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Thiazolylketol Acetates as Glycosyl Donors. Stereoselective Synthesis of α-Linked Ketodisaccharides[¶]

Alessandro Dondoni,* Alberto Marra, Isabel Rojo, and Marie-Christine Scherrmann

Dipartimento di Chimica, Laboratorio di Chimica Organica, Università, Ferrara, Italy

Abstract: TMSOTf-promoted glycosidation of 1-*C*-(2-thiazolyl)-α-D-galactopyranosyl acetate (α)-**2** and 1-*C*-(2-thiazolyl)-α-D-mannofuranosyl acetate **7** donors with 1 equiv of primary **3** and secondary **5** sugar alcohols acceptors gave exclusively the corresponding α-D-ketodisaccharides **4a, 8a, 11a,** and **12a** in 60-73% yield. On the other hand glycosidation of the 1-*C*-(2-thiazolyl)-α-D-glucopyranosyl acetate **6** with the primary alcohol **3** under the above conditions afforded a mixture of α- and β-D-ketodisaccharides **9a** and **10a** in ca. 1:1 ratio. The important role of the thiazole ring for the easy glycosidation of these ketol acetates was pointed out by comparison with ketoses bearing a methyl, carboxymethyl, and 2-furyl group. Application of the thiazolyl-to-formyl deblocking reaction sequence to the thiazolylketodisaccharides gave the corresponding aldehydes which in turn were converted into alcohols and esters by reduction and oxidation, respectively.

Recent work from this laboratory showed the synthetic utility of furanose and pyranose thiazolylketol acetates **B** (Figure 1) as key intermediates for the preparation of *C*-formyl glycosides **C** via reductive displacement of the acetoxy group and cleavage of the thiazole ring.[1] Compounds **B** were readily available in either diastereomeric form by addition of 2-lithiothiazole (**1**) to 1,4- and 1,5-glyconolactones **A** followed by acetylation of the resultant ketols. It has been also shown[2] that ketol acetates **B** upon treatment with $TMSN_3$-TMSOTf behave as very effective glycosyl donors to give thiazolyl azido glycosides. These products were then transformed into anomeric α-amino acids **D**.

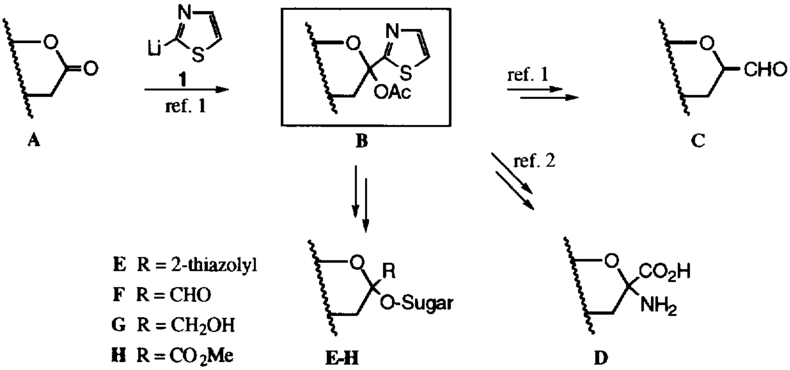


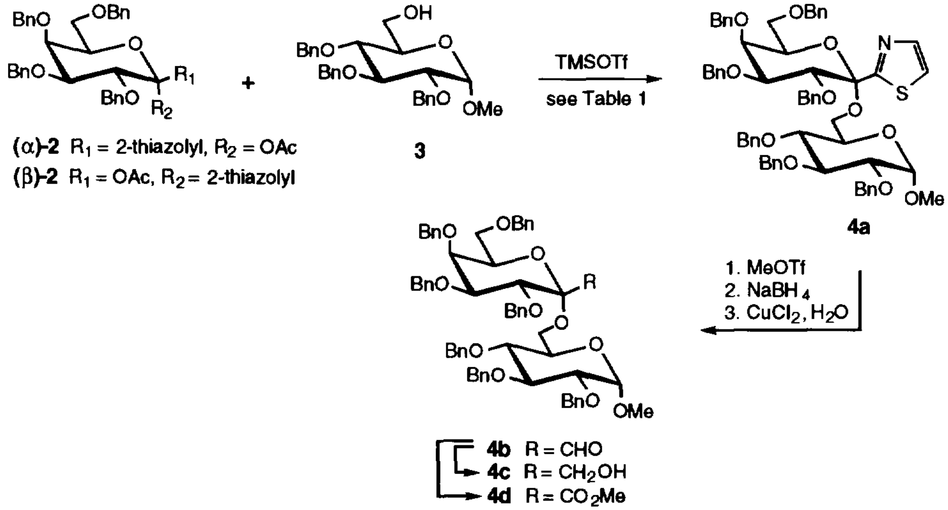
Figure 1

We now report the use of ketol acetates **B** as glycosyl donors toward model primary and secondary sugar alcohols under TMSOTf activation to give in most of the cases α-linked thiazolylketodisaccharides **E** stereoselectively and in good yields. Compounds **E**, subjected to a set of simple transformations, *i. e.* the metal catalysed hydrolytic cleavage of the thiazole ring to the formyl group and reduction or oxidation of the latter, were converted into ketosides **F-H** bearing different substituents at the anomeric carbon.

While numerous oligosaccharides have been prepared by efficient *O*-glycosylation methods with aldofuranoses and aldopyranoses,[3] the stereoselective synthesis of oligosaccharides containing ketopyranosyl and ketofuranosyl units is still a difficult problem in carbohydrate chemistry. Recent methods have been described involving the use of phosphite activated fructofuranose[4] and variously activated ketopyranoses obtained by different alkoxymethylenation procedures of sugar lactones.[5] Anomeric spiroepoxides derived from exocyclic enol ethers[6] have been also used as direct glycosyl donors[7] and precursors to activated ketoses.[8] We report below the results of our own approach to this problem.

RESULTS AND DISCUSSION

Synthesis of Thiazolylketodisaccharides. An initial glycosidation model was generated from the 1-*C*-(2-thiazolyl)-α-D-galactopyranosyl acetate donor (α)-**2** with methyl 2,3,4-tri-*O*-benzyl-α-D-glucopyranoside[9] acceptor (**3**) (Scheme 1). Thus, treatment of an equimolar solution of **2** and **3** in CH_2Cl_2 with 1 equiv of the promoter TMSOTf at room temperature (20-24 °C) produced after 1 h exclusively the α-ketodisaccharide[10] **4a** in good isolated yield (entry 1, Table 1). The reaction became quite slow at 0 °C, while was still uncompleted after 4 h at -20 °C and did not occur at all at -40 °C. However, compound **4a** was still the only condensation product observed under these conditions. Attempts at reversing the stereoselectivity in favour of the β-linked stereoisomer by the use of CH_3CN as participating solvents[11] were unsuccessful (entry 2). Also the use of the anomer (β)-**2** gave the same α-linked ketodisaccharide **4a** in a similar yield (entry 3). The configuration at the anomeric center of **4a** is in agreement in all cases with a chair-like transition state[12] derived from a stereoselective axial attack of the primary hydroxyl group of the acceptor **3** to the less hindered face of a pyran oxycarbenium ion intermediate generated from **2** by the TMSOTf promoted removal of the acetoxy group.



Scheme 1

Table 1. Glycosylation of Primary and Secondary Sugar Alcohols by Thiazolylketol Acetates[a]

entry	donor	acceptor[b]	solvent	disaccharide (yield, %)[c]
1	**(α)-2**	**3**	CH_2Cl_2	**4a** (73)
2	**(α)-2**	**3**	CH_3CN	**4a** (71)
3	**(β)-2**	**3**	CH_2Cl_2	**4a** (71)
4	**(α)-2**	**5**	CH_2Cl_2	**8a** (60)
5	**6**	**3**	CH_2Cl_2	**9a** (38), **10a** (25)
6	**6**	**3**	CH_3CN	**9a** (34), **10a** (30)
7	**7**	**3**	CH_2Cl_2	**11a** (70)
8	**7**	**3**	CH_3CN	**11a** (68)
9	**7**	**5**	CH_2Cl_2	**12a** (62)

[a] At r. t. in the presence of 1 equiv of TMSOTf (with **3**) or 2 equiv of TMSOTf (with **5**).
[b] Donor/acceptor ratio = 1:1. [c] Yields refer to isolated products.

Also the glycosidation of **2** with methyl 2,3,6-tri-*O*-benzyl-α-D-glucopyranoside[13] acceptor (**5**) (Chart 1) under the above conditions afforded the α-ketodisaccharide[10] **8a** as a single diastereoisomer although in lower yield (30%). However, the yield was doubled by the slow addition of the donor **(α)-2** to the solution of **5** and TMSOTf in a 1:2 ratio[14] (entry 4, Table 1).

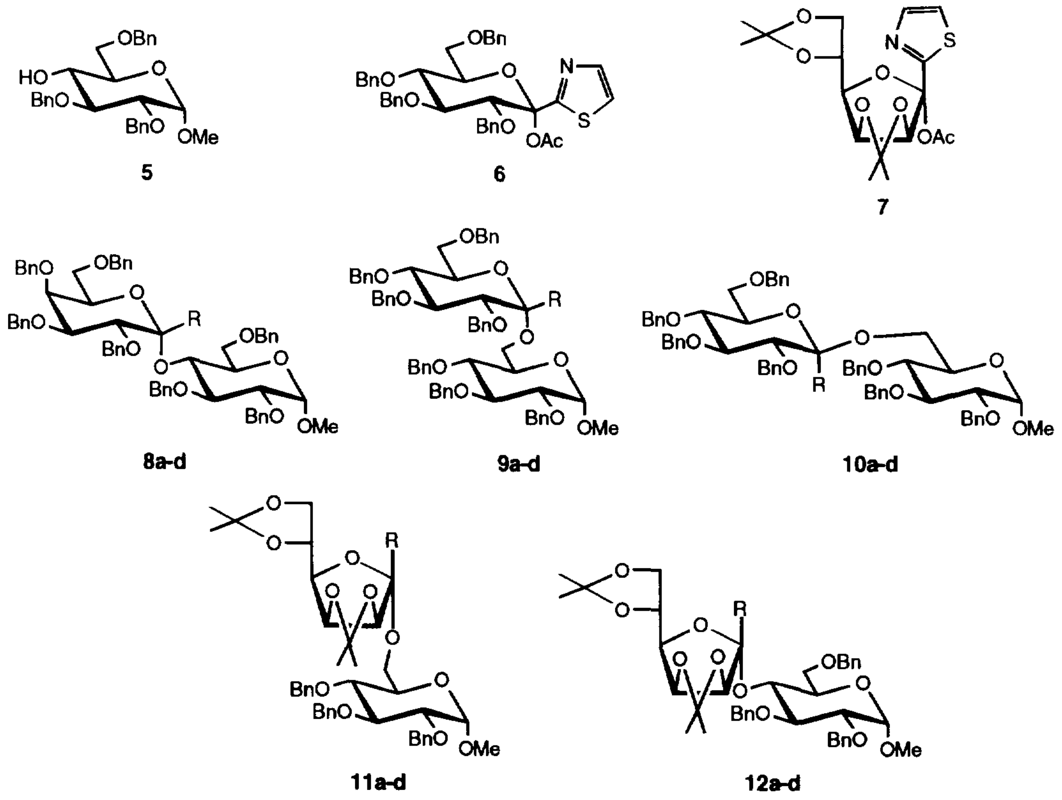
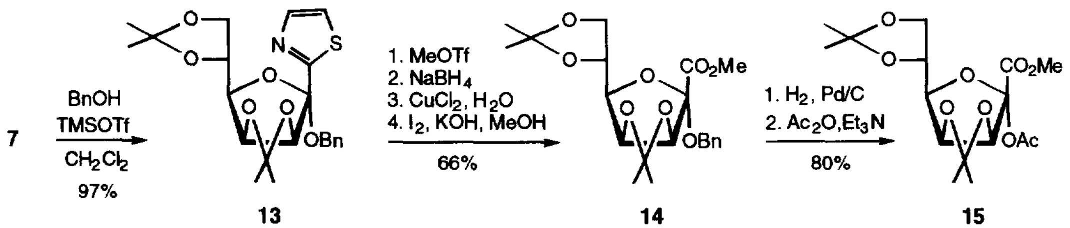


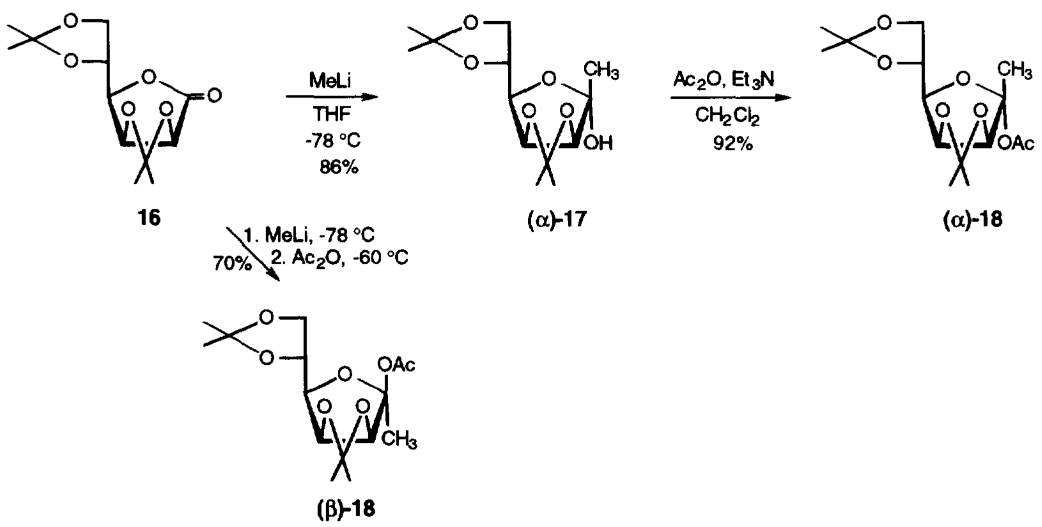
Chart 1. For compounds **8**-**12**: **a**, R = 2-thiazolyl; **b**, R = CHO; **c**, R = CH_2OH; **d**, R = CO_2Me.

Having established satisfactory glycosidation conditions of the thiazolylketol acetate **2**, the reaction was extended to other glycosyl donors. The condensation of the 1-*C*-(2-thiazolyl)-α-D-glucopyranosyl acetate derivative[1] **6** (Chart 1) with the primary hydroxy group of the acceptor **3** occurred smoothly in CH_2Cl_2 and CH_3CN under the agency of TMSOTf to give in both cases a mixture of α- and β-linked disaccharides[10] **9a** and **10a** in ca. 1:1 ratio (entries 5 and 6, Table 1). Evidently, unlike the galactopyranosyl donor **2**, the *gluco* derivative **6** leads to a pyran oxycarbenium ion intermediate whose diastereotopic faces are sterically equivalents and therefore undergo unselective attack by the nucleophile. The lack of selectivity had been previously observed in the TMSOTf-promoted removal of the acetoxy group from **6** by reduction with triethylsilane whereas the same reaction with **2** was highly stereoselective.[1b]

The use of the 1-*C*-(2-thiazolyl)-α-D-mannofuranosyl acetate derivative[1] **7** as glycosyl donor (Chart 1) produced other stereoselective reactions with both model primary and secondary sugar alcohols **3** and **5**. These glycosidations proceeded under the usual conditions giving rise to the corresponding α-ketodisaccharide[15] **11a** and **12a** in satisfactory yields (entries 7-9, Table 1). The stereochemical outcome indicates that also these reactions proceed through a nucleophilic addition of the acceptor hydroxyl group to the less hindered side of furan oxycarbenium ion intermediate.

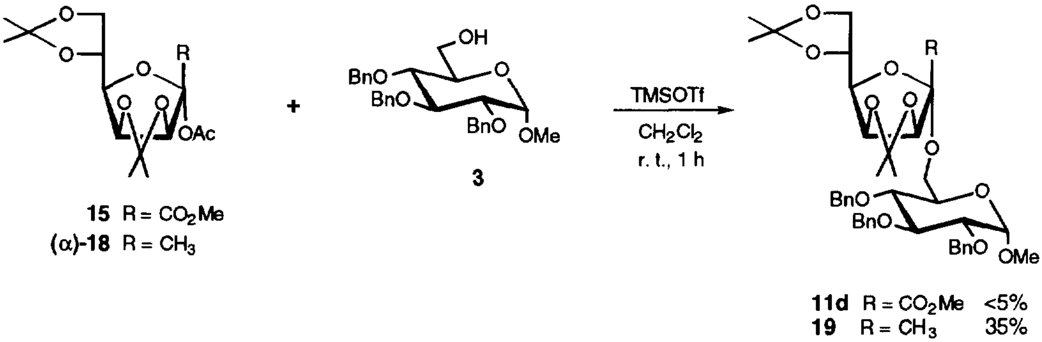


Scheme 2



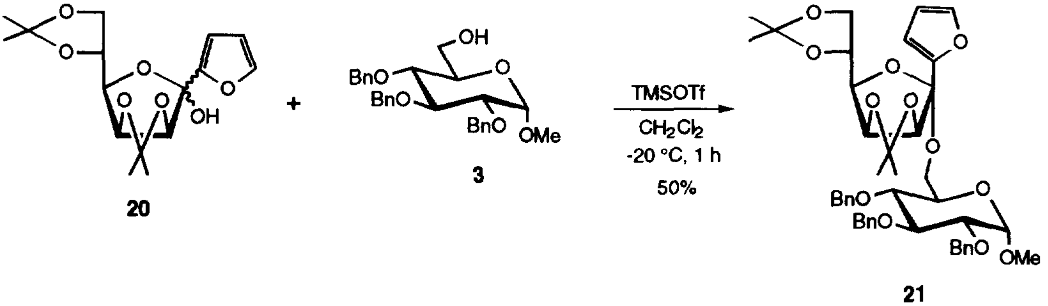
Scheme 3

The ease of glycosidation of the above thiazolylketol acetates was quite surprising when considering the modest reactivity of the acetoxy as leaving group[16] and the electron-poor character of the thiazole ring[17] which contrasts with the formation of the oxycarbenium ion intermediate discussed above. Nevertheless, this heterocycle appeared to favour considerably the reaction in comparison with a carbomethoxy and a methyl group. The glycosidations of the ketofuranosyl acetates **15** and (α)-**18**, prepared as shown in Schemes 2 and 3 respectively,[18,19] with the primary sugar alcohol **3** (Scheme 4) were sluggish in comparison with the same reaction of **7** and much less efficient[20] as judged from the lower yields of the isolated α-ketodisaccharides **11d** and **19**[21] (~5 and 35%, respectively). Accordingly, satisfactory glycosidation reactions of ketoses[4,5] and ulosonic acid[22] bearing at the anomeric position highly reactive leaving groups have been reported.



Scheme 4

Thiazolylketols appeared to be less reactive than the furyl analogues. For instance the glycosidation of the unactivated ketofuranosyl donor[23] **20** with **3** (Scheme 5) occurred readily even at -20 °C to give the corresponding ketofuranoside[21] **21** in 50% yield. Owing to its electrondonor character, furan has been conveniently employed as activating group of glycosyl donors and then converted to carboxyl group by oxidative cleavage.[24] However, the harsh oxidative conditions for the unmasking of the carboxylic acid may represent a serious limitation in synthetic methodology.[25] Hence the heretofore unexploited use of the thiazole ring in glycosyl donors appears to be of considerable synthetic importance since this heterocycle provides enough reactivity[26] and undergoes a facile conversion to a key functionality such as the formyl group under almost neutral conditions.



Scheme 5

Synthesis of Functionalized Ketodisaccharides. The actual synthetic utility arising from the presence of the thiazole ring in the above ketodisaccharides was proved by conversion to products bearing three different functionalities such as an aldehyde, an alcohol, and an ester group. A set of model transformations was generated starting from the disaccharide **4a** (Scheme 1). Application of the improved thiazolyl-to-formyl deblocking procedure[27] to this compound gave, without any epimerization, the corresponding aldehyde **4b** (75% yield) showing by ^{1}H NMR to be at least 90% pure. Crude **4b** was readily reduced by $NaBH_4$ in Et_2O-MeOH to the alcohol **4c** which was isolated in 65% yield based on the thiazole derivative **4a**. The oxidation of the formyl group of **4b** failed by the use of Ag_2O in THF-H_2O and KMnO4 in *t*BuOH-H_2O, in part because of the low solubility of the aldehyde in the solvents employed for these reactions. On the other hand a very efficient oxidation-esterification reaction[28] was carried out by I_2 in the presence of KOH in a Et_2O/MeOH mixture as a solvent. Pure methyl heptulosonate derivative **4d** was isolated in 67% yield based on the thiazole derivative **4a**. The application of the same reactions to the disaccharides **8a-12a** produced in all cases the corresponding products[29] **8b,c,d-12b,c,d** in comparable yields to those of **4b-d** (see Experimental).

In conclusion, the synthesis of ketodisaccharides starting from sugar lactones through thiazolylketol acetates appears a simple and efficient method which is expected to be of large application. In fact, various thiazole-armed glycosyl donors have been prepared from sugar lactones[1b] and many others are in principle available. The importance of highly functionalized ketodisaccharides is apparent when considering their possible use in the design and synthesis of multisubstrate analogues[30] for glycosyltransferases. Neither to say the role of the thiazole ring is noteworthy in this methodology as well.

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EXPERIMENTAL

All moisture-sensitive reactions were performed under a nitrogen atmosphere using oven-dried glassware. All solvents were dried over standard drying agents[31] and freshly distilled prior to use. Flash column chromatography[32] 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. Melting points were determined with a capillary apparatus and are uncorrected. Optical rotations were measured at 20 ± 2 °C in chloroform. ^{1}H (300 MHz) and ^{13}C (75 MHz) NMR were recorded at 295 °K for $CDCl_3$ solutions, unless otherwise specified. Assigments were aided by decoupling and/or homo- and heteronuclear two-dimensional experiments. Lactone **16**[33] was prepared in 80% yield by oxidation of 2,3:5,6-di-*O*-isopropylidene-α-D-mannofuranose[34] with pyridinium chlorochromate[35] in the presence of activated 4 Å powdered molecular sieves.

Methyl 2,3,4-tri-O-benzyl-6-O-[2,3,4,6-tetra-O-benzyl-1-C-(2-thiazolyl)-α-D-galactopyranosyl]-α-D-glucopyranoside (**4a**). A mixture of acetate (α)-**2** (333 mg, 0.5 mmol), alcohol **3** (232 mg, 0.5 mmol), activated 4 Å powdered molecular sieves (1.0 g), and anhydrous CH_2Cl_2 (5 mL) was stirred at r. t. for 15 min, then trimethylsilyl triflate (90 μL, 0.5 mmol) was added. The suspension was stirred at r. t. for 1 h, 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 3:2 cyclohexane-Et_2O to afford **4a** (390 mg, 73%) as a syrup; $[\alpha]_D = +17.3$ (*c* 1). ^{1}H NMR: δ 7.82 (d, 1 H, $J = 3.2$ Hz, Th), 7.40-7.08 (m, 36 H, 7 Ph, Th), 4.99 and 4.67 (2 d, 2 H, $J = 11.3$

Hz, PhCH_2), 4.96 and 4.79 (2 d, 2 H, J = 10.8 Hz, PhCH_2), 4.76 and 4.66 (2 d, 2 H, J = 12.0 Hz, PhCH_2), 4.73 and 4.34 (2 d, 2 H, J = 11.0 Hz, PhCH_2), 4.69 (s, 2 H, PhCH_2), 4.66 and 4.36 (2 d, 2 H, J = 11.2 Hz, PhCH_2), 4.54 (d, 1 H, $J_{1,2}$ = 3.5 Hz, H-1), 4.50 and 4.44 (2 d, 2 H, J = 11.7 Hz, PhCH_2), 4.23 (ddd, 1 H, $J_{4',5'}$ = 1.0, $J_{5',6'a}$ = 7.1, $J_{5',6'b}$ = 6.0 Hz, H-5'), 4.15 (dd, 1 H, $J_{2',3'}$ = 9.8, $J_{3',4'}$ = 2.2 Hz, H-3'), 4.10 (d, 1 H, H-2'), 4.05 (dd, 1 H, H-4'), 3.99 (ddd, 1 H, $J_{4,5}$ = 10.0, $J_{5,6a}$ = 1.5, $J_{5,6b}$ = 8.5 Hz, H-5), 3.97 (dd, 1 H, $J_{3,4}$ = 8.8, $J_{2,3}$ = 9.4 Hz, H-3), 3.83 (dd, 1 H, $J_{6a,6b}$ = 10.3 Hz, H-6a), 3.73 (dd, 1 H, $J_{6'a,6'b}$ = 9.4 Hz, H-6'a), 3.66 (dd, 1 H, H-6'b), 3.47 (dd, 1 H, H-2), 3.36 (dd, 1 H, H-6b), 3.25 (s, 3 H, OMe), 3.12 (dd, 1 H, H-4). ^{13}C NMR: δ 167.0, 142.4, and 120.8 (Th), 138.9-138.0 and 128.3-127.2 (7 Ph), 100.7 (C-1'), 97.3 (C-1), 82.2 (C-3), 79.8 (C-2), 79.6 and 79.5 (C-2' and C-3'), 78.9 (C-4), 75.7, 74.8 (2 C), 74.4, 73.1 (2 C), and 72.4 (7 PhCH_2), 74.8 (C-4'), 71.0 (C-5'), 69.6 (C-5), 68.6 (C-6'), 62.8 (C-6), 54.7 (OMe). Anal. Calcd for $C_{65}H_{67}NO_{11}S$: C, 72.94; H, 6.31; N, 1.31. Found: C, 72.80; H, 6.25; N, 1.56. When the glycosylation was performed in anhydrous CH_3CN instead of CH_2Cl_2, **4a** was recovered in 71% yield. The use of (β)-**2** as glycosyl donor (in CH_2Cl_2) gave similar results (71%). The isolated yield of **4a** was not improved by the application[14] of the "inverse procedure" described for the preparation of **8a** and **11a** (see below).

Methyl 2,3,6-tri-O-benzyl-4-O-[2,3,4,6-tetra-O-benzyl-1-C-(2-thiazolyl)-α-D-galactopyranosyl]-α-D-glucopyranoside (**8a**). A mixture of alcohol **5** (232 mg, 0.5 mmol), activated 4 Å powdered molecular sieves (1.0 g), and anhydrous CH_2Cl_2 (3 mL) was stirred at r. t. for 15 min, then trimethylsilyl triflate (180 μL, 1.0 mmol) was added and stirring was continued at r. t. for 5 min. To the suspension was added dropwise a solution of acetate (α)-**2** (333 mg, 0.5 mmol) in anhydrous CH_2Cl_2 (2 mL). After an additional 2 h the mixture was treated with an excess of Et_3N, diluted with CH_2Cl_2, filtered through Celite, and concentrated. In order to allow a better chromatographic separation, the unreacted alcohol **5** was acetylated as follows. A solution of the crude reaction mixture in anhydrous CH_2Cl_2 (3 mL), Et_3N (1.5 mL), and Ac_2O (1.0 mL) was kept at r. t. overnight, then concentrated. The residue was eluted from a column of silica gel with 4:1 cyclohexane-Et_2O to give **8a** (320 mg, 60%) as a syrup; $[\alpha]_D$ = +37.3 (*c* 1). ^{1}H NMR: δ 7.78 (d, 1 H, J = 3.2 Hz, Th), 7.32-7.10 (m, 36 H, 7 Ph, Th), 4.96 and 4.61 (2 d, 2 H, J = 11.7 Hz, PhCH_2), 4.90 and 4.57 (2 d, 2 H, J = 11.3 Hz, PhCH_2), 4.66 and 4.46 (2 d, 2 H, J = 12.2 Hz, PhCH_2), 4.66 and 4.63 (2 d, 2 H, J = 12.1 Hz, PhCH_2), 4.58 and 4.26 (2 d, 2 H, J = 10.7 Hz, PhCH_2), 4.53 (d, 1 H, $J_{1,2}$ = 3.6 Hz, H-1), 4.44 and 4.36 (2 d, 2 H, J = 11.8 Hz, PhCH_2), 4.38 (dd, 1 H, $J_{3,4}$ = 6.9, $J_{4,5}$ = 8.8 Hz, H-4), 4.30 (ddd, 1 H, $J_{4',5'}$ = 1.3, $J_{5',6'a}$ = $J_{5',6'b}$ = 6.5 Hz, H-5'), 4.22 (s, 2 H, PhCH_2), 4.16 (dd, 1 H, $J_{2',3'}$ = 10.0, $J_{3',4'}$ = 2.5 Hz, H-3'), 4.08 (d, 1 H, H-2'), 4.04 (dd, 1 H, $J_{2,3}$ = 8.7 Hz, H-3), 3.99 (dd, 1 H, H-4'), 3.88 (ddd, 1 H, $J_{5,6a}$ = 2.1, $J_{5,6b}$ = 4.8 Hz, H-5), 3.66 (d, 2 H, 2 H-6'), 3.65 (dd, 1 H, $J_{6a,6b}$ = 10.8 Hz, H-6a), 3.59 (dd, 1 H, H-6b), 3.42 (dd, 1 H, H-2), 3.35 (s, 3 H, OMe). ^{13}C NMR: δ 166.5, 142.3, and 120.9 (Th), 139.6-138.0 and 128.7-126.8 (7 Ph), 101.4 (C-1'), 97.3 (C-1), 81.2 (C-2'), 80.4 (C-3), 79.2 (C-3'), 78.2 (C-2), 75.8, 74.7, 74.6, 73.4, 73.0, 72.7, and 72.6 (7 PhCH_2), 74.9 (C-4'), 74.4 (C-4), 71.6 (C-5'), 70.9 (C-5), 70.2 (C-6), 68.9 (C-6'), 55.4 (OMe). Anal. Calcd for $C_{65}H_{67}NO_{11}S$: C, 72.94; H, 6.31; N, 1.31. Found: C, 72.75; H, 6.21; N, 1.45.

*Methyl 2,3,4-tri-O-benzyl-6-O-[2,3,4,6-tetra-O-benzyl-1-C-(2-thiazolyl)-*α- and -β-D-*glucopyranosyl]-α-D-glucopyranoside* (**9a** and **10a**). Acetate **6** (333 mg, 0.5 mmol) was reacted in CH_2Cl_2 with **3** (232 mg, 0.5 mmol) as described for the preparation of **4a**. Column chromatography (5:1 cyclohexane-AcOEt) of the residue afforded first **10a** (134 mg, 25%) as a syrup; $[\alpha]_D$ = +33.8 (*c* 1). ^{1}H NMR: δ 7.79 (d, 1 H, J = 3.3 Hz, Th), 7.37-7.14 (m, 36 H, 7 Ph, Th), 4.96-4.48 (m, 14 H, 7 PhCH_2), 4.51 (d, 1 H, $J_{1,2}$ = 3.6 Hz, H-1), 4.22 (ddd, 1 H, $J_{4',5'}$ = 9.7, $J_{5',6'a}$ = 2.4, $J_{5',6'b}$ = 3.5 Hz, H-5'), 4.07 (dd, 1 H, $J_{5,6a}$ = 2.0, $J_{6a,6b}$ = 10.5 Hz, H-6a), 4.04-

3.97 (m, 3 H), 3.95 (dd, 1 H, $J_{2,3}$ = 9.6, $J_{3,4}$ = 8.9 Hz, H-3), 3.82-3.72 (m, 3 H), 3.63 (dd, 1 H, $J_{5,6}$ = 4.3 Hz, H-6b), 3.60 (dd, 1 H, $J_{4,5}$ = 10.0 Hz, H-4), 3.46 (dd, 1 H, H-2), 3.30 (s, 3 H, OMe). ^{13}C NMR (selected data): δ 166.8, 142.0, and 120.8 (Th), 100.8 (C-1'), 97.8 (C-1), 54.9 (OMe). Anal. Calcd for $C_{65}H_{67}NO_{11}S$: C, 72.94; H, 6.31; N, 1.31. Found: C, 72.63; H, 6.19; N, 1.43.

Eluted second was syrupy **9a** (203 mg, 38%); $[\alpha]_D$ = +30.7 (*c* 1.1). ^{1}H NMR: δ 7.83 (d, 1 H, *J* = 3.3 Hz, Th), 7.39-7.10 (m, 36 H, 7 Ph, Th), 4.96 and 4.78 (2 d, 2 H, *J* = 10.6 Hz, PhCH_2), 4.87 and 4.59 (2 d, 2 H, *J* = 11.0 Hz, PhCH_2), 4.83 and 4.77 (2 d, 2 H, *J* = 10.8 Hz, PhCH_2), 4.78 and 4.40 (2 d, 2 H, *J* = 11.2 Hz, PhCH_2), 4.76 and 4.68 (2 d, 2 H, *J* = 12.0 Hz, PhCH_2), 4.66 and 4.56 (2 d, 2 H, *J* = 12.2 Hz, PhCH_2), 4.60 (d, 1 H, $J_{1,2}$ = 3.6 Hz, H-1), 4.53 and 4.19 (2 d, 2 H, *J* = 11.0 Hz, PhCH_2), 4.17 (dd, 1 H, $J_{2',3'}$ = 9.6, $J_{3',4'}$ = 8.9 Hz, H-3'), 4.14 (ddd, 1 H, $J_{4',5'}$ = 10.0, $J_{5',6'a}$ = 4.0, $J_{5',6'b}$ = 2.0 Hz, H-5'), 4.04 (ddd, 1 H, $J_{4,5}$ = 10.3, $J_{5,6a}$ = 1.7, $J_{5,6b}$ = 8.3 Hz, H-5), 3.99 (dd, 1 H, $J_{2,3}$ = 9.6, $J_{3,4}$ = 8.7 Hz, H-3), 3.90 (dd, 1 H, $J_{6a,6b}$ = 11.2 Hz, H-6a), 3.78 (dd, 1 H, H-4'), 3.77 (dd, 1 H, $J_{6'a,6'b}$ = 11.5 Hz, H-6'a), 3.70 (dd, 1 H, H-6'b), 3.59 (d, 1 H, H-2'), 3.49 (dd, 1 H, H-2), 3.42 (dd, 1 H, H-6b), 3.42 (s, 3 H, OMe), 3.17 (dd, 1 H, H-4). ^{13}C NMR (selected data): δ 167.2, 142.7, and 120.8 (Th), 100.3 (C-1'), 97.3 (C-1), 55.0 (OMe). Anal. Calcd for $C_{65}H_{67}NO_{11}S$: C, 72.94; H, 6.31; N, 1.31. Found: C, 72.79; H, 6.26; N, 1.42. When the glycosylation was carried out in anhydrous CH_3CN instead of CH_2Cl_2, **10a** and **9a** were recovered in 30 and 34% yield, respectively.

Methyl 2,3,4-tri-O-benzyl-6-O-[2,3:5,6-di-O-isopropylidene-1-C-(2-thiazolyl)-α-D-mannofuranosyl]-α-D-glucopyranoside (**11a**). Acetate **7** (193 mg, 0.5 mmol) was reacted in CH_2Cl_2 with **3** (232 mg, 0.5 mmol) as described for the preparation of **4a**. Column chromatography (1:1 cyclohexane-Et_2O) of the residue afforded **11a** (276 mg, 70%) as a syrup; $[\alpha]_D$ = +59.5 (*c* 1). ^{1}H NMR: δ 7.88 and 7.36 (2 d, 2 H, *J* = 3.2 Hz, Th), 7.39-7.21 and 7.15-7.09 (2 m, 15 H, 3 Ph), 4.96 and 4.76 (2 d, 2 H, *J* = 10.7 Hz, PhCH_2), 4.87 (d, 1 H, $J_{2',3'}$ = 5.8 Hz, H-2'), 4.85 (dd, 1 H, $J_{3',4'}$ = 3.0 Hz, H-3'), 4.78 and 4.66 (2 d, 2 H, *J* = 12.1 Hz, PhCH_2), 4.77 and 4.46 (2 d, 2 H, *J* = 11.2 Hz, PhCH_2), 4.59 (d, 1 H, $J_{1,2}$ = 3.5 Hz, H-1), 4.49 (ddd, 1 H, $J_{4',5'}$ = 7.4, $J_{5',6'a}$ = 6.3, $J_{5',6'b}$ = 4.8 Hz, H-5'), 4.22 (dd, 1 H, H-4'), 4.17 (dd, 1 H, $J_{6'a,6'b}$ = 8.7 Hz, H-6'a), 4.07 (dd, 1 H, H-6'b), 3.96 (dd, 1 H, $J_{2,3}$ = 9.6, $J_{3,4}$ = 8.6 Hz, H-3), 3.78 (ddd, 1 H, $J_{4,5}$ = 10.2, $J_{5,6a}$ = 2.3, $J_{5,6b}$ = 7.6 Hz, H-5), 3.60 (dd, 1 H, $J_{6a,6b}$ = 10.4 Hz, H-6a), 3.49 (dd, 1 H, H-2), 3.40 (s, 3 H, OMe), 3.38 (dd, 1 H, H-6b), 3.19 (dd, 1 H, H-4), 1.41, 1.40, 1.31, and 1.24 (4 s, 12 H, 4 Me). ^{13}C NMR: δ 165.6, 143.2, and 120.2 (Th), 138.6, 138.0, 137.8, and 128.3-127.5 (3 Ph), 113.1 and 109.1 (2 O-C-O), 108.1 (C-1'), 97.4 (C-1), 86.9 (C-2'), 81.9 (C-3), 80.0 (2 C, C-3' and C-4'), 79.8, (C-2), 78.3 (C-4), 75.6, 74.5, and 73.2 (3 PhCH_2), 72.9 (C-5'), 69.4 (C-5), 66.8 (C-6'), 63.0 (C-6), 54.9 (OMe), 26.7, 25.4, 25.3, and 24.2 (4 Me). Anal. Calcd for $C_{43}H_{51}NO_{11}S$: C, 65.38; H, 6.51; N, 1.77. Found: C, 65.17; H, 6.40; N, 1.65. When the glycosylation was performed in anhydrous CH_3CN instead of CH_2Cl_2, **11a** was recovered in 68% yield

Methyl 2,3,6-tri-O-benzyl-4-O-[2,3:5,6-di-O-isopropylidene-1-C-(2-thiazolyl)-α-D-mannofuranosyl]-α-D-glucopyranoside (**12a**). A mixture of alcohol **5** (232 mg, 0.5 mmol), activated 4 Å powdered molecular sieves (1.0 g), and anhydrous CH_2Cl_2 (3 mL) was stirred at r. t. for 15 min, then trimethylsilyl triflate (180 μL, 1.0 mmol) was added and stirring was continued at r. t. for 5 min. To the suspension was added dropwise a solution of acetate **7** (193 mg, 0.5 mmol) in anhydrous CH_2Cl_2 (2 mL). After an additional 2 h the mixture was 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 1:1 cyclohexane-Et_2O to give **12a** (245 mg, 62%) as a syrup; $[\alpha]_D$ = +63.6 (*c* 0.9). ^{1}H NMR: δ 7.78 and 7.17 (2 d, 2 H, *J* = 3.2 Hz, Th), 7.38-7.20 (m, 15 H, 3 Ph), 5.10 (d, 1 H, $J_{2',3'}$ = 5.8 Hz, H-2'), 4.91 and 4.28 (2 d, 2 H, *J* = 11.9 Hz, PhCH_2), 4.62 and 4.50 (2 d, 2 H, *J* =

12.2 Hz, PhCH_2), 4.55 (d, 1 H, $J_{1,2}$ = 3.5 Hz, H-1), 4.48 and 4.36 (2 d, 2 H, J = 12.2 Hz, PhCH_2), 4.45-4.38 (m, 2 H, H-3', H-5'), 4.33 (dd, 1 H, $J_{3',4'}$ = 3.8, $J_{4',5'}$ = 5.7 Hz, H-4'), 4.18 (dd, 1 H, $J_{3,4}$ = 8.4, $J_{4,5}$ = 9.5 Hz, H-4), 4.16-4.09 (m, 2 H, 2 H-6'), 3.88 (dd, 1 H, $J_{2,3}$ = 9.2 Hz, H-3), 3.85 (ddd, 1 H, $J_{5,6a}$ = 2.8, $J_{5,6b}$ = 6.1 Hz, H-5), 3.51 (dd, 1 H, H-2), 3.37 (s, 3 H, OMe), 3.27-3.18 (m, 2 H, 2 H-6), 1.50, 1.41, 1.16, and 1.01 (4 s, 12 H, 4 Me). ^{13}C NMR: δ 166.6, 142.7, and 120.1 (Th), 139.3, 138.2, 137.9, and 128.3-126.6 (3 Ph), 112.7 and 108.9 (2 O-C-O), 107.9 (C-1'), 97.2 (C-1), 87.1 (C-2'), 80.9 (C-4'), 79.8 (C-3'), 79.7 (2 C, C-2 and C-3), 73.9 (C-5'), 73.3, 73.1, and 72.9 (3 PhCH_2), 71.9 (C-4), 70.4 (C-5), 68.7 (C-6), 66.2 (C-6'), 55.1 (OMe), 26.7, 25.4, 25.3, and 23.9 (4 Me). Anal. Calcd for $C_{43}H_{51}NO_{11}S$: C, 65.38; H, 6.51; N, 1.77. Found: C, 65.10; H, 6.45; N, 1.60.

*Methyl 2,3,4-tri-O-benzyl-6-O-(3,4,5,7-tetra-O-benzyl-α-D-*galacto*-heptosulopyranosyl)-α-D-glucopyranoside* (**4b**). A mixture of thiazolylketodisaccharide **4a** (320 mg, 0.3 mmol), activated 4 Å powdered molecular sieves (0.6 g), and anhydrous CH_3CN (3 mL) was stirred at r. t. for 10 min, then methyl triflate (43 µL, 0.39 mmol) was added. The suspension was stirred at r. t. for 15 min and then concentrated to dryness. The crude *N*-methylthiazolium salt was suspended in 1:1 MeOH-Et_2O (3 mL), cooled to 0 °C, and treated with $NaBH_4$ (25 mg, 0.66 mmol). The mixture was stirred at r. t. for an additional 5 min, diluted with acetone (3 mL), and concentrated. A solution of the crude thiazolidines in CH_2Cl_2 (1 mL) was diluted with CH_3CN (3 mL) and H_2O (0.3 mL), and then treated with CuO (190 mg, 2.4 mmol) and $CuCl_2 \cdot 2H_2O$ (51 mg, 0.3 mmol). The mixture was sonicated at r. t. for 10 min in an ultrasonic cleaning bath, then concentrated to dryness (temperature not exceeding 40 °C). The brown solid was triturated with Et_2O (4 x 3 mL) and the liquid phase was pipetted and filtered though a pad (0.5 x 3 cm, h x d) of Florisil (100-200 mesh) to afford a colorless solution. After a further washing of Florisil with AcOEt (3 mL) the combined organic phases were concentrated to yield syrupy **4b** (228 mg, 75%; at least 90% pure by ^{1}H-NMR analysis) which was used in the next step without further purification. ^{1}H NMR (selected data): δ 9.35 (s, 1 H, CHO), 7.40-7.18 (m, 35 H, 7 Ph), 4.54 (d, 1 H, $J_{1,2}$ = 3.5 Hz, H-1), 4.14 (d, 1 H, $J_{3',4'}$ = 9.7 Hz, H-3'), 3.23 (s, 3 H, OMe).

*Methyl 2,3,6-tri-O-benzyl-4-O-(3,4,5,7-tetra-O-benzyl-α-D-*galacto*-heptosulopyranosyl)-α-D-glucopyranoside* (**8b**). Thiazolylketodisaccharide **8a** (320 mg, 0.3 mmol) was treated as described for the preparation of **4b** to give syrupy **8b** (234 mg, 77%; at least 90% pure by ^{1}H-NMR analysis) which was used in the next step without further purification. ^{1}H NMR: δ 9.25 (s, 1 H, CHO), 7.38-7.15 (m, 35 H, 7 Ph), 4.86 and 4.54 (2 d, 2 H, J = 11.5 Hz, PhCH_2), 4.85 and 4.60 (2 d, 2 H, J = 12.1 Hz, PhCH_2), 4.74 and 4.64 (2 d, 2 H, J = 11.2 Hz, PhCH_2), 4.62 (s, 2 H, PhCH_2), 4.53 (d, 1 H, $J_{1,2}$ = 3.6 Hz, H-1), 4.47 and 4.34 (2 d, 2 H, J = 11.8 Hz, PhCH_2), 4.44 and 4.35 (2 d, 2 H, J = 12.0 Hz, PhCH_2), 4.42 and 4.30 (2 d, 2 H, J = 11.9 Hz, PhCH_2), 4.06 (d, 1 H, $J_{3',4'}$ = 10.0 Hz, H-3'), 4.04 (dd, 1 H, $J_{3,4}$ = 8.5, $J_{4,5}$ = 10.0 Hz, H-4), 4.04 (ddd, 1 H, $J_{5',6'}$ = 1.3, $J_{6',7'a}$ = 6.1, $J_{6',7'b}$ = 5.3 Hz, H-6'), 3.94 (dd, 1 H, $J_{2,3}$ = 9.3 Hz, H-3), 3.89 (ddd, 1 H, $J_{5,6a}$ = 3.9, $J_{5,6b}$ = 2.1 Hz, H-5), 3.84 (dd, 1 H, $J_{4',5'}$ = 2.7 Hz, H-4'), 3.78 (dd, 1 H, H-5'), 3.72 (dd, 1 H, $J_{6a,6b}$ = 10.9 Hz, H-6a), 3.61 (dd, 1 H, H-6b), 3.57 (dd, 1 H, $J_{7'a,7'b}$ = 9.6 Hz, H-7'a), 3.43 (dd, 1 H, H-7'b), 3.43 (dd, 1 H, H-2), 3.34 (s, 3 H, OMe).

*Methyl 2,3,4-tri-O-benzyl-6-O-(3,4:6,7-di-O-isopropylidene-α-D-*manno*-heptosulofuranosyl)-α-D-glucopyranoside* (**11b**). Thiazolylketodisaccharide **11a** (237 mg, 0.3 mmol) was treated as described for the preparation of **4b** to give syrupy **11b** (172 mg, 78%; at least 90% pure by ^{1}H-NMR analysis) which was used in the next step without further purification. ^{1}H NMR: δ 9.40 (s, 1 H, CHO), 7.39-7.22 (m, 15 H, 3 Ph), 4.98 and 4.78 (2 d, 2 H, J = 10.8 Hz, PhCH_2), 4.86 and 4.55 (2 d, 2 H, J = 11.1 Hz, PhCH_2), 4.80 (dd, 1 H, $J_{3',4'}$ = 5.8, $J_{4',5'}$ = 3.2 Hz, H-4'), 4.78 and 4.66 (2 d, 2 H, J = 12.0 Hz, PhCH_2), 4.72 (d, 1 H, H-3'), 4.60 (d, 1 H, $J_{1,2}$ =

3.5 Hz, H-1), 4.47 (ddd, 1 H, $J_{5',6'}$ = 7.6, $J_{6',7'a}$ = 6.4, $J_{6',7'b}$ = 4.2 Hz, H-6'), 4.53 (dd, 1 H, $J_{7'a,7'b}$ = 9.0 Hz, H-7'a), 4.04-3.96 (m, 3 H, H-3, H-5', H-7'b), 3.73 (ddd, 1 H, $J_{4,5}$ = 10.3, $J_{5,6a}$ = 2.1, $J_{5,6b}$ = 6.3 Hz, H-5), 3.59 (dd, 1 H, $J_{6a,6b}$ = 11.2 Hz, H-6a), 3.50 (dd, 1 H, $J_{2,3}$ = 9.7 Hz, H-2), 3.49 (dd, 1 H, H-6b), 3.36 (dd, 1 H, $J_{3,4}$ = 8.5 Hz, H-4), 3.35 (s, 3 H, OMe), 1.42, 1.38, and 1.26 (3 s, 12 H, 4 Me).

*Methyl 2,3,6-tri-O-benzyl-4-O-(3,4:6,7-di-O-isopropylidene-*α-D-manno-*heptosulofuranosyl)*-α-D-*glucopyranoside* (**12b**). Thiazolylketodisaccharide **12a** (237 mg, 0.3 mmol) was treated as described for the preparation of **4b** to give syrupy **12b** (159 mg, 72%; at least 90% pure by ^{1}H-NMR analysis) which was used in the next step without further purification. ^{1}H NMR: δ 9.05 (s, 1 H, CHO), 7.39-7.25 (m, 15 H, 3 Ph), 5.09 and 4.55 (2 d, 2 H, *J* = 11.9 Hz, PhCH_2), 4.65 and 4.54 (2 d, 2 H, *J* = 12.3 Hz, PhCH_2), 4.63 and 4.52 (2 d, 2 H, *J* = 11.9 Hz, PhCH_2), 4.58-4.55 (m, 3 H, H-1, H-3', H-4'), 4.41 (ddd, 1 H, $J_{5',6'}$ = 5.6, $J_{6',7'a}$ = $J_{6',7'b}$ = 6.2 Hz, H-6'), 4.13-4.06 (m, 3 H, H-5', 2 H-7'), 3.82 (dd, 1 H, $J_{2,3}$ = 9.4, $J_{3,4}$ = 8.7 Hz, H-3), 3.80 (ddd, 1 H, $J_{4,5}$ = 9.7, $J_{5,6a}$ = 2.8, $J_{5,6b}$ = 4.8 Hz, H-5), 3.63 (dd, 1 H, H-4), 3.62-3.55 (m, 2 H, 2 H-6), 3.52 (dd, 1 H, $J_{1,2}$ = 3.5 Hz, H-2), 3.37 (s, 3 H, OMe), 1.45, 1.40, 1.32, and 1.22 (4 s, 12 H, 4 Me).

*Methyl 2,3,4-tri-O-benzyl-6-O-(3,4,5,7-tetra-O-benzyl-*α-D-galacto-*heptulopyranosyl)*-α-D-*glucopyranoside* (**4c**). To a stirred solution of crude aldehyde **4b** (228 mg, ~0.2 mmol) in 1:1 MeOH-Et$_2$O (2 mL) was added NaBH$_4$ (8 mg, 0.2 mmol). Stirring was continued at r. t. for 10 min, then acetone (0.5 mL) was added and the mixture was concentrated. The residue was suspended in CH$_2$Cl$_2$, filtered through Celite, and concentrated. The crude alcohol was eluted from a column of silica gel with 1:1 cyclohexane-Et$_2$O to give **4c** (198 mg, 65% from **4a**) as a syrup; $[\alpha]_D$ = +40.3 (*c* 1.3). ^{1}H NMR: δ 7.39-7.20 (m, 35 H, 7 Ph), 4.96 and 4.80 (2 d, 2 H, *J* = 10.8 Hz, PhCH_2), 4.96 and 4.76 (2 d, 2 H, *J* = 11.2 Hz, PhCH_2), 4.95 and 4.59 (2 d, 2 H, *J* = 11.5 Hz, PhCH_2), 4.82 and 4.53 (2 d, 2 H, *J* = 11.1 Hz, PhCH_2), 4.75 and 4.64 (2 d, 2 H, *J* = 12.0 Hz, PhCH_2), 4.68 (s, 2 H, PhCH_2), 4.54 (d, 1 H, $J_{1,2}$ = 3.5 Hz, H-1), 4.44 and 4.40 (2 d, 2 H, *J* = 11.8 Hz, PhCH_2), 4.16 (d, 1 H, $J_{3',4'}$ = 9.9 Hz, H-3'), 4.02-3.92 (m, 4 H, H-3, H-4', H-5', H-6'), 3.87-3.78 (m, 2 H, H-5, H-6a), 3.60 (d, 2 H, $J_{1',OH}$ = 6.0 Hz, 2 H-1'), 3.56-3.43 (m, 4 H, H-2, H-6b, 2 H-7'), 3.32 (dd, 1 H, $J_{3,4}$ = 8.8, $J_{4,5}$ = 10.2 Hz, H-4), 3.22 (s, 3 H, OMe), 2.32 (t, 1 H, OH). Anal. Calcd for $C_{63}H_{68}O_{12}$: C, 74.39; H, 6.74. Found: C, 74.16; H, 6.82.

*Methyl 2,3,6-tri-O-benzyl-4-O-(3,4,5,7-tetra-O-benzyl-*α-D-galacto-*heptulopyranosyl)*-α-D-*glucopyranoside* (**8c**). Crude aldehyde **8b** (234 mg, ~0.2 mmol) was reduced as described for the preparation of **4c**. Column chromatography (4:1 cyclohexane-AcOEt) of the residue afforded **8c** (204 mg, 67% from **8a**) as a syrup; $[\alpha]_D$ = +23.0 (*c* 1). ^{1}H NMR: δ 7.36-7.05 (m, 35 H, 7 Ph), 5.01 and 4.80 (2 d, 2 H, *J* = 12.0 Hz, PhCH_2), 4.92 and 4.53 (2 d, 2 H, *J* = 11.4 Hz, PhCH_2), 4.72 (s, 2 H, PhCH_2), 4.65 and 4.52 (2 d, 2 H, *J* = 11.6 Hz, PhCH_2), 4.59 and 4.47 (2 d, 2 H, *J* = 12.2 Hz, PhCH_2), 4.57 (d, 1 H, $J_{1,2}$ = 3.6 Hz, H-1), 4.43 (s, 2 H, PhCH_2), 4.37 (s, 2 H, PhCH_2), 4.23 (dd, 1 H, $J_{3,4}$ = 8.3, $J_{4,5}$ = 9.2 Hz, H-4), 4.05 (s, 2 H, H-3', H-4'), 4.00-3.95 (m, 2 H, H-5', H-6'), 3.83 (dd, 1 H, $J_{2,3}$ = 9.7 Hz, H-3), 3.78 (dd, 1 H, $J_{1'a,1'b}$ = 12.2, $J_{1'a,OH}$ = 6.5 Hz, H-1'a), 3.72-3.62 (m, 4 H, H-5, 2 H-6, H-1'b), 3.55 (dd, 1 H, $J_{6',7'a}$ = 8.0, $J_{7'a,7'b}$ = 8.9 Hz, H-7'a), 3.50 (dd, 1 H, H-2), 3.39 (s, 3 H, OMe), 3.36 (dd, 1 H, H-7'b), 2.77 (dd, 1 H, $J_{1'b,OH}$ = 6.0 Hz, OH). Anal. Calcd for $C_{63}H_{68}O_{12}$: C, 74.39; H, 6.74. Found: C, 74.10; H, 6.85.

*Methyl 2,3,4-tri-O-benzyl-6-O-(3,4:6,7-di-O-isopropylidene-*α-D-manno-*heptulofuranosyl)*-α-D-*glucopyranoside* (**11c**). Crude aldehyde **11b** (172 mg, ~0.2 mmol) was reduced as described for the preparation of **4c**. Column chromatography (2:1 cyclohexane-AcOEt) of the residue afforded **11c** (150 mg, 68% from **11a**) as a syrup; $[\alpha]_D$ = +39.5 (*c* 0.8). ^{1}H NMR: δ 7.39-7.26 (m, 15 H, 3 Ph), 4.99 and 4.83 (2 d, 2 H, *J* = 10.8 Hz, PhCH_2), 4.86 and 4.60 (2 d, 2 H, J = 10.9 Hz, PhCH_2), 4.78 and 4.64 (2 d, 2 H, J = 11.6 Hz, PhCH_2), 4.77 (dd, 1 H, $J_{3',4'}$ = 6.0, $J_{4',5'}$ = 3.7 Hz, H-4'), 4.59 (d, 1 H, $J_{1,2}$ = 3.5 Hz, H-1), 4.51 (d, 1 H, H-3'), 4.36 (ddd, 1 H, $J_{5',6'}$ = 7.9, $J_{6',7'a}$ = 6.2, $J_{6',7'b}$ = 4.5 Hz, H-6'), 4.08 (dd, 1 H, $J_{7'a,7'b}$ = 8.6 Hz, H-7'a), 3.98 (dd, 1 H, $J_{2,3}$ = 9.6, $J_{3,4}$ = 7.4 Hz, H-3), 3.92 (dd, 1 H, H-7'b), 3.79 (dd, 1 H, H-5'), 3.76-3.61 (m, 6 H, H-4, H-5, 2 H-6, 2 H-1'), 3.50 (dd, 1 H, H-2), 3.36 (s, 3 H, OMe), 3.03 (dd, 1 H, $J_{1'a,OH}$ = 4.8, $J_{1'b,OH}$ = 9.6 Hz, OH), 1.49, 1.39, 1.37, and 1.34 (4 s, 12 H, 4 Me). Anal. Calcd for $C_{41}H_{52}O_{12}$: C, 66.83; H, 7.11. Found: C, 66.61; H, 7.20.

Methyl 2,3,6-tri-O-benzyl-4-O-(3,4:6,7-di-O-isopropylidene-α-D-manno-*heptulofuranosyl)*-α-D-*gluco-pyranoside* (**12c**). Crude aldehyde **12b** (159 mg, ~0.2 mmol) was reduced as described for the preparation of **4c**. Column chromatography (1:1 cyclohexane-Et_2O) of the residue afforded **12c** (148 mg, 67% from **12a**) as a syrup; $[\alpha]_D$ = +32.0 (*c* 0.7). ^{1}H NMR: δ 7.40-7.25 (m, 15 H, 3 Ph), 4.95 and 4.88 (2 d, 2 H, J = 11.4 Hz, PhCH_2), 4.72 and 4.58 (2 d, 2 H, J = 11.9 Hz, PhCH_2), 4.70 (dd, 1 H, $J_{3',4'}$ = 5.8, $J_{4',5'}$ = 4.6 Hz, H-4'), 4.59 (d, 1 H, $J_{1,2}$ = 3.5 Hz, H-1), 4.58 and 4.51 (2 d, 2 H, J = 11.5 Hz, PhCH_2), 4.48 (d, 1 H, $J_{1'b,OH}$ = 12.0 Hz, OH), 4.34 (ddd, 1 H, $J_{5',6'}$ = 5.8, $J_{6',7'a}$ = $J_{6',7'b}$ = 6.1 Hz, H-6'), 4.16 (d, 1 H, H-3'), 4.15 (dd, 1 H, H-5'), 4.10 (dd, 1 H, $J_{3,4}$ = 8.9, $J_{4,5}$ = 9.6 Hz, H-4), 4.00 (dd, 1 H, $J_{7'a,7'b}$ = 8.6 Hz, H-7'a), 3.99 (d, 1 H, $J_{1'a,1'b}$ = 13.1 Hz, H-1'a), 3.91 (dd, 1 H, H-7'b), 3.88 (dd, 1 H, $J_{2,3}$ = 9.9 Hz, H-3), 3.83 (dd, 1 H, $J_{5,6a}$ = 3.6, $J_{6a,6b}$ =10.7 Hz, H-6a), 3.75 (dd, 1 H, H-1'b), 3.73 (dd, 1 H, H-6b), 3.62 (ddd, 1 H, H-5), 3.54 (dd, 1 H, H-2), 3.38 (s, 3 H, OMe), 1.47, 1.41, 1.35, and 1.31 (4 s, 12 H, 4 Me). Anal. Calcd for $C_{41}H_{52}O_{12}$: C, 66.83; H, 7.11. Found: C, 66.59; H, 7.18.

Methyl 2,3,4-tri-O-benzyl-6-O-(methyl 3,4,5,7-tetra-O-benzyl-α-D-galacto-*heptulopyranosylonate)*-α-D-*glucopyranoside* (**4d**). To a vigorously stirred solution of crude aldehyde **4b** in 1:1 MeOH-Et_2O (~0.05 M) 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 ($MgSO_4$), and concentrated. The residue was eluted from a column of silica gel with 7:3 cyclohexane-Et_2O to give syrupy **4d** (67% from **4a**); $[\alpha]_D$ = +24.4 (*c* 0.8). ^{1}H NMR: δ 7.39-7.20 (m, 35 H, 7 Ph), 4.97 and 4.67 (2 d, 2 H, J = 11.6 Hz, PhCH_2), 4.95 and 4.77 (2 d, 2 H, J = 10.7 Hz, PhCH_2), 4.84 and 4.66 (2 d, 2 H, J = 11.6 Hz, PhCH_2), 4.81 and 4.49 (2 d, 2 H, J = 10.5 Hz, PhCH_2), 4.74 and 4.64 (2 d, 2 H, J = 12.0 Hz, PhCH_2), 4.68 (s, 2 H, PhCH_2), 4.53 (d, 1 H, $J_{1,2}$ = 3.5 Hz, H-1), 4.45 and 4.38 (2 d, 2 H, J = 11.8 Hz, PhCH_2), 4.34 (d, 1 H, $J_{3',4'}$ = 9.7 Hz, H-3'), 4.20 (dd, 1 H, $J_{5,6a}$ = 1.6, $J_{6a,6b}$ = 10.3 Hz, H-6a), 4.12 (ddd, 1 H, $J_{5',6'}$ = 1.0, $J_{6',7'a}$ = 7.0, $J_{6',7'b}$ = 6.0 Hz, H-6'), 4.04 (ddd, 1 H, $J_{4,5}$ = 10.0, $J_{5,6b}$ = 9.4 Hz, H-5), 4.03-3.95 (m, 3 H, H-3, H-4', H-5'), 3.59 (dd, 1 H, $J_{7'a,7'b}$ = 9.6 Hz, H-7'a), 3.53 (dd, 1 H, H-7'b), 3.49 (s, 3 H, CO_2Me), 3.47 (dd, 1 H, H-6b), 3.46 (dd, 1 H, $J_{2,3}$ = 9.7 Hz, H-2), 3.20 (s, 3 H, OMe), 3.15 (dd, 1 H, $J_{3,4}$ = 8.8 Hz, H-4). ^{13}C NMR (selected data): δ 167.5 (C=O), 99.7 (C-2'), 97.3 (C-1), 54.7 (OMe), 52.3 (CO_2*Me*). Anal. Calcd for $C_{64}H_{68}O_{13}$: C, 73.54; H, 6.56. Found: C, 73.35; H, 6.45.

Methyl 2,3,6-tri-O-benzyl-4-O-(methyl 3,4,5,7-tetra-O-benzyl-α-D-galacto-*heptulopyranosylonate)*-α-D-*glucopyranoside* (**8d**). Crude aldehyde **8b** was oxidised as described for the preparation of **4d**. Column chromatography (4:1 cyclohexane-AcOEt) of the residue afforded syrupy **8d** (65% from **8a**); $[\alpha]_D$ = +39.0 (*c* 1). ^{1}H NMR: δ 7.38-7.12 (m, 35 H, 7 Ph), 4.90 and 4.63 (2 d, 2 H, J = 11.7 Hz, PhCH_2), 4.79 and 4.74 (2 d, 2 H, J = 11.4 Hz, PhCH_2), 4.77 and 4.56 (2 d, 2 H, J = 12.0 Hz, PhCH_2), 4.63 and 4.60 (2 d, 2 H, J = 11.8 Hz, PhCH_2), 4.54 (d, 1 H, $J_{1,2}$ = 3.6 Hz, H-1), 4.47 and 4.33 (2 d, 2 H, J = 11.7 Hz, PhCH_2), 4.44 and 4.29 (2 d, 2 H, J = 12.0 Hz, PhCH_2), 4.41 and 4.22 (2 d, 2 H, J = 11.9 Hz, PhCH_2), 4.31 (dd, 1 H, $J_{3,4}$ = 8.3, $J_{4,5}$ = 9.5 Hz, H-4), 4.21 (d, 1 H, $J_{3',4'}$ = 10.0 Hz, H-3'), 4.12 (dd, 1 H, $J_{2,3}$ = 9.4 Hz, H-3), 4.12 (ddd, 1 H, $J_{5',6'}$ = 1.3, $J_{6',7'a}$ = 6.6, $J_{6',7'b}$ = 5.5 Hz, H-6'), 3.94 (ddd, 1 H, $J_{5,6a}$ = 3.8, $J_{5,6b}$ = 1.8 Hz, H-5), 3.89 (dd, 1 H, $J_{4',5'}$ = 2.6 Hz, H-4'), 3.81 (dd, 1 H, $J_{6a,6b}$ = 10.9 Hz, H-6a), 3.73 (dd, 1 H, H-5'), 3.65 (dd, 1 H, $J_{7'a,7'b}$ = 9.8 Hz, H-7'a), 3.59 (dd, 1 H, H-6b), 3.43 (dd, 1 H, H-2), 3.38 (dd, 1 H, H-7'b), 3.31 (s, 3 H, OMe), 3.17 (s, 3 H, CO_2Me). ^{13}C NMR (selected data): δ 166.8 (C=O), 99.5 (C-2'), 97.5 (C-1), 55.0 (OMe), 51.9 (CO_2*Me*). Anal. Calcd for $C_{64}H_{68}O_{13}$: C, 73.54; H, 6.56. Found: C, 73.40; H, 6.48.

*Methyl 2,3,4-tri-O-benzyl-6-O-(methyl 3,4,5,7-tetra-O-benzyl-*α-D-gluco-*heptulopyranosylonate)*-α-D-*glucopyranoside* (**9d**). Thiazolylketodisaccharide **9a** (320 mg, 0.3 mmol) was treated as described for the preparation of **4b** to give crude **9b** which was oxidised as described for the preparation of **4d**. Column chromatography (5:1 cyclohexane-AcOEt) of the residue afforded syrupy **9d** (194 mg, 62% from **9a**); $[\alpha]_D$ = +36.4 (*c* 0.9). ^1H NMR (C_6D_6): δ 7.35-7.02 (m, 35 H, 7 Ph), 4.99 and 4.72 (2 d, 2 H, *J* = 11.3 Hz, PhC*H*$_2$), 4.94 and 4.87 (2 d, 2 H, *J* = 11.5 Hz, PhC*H*$_2$), 4.94 and 4.60 (2 d, 2 H, *J* = 11.5 Hz, PhC*H*$_2$), 4.93 and 4.59 (2 d, 2 H, *J* = 11.3 Hz, PhC*H*$_2$), 4.81 and 4.64 (2 d, 2 H, *J* = 11.4 Hz, PhC*H*$_2$), 4.69 (d, 1 H, $J_{1,2}$ = 3.5 Hz, H-1), 4.66 (dd, 1 H, $J_{6a,6b}$ = 10.2 Hz, H-6a), 4.52 and 4.39 (2 d, 2 H, *J* = 12.0 Hz, PhC*H*$_2$), 4.46-4.32 (m, 5 H, H-4', H-6', H-5, PhC*H*$_2$), 4.24 (dd, 1 H, $J_{2,3}$ = 9.5, $J_{3,4}$ = 8.6 Hz, H-3), 4.13 (d, 1 H, $J_{3',4'}$ = 9.6 Hz, H-3'), 3.98 (dd, 1 H, $J_{5,6b}$ = 8.1 Hz, H-6b), 3.90 (dd, 1 H, H-5'), 3.77 (dd, 1 H, $J_{6',7'a}$ = 4.3, $J_{7'a,7'b}$= 11.2 Hz, H-7'a), 3.70 (dd, 1 H, $J_{6',7'b}$ = 1.5 Hz, H-7'b), 3.53 (dd, 1 H, H-2), 3.40 (dd, 1 H, $J_{4,5}$ = 10.3 Hz, H-4), 3.34 (s, 3 H, OMe), 3.22 (s, 3 H, CO_2Me). ^{13}C NMR (C_6D_6, selected data): δ 168.3 (C=O), 99.6 (C-2'), 97.8 (C-1). Anal. Calcd for $C_{64}H_{68}O_{13}$: C, 73.54; H, 6.56. Found: C, 73.28; H, 6.60.

*Methyl 2,3,4-tri-O-benzyl-6-O-(methyl 3,4,5,7-tetra-O-benzyl-*β-D-gluco-*heptulopyranosylonate)*-α-D-*glucopyranoside* (**10d**). Thiazolylketodisaccharide **10a** (320 mg, 0.3 mmol) was treated as described for the preparation of **4b** to give crude **10b** which was oxidised as described for the preparation of **4d**. Column chromatography (5:1 cyclohexane-AcOEt) of the residue afforded syrupy **10d** (207 mg, 66% from **10a**); $[\alpha]_D$ = +32.8 (*c* 1.4). ^1H NMR (C_6D_6, selected data): δ 7.39-7.02 (m, 35 H, 7 Ph), 4.65 (d, 1 H, $J_{1,2}$ = 3.4 Hz, H-1), 4.67 (ddd, 1 H, $J_{5',6'}$ = 8.8, $J_{6',7'a}$ = 3.5, $J_{6',7'b}$ = 1.8 Hz, H-6'), 4.33 (dd, 1 H, $J_{5,6a}$ = 1.7, $J_{6a,6b}$ = 10.5 Hz, H-6a), 4.27 (dd, 1 H, $J_{3',4'}$ = 7.8, $J_{4',5'}$ = 9.2 Hz, H-4'), 4.16 (dd, 1 H, $J_{5,6b}$ = 4.4 Hz, H-6b), 4.07 (dd, 1 H, H-5'), 4.05 (d, 1 H, H-3'), 3.80 (dd, 1 H, $J_{7'a,7'b}$ = 11.3 Hz, H-7'a), 3.68 (dd, 1 H, H-7'b), 3.62 (dd, 1 H, $J_{2,3}$ = 9.6 Hz, H-2), 3.30 (s, 3 H, CO_2Me), 3.17 (s, 3 H, OMe). ^{13}C NMR (C_6D_6, selected data): δ 169.4 (C=O), 101.5 (C-2'), 98.3 (C-1). Anal. Calcd for $C_{64}H_{68}O_{13}$: C, 73.54; H, 6.56. Found: C, 73.46; H, 6.69.

*Methyl 2,3,4-tri-O-benzyl-6-O-(methyl 3,4:6,7-di-O-isopropylidene-*α-D-manno-*heptulofuranosylonate)*-α-D-*glucopyranoside* (**11d**). (Route *a*). Crude aldehyde **11b** was oxidised as described for the preparation of **4d**. Column chromatography (3:1 cyclohexane-AcOEt) of the residue afforded syrupy **11d** (70% from **11a**); $[\alpha]_D$ = +53.2 (*c* 1). ^1H NMR: δ 7.39-7.22 (m, 15 H, 3 Ph), 4.98 and 4.78 (2 d, 2 H, *J* = 10.6 Hz, PhC*H*$_2$), 4.86 and 4.54 (2 d, 2 H, *J* = 11.0 Hz, PhC*H*$_2$), 4.78 and 4.66 (2 d, 2 H, *J* = 11.3 Hz, PhC*H*$_2$), 4.77 (dd, 1 H, $J_{3',4'}$ = 5.8 , $J_{4',5'}$ = 3.4 Hz, H-4'), 4.67 (d, 1 H, H-3'), 4.58 (d, 1 H, $J_{1,2}$ = 3.5 Hz, H-1), 4.47 (ddd, 1 H, $J_{5',6'}$ = 8.5, $J_{6',7'a}$ = 6.2, $J_{6',7'b}$ = 3.9 Hz, H-6'), 4.13 (dd, 1 H, $J_{7'a,7'b}$ = 8.8 Hz, H-7'a), 4.01 (dd, 1 H, H-7'b), 3.99 (dd, 1 H, $J_{2,3}$ = 9.7, $J_{3,4}$ = 8.7 Hz, H-3), 3.97 (dd, 1 H, H-5'), 3.75 (ddd, 1 H, $J_{4,5}$ = 10.2, $J_{5,6a}$ = 2.6, $J_{5,6b}$ = 6.3 Hz, H-5), 3.71 and 3.37 (2 s, 6 H, CO_2Me and OMe), 3.58 (dd, 1 H, $J_{6a,6b}$ = 10.7 Hz, H-6a), 3.52 (dd, 1 H, H-6b), 3.51 (dd, 1 H, H-2), 3.31 (dd, 1 H, H-4), 1.42, 1.38, 1.36, and 1.30 (4 s, 12 H, 4 Me). Anal. Calcd for $C_{42}H_{52}O_{13}$: C, 65.95; H, 6.85. Found: C, 65.78; H, 6.92. (Route *b*). Acetate **15** (108 mg, 0.3 mmol) was reacted in CH_2Cl_2 with **3** (139 mg, 0.3 mmol) as described for the preparation of **4a**. In order to allow a better chromatographic separation, the unreacted alcohol **5** was acetylated as follows. A solution of the crude reaction mixture in anhydrous CH_2Cl_2 (2 mL), Et_3N (1.0 mL), and Ac_2O (0.8 mL) was kept at r. t. overnight, then concentrated. Column chromatography (3:1 cyclohexane-AcOEt) of the residue gave first a mixture of silylated and acetylated acceptor **3**. Eluted second was **11d** (11 mg, ~5%) contaminated by **15**. Eluted third was unreacted **15** (99 mg, 92%).

*Methyl 2,3,6-tri-*O*-benzyl-4-*O*-(methyl 3,4:6,7-di-*O*-isopropylidene-*α-D-manno-*heptulofuranosylonate)-*α-D-*glucopyranoside* (**12d**). Crude aldehyde **12b** was oxidised as described for the preparation of **4d**. Column chromatography (1:1 cyclohexane-Et_2O) of the residue afforded syrupy **12d** (67% from **12a**); $[\alpha]_D$ = +63.3 (*c* 1). ^{1}H NMR: δ 7.38-7.16 (m, 15 H, 3 Ph), 4.98 and 4.63 (2 d, 2 H, J = 12.5 Hz, PhCH_2), 4.67 and 4.53 (2 d, 2 H, J = 12.3 Hz, PhCH_2), 4.57 (d, 1 H, $J_{1,2}$ = 3.5 Hz, H-1), 4.54 (d, 1 H, $J_{3',4'}$ = 5.7 Hz, H-3'), 4.51 and 4.39 (2 d, 2 H, J = 11.8 Hz, PhCH_2), 4.45 (ddd, 1 H, $J_{5',6'}$ = 6.4, $J_{6',7'a}$ = 5.5, $J_{6',7'b}$ = 6.3 Hz, H-6'), 4.44 (dd, 1 H, $J_{4',5'}$ = 3.7 Hz, H-4'), 4.20-4.12 (m, 2 H, 2 H-7'), 4.09 (dd, 1 H, H-5'), 4.00-3.94 (m, 1 H, H-3), 3.91-3.81 (m, 2 H, H-4, H-5), 3.68-3.55 (m, 2 H, 2 H-6), 3.52 (dd, 1 H, $J_{2,3}$ = 9.3 Hz, H-2), 3.36 and 3.31 (2 s, 6 H, CO_2Me and OMe), 1.48, 1.41, 1.35, and 1.21 (4 s, 12 H, 4 Me). Anal. Calcd for $C_{42}H_{52}O_{13}$: C, 65.95; H, 6.85. Found: C, 65.70; H, 6.75.

*Benzyl 2,3:5,6-di-*O*-isopropylidene-1-*C*-(2-thiazolyl)-*α-D-*mannofuranoside* (**13**). A mixture of acetate **7** (578 mg, 1.5 mmol), anhydrous benzyl alcohol (310 μL, 3 mmol), activated 4 Å powdered molecular sieves (1.5 g), and anhydrous CH_2Cl_2 (15 mL) was stirred at r. t. for 15 min, then trimethylsilyl triflate (270 μL, 1.5 mmol) was added. The suspension was stirred at r. t. for 30 min and 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 3:1 cyclohexane-AcOEt to afford **13** (630 mg, 97%) as a syrup; $[\alpha]_D$ = +59.4 (*c* 1). ^{1}H NMR: δ 7.96 and 7.42 (2 d, 2 H, J = 3.4 Hz, Th), 7.39-7.28 (m, 5 H, Ph), 4.96 (d, 1 H, $J_{2,3}$ = 5.9 Hz, H-2), 4.92 (dd, 1 H, $J_{3,4}$ = 3.4 Hz, H-3), 4.54 (ddd, 1 H, $J_{4,5}$ = 7.3, $J_{5,6a}$ = 6.3, $J_{5,6b}$ = 4.8 Hz, H-5), 4.44 and 4.38 (2 d, 2 H, J = 11.4 Hz, PhCH_2), 4.20 (dd, 1 H, $J_{6a,6b}$ = 8.8 Hz, H-6a), 4.12 (dd, 1 H, H-4), 4.09 (dd, 1 H, H-6b), 1.47, 1.42, 1.34, and 1.25 (4 s, 12 H, 4 Me). Anal. Calcd for $C_{22}H_{27}NO_6S$: C, 60.95; H, 6.28; N, 3.23. Found: C, 60.72; H, 6.19; N, 3.31.

*Methyl (benzyl 3,4:6,7-di-*O*-isopropylidene-*α-D-manno-*heptulofuranosid)onate* (**14**). Thiazolylketoside **13** (433 mg, 1 mmol) was treated as described for the preparation of **4b** to give the corresponding crude aldehyde which was oxidised as described for the preparation of **4d**. Column chromatography (5:1 cyclohexane-AcOEt) of the residue afforded **14** (270 mg, 66%) as a syrup; $[\alpha]_D$ = +52.9 (*c* 1). ^{1}H NMR: δ 7.40-7.30 (m, 5 H, Ph), 4.84 (dd, 1 H, $J_{3,4}$ = 5.7, $J_{4,5}$ = 3.3 Hz, H-4), 4.77 (d, 1 H, H-3), 4.53 (ddd, 1 H, $J_{5,6}$ = 8.3, $J_{6,7a}$ = 6.1, $J_{6,7b}$ = 4.0 Hz, H-6), 4.51 and 4.37 (2 d, 2 H, J = 11.3 Hz, PhCH_2), 4.18 (dd, 1 H, $J_{7a,7b}$ = 9.0 Hz, H-7a), 4.03 (dd, 1 H, H-7b), 3.92 (dd, 1 H, H-5), 3.80 (s, 3 H, OMe), 1.44, 1.40, and 1.30 (3 s, 12 H, 4 Me). Anal. Calcd for $C_{21}H_{28}O_8$: C, 61.75; H, 6.91. Found: C, 61.60; H, 6.94.

*Methyl 2-*O*-acetyl-3,4:6,7-di-*O*-isopropylidene-*α-D-manno-*heptulofuranosonate* (**15**). A vigorously stirred mixture of **14** (204 mg, 0.5 mmol) and 10% palladium on activated carbon (50 mg) in AcOEt (5 mL) was degassed under vacuum and saturated with hydrogen (by a H_2-filled balloon) three times. The suspension was stirred at r. t. overnight under a slightly positive pressure of H_2 (balloon), then filtered through a plug of cotton, and concentrated. A solution of the residue in anhydrous CH_2Cl_2 (1 mL) was treated at r. t. for 48 h with Et_3N (1.4 mL, 10 mmol) and Ac_2O (1 mL, 10 mmol), then concentrated. The residue was eluted from a column of silica gel with 2:1 cyclohexane-AcOEt to give **15** (144 mg, 80%) as a solid; mp 139-140 °C (from *i*Pr$_2$O); $[\alpha]_D$ = +111.8 (*c* 0.8). ^{1}H NMR: δ 4.92 (dd, 1 H, $J_{3,4}$ = 5.8, $J_{4,5}$ = 3.1 Hz, H-4), 4.88 (d, 1 H, H-3), 4.52 (ddd, 1 H, $J_{5,6}$ = 8.5, $J_{6,7a}$ = 5.7, $J_{6,7b}$ = 3.6 Hz, H-6), 4.15 (dd, 1 H, $J_{7a,7b}$ = 9.2 Hz, H-7a), 4.10 (dd, 1 H, H-7b), 3.99 (dd, 1 H, H-5), 3.81 (s, 3 H, OMe), 2.10 (s, 3 H, Ac), 1.43, 1.42, 1.39, and 1.37 (4 s, 12 H, 4 Me). ^{13}C NMR (selected data): δ 168.4 and 165.1 (2 C=O), 114.1 and 109.4 (2 O-C-O), 105.0 (C-2), 52.7 (OMe). Anal. Calcd for $C_{16}H_{24}O_9$: C, 53.33; H, 6.71. Found: C, 53.25; H, 6.68.

*2,3:5,6-Di-*O*-isopropylidene-1-*C*-methyl-α-*D*-mannofuranose* (**α-17**). To a stirred, cooled (-78 °C) solution of lactone **16** (516 mg, 2.0 mmol) in anhydrous THF (5 mL) was added dropwise methyllithium (1.4 mL of a 1.6 M solution in Et$_2$O, 2.2 mmol). The solution was stirred at -78 °C for 30 min, then allowed to warm to -60 °C in 1 h, poured into 50 mL of a 1 M phosphate buffer (pH = 7), and extracted with CH$_2$Cl$_2$ (2 x 50 mL). The combined organic layers were dried (MgSO$_4$) and concentrated to give almost pure (NMR analysis) (α)-**17** as a solid (472 mg, 86%). An analytical sample was obtained by crystallization; mp 106-107 °C (from cyclohexane), lit.[19] mp 102 °C; $[\alpha]_D$ (2 min) = +9.0 (*c* 1), lit.[19] $[\alpha]_D$ = +8.33. ^{1}H NMR: δ 4.84 (dd, 1 H, $J_{2,3}$ = 5.9, $J_{3,4}$ = 3.9 Hz, H-3), 4.46 (d, 1 H, H-2), 4.38 (ddd, 1 H, $J_{4,5}$ = 7.5, $J_{5,6a}$ = 6.1, $J_{5,6b}$ = 4.7 Hz, H-5), 4.11 (dd, 1 H, H-4), 4.08 (dd, 1 H, $J_{6a,6b}$ = 8.5 Hz, H-6a), 4.00 (dd, 1 H, H-6b), 2.02 (s, 1 H, OH), 1.50, 1.48, 1.45, 1.38, and 1.34 (5 s, 15 H, 5 Me). ^{13}C NMR (selected data): δ 112.7 and 109.1 (2 O-C-O), 105.4 (C-1). Anal. Calcd for $C_{13}H_{22}O_6$: C, 56.92; H, 8.08. Found: C, 56.80; H, 8.11. Compound (α)-**17** slowly equilibrated in solution of CDCl$_3$ to give a mixture of anomers (α:β = 3:1, 72 h). (β)-**17**: ^{1}H NMR (selected data) δ 4.80 (dd, 1 H, $J_{2,3}$ = 5.9, $J_{3,4}$ = 3.6 Hz, H-3), 4.31 (d, 1 H, H-2), 4.07 (s, 1 H, OH), 3.50 (dd, 1 H, $J_{4,5}$ = 8.4 Hz, H-4). ^{13}C NMR (selected data): δ 113.2 and 109.4 (2 O-C-O), 102.8 (C-1).

*1-*O*-Acetyl-2,3:5,6-di-*O*-isopropylidene-1-*C*-methyl-α-*D*-mannofuranose* (**α-18**). A solution of (α)-**17** (274 mg, 1.0 mmol) in anhydrous CH$_2$Cl$_2$ (2 mL) was treated at r. t. for 48 h with Et$_3$N (2.8 mL, 20 mmol) and Ac$_2$O (2.0 mL, 20 mmol), then concentrated. The residue was eluted from a column of silica gel with 4:1 cyclohexane-AcOEt to give (α)-**18** (290 mg, 92%) as a syrup; $[\alpha]_D$ = +3.6 (*c* 1.2). ^{1}H NMR: δ 4.85-4.80 (m, 2 H, H-2, H-3), 4.37 (ddd, 1 H, $J_{4,5}$ = 7.9, $J_{5,6a}$ = 6.2, $J_{5,6b}$ = 4.6 Hz, H-5), 4.10 (dd, 1 H, $J_{6a,6b}$ = 8.8 Hz, H-6a), 4.06-4.02 (m, 1 H, H-4), 4.02 (dd, 1 H, H-6b), 2.03 (s, 3 H, Ac), 1.70, 1.48, 1.46, 1.38, and 1.34 (5 s, 15 H, 5 Me). ^{13}C NMR (selected data): δ 170.0 (C=O), 113.1 and 109.3 (2 O-C-O), 112.5 (C-1). Anal. Calcd for $C_{15}H_{24}O_7$: C, 56.95; H, 7.65. Found: C, 56.69; H, 7.75.

*1-*O*-Acetyl-2,3:5,6-di-*O*-isopropylidene-1-*C*-methyl-β-*D*-mannofuranose* (**β-18**). To a stirred, cooled (-78 °C) solution of lactone **16** (258 mg, 1.0 mmol) in anhydrous THF (3 mL) was added dropwise methyllithium (0.7 mL of a 1.6 M solution in Et$_2$O, 1.1 mmol). The solution was stirred at -78 °C for 30 min, then allowed to warm to -60 °C in 1 h, and treated with Ac$_2$O (1.0 mL, 10 mmol). The mixture was stirred for an additional 60 min at -60 °C, then poured into 20 mL of a 1 M phosphate buffer (pH = 7), and extracted with CH$_2$Cl$_2$ (2 x 30 mL). The combined organic layers were dried (MgSO$_4$) and concentrated. The residue was eluted from a column of silica gel with 5:1 cyclohexane-AcOEt to give (β)-**18** (220 mg, 70%), as a solid; mp 72-74 °C; $[\alpha]_D$ = +38.8 (*c* 1). ^{1}H NMR: δ 4.81 (dd, 1 H, $J_{2,3}$ = 6.0, $J_{3,4}$ = 3.6 Hz, H-3), 4.74 (d, 1 H, H-2), 4.46 (ddd, 1 H, $J_{4,5}$ = 8.4, $J_{5,6a}$ = 6.0, $J_{5,6b}$ = 4.0 Hz, H-5), 4.13 (dd, 1 H, $J_{6a,6b}$ = 9.0 Hz, H-6a), 4.07 (dd, 1 H, H-6b), 3.61 (dd, 1 H, H-4), 2.11 (s, 3 H, Ac), 1.62, 1.50, 1.47, 1.38, and 1.37 (5 s, 15 H, 5 Me). ^{13}C NMR (selected data): δ 168.4 (C=O), 113.4 and 108.7 (2 O-C-O), 109.5 (C-1). Anal. Calcd for $C_{15}H_{24}O_7$: C, 56.95; H, 7.65. Found: C, 57.10; H, 7.60.

*Methyl 2,3,4-tri-*O*-benzyl-6-*O*-(2,3:5,6-di-*O*-isopropylidene-1-*C*-methyl-α-*D*-mannofuranosyl)-α-*D*-glucopyranoside* (**19**). Acetate (α)-**18** (95 mg, 0.3 mmol) was reacted in CH$_2$Cl$_2$ with **3** (139 mg, 0.3 mmol) as described for the preparation of **4a**. Column chromatography (4:1, then 2:1 cyclohexane-AcOEt) of the residue gave first **19** (75 mg, 35%) as a syrup; $[\alpha]_D$ = +40.3 (*c* 1.3). ^{1}H NMR: δ 7.40-7.28 (m, 15 H, 3 Ph), 4.99 and 4.80 (2 d, 2 H, *J* = 10.8 Hz, PhCH_2), 4.89 and 4.59 (2 d, 2 H, *J* = 11.0 Hz, PhCH_2), 4.79 and 4.67 (2 d, 2 H, *J* = 12.0 Hz, PhCH_2), 4.75 (dd, 1 H, $J_{2',3'}$ = 6.0, $J_{3',4'}$ = 3.7 Hz, H-3'), 4.58 (d, 1 H, $J_{1,2}$ = 3.6 Hz, H-1), 4.40 (d, 1 H, H-2'), 4.34 (ddd, 1 H, $J_{4',5'}$ = 8.1, $J_{5',6'a}$ = 6.3, $J_{5',6'b}$ = 4.6 Hz, H-5'), 4.08 (dd, 1 H, $J_{6'a,6'b}$ = 8.6 Hz, H-6'a), 4.00 (dd, 1 H, $J_{2,3}$ = 9.6, $J_{3,4}$ = 8.8 Hz, H-3), 3.92 (dd, 1 H, H-6'b), 3.88 (dd, 1 H, H-4'), 3.74-3.68 (m, 2 H, H-5, H-6a), 3.52 (dd, 1 H, H-2), 3.46-3.40 (m, 1 H, H-6b), 3.36 (s, 3 H, OMe), 1.47, 1.37, 1.36, 1.34, and 1.32 (5 s, 15 H, 5 Me). Anal. Calcd for $C_{41}H_{52}O_{11}$: C, 68.31; H, 7.27. Found: C, 68.18; H, 7.19. Eluted second was unreacted **3** (185 mg, 40%). The use of (β)-**18** as glycosyl donor gave similar results.

1-C-(2-Furyl)-2,3:5,6-di-O-isopropylidene-α,β-D-mannofuranose (**20**). To a stirred, cooled (-78 °C) solution of butyllithium (1.4 mL of a 1.6 M solution in hexanes, 2.2 mmol) in anhydrous THF (2 mL) was added dropwise a solution of anhydrous furan (210 μL, 3.0 mmol; distilled under nitrogen from KOH immediately before use) in anhydrous THF (6 mL). The solution was allowed to warm to r. t. in 2 h, then stirred at r. t. for an additional 2 h, and cooled to -78 °C. To the mixture was added dropwise a solution of lactone **16** (516 mg, 2.0 mmol) in anhydrous THF (2 mL). The solution was stirred at -78 °C for 30 min, then allowed to warm to -30 °C in 1 h, poured into 50 mL of a 1 M phosphate buffer (pH = 7), and extracted with Et_2O (3 x 50 mL). The combined organic layers were dried (Na_2SO_4) and concentrated. The residue was eluted from a column of silica gel with 5:1 cyclohexane-AcOEt to give **20** (457 mg, 70%) as syrup. The ^{1}H NMR spectrum (in $CDCl_3$ at r. t. and in $C_2D_2Cl_4$ at 20-120 °C) of this compound was complex due to its existence as a mixture of anomers and the presence of the open-chain hydroxy ketone. ^{1}H NMR (α-**20**, selected data): δ 7.45 (dd, 1 H, $J_{3,5}$ = 0.8, $J_{4,5}$ = 1.8 Hz, furyl H-5), 6.50 (dd, 1 H, $J_{3,4}$ = 3.2 Hz, furyl H-3), 6.39 (dd, 1 H, furyl H-4), 4.94 (dd, 1 H, $J_{2,3}$ = 5.8, $J_{3,4}$ = 3.7 Hz, H-3), 4.76 (d, 1 H, H-2), 4.50 (ddd, 1 H, $J_{4,5}$ = 7.6, $J_{5,6a}$ = 6.0, $J_{5,6b}$ = 4.9 Hz, H-5), 4.26 (dd, 1 H, H-4). Anal. Calcd for $C_{16}H_{22}O_7$: C, 58.89; H, 6.79. Found: C, 59.25; H, 6.61.

Methyl 2,3,4-tri-O-benzyl-6-O-[1-C-(2-furyl)-2,3:5,6-di-O-isopropylidene-α-D-mannofuranosyl]-α-D-glucopyranoside (**21**). Ketol **20** (98 mg, 0.3 mmol) was reacted with **3** (139 mg, 0.3 mmol) at -20 °C for 1 h in CH_2Cl_2 (3 mL) as described for the preparation of **4a**. Column chromatography (5:1 cyclohexane-AcOEt, containing 0.3% of Et_3N) of the residue afforded **21** (116 mg, 50%) as a syrup; $[\alpha]_D$ = +61.6 (*c* 1.2). ^{1}H NMR: δ 7.44 (dd, 1 H, $J_{3,5}$ = 1.1, $J_{4,5}$ = 2.2 Hz, furyl H-5), 7.39-7.26 and 7.17-7.13 (2 m, 15 H, 3 Ph), 6.44 (dd, 1 H, $J_{3,4}$ = 3.7 Hz, furyl H-3), 6.36 (dd, 1 H, furyl H-4), 4.97 and 4.77 (2 d, 2 H, *J* = 10.8 Hz, PhCH_2), 4.84 (dd, 1 H, $J_{2',3'}$ = 5.7, $J_{3',4'}$ = 3.6 Hz, H-3'), 4.79 and 4.47 (2 d, 2 H, *J* = 10.9 Hz, PhCH_2), 4.78 and 4.66 (2 d, 2 H, *J* = 12.0 Hz, PhCH_2), 4.77 (d, 1 H, H-2'), 4.59 (d, 1 H, $J_{1,2}$ = 3.5 Hz, H-1), 4.45 (ddd, 1 H, $J_{4',5'}$ = 7.7, $J_{5',6'a}$ = 6.3, $J_{5',6'b}$ = 4.7 Hz, H-5'), 4.14 (dd, 1 H, $J_{6'a,6'b}$ = 8.7 Hz, H-6'a), 4.08 (dd, 1 H, H-4'), 4.03 (dd, 1 H, H-6'b), 3.96 (dd, 1 H, $J_{2,3}$ = 9.7, $J_{3,4}$ = 8.8 Hz, H-3), 3.67 (ddd, 1 H, $J_{4,5}$ = 10.1, $J_{5,6a}$ = 2.3, $J_{5,6b}$ = 7.3 Hz, H-5), 3.54 (dd, 1 H, $J_{6a,6b}$ = 10.8 Hz, H-6a), 3.50 (dd, 1 H, H-2), 3.39 (s, 3 H, OMe), 3.39 (dd, 1 H, H-6b), 3.22 (dd, 1 H, H-4), 1.39, 1.32, and 1.27 (3 s, 12 H, 4 Me). Anal. Calcd for $C_{44}H_{52}O_{12}$: C, 68.38; H, 6.78. Found: C, 68.60; H, 6.68. When the glycosylation was performed at higher temperatures complex mixtures of decomposition products were obtained.

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10. The anomeric configuration of **4a** and other pyranose thiazolylketodisaccharides **8a**, **9a**, and **10a** obtained afterwards could not be unambiguously established by NOESY and ^{13}C-NMR experiments. Thus, the configuration was assigned through the corresponding methyl ester derivatives **4d**, **8d**, **9d**, and **10d** on the basis of the vicinal coupling constants between the carboxyl carbon C-1' and the axial proton H-3' (ulosonic acid numbering) following a rule established for sialic acids (Haverkamp, J.; Spoormaker, T.; Dorland, L.; Vliegenthart, J. F. G.; Schauer, R. *J. Am. Chem. Soc.* **1979**, *101*, 4851) and sialic acid methyl esters (Hori, H.; Nakajima, T. Nishida, Y.; Ohrui, H.; Meguro, H. *Tetrahedron Lett.* **1988**, *29*, 6317; for a reinvestigation see: Prytulla, S.; Lauterwein, J.; Klessinger, M.; Thiem, J. *Carbohydr. Res.* **1991**, *215*, 345). The ^{13}C-NMR spectra, recorded with selective decoupling of the methyl ester protons, showed the C-1' signal as a singlet ($^3J_{C\text{-}1', H\text{-}3'} < 1$ Hz) in the case of α-disaccharides **4d**, **8d**, and **9d** (equatorial CO_2Me group) and as a doublet ($^3J_{C\text{-}1', H\text{-}3'} = 4.0$ Hz) in the case of β-disaccharide **10d**. This feature was expected for α- and β-D-ulosonate derivatives in a $^4C_1$ conformation having nearly 60° and 180° dihedral angles C-1–C-2–C-3–H-3, respectively. In each series, the stereochemistry assigned to esters was assumed for their precursors as well.
11. The intermediacy of α-nitrilium ions by use of acetonitrile or propionitrile as the solvents is well established, see: Braccini, I.; Derouet, C.; Esnault, J.; Hervé du Penhoat, C.; Mallet, J.-M.; Michon, V.; Sinaÿ, P. *Carbohydr. Res.* **1993**, *246*, 23 and references cited therein.
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14. When this glycosidation was carried out in the presence of 1 equiv of TMSOTf the disaccharide **8a** was recovered in ~55% yield. The efficiency of the so-called "inverse procedure" has been already proven using trichloroacetimidate derivatives as glycosyl donors (Schmidt, R. R.; Toepfer, A. *Tetrahedron Lett.* **1991**, *32*, 3353).
15. The α-configuration of the furanose thiazolylketodisaccharides **11a** and **12a** was assigned by NOESY experiments showing enhancements between H-4' and H-6b (for **11a**), H-4' and H-3, H-2' and H-4 (for **12a**).

16. Lewis acid-promoted glycosidation of 1-*O*-acetyl-aldofuranose and -aldopyranose derivatives has been reported. See: Mukaiyama, T.; Takashima, T.; Katsurada, M.; Aizawa, H. *Chem. Lett.* **1991**, 533 and previous papers cited therein.
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18. The ^{1}H-NMR spectra of the thiazolylketoside **13** and the methyl ester (α)-**15** showed chemical shifts and coupling constants values similar to those displayed by the corresponding α-thiazolylketol (see product **3e** in ref. 1b) and the methyl ester (α)-**18** (see Experimental), respectively. This allowed to assign the α-configuration to **13** and (α)-**15**.
19. Compound (α)-**17** was synthesised by addition of MeLi to the lactone **16**. The same procedure was employed earlier by Tam, T. F.; Fraser-Reid, B. *J. Org. Chem.* **1980**, *45*, 1344. However these Authors assigned to the resulting product the β-configuration on the basis of a hydrogen bonding of the hydroxyl proton to the vicinal oxygen atom (the ^{1}H-NMR data were not given). The physical data of (α)-**17** compared quite well with those reported for the product obtained by Tam and Fraser-Reid (see Experimental). Our assignement is based on the following observations. Product (α)-**17** slowly equilibrated in solution of $CDCl_3$ to give, after 3 days at r. t., a 3:1 mixture of anomers which were unambiguously characterised by NMR by comparison of their $\delta_{C\text{-}1}$ values (downfield chemical shifts have been reported for the ketofuranose anomers having the C-1–O-1 and C-2–O-2 bonds in a trans orientation; see: ref. 1b and Boschetti, A.; Panza, L.; Ronchetti, F.; Russo, G.; Toma, L. *J. Chem. Soc. Perkin Trans. I* **1988**, 3353). The anomeric configuration of the thermodynamic acetate (α)-**18** and the kinetic anomer (β)-**18** was determined by the same method.
20. Although it is quite obvious, this result clearly demonstrates that the intermediate oxycarbenium ion generated from donors bearing a carboxymethyl function is not stabilised by conjugation with the carbonyl oxygen. An opposite conclusion has been reported by others. See: Kirchner, E.; Thiem, F.; Dernick, R.; Heukeshoven, J.; Thiem, J. *J. Carbohydr. Chem.* **1988**, *7*, 453.
21. The ^{1}H-NMR spectra of the ketodisaccharides **19** and **21** showed chemical shifts and coupling constants values similar to those displayed by the ketol (α)-**17** and the thiazolylketodisaccharide **11a** (see Experimental), respectively. This allowed to assign the α-configuration to **19** and **21**.
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23. The addition of 2-lithiofuran (prepared according to: Mukaiyama, T.; Suzuki, K.; Yamada, T.; Tabusa, F. *Tetrahedron* **1990**, *46*, 265) to the sugar lactone **16** gave an anomeric mixture of 1-*C*-(2-furyl)-D-mannofuranose derivative **20** (70%) which, on treatment with acetic anhydride and triethylamine, afforded the crude anomeric acetates. However, upon purification on silica gel column the extremely acid sensitive 1-*O*-acetyl-1-*C*-(2-furyl)-2,3:5,6-di-*O*-isopropylidene-α,β-D-mannofuranose hydrolysed completely to afford **20**.
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I **II**

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