH_3), 62.2 (d, J = 6.3 Hz, CH_2CH_3), 63.3 (d, J = 7.8 Hz, C-1), 69.1 (C-7), 73.1, 74.4, 75.2, and 75.9 (4 PhCH_2), 75.6 (C-6), 77.9 (C-5), 78.5 (C-3), 81.2 (d, J = 151.2 Hz, C-2), 83.1 (C-4), 127.3-128.2 and 137.9-138.6 (4 Ph). ^{31}P NMR: δ 21.8. Anal. Calcd for $C_{39}H_{47}O_9P$: C, 67.81; H, 6.86. Found: C, 67.69; H, 6.82.

Diethyl (2,3,4,6-tetra-*O*-benzyl-β-D-*gluco*-heptulopyranosyl)phosphonate (β-4e). Thiazolylketoside β-**2e** (372 mg, 0.50 mmol) was treated as described for the preparation of **3a** to give β-**3e** (270 mg) as a syrup. ^{1}H NMR: δ 1.20 and 1.27 (2 t, 6 H, J = 7.0 Hz, 2 CH_2CH_3), 3.58 (dd, 1 H, $J_{3,4}$ = $J_{4,5}$ = 9.8 Hz, H-4), 3.71 (dd, 1 H, $J_{6,7a}$ = 4.0, $J_{7a,7b}$ = 10.8 Hz, H-7a), 3.72 (dd, 1 H, $J_{5,6}$ = 9.9 Hz, H-5), 3.75 (dd, 1 H, $J_{6,7b}$ = 2.2 Hz, H-7b), 3.93 (dddd, 1 H, $J_{6,P}$ = 2.7 Hz, H-6), 4.02-4.30 (m, 4 H, 2 CH_2CH3), 4.35 (dd, 1 H, $J_{3,P}$ = 13.8 Hz, H-3), 4.52 and 4.58 (2 d, 2 H, J = 11.7 Hz, PhCH_2), 4.60 and 4.81 (2 d, 2 H, J = 11.0 Hz, PhCH_2), 4.57 (dd, 1 H, $J_{5,6}$ = 9.7 Hz, H-5), 4.83 (s, 2 H, PhCH_2), 4.98 and 5.11 (2 d, 2 H, J = 10.8 Hz, PhCH_2), 7.15-7.41 (m, 20 H, 4 Ph), 10.08 (s, 1 H, H-1). Crude aldehyde β-**3e** was reduced as described for the preparation of **4a**. Column chromatography (1:1 cyclohexane-AcOEt) of the residue afforded β-**4e** (194 mg, 56%) as a syrup; $[\alpha]_D$ = +39.0 (c 1.2, $CHCl_3$). ^{1}H NMR: δ 1.19 and 1.25 (2 t, 6 H, J = 7.0 Hz, 2 CH_2CH_3), 2.84 (dd, 1 H, $J_{1a,OH}$ = $J_{1b,OH}$ = 6.0 Hz, OH), 3.72 (dd, 1 H, $J_{3,4}$ = $J_{3,P}$ = 9.5 Hz, H-3), 3.73-3.83 (m, 3 H, 2 H-7 and H-6), 3.89 (dd, 1 H, $J_{4,5}$ = 9.5 Hz, H-4), 4.06-4.26 (m, 7 H, 2 CH_2CH_3, H-5, 2 H-1), 4.51 and 4.57 (2 d, 2 H, J = 11.7 Hz, PhCH_2), 4.64 and 4.89 (2 d, 2 H, J = 11.0 Hz, PhCH_2), 4.84 (s, 2 H, PhCH_2), 7.40-7.65 (m, 20 H, 4 Ph). ^{13}C NMR: δ 16.3 (2 CH_2CH_3), 59.0 (C-1), 63.2 (d, J = 7.1 Hz, CH_2CH_3), 63.9 (d, J = 6.4 Hz, CH_2CH_3), 68.7 (C-7), 73.0 (d, J = 13.5 Hz, C-6), 73.1, 74.9, and 75.7 (4 PhCH_2), 77.8 (C-5), 79.1 (d, J = 170.3 Hz, C-2), 84.3 (d, J = 13.4 Hz, C-4), 126.8-128.3, 137.9, 138.0, 138.1, and 138.3 (4 Ph). ^{31}P NMR: δ 22.2. Anal. Calcd for $C_{39}H_{47}O_9P$: C, 67.81; H, 6.86. Found: C, 68.14; H, 6.97.

Diethyl (methyl 2,3,4,6-tetra-*O*-benzyl-α-D-*galacto*-heptulopyranosylonate)-phosphonate (5a). Thiazolylketoside **2a** (372 mg, 0.50 mmol) was converted into the aldehyde **3a** as described for the preparation of **4a**. To a vigorously stirred solution of crude

aldehyde **3a** in 1:1 MeOH-Et_2O (5 mL) were added, dropwise and simultaneously, a 1 M solution of KOH in MeOH and a 0.5 M solution of I_2 in MeOH until the intermediate methyl hemiacetals formed *in situ* had disappeared (TLC analysis), then the mixture was neutralized with AcOH and concentrated. The crude methyl ester was diluted with CH_2Cl_2, washed with aqueous 10% $Na_2S_2O_3 \cdot 5H_2O$, dried (Na_2SO_4), and concentrated. The residue was eluted from a column of silica gel with 3:1 cyclohexane-AcOEt to give **5a** (223 mg, 62%) as a syrup; $[\alpha]_D$ = +28.1 (*c* 0.8, $CHCl_3$). ^1H NMR: δ 1.05 and 1.20 (2 t, 6 H, J = 7.5 Hz, 2 CH_2CH_3), 3.57 (dd, 1 H, $J_{6,7a}$ = 7.2, $J_{7a,7b}$ = 9.4 Hz, H-7a), 3.63 (dd, 1 H, $J_{6,7b}$ = 5.8 Hz, H-7b), 3.79 (s, 3 H, OCH_3), 3.80-3.89 (m, 1 H, CH_2CH_3), 3.94-4.23 (m, 3 H, CH_2CH_3) 3.95 (dd, 1 H, $J_{4,5}$ = 2.8, $J_{5,6}$ = 1.0 Hz, H-5), 4.31 (dddd, 1 H, $J_{6,P}$ = 1.8 Hz, H-6), 4.44 and 4.49 (2 d, 2 H, J = 12.0 Hz, $PhCH_2$), 4.46 (dd, 1 H, $J_{3,4}$ = 9.6, $J_{3,P}$ = 26.5 Hz, H-3), 4.53 (dd, 1 H, H-4), 4.59-4.92 (2 d, 2 H, J = 11.6 Hz, $PhCH_2$), 4.76 (s, 2 H , $PhCH_2$), 4.97 (s, 2 H , $PhCH_2$), 7.20-7.41 (m, 20 H, 4 Ph). ^{13}C NMR: δ 16.2 (d, J = 7.3 Hz, CH_2CH_3), 16.5 (d, J = 6.1 Hz, CH_2CH_3), 52.9 (OCH_3), 63.3 (d, J = 7.3 Hz, 2 CH_2CH_3), 68.7 (C-7), 72.6, 73.2, 74.9, 75.9 (4 $PhCH_2$), 73.2 (C-5), 74.4 (C-6), 77.6 (C-3), 80.9 (C-4), 83.2 (d, J = 145.2 Hz, C-2), 127.2-128.3 and 138.0-138.7 (4 Ph), 168.4 (C-1). ^{31}P NMR: δ 16.8. Anal. Calcd for $C_{40}H_{47}O_{10}P$: C, 66.84; H, 6.59. Found: C, 66.59 H, 6.57.

Diethyl (methyl 2-azido-3,4,6-tri-*O*-benzyl-2-deoxy-α-D-*galacto*-heptulopyranosylonate)phosphonate (5b). Thiazolylketoside **2b** (339 mg, 0.50 mmol) was treated as described for the preparation of **5a**. Column chromatography (5:2 cyclohexane-AcOEt) of the residue afforded **5b** (193 mg, 59%) as a syrup; $[\alpha]_D$ = +13.5 (*c* 0.9, $CHCl_3$). ^1H NMR: δ 1.25 and 1.31 (2 t, 6 H, J = 7.0 Hz, 2 CH_2CH_3), 3.52 (dd, 1 H, $J_{6,7a}$ = 7.0, $J_{7a,7b}$ = 9.3 Hz, H-7a), 3.59 (dd, 1 H, $J_{6,7b}$ = 5.7 Hz, H-7b), 3.83 (s, 3 H, OCH_3), 3.93 (dd, 1 H, $J_{4,5}$ = 2.8, $J_{5,6}$ = 0.8 Hz, H-5), 4.09-4.28 (m, 5 H, 2 CH_2CH_3 and H-6), 4.28 (dd, 1 H, $J_{3,4}$ = 10.3 Hz, H-4), 4.39 (dd, 1 H, $J_{3,P}$ = 29.2 Hz, H-3), 4.42 and 4.47 (2 d, 2 H, J = 12.0 Hz, $PhCH_2$), 4.53 and 4.87 (2 d, 2 H, J = 11.4 Hz, $PhCH_2$), 4.74 and 4.81 (2 d, 2 H, J = 11.3 Hz, $PhCH_2$), 7.25-7.47 (m, 15 H, 3 Ph). ^{13}C NMR: δ 16.2 (d, J = 6.2 Hz, CH_2CH_3), 16.4 (d, J = 5.6 Hz, CH_2CH_3), 53.3 (OCH_3), 61.9 (C-3), 63.5 (d, J = 7.0 Hz, CH_2CH_3), 63.8 (d, J = 7.3 Hz, CH_2CH_3), 68.6 (C-7), 72.3 (C-5), 72.9, 73.3, and 74.6 (3 $PhCH_2$), 75.1 (C-6), 78.8 (C-4), 82.2 (d, J = 145.0 Hz, C-2), 127.6-128.4, 137.8, and 138.0 (3 Ph), 167.9 (C-1). ^{31}P NMR: δ 15.4. Anal. Calcd for $C_{33}H_{40}N_3O_9P$: C, 60.64; H, 6.17; N, 6.43. Found: C, 60.45; H, 6.26; N, 6.54.

Diethyl (methyl 2,3,4,6-tetra-*O*-benzyl-α-D-*manno*-heptulopyranosylonate)-phosphonate (5c). Thiazolylketoside **2c** (372 mg, 0.50 mmol) was treated as described for the preparation of **5a**. Column chromatography (3:1 cyclohexane-AcOEt) of the residue afforded **5c** (183 mg, 51%) as a syrup; $[\alpha]_D$ = +5.4 (*c* 0.9, $CHCl_3$). ^1H NMR: δ 1.28 and 1.34 (2 t, 6 H, J = 7.0 Hz, 2 CH_2CH_3), 3.69 (s, 3 H, OCH_3), 3.79 (dd, 1 H, $J_{6,7a}$ = 2.4, $J_{7a,7b}$ = 11.6 Hz, H-7a), 3.85 (dd, 1 H, $J_{6,7b}$ = 4.3 Hz, H-7b), 4.02-4.26 (m, 5 H, 2 CH_2CH_3 and H-5), 4.29 (dd, 1 H, $J_{3,4}$ = 2.4, $J_{4,5}$ = 9.2 Hz, H-4), 4.57-4.63 (m, 2 H, H-3 and H-6), 4.59 and 4.79 (2 d, 2 H, J = 11.6 Hz, $PhCH_2$), 4.59 and 5.06 (2 d, 2 H, J = 11.0 Hz, $PhCH_2$), 4.63 and 4.89 (2 d, 2 H, J = 11.0 Hz, $PhCH_2$), 4.83 (s, 2 H, $PhCH_2$), 7.20-7.45 (m, 20 H, 4 Ph). ^1H NMR (C_6D_6) selected data: δ 3.86 (dd, 1 H, $J_{6,7a}$ = 2.0, $J_{7a,7b}$ = 11.5 Hz, H-7a), 3.92 (dd, 1 H, $J_{6,7b}$ = 4.8 Hz, H-7b), 4.40 (dd, 1 H, $J_{4,5}$ = 9.5, $J_{5,6}$ = 10.0 Hz, H-5), 4.76 (dd, 1 H, $J_{3,4}$ = 2.6 Hz, H-4), 4.87 (dd, 1 H, $J_{3,P}$ = 2.2 Hz, H-3), 5.23 (dddd, 1 H, $J_{6,P}$ = 2.7 Hz, H-6). ^{13}C NMR: δ

16.3 (d, J = 5.3 Hz, CH_2CH_3), 16.5 (d, J = 4.1 Hz, CH_2CH_3), 52.6 (OCH_3), 63.5 (d, J = 8.0 Hz, CH_2CH_3), 64.5 (d, J = 6.7 Hz, CH_2CH_3), 69.4 (C-7), 72.7, 73.3, 74.7, and 75.7 (4 $PhCH_2$), 73.9 (C-5), 77.4 (C-6), 77.8 (d, J = 14.6 Hz, C-3), 80.8 (C-4), 84.6 (d, J = 144.7 Hz, C-2), 127.1-128.4, 138.4, 138.6, and 138.9 (4 Ph), 167.5 (C-1). ^{31}P NMR: δ 14.9. Anal. Calcd for $C_{40}H_{47}O_{10}P$: C, 66.84; H, 6.59. Found: C, 67.11; H, 6.78

Diethyl (methyl 2,3:5,6-di-*O*-isopropylidene-α-D-*manno*-heptulofuranosylonate)phosphonate (5d). Thiazolylketoside **2d** (232 mg, 0.50 mmol) was treated as described for the preparation of **5a**. Column chromatography (1:1 cyclohexane-AcOEt) of the residue afforded **5d** (118 mg, 54%) as a syrup; $[\alpha]_D$ = +31.9 (*c* 0.9, $CHCl_3$). ^1H NMR (500 MHz, $CDCl_3$): δ 1.34, 1.38, 1.42, and 1.45 (4 s, 12 H, 4 CH_3), 1.33 and 1.37 (2 t, 6 H, J = 7.0 Hz, 2 CH_2CH_3), 3.82 (s, 3 H, OCH_3), 4.13-4.18 (m, 2 H, 2 H-7), 4.19-4.28 (m, 4 H, 2 CH_2CH_3), 4.46-4.50 (m, 2 H, H-5 and H-6), 4.91 (dd, 1 H, $J_{4,5}$ = 3.0, $J_{3,4}$= 6.0 Hz, H-4), 5.25 (dd, 1 H, $J_{3,P}$ = 7.5 Hz, H-3). ^{13}C NMR: δ 16.2 (2 CH_2CH_3), 24.3, 25.2, 25.4, and 26.7 (4 CH_3), 52.4 (OCH_3), 63.4 (d, J = 7.9 Hz, CH_2CH_3), 64.4 (d, J = 6.3 Hz, CH_2CH_3), 66.7 (C-7), 73.1 (C-5), 80.7 (C-4), 81.9 (C-6), 83.8 (d, J = 9.5 Hz, C-3), 89.1 (d, J = 159.0 Hz, C-2), 109.1 and 113.6 (2 OCO), 165.9 (d, J = 6.0 Hz, C-1). ^{31}P NMR: δ 15.5. Anal. Calcd for $C_{18}H_{31}O_{10}P$: C, 49.31; H, 7.13. Found: C, 49.60; H, 7.27.

Diethyl (methyl 2,3,4,6-tetra-*O*-benzyl-α-D-*gluco*-heptulopyranosylonate)-phosphonate (α-5e). Thiazolylketoside **2b** (372 mg, 0.50 mmol) was treated as described for the preparation of **5a**. Column chromatography (5:2 cyclohexane-AcOEt) of the residue afforded **α-5e** (223 mg, 62%) as a syrup; $[\alpha]_D$ = +31.8 (*c* 0.7, $CHCl_3$). ^1H NMR: δ 1.16 and 1.21 (2 t, 6 H, J = 7.0 Hz, 2 CH_2CH_3), 3.67 (dd, 1 H, $J_{4,5}$ = 4.0, $J_{5,6}$ = 10.4 Hz, H-5), 3.68 (s, 3 H, OCH_3), 3.73 (dd, 1 H, $J_{6,7a}$ = 4.7, $J_{7a,7b}$ = 11.6 Hz, H-7a), 3.78 (dd, 1 H, $J_{6,7b}$ = 2.4 Hz, H-7b), 3.93 (ddd, 1 H, $J_{4,P}$ = 3.0, $J_{3,4}$ = 4.5 Hz, H-4), 4.00-4.21 (m, 4 H, 2 CH_2CH_3), 4.36 (ddd, 1 H, H-6), 4.38 and 4.49 (2 d, 2 H, J = 11.5 Hz, $PhCH_2$), 4.39 and 4.55 (2 d, 2 H, J = 11.8 Hz, $PhCH_2$), 4.56 (dd, 1 H, $J_{3,P}$ = 8.7 Hz, H-3), 4.58 and 4.70 (2 d, 2 H, J = 12.0 Hz, $PhCH_2$), 4.76 and 4.91 (2 d, 2 H, J = 11.0 Hz, $PhCH_2$), 7.10-7.45 (m, 20 H, 4 Ph). ^{13}C NMR: δ 16.2 (d, J = 5.6 Hz, 2 CH_2CH_3), 52.8 (OCH_3), 63.2 (d, J = 7.1 Hz, CH_2CH_3), 63.7 (d, J = 7.1 Hz, CH_2CH_3), 69.6 (C-7), 72.2, 73.0, and 74.2 (4 $PhCH_2$), 74.1 (d, J = 12.7 Hz, C-6), 77.3 (C-5), 78.1 (d, J = 3.0 Hz, C-4), 78.4 (C-3), 83.0 (d, J = 156.0 Hz, C-2), 127.2-128.2, 137.5, 137.7, 137.9, and 138.6 (Ph), 168.6 (C-1). ^{31}P NMR: δ 15.8. Anal. Calcd for $C_{40}H_{47}O_{10}P$: C, 66.84; H, 6.59. Found: C, 66.57; H, 6.62.

Diethyl (methyl 2,3,4,6-tetra-*O*-benzyl-β-D-*gluco*-heptulopyranosylonate)-phosphonate (β-5e). Thiazolylketoside **2b** (372 mg, 0.50 mmol) was treated as described for the preparation of **5a**. Column chromatography (5:3 cyclohexane-AcOEt) of the residue afforded **β-5e** (212 mg, 59%) as a syrup; $[\alpha]_D$ = +28.1 (*c* 0.8, $CHCl_3$). ^1H NMR: δ 1.15 and 1.19 (2 t, 6 H, J = 7.0 Hz, 2 CH_2CH_3), 3.76 (dd, 1 H, $J_{3,P}$ = 10.0, $J_{3,4}$ = 8.5 Hz, H-3), 3.78 (d, 2 H, $J_{7a,7b}$ = 2.5 Hz, 2 H-7), 3.83 (s, 3 H, OCH_3), 4.03 (dd, 1 H, $J_{4,5}$ = 8.5 Hz, H-4), 4.06-4.30 (m, 6 H, 2 CH_2CH_3, H-5, H-6), 4.50 and 4.57 (2 d, 2 H, J = 12.0 Hz, $PhCH_2$), 4.62 and 4.84 (2 d, 2 H, J = 11.0 Hz, $PhCH_2$), 4.80 and 4.83 (2 d, 2 H, J = 11.0 Hz, $PhCH_2$), 4.89 and 4.98 (2 d, 2 H, J = 11.5 Hz, $PhCH_2$), 7.20-7.35 (m, 20 H, Ph). ^{13}C NMR: δ 16.2 (d, J = 6.6 Hz, CH_2CH_3), 16.4 (d, J = 6.5 Hz, CH_2CH_3), 52.4 (OCH_3), 64.1 (d, J = 6.2 Hz, CH_2CH_3), 64.4 (d, J = 6.6 Hz, CH_2CH_3), 68.7 (C-7), 73.2, 74.8, 74.9, and 75.3 (4 $PhCH_2$), 76.3 (d, J = 13.4 Hz,

C-6), 77.2 (C-3), 79.5 (C-5), 82.1 (d, J = 161.6 Hz, C-1), 83.1 (d, J = 12.1 Hz, C-4) 126.8-128.4, 138.1, 138.2, 138.3, and 138.7 (4 Ph), 168.3 (C-1). ^{31}P NMR: δ 15.6. Anal. Calcd for $C_{40}H_{47}O_{10}P$: C, 66.84; H, 6.59. Found: C, 67.02; H, 6.73.

(α-D-*Galacto*-heptulopyranosyl)phosphonic acid (6a). A solution of **4a** (138 mg, 0.20 mmol) and bromotrimethylsilane (158 μL, 1.20 mmol) in anhydrous CH_2Cl_2 (2 mL) was kept at room temperature overnight, then concentrated. A vigorously stirred mixture of the residue, 10% palladium on activated carbon (70 mg), and MeOH (3 mL) was degassed under vacuum and saturated with hydrogen (by a H_2-filled balloon) three times. The suspension was stirred at room temperature for 2 h under a slightly positive pressure of hydrogen (balloon), then filtered through a plug of cotton and concentrated. Purification by anion-exchange chromatography (Dowex 2 x 8, HCO_2^- form, 0-1 M HCO_2H gradient) followed by lyophilization gave **6a** (44 mg, 81%) as an amorphous solid; $[\alpha]_D$ = +56.6 (*c* 0.9, MeOH). ^{1}H NMR (MeOD): δ 3.49 (dd, 1 H, $J_{6,7a}$ = 4.5, $J_{7a,7b}$ = 11.0 Hz, H-7a), 3.59 (dd, 1 H, $J_{6,7b}$ = 7.0 Hz, H-7b), 3.67-3.76 (m, 3 H, 2 H-1 and H-5), 3.87 (dd, 1 H, $J_{3,P}$ = 30.0, $J_{3,4}$ = 9.8 Hz, H-3), 3.99 (ddd, 1 H, H-6), 4.06 (dd, 1 H, $J_{4,5}$ = 2.5 Hz, H-4). ^{13}C NMR (D_2O): δ 64.1 (C-7), 66.3 (d, J = 7.0 Hz, C-1), 69.9 (C-3), 71.3 (C-5), 72.8 (C-4), 77.9 (C-6), 84.0 (d, J = 147.7 Hz, C-2).^{31}P NMR (D_2O): δ 22.6. Anal. Calcd for $C_7H_{15}O_9P{\cdot}H_2O$: C, 28.77; H, 5.86. Found: C, 29.06; H, 6.02.

(α-D-*Galacto*-heptulopyranosylonic)phosphonic acid (7a). A solution of **5a** (216 mg, 0.30 mmol) and bromotrimethylsilane (317 μL, 2.40 mmol) in anhydrous CH_2Cl_2 (3 mL) was kept at room temperature overnight, then concentrated. A vigorously stirred mixture of the residue, 10% palladium on activated carbon (100 mg), and MeOH (5 mL) was degassed under vacuum and saturated with hydrogen (by a H_2-filled balloon) three times. The suspension was stirred at room temperature for 2 h under a slightly positive pressure of hydrogen (balloon), then filtered through a plug of cotton and concentrated to give (methyl α-D-*galacto*-heptulopyranosylonate)phosphonic acid (95 mg). ^{1}H NMR (D_2O): δ 3.49 (dd, 1 H, $J_{6,7a}$ = 4.8, $J_{7a,7b}$ = 11.9 Hz, H-7a), 3.57 (dd, 1 H, $J_{6,7b}$ = 7.2 Hz, H-7b), 3.63 (s, 3 H, OCH_3), 3.77 (dd, 1 H, $J_{4,5}$ = 3.2, $J_{5,6}$ = 0.8 Hz, H-5), 3.96 (dd, 1 H, $J_{3,4}$ = 9.9, $J_{3,P}$ = 25.0 Hz, H-3), 4.06 (dddd, 1 H, $J_{6,P}$ = 1.7 Hz, H-6), 4.07 (dd, 1 H, H-4). ^{31}P NMR (D_2O): δ 11.0. To a solution of the methyl ester in 4:1 H_2O-MeOH (3 mL) was added 6 M aqueous NaOH (1.5 mL). After 6 h at room temperature the solution was eluted from a column of Dowex 50W x 2 (H^+ form) with 4:1 H_2O-MeOH and lyophilized. The residue was purified by anion-exchange chromatography (Dowex 2 x 8, HCO_2^- form, 1-4 M HCO_2H gradient) followed by lyophilization to give **7a** (73 mg, 85%) as an amorphous solid; $[\alpha]_D$ = +48.2 (*c* 0.8, H_2O). ^{1}H NMR (D_2O): δ 3.52 (dd, 1 H, $J_{6,7a}$ = 4.4, $J_{7a,7b}$ = 12.0 Hz, H-7a), 3.62 (dd, 1 H, $J_{6,7b}$ = 7.5 Hz, H-7b), 3.78 (dd, 1 H, $J_{4,5}$ = 3.1, $J_{5,6}$ = 0.6 Hz, H-5), 3.93 (dd, 1 H, $J_{3,4}$ = 10.0, $J_{3,P}$ = 25.6 Hz, H-3), 4.11 (dd, 1 H, H-4), 4.15 (dddd, 1 H, $J_{6,P}$ = 1.0 Hz, H-6). ^{31}P NMR (D_2O): δ 10.7. Anal. Calcd for $C_7H_{13}O_{10}P{\cdot}2H_2O$: C, 25.93; H, 5.29. Found: C, 26.24; H, 5.38.

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