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Selectivity in the SmI_2-induced deoxygenation of thiazolylketoses for formyl *C*-glycoside synthesis and revised structure of *C*-ribofuranosides

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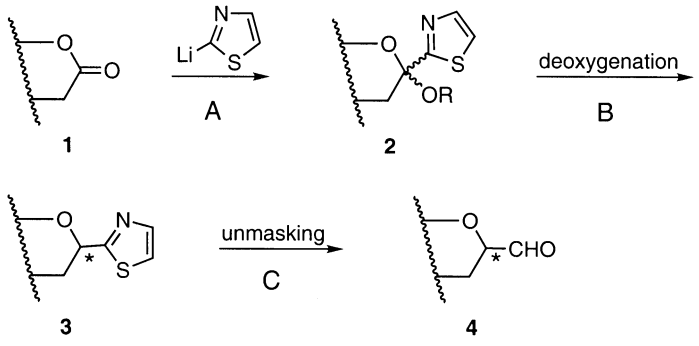
Abstract—Deoxygenation of thiazolylketose acetates using SmI_2–$(CH_2OH)_2$ or TMSOTf–Et_3SiH affords thiazolyl *C*-glycosides with opposite α/β ratios. Examination of the thiazolyl α- and β-*C*-ribofuranoside pair by NOE experiments reveals that the earlier configuration assigned to one of these isomers has to be revised. Having prepared authentic anomeric α- and β-ribofuranose aldehydes from the corresponding thiazolyl *C*-glycosides by cleavage of the thiazole ring, each aldehyde was transformed into (1→6)-*C*-disaccharides via Wittig olefination with a galactose 6-phosphorane.

In an earlier publication from our laboratory[1] we reported on a method of preparation of anomeric sugar aldehydes (formyl *C*-glycosides, **4**) from sugar lactones **1** by a three-step route involving: (A) the addition of 2-lithiothiazole (2-LTT) to **1**; (B) the removal of the hydroxy group in the resulting thiazolylketose **2** by acetylation and deoxygenation with TMSOTf–Et_3SiH; (C) the transformation of the thiazole ring of **3** into the formyl group by a one-pot reaction sequence (N-methylation, reduction, hydrolysis) (Scheme 1). The scope of this method is documented by the synthesis of various formyl *C*-glycosides bearing different hydroxy protective groups[1,2] as well as an azido group at C-2 of the galactopyranose ring.[1]

Since no epimerization occurs in the formyl unmasking step (C), the formyl group in compounds **4** has the same α- or β-disposition as the thiazole ring in their precursors **3**. The anomeric configuration of these glycosides which is established in the deoxygenation step (B) is in agreement with hydride addition to the less hindered face of a sugar oxycarbenium ion intermediate. Hence, since the silane-based deoxygenation was a highly stereoselective reaction (Table 1), a single formyl *C*-glycoside stereoisomer was obtained from the majority of the thiazolylketose acetates **2** which were examined. Consequently we have been searching for other deoxygenative methods which would lead to *C*-glycosides **3** with opposite configuration to that resulting by the use of TMSOTf–Et_3SiH. The tunable stereoselective synthesis of α- and β-linked sugar aldehydes **4** from the same thiazolylketose acetate **2** would broaden the scope of these compounds as synthetic tools in *C*-glycoside synthesis.[3] Stimulated by the recent work of Hanessian



Scheme 1.

Keywords: deoxygenation; *C*-glycosides; samarium diiodide; thiazole; Wittig reactions.
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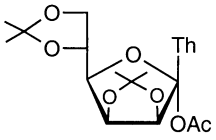
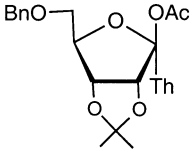
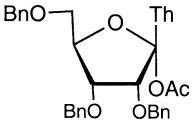
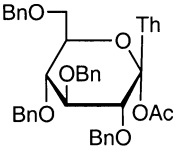
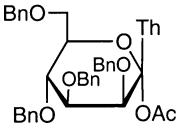
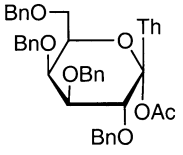
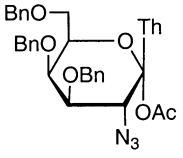
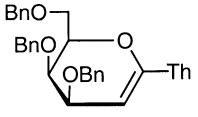
Table 1. Deoxygenation of thiazolylketose acetates **2**

Ketose acetate	SmI_2–$(CH_2OH)_2$	TMSOTf–Et_3SiH
	Product (α/β ratio)[a]	Product (α/β ratio)[b]
 **2a**	**3a** (11.5:1)	**3a** (0:1)
 **2b**	**3b** (1:9)	**3b** (4:1)
 **2c**	**3c** (1:4)	**3c** (0:1)
 **2d**	**3d** (2:1)	**3d** (1:1)
 **2e**	**3e** (4:1)	**3e** (0:1)
 **2f**	**3f** (1.4:1)	**3f** (0:1)
 **2g**  **5**	**3g** (0:1)	

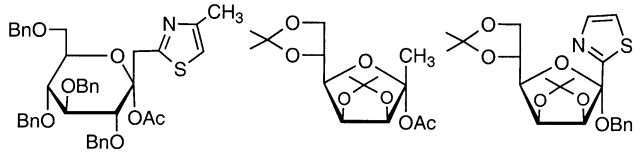
Samarium-promoted reactions were performed at rt by adding 0.1 M SmI_2 in THF to a mixture of **2** and ethylene glycol (12 equiv.) until persistent blue color.

[a] Ratio determined by ^1H NMR analysis of the reaction mixture after the aqueous workup.

[b] Data taken from Ref. 1.

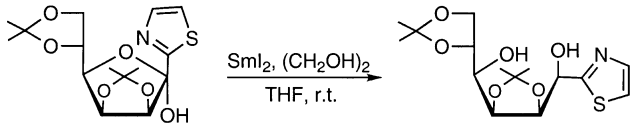
and Girard regarding the SmI_2-induced anomeric deoxygenation of ulosonic acids,[4] we focused our attention on the use of the same reducing reagent[5] and conditions for our purposes. Quite rewardingly, initial experiments showed[6] that treatment of the bis-acetonide-protected thiazolylmannofuranose acetate **2a** with SmI_2 and anhydrous ethylene glycol in THF resulted in the formation of the corresponding α-linked thiazolyl glycoside α-**3a** with high selectivity (Table 1) whereas the silane-based reaction afforded the β-isomer as a single product.[1] It was proved that individual α-**3a** and β-**3a** could be transformed into the corresponding anomeric sugar aldehydes α-**4a** and β-**4a** without epimerization.[1,6] We now report that the same change of reagents produces a substantial inversion of α/β selectivity also in the deoxygenation of the 5-*O*-benzyl-2,3-*O*-isopropylidene-thiazolylribofuranose acetate **2b**. Variation of selectivity, although at lower extent, was also observed in the deoxygenation of the tri-*O*-benzyl derivative **2c** and tetra-*O*-benzylated gluco-, manno-, and galactopyranose **2d**–**f**. In all cases the SmI_2-induced reaction appeared to be a remarkably efficient process as it occurred quite rapidly[7] and afforded the α- and/or β-linked *C*-thiazolyl glycoside **3** in almost quantitative overall yield without glycal side-product.[8] However, this method appears to fail with azido derivatives since the 2-azido-galactopyranose derivative **2g** afforded the compound **5** resulting from the deoxygenation process and the β-elimination of the azido group.[9]

The presence of the thiazole ring directly linked to the anomeric carbon atom and the activation of the hydroxy group as acetate were crucial for a successful deoxygenation reaction. For instance compounds **6**–**9** lacking one of these features were recovered unaltered or afforded the reduced open-chain product **10** (Scheme 2).



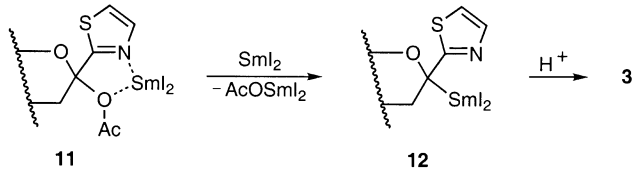
6 **7** **8**

The thiazole ring may serve to assist the two-electron reduction process through the formation of a chelate structure **11** (Scheme 3) in a similar way to that suggested for the deoxygenation of α-oxygenated esters.[10] Quenching of the anomeric organosamarium(III) intermediate **12** by the proton source would lead to the thiazolyl glycoside **3**. It has been suggested that the stereoselectivity of *C*-glycosidation and reduction reactions proceeding through glycosyl



9 **10**

Scheme 2.

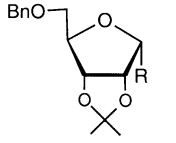


11 **12**

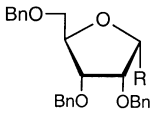
Scheme 3.

samarium intermediates is controlled by the configuration of the major isomer having the bulky $I_2Sm(III)$-substituent in the more thermodynamically stable position.[8,11] The application of the same concept to the results of Table 1 may be used to establish the preferred anomeric configuration of the samariated thiazolyl *C*-glycoside **12** considering that the protodesamariation reaction occurs with retention of configuration.

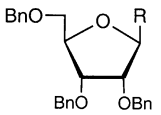
Having both the α- and β-linked isomers of the thiazolyl glycoside **3c** via the SmI_2-induced deoxygenation of **2c**, their anomeric configuration was established by NOE experiments with a high degree of confidence despite the relatively small effects which were observed. The isomer α-**3c** showed a significant NOE (ca. 5%) between H-1 and H-3, upon irradiation of the former, and absence of any effect between H-1 and H-4. On the other hand, the isomer β-**3c** showed a 2.5% NOE between H-1 and H-4. Since β-**3c** was identical in all respects to the product obtained via the TMSOTf–Et_3SiH deoxygenation,[1] we had to conclude that the α-D-configuration established in our earlier report was incorrect. Hence the β-D-configuration is now assigned as shown in Table 1. Adequately characterized ribofuranosides α-**3c** and β-**3c** were transformed into the corresponding aldehydes α-**4c** and β-**4c** by the thiazole-to-formyl protocol.[12] Optimized conditions were established for this transformation by replacing copper(II) chloride or mercury(II) chloride with silver nitrate in the final step of the unmasking reaction sequence.[13] Both aldehydes were stable as pure material and in solution under neutral conditions. However, the α-isomer epimerized to the β-isomer by mild basic treatment (CH_2Cl_2–*i*PrOH–Et_3N, rt, 36 h).[14] As a confirmation of the structure, the reduction of β-**4c** to alcohol and benzylation afforded the *meso*-product **16**. Hence, the structure of the α-configured formyl *C*-ribofuranoside reported in our earlier paper[15] also has to be changed into that of β-**4c**.



α-**3b** R = thiazolyl
α-**4b** R = CHO
13 R = CH_2OH
14 R = CH_2OBn



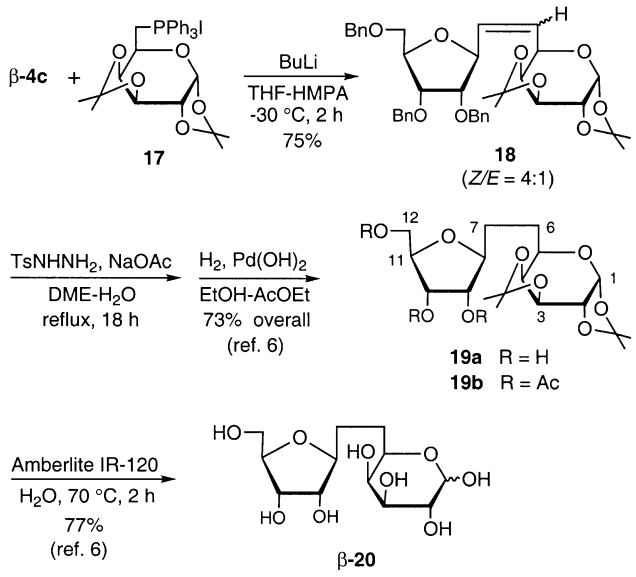
α-**3c** R = thiazolyl
α-**4c** R = CHO



β-**3c** R = thiazolyl
β-**4c** R = CHO
15 R = CH_2OH
16 R = CH_2OBn

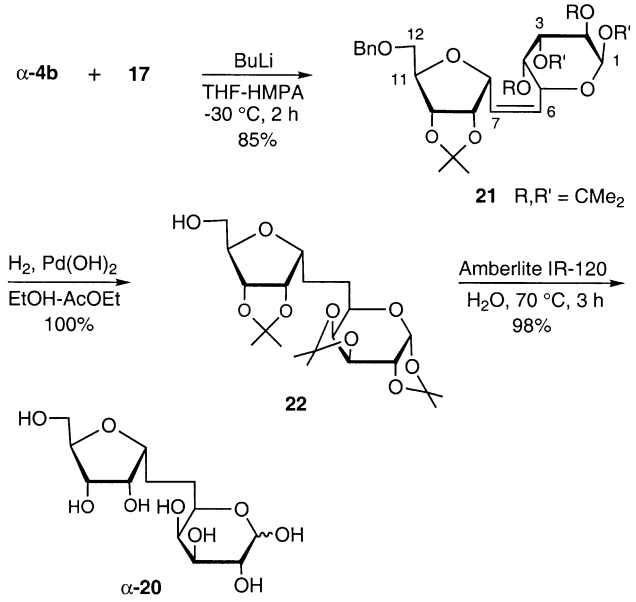
The repetition of the Wittig-based (1→6)-*C*-disaccharide synthesis[6] using the aldehyde β-**4c** and the galactose 6-phosphonium salt **17** (Scheme 4) under improved conditions (see Section 1) afforded as a final product the β-linked *C*-disaccharide β-**20** ($[\alpha]_D^{20}=-16$), identical to the product erroneously characterized as an α-isomer in our earlier publication.[16] The NMR analysis of the triacetate derivative **19b**, obtained from the intermediate **19a** in this synthesis, confirmed the β-linkage. In fact, the NOE experiments carried out with compound **19b** (500 MHz, acetone-d_6) turned out to be more conclusive than with the initial adduct **18** as reported in our original publication.[6] The H-8 proton of **19b** showed an NOE interaction with H-11 (2.5%) but not with H-10.

Since the tri-*O*-benzyl protected formyl *C*-ribofuranoside



Scheme 4.

α-**4c** was unstable under basic conditions, authentic α-D-(1→6)-*C*-disaccharide α-**20** was prepared starting from the more readily accessible[1] and quite stable acetonide-protected aldehyde[17] α-**4b** (Scheme 5). The Wittig coupling of this aldehyde with an equimolar amount of the ylide derived from the phosphonium iodide **17** afforded the (*Z*)-alkene **21** ($J_{6,7}$=11.5 Hz) in remarkably high yield (85%) (Scheme 5). Then reduction of the double bond and debenzylation by hydrogenation over $Pd(OH)_2$ quantitatively converted **21** into the alcohol **22** which upon treatment with Amberlite IR-120 afforded the free *C*-disaccharide α-**20** ($[\alpha]_D^{20}=+41$) in 98% yield. That the original α-linkage was retained in this product was demonstrated by NOE experiments on the alkene **21** and the reduced product **22**. Irradiation of H-8 or H-11 of **21** did not show an NOE interaction between these protons and induced an enhancement of the signal for the H-10 proton



Scheme 5.

(2 and 2.5%, respectively). An NOE interaction was also observed between H-8 and H-10 (1.5%) in compound **22** upon irradiation of the former.

In conclusion, the Sm(II)-based deoxygenation of thiazolylketose acetates **2** may serve to broaden the synthetic utility of these ketosides as precursors to anomeric sugar aldehydes. In some cases the method appears to be of preparative value. This study led to the preparation of α- and β-linked formyl *C*-ribofuranosides and their transformation into diastereomeric (1→6)-*C*-disaccharides containing a galactose unit as the second sugar moiety.

1. Experimental

1.1. General

All moisture-sensitive reactions were performed under a nitrogen atmosphere using oven-dried glassware. Anhydrous solvents were dried over standard drying agents[18] and freshly distilled prior to use. Commercially available powdered 4 Å molecular sieves (5 μm average particle size) were used without further activation. Reactions were monitored by TLC on silica gel 60 F_{254} with detection by charring with sulfuric acid. Flash column chromatography[19] was performed on silica gel 60 (230–400 mesh). Optical rotations were measured at 20 ± 2°C in the stated solvent. IR spectra were recorded in $CHCl_3$. ^{1}H- (300 and 500 MHz) and ^{13}C (75 MHz) NMR were recorded at room temperature unless otherwise specified. Assignments were aided by homo- and heteronuclear two-dimensional experiments. MALDI-TOF mass spectra were acquired using α-cyano-4-hydroxycinnamic acid as the matrix. The (ca. 0.1 M) samarium(II) iodide THF solution was prepared as described,[20] stored at rt, and used within two days. Compound **6** was prepared by addition of 2-lithiomethyl-4-methyl-thiazole to the gluconolactone followed by acetylation.[21] The syntheses of compounds **7** and **8** have been already reported.[22]

1.1.1. 2-(2,3:5,6-Di-*O*-isopropylidene-α-D-mannofuranosyl)thiazole (α-3a). A vigorously stirred solution of **2a** (193 mg, 0.50 mmol) and anhydrous ethylene glycol (372 mg, 6.00 mmol) in anhydrous THF (2.5 mL) was degassed under vacuum and saturated with argon three times, then a ca. 0.1 M solution of SmI_2 in THF was added dropwise by means of a gas-tight syringe until the reaction mixture turned to a persistent blue color (usually after 10–20 min). The mixture was stirred for an additional 10 min, then diluted with saturated aqueous $NaHCO_3$ (50 mL) and concentrated to remove the THF. The residue was extracted with AcOEt (2×50 mL), the combined organic phases were dried (Na_2SO_4) and concentrated. The residue was eluted from a column of silica gel with 2:1 cyclohexane–AcOEt (containing 0.1% of Et_3N) to give α-**3a** (154 mg, 83%) as a low melting solid; $[\alpha]_D$=+22.0 (c=0.9, $CHCl_3$). IR: 2980, 2940, 2880, 1450, 1370, 1300, 1150, 1115, 1060, 975, 945, 910, 890 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ=7.76 and 7.36 (2d, 2H, J=3.2 Hz, Th), 5.44 (dd, 1H, $J_{1,2}$=0.5, $J_{2,3}$=6.1 Hz, H-2), 5.31 (d, 1H, H-1), 4.85 (dd, 1H, $J_{3,4}$=3.7 Hz, H-3), 4.48 (ddd, 1H, $J_{4,5}$=7.5, $J_{5,6a}$=6.2, $J_{5,6b}$=4.5 Hz, H-5), 4.15 (dd, 1H, $J_{6a,6b}$=8.8 Hz, H-6a), 4.10 (dd, 1H, H-6b), 3.87 (dd, 1H, H-4), 1.56, 1.43, 1.39, and 1.38 (4s, 12H, 4CH_3). ^{13}C NMR ($CDCl_3$): δ=168.9, 143.0, and 120.2 (Th), 112.9 and 109.3 (OCO), 85.0 (C-2), 83.2 (C-1), 82.0 (C-4), 80.8 (C-3), 73.1 (C-5), 66.9 (C-6), 26.8, 26.0, 25.1, and 24.6 (CH_3). MALDI-TOF MS (327.4): 328.6 (M+H). Anal. Calcd for $C_{15}H_{21}NO_5S$: C, 55.03; H, 6.47; N, 4.28. Found: C, 55.28; H, 6.40; N, 4.50.

1.1.2. 2-(5-*O*-Benzyl-2,3-*O*-isopropylidene-D-ribofuranosyl)thiazole (3b). Thiazolylketose acetate **2b** was treated with SmI_2 as described for the preparation of α-**3a** to give, after the same workup, a 1:9 α,β mixture of the known[1] *C*-glycosides **3b**. Column chromatography (5:2 cyclohexane–AcOEt) of the crude products gave first β-**3b** (73%) as a syrup; $[\alpha]_D$=−40.3 (c=1.0, $CHCl_3$), lit.[1] $[\alpha]_D$=−40.6 (c=1.0, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ=7.76 (d, 1H, J=3.2 Hz, Th), 7.40–7.20 (m, 6H, Ph, Th), 5.27 (d, 1H, $J_{1,2}$=4.0 Hz, H-1), 5.03 (dd, 1H, $J_{2,3}$=6.5 Hz, H-2), 4.75 (dd, 1H, $J_{3,4}$=3.0 Hz, H-3), 4.53 and 4.49 (2d, 2H, J=12.0 Hz, PhCH_2), 4.40 (ddd, 1H, $J_{4,5a}$=$J_{4,5b}$=4.5 Hz, H-4), 3.62 (dd, 1H, $J_{5a,5b}$=10.0 Hz, H-5a), 3.58 (dd, 1H, H-5b), 1.61 and 1.37 (2s, 6H, 2CH_3). ^{13}C NMR ($CDCl_3$): δ=170.4, 142.9, and 119.3 (Th), 137.8, 128.4, and 127.6 (Ph), 114.4 (OCO), 85.6 (C-2), 84.5 (C-4, C-1), 82.4 (C-3), 73.4 (PhCH_2), 70.3 (C-5), 27.2 and 25.3 (CH_3). MALDI-TOF MS (347.4): 348.5 (M+H).

Eluted second was α-**3b** (7%) as a syrup; $[\alpha]_D$=−63.8 (c=1.0, $CHCl_3$), lit.[1] $[\alpha]_D$=−63.2 (c=1.0, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ=7.80 (d, 1H, J=3.2 Hz, Th), 7.40–7.25 (m, 6H, Ph, Th), 5.64 (d, 1H, $J_{1,2}$=4.5 Hz, H-1), 5.04 (dd, 1H, $J_{2,3}$=6.0 Hz, H-2), 4.96 (dd, 1H, $J_{3,4}$~0.5 Hz, H-3), 4.72 (ddd, 1H, $J_{4,5a}$=3.5, $J_{4,5b}$=3.5 Hz, H-4), 4.59 and 4.50 (2d, 2H, J=12.0 Hz, PhCH_2), 3.75 (dd, 1H, $J_{5a,5b}$=10.5 Hz, H-5a), 3.65 (dd, 1H, H-5b),1.29 and 1.42 (2s, 6H, 2CH_3). ^{13}C NMR ($CDCl_3$): δ=168.0, 141.9, and 119.2 (Th), 137.4, 128.3, 127.7, and 127.4 (Ph), 112.6 (OCO), 83.2 (C-3), 83.1 (C-4), 82.7 (C-1), 82.3 (C-2), 73.4 (PhCH_2), 71.6 (C-5), 25.6 and 24.3 (CH_3). MALDI-TOF MS (347.4): 348.4 (M+H).

1.1.3. 2-(2,3,5-Tri-*O*-benzyl-D-ribofuranosyl)thiazole (3c). Thiazolylketose acetate **2c** was treated with SmI_2 as described for the preparation of α-**3a** to give, after column chromatography (from 6:1 to 3:1 cyclohexane–AcOEt), first, the known[1] *C*-glycoside β-**3c** (70%) as a syrup; $[\alpha]_D$=+18.3 (c=1.0, $CHCl_3$), lit.[1] $[\alpha]_D$=+18.0 (c=1.0, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ=7.78 (d, 1H, J=3.3 Hz, Th), 7.40–7.25 (m, 16H, 3Ph, Th), 5.42 (d, 1H, $J_{1,2}$=3.6 Hz, H-1), 4.78 and 4.66 (2d, 2H, J=12.0 Hz, PhCH_2), 4.63 and 4.56 (2d, 2H, J=12.0 Hz, PhCH_2), 4.59 and 4.45 (2d, 2H, J=11.7 Hz, PhCH_2), 4.42 (ddd, 1H, $J_{3,4}$=6.5, $J_{4,5a}$=3.5, $J_{4,5b}$=4.7 Hz, H-4), 4.24 (dd, 1H, $J_{2,3}$=5.0 Hz, H-2), 3.96 (dd, 1H, H-3), 3.75 (dd, 1H, $J_{5a,5b}$=10.5 Hz, H-5a), 3.65 (dd, 1H, H-5b). ^{13}C NMR ($CDCl_3$): δ=138.1–137.6 and 128.3–127.5 (Ph), 171.2, 142.9, and 119.3 (Th), 81.8 (C-1), 81.7 (C-2), 81.2 (C-4), 77.4 (C-3), 73.2, 72.0, and 71.8 (PhCH_2), 69.8 (C-5). MALDI-TOF MS (487.6): 488.8 (M+H).

Eluted second was α-**3c** (14%) as a syrup; $[\alpha]_D$=+71.0 (c=1.0, $CHCl_3$). IR: 2930, 2860, 1720, 1600, 1450, 1360,

1125, 1080, 1040, 1020 cm^{-1}. ^{13}H NMR (300 MHz, $CDCl_3$): δ=7.81 and 7.39 (2d, 2H, J=3.2 Hz, Th), 7.38–7.22 and 7.12–7.07 (2m, 15H, 3Ph), 5.50 (d, 1H, $J_{1,2}$=3.2 Hz, H-1), 4.63 and 4.53 (2d, 2H, J=12.1 Hz, PhCH_2), 4.54 and 4.42 (2d, 2H, J=11.8 Hz, PhCH_2), 4.48 (ddd, 1H, $J_{3,4}$=8.2, $J_{4,5a}$=2.6, $J_{4,5b}$=3.6 Hz, H-4), 4.33 (dd, 1H, $J_{2,3}$=4.0 Hz, H-2), 4.29 (dd, 1H, H-3), 4.21 (s, 2H, PhCH_2), 3.83 (dd, 1H, $J_{5a,5b}$=11.0 Hz, H-5a), 3.64 (dd, 1H, H-5b). ^{13}C NMR ($CDCl_3$): δ=169.7, 142.0, and 119.8 (Th), 138.2, 137.7, 137.6, and 128.4–127.6 (Ph), 81.1 (C-1), 80.2 (C-4), 79.5 (C-3), 78.6 (C-2), 73.5, 73.2, and 72.6 (PhCH_2), 69.4 (C-5). MALDI-TOF MS (487.6): 488.7 (M+H). Anal. Calcd for $C_{29}H_{29}NO_4S$: C, 71.43; H, 5.99; N, 2.87. Found: C, 71.62; H, 6.10; N, 3.03.

1.1.4. 2-(2,3,4,6-Tetra-*O*-benzyl-D-glucopyranosyl)thiazole (3d). Thiazolylketose acetate **2d** was treated with SmI_2 as described for the preparation of α-**3a** to give, after the same workup, a 2:1 α,β mixture of the known[1] *C*-glycosides **3d**. Analytical samples were obtained by column chromatography (30:1 toluene–acetone). Eluted first was α-**3d** as a syrup; $[\alpha]_D$=+38.4 (c=1.0, $CHCl_3$), lit.[1] $[\alpha]_D$=+38.3 (c=1.0, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$): δ=7.85 (d, 1H, J=3.1 Hz, Th), 7.40–7.05 (m, 21H, 4Ph, Th), 5.29 (d, 1H, $J_{1,2}$=6.0 Hz, H-1), 4.95 and 4.80 (2d, 2H, J=11.3 Hz, PhCH_2), 4.81 and 4.50 (2d, 2H, J=10.7 Hz, PhCH_2), 4.76 and 4.68 (2d, 2H, J=12.0 Hz, PhCH_2), 4.62 and 4.47 (2d, 2H, J=12.0 Hz, PhCH_2), 4.30 (dd, 1H, $J_{2,3}$=8.7, $J_{3,4}$=8.7 Hz, H-3), 4.03 (dd, 1H, H-2), 3.96 (ddd, 1H, $J_{4,5}$=10.0, $J_{5,6a}$=3.3, $J_{5,6b}$=2.0 Hz, H-5), 3.79 (dd, 1H, H-4), 3.73 (dd, 1H, $J_{6a,6b}$=10.6 Hz, H-6a), 3.66 (dd, 1H, H-6b). ^{13}C NMR ($CDCl_3$): δ=165.8, 142.8, and 120.2 (Th), 138.8, 138.4, 138.1, 137.9, and 128.5–127.8 (Ph), 82.1 (C-3), 79.6 (C-2), 77.8 (C-4), 75.3, 75.0, and 73.7 (PhCH_2), 73.6 (C-5, PhCH_2), 73.2 (C-1), 68.7 (C-6). MALDI-TOF MS (607.8): 608.7 (M+H).

Eluted second was β-**3d** as a white solid; mp 112–113°C (AcOEt–hexane), lit[1] mp 112–113°C (AcOEt–hexane); $[\alpha]_D$=+10.6 (c=1.0, $CHCl_3$), lit.[1] $[\alpha]_D$=+10.4 (c=1.0, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$): δ=7.84 and 7.40 (2d, 2H, J=3.1 Hz, Th), 7.40–7.00 (m, 20H, 4Ph), 4.95 and 4.89 (2d, 2H, J=10.8 Hz, PhCH_2), 4.86 and 4.60 (2d, 2H, J=10.8 Hz, PhCH_2), 4.74–4.67 (m, 1H, H-1), 4.62 and 4.56 (2d, 2H, J=11.5 Hz, PhCH_2), 4.52 and 4.15 (2d, 2H, J=10.1 Hz, PhCH_2), 3.88–3.70 (m, 5H, H-2, H-3, H-4, 2H-6), 3.65 (ddd, 1H, $J_{4,5}$=9.0, $J_{5,6a}$=$J_{5,6b}$=3.1 Hz, H-5). ^{13}C NMR ($CDCl_3$): δ=167.6, 142.5, and 119.9 (Th), 138.5, 138.2, 137.9, 137.7, and 128.4–127.6 (Ph), 86.4, 83.1, and 77.9 (C-2, C-3, C-4), 79.7 (C-5), 78.3 (C-1), 75.6, 75.1, 74.9, and 73.4 (PhCH_2), 68.9 (C-6). MALDI-TOF MS (607.8): 608.8 (M+H).

1.1.5. 2-(2,3,4,6-Tetra-*O*-benzyl-D-mannopyranosyl)thiazole (3e). Thiazolylketose acetate **2e** was treated with SmI_2 as described for the preparation of α-**3a** to give, after column chromatography (from 6:1 to 3:1 cyclohexane–AcOEt), first α-**3e** (75%) as a syrup; $[\alpha]_D$=+45.0 (c=0.9, $CHCl_3$). IR: 2930, 2870, 1605, 1450, 1365, 1090, 1025 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ=7.71 (d, 1H, J=3.2 Hz, Th), 7.46–7.24 and 7.17–7.12 (2m, 21H, Th, 4Ph), 5.41 (d, 1H, $J_{1,2}$=2.6 Hz, H-1), 4.86 and 4.52 (2d, 2H, J=10.9 Hz, PhCH_2), 4.80 (s, 2H, PhCH_2), 4.77 (dd, 1H, $J_{2,3}$=3.0 Hz, H-2), 4.72 and 4.62 (2d, 2H, J=11.6 Hz, PhCH_2), 4.72 and 4.60 (2d, 2H, J=12.0 Hz, PhCH_2), 4.08 (dd, 1H, $J_{3,4}$=9.2, $J_{4,5}$=8.5 Hz, H-4), 3.89 (dd, 1H, H-3), 3.86–3.77 (m, 3H, H-5, 2H-6). ^{13}C NMR ($CDCl_3$): δ=168.8, 142.3, and 120.5 (Th), 138.3, 138.2, and 128.2–127.4 (Ph), 79.6 (C-3), 75.0 (C-1, C-2, C-5), 74.8 (PhCH_2), 74.5 (C-4), 73.3, 72.4, and 71.8 (PhCH_2), 69.3 (C-6). MALDI-TOF MS (607.8): 608.9 (M+H). Anal. Calcd for $C_{37}H_{37}NO_5S$: C, 73.12; H, 6.14; N, 2.30. Found: C, 73.40; H, 6.19; N, 2.46.

Eluted second was the known[1] *C*-glycoside β-**3e** (19%) as a syrup; $[\alpha]_D$=−19.2 (c=1.0, $CHCl_3$), lit.[1] $[\alpha]_D$=−19.8 (c=1.0, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$): δ=7.75 (d, 1H, J=3.2 Hz, Th), 7.42–6.95 (m, 21H, 4Ph, Th), 4.86 (d, 1H, $J_{1,2}$=0.9 Hz, H-1), 4.77 and 4.65 (2d, 2H, J=11.5 Hz, PhCH_2), 4.93 and 4.62 (2d, 2H, J=11.0 Hz, PhCH_2), 4.75 and 4.64 (2d, 2H, J=12.0 Hz, PhCH_2), 4.61 and 4.27 (2d, 2H, J=11.5 Hz, PhCH_2), 4.42 (dd, 1H, $J_{2,3}$=2.9 Hz, H-2), 4.05 (dd, 1H, $J_{3,4}$=9.5, $J_{4,5}$=9.5 Hz, H-4), 3.85 (d, 2H, $J_{5,6}$=3.6 Hz, 2H-6), 3.82 (dd, 1H, H-3), 3.70 (dt, 1H, H-5). ^{13}C NMR ($CDCl_3$): δ=169.5, 142.0, and 119.4 (Th), 138.6–138.2 and 128.5–127.3 (Ph), 83.7 (C-3), 80.4 (C-5), 78.5 (C-1), 76.5 (C-2), 75.2 (PhCH_2), 74.6 (C-4, PhCH_2), 71.9 and 73.6 (PhCH_2), 69.4 (C-6). MALDI-TOF MS (607.8): 609.0 (M+H).

1.1.6. 2-(2,3,4,6-Tetra-*O*-benzyl-D-galactopyranosyl)thiazole (3f). Thiazolylketose acetate **2f** was treated with SmI_2 as described for the preparation of α-**3a** to give, after column chromatography (from 6:1 to 4:1 cyclohexane–AcOEt), first α-**3f** (50%) as a syrup; $[\alpha]_D$=+40.0 (c=1.0, $CHCl_3$). IR: 2990, 2930, 2870, 1605, 1490, 1450, 1370, 1355, 1315, 1090, 1025, 910, 880 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ=7.81 and 7.36 (2d, 2H, J=3.2 Hz, Th), 7.35–7.25 and 7.11–7.07 (2m, 20H, 4Ph), 5.32 (d, 1H, $J_{1,2}$=3.3 Hz, H-1), 4.65 and 4.57 (2d, 2H, J=11.9 Hz, PhCH_2), 4.64 (s, 2H, PhCH_2), 4.57 and 4.52 (2d, 2H, J=12.2 Hz, PhCH_2), 4.49 (ddd, 1H, $J_{4,5}$=2.8, $J_{5,6a}$=8.0, $J_{5,6b}$=3.7 Hz, H-5), 4.39 and 4.35 (2d, 2H, J=11.5 Hz, PhCH_2), 4.18 (dd, 1H, $J_{2,3}$=5.8 Hz, H-2), 4.16 (dd, 1H, H-4), 4.04 (dd, 1H, $J_{6a,6b}$=11.3 Hz, H-6a), 3.95 (dd, 1H, H-3), 3.79 (dd, 1H, H-6b). ^{13}C NMR ($CDCl_3$): δ=168.6, 142.0, and 119.4 (Th), 138.2, 137.7, and 128.2–127.5 (Ph), 77.1 (C-2), 75.5 (C-3), 74.8 (C-5), 73.6 (C-4, PhCH_2), 73.0, 72.9, and 72.4 (PhCH_2), 70.6 (C-1), 66.2 (C-6). MALDI-TOF MS (607.8): 608.8 (M+H). Anal. Calcd for $C_{37}H_{37}NO_5S$: C, 73.12; H, 6.14; N, 2.30. Found: C, 73.00; H, 6.21; N, 2.48.

Eluted second was the known[1] *C*-glycoside β-**3f** (36%) as a syrup; $[\alpha]_D$=0.0 (c=1.0, $CHCl_3$), lit.[1] $[\alpha]_D$=0 (c=1.0, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$): δ=7.80 (d, 1H, J=3.2 Hz, Th), 7.40–7.20 (m, 21H, 4Ph, Th), 5.01 and 4.67 (2d, 2H, J=11.8 Hz, PhCH_2), 4.78 and 4.73 (2d, 2H, J=10.6 Hz, PhCH_2), 4.66 (d, 1H, $J_{1,2}$=9.4 Hz, H-1), 4.66 and 4.28 (2d, 2H, J=10.6 Hz, PhCH_2), 4.47 and 4.41 (2d, 2H, J=11.8 Hz, PhCH_2), 4.24 (dd, 1H, $J_{2,3}$=9.4 Hz, H-2), 4.05 (dd, 1H, $J_{3,4}$=2.9, $J_{4,5}$~0.6 Hz, H-4), 3.75 (dt, 1H, $J_{5,6}$=6.5 Hz, H-5), 3.73 (dd, 1H, H-3), 3.63 (d, 2H, 2H-6). ^{13}C NMR ($CDCl_3$): δ=167.9, 142.5, and 119.8 (Th), 138.9–137.9 and 128.4–127.5 (Ph), 79.4 (C-2), 78.7 (C-1), 84.0 and 77.7 (C-3, C-5), 75.0, 74.4, 73.4, and 72.5 (PhCH_2),

73.8 (C-4), 68.6 (C-6). MALDI-TOF MS (607.8): 608.6 (M+H).

1.1.7. 1,5-Anhydro-3,4,6-tri-*O*-benzyl-2-deoxy-1-*C*-(2-thiazolyl)-D-*lyxo*-hex-1-enitol (5). Thiazolylketose acetate **2g** was treated with SmI_2 as described for the preparation of α-**3a** to give, after the same workup, the glycal **5** contaminated by uncharacterized byproducts. Upon trituration of the residue with *n*-pentane, pure **5** was isolated as a white solid; mp 72–73°C; $[\alpha]_D=-84.3$ ($c=0.5$, $CHCl_3$). IR: 2990, 2930, 2870, 1725, 1650, 1605, 1490, 1450, 1350, 1265, 1150, 1090, 1030, 920, 880 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): $\delta=7.81$ (d, 1H, $J=3.2$ Hz, Th), 7.40–7.26 (m, 16H, 3Ph, Th), 6.11 (dd, 1H, $J_{2,3}=3.3$, $J_{2,4}=1.0$ Hz, H-2), 4.91 and 4.68 (2d, 2H, $J=11.9$ Hz, PhCH_2), 4.78 and 4.67 (2d, 2H, $J=12.0$ Hz, PhCH_2), 4.54 and 4.49 (2d, 2H, $J=12.0$ Hz, PhCH_2), 4.44 (dddd, 1H, $J_{3,5}=1.2$, $J_{4,5}=2.5$, $J_{5,6a}=6.9$, $J_{5,6b}=5.6$ Hz, H-5), 4.37 (ddd, 1H, $J_{3,4}=4.1$ Hz, H-3), 4.06 (ddd, 1H, H-4), 3.90 (dd, 1H, $J_{6a,6b}=10.5$ Hz, H-6a), 3.83 (dd, 1H, H-6b). ^{13}C NMR ($CDCl_3$): $\delta=146.6$, 143.3, and 119.5 (Th), 138.3, 138.1, and 128.4–127.5 (Ph, C-1), 98.5 (C-2), 77.1 (C-5), 73.5, 73.3, and 70.9 (Ph*C*H_2), 71.1 (C-4), 70.9 (C-3), 68.0 (C-6). MALDI-TOF MS (499.6): 500.6 (M+H). Anal. Calcd for $C_{30}H_{29}NO_4S$: C, 72.12; H, 5.85; N, 2.80. Found: C, 72.25; H, 5.88; N, 2.99.

1.1.8. 2,3:5,6-Di-*O*-isopropylidene-1-*C*-thiazolyl-D-hexitol (10). Thiazolylketose **9** was treated with SmI_2 as described for the preparation of α-**3a** to give, after the same workup, the diol **10** contaminated by uncharacterized byproducts. ^1H NMR (300 MHz, $CDCl_3$): $\delta=7.77$ and 7.38 (2d, 2H, $J=3.3$ Hz, Th), 5.38 (dd, 1H, $J_{1,2}=6.6$, $J_{1,OH}=6.2$ Hz, H-1), 4.82 (d, 1H, OH-1), 4.72 (dd, 1H, $J_{2,3}=6.8$ Hz, H-2), 4.51 (dd, 1H, $J_{3,4}=0.6$ Hz, H-3), 4.10–4.02 (m, 3H, H-5, 2H-6), 3.69 (ddd, 1H, $J_{4,5}=6.5$, $J_{4,OH}=7.9$ Hz, H-4), 3.12 (d, 1H, OH-4), 1.57, 1.44, 1.34, and 1.31 (4s, 12H, 4CH_3). MALDI-TOF MS (345.4): 346.5 (M+H).

1.1.9. 2,5-Anhydro-3,4,6-tri-*O*-benzyl-*aldehydo*-D-*altro*-hexofuranose (α-4c). A mixture of α-**3c** (49 mg, 0.10 mmol), activated 4 Å powdered molecular sieves (50 mg), and anhydrous CH_3CN (1 mL) was stirred at room temperature for 10 min, then methyl triflate (15 μL, 0.13 mmol) was added. The suspension was stirred at room temperature for 15 min and then concentrated to dryness without filtering off the molecular sieves. To a stirred suspension of the crude *N*-methylthiazolium salt in MeOH (1 mL) was added $NaBH_4$ (8 mg, 0.20 mmol). The mixture was stirred at room temperature for an additional 5 min, diluted with acetone, filtered through a pad of Celite, and concentrated. To a vigorously stirred solution of the crude mixture of diastereomeric thiazolidines in CH_3CN (1 mL) was added H_2O (0.1 mL) and then $AgNO_3$ (17 mg, 0.10 mmol). The mixture was stirred at room temperature for 10 min, then diluted with 1 M phosphate buffer at pH 7 (10 mL) and concentrated to remove acetonitrile (bath temperature not exceeding 40°C). The mixture was extracted with CH_2Cl_2 (2×20 mL), the combined organic phases were dried (Na_2SO_4), filtered through a pad of Celite to remove the silver salts, and concentrated to afford α-**4c** (43 mg, 99%, ca. 90% pure by ^1H NMR analysis) as a syrup. ^1H NMR (300 MHz, $CDCl_3$): $\delta=9.75$ (d, 1H, $J_{1,2}=2.0$ Hz, H-1), 7.43–7.22 (m, 15H, 3Ph), 4.68 and 4.62 (2d, 2H, $J=11.6$ Hz, PhCH_2), 4.64 and 4.53 (2d, 2H, $J=11.8$ Hz, PhCH_2), 4.58 and 4.51 (2d, 2H, $J=12.0$ Hz, PhCH_2), 4.46 (ddd, 1H, $J_{4,5}=4.1$, $J_{5,6a}=3.4$, $J_{5,6b}=3.7$ Hz, H-5), 4.45 (dd, 1H, $J_{2,3}=6.0$, $J_{3,4}=5.6$ Hz, H-3), 4.40 (dd, 1H, H-2), 4.06 (dd, 1H, H-4), 3.68 (dd, 1H, $J_{6a,6b}=10.9$ Hz, H-6a), 3.56 (dd, 1H, H-6b). ^1H NMR (300 MHz, DMSO-d_6, 140°C): $\delta=9.64$ (d, 1H, $J_{1,2}=2.0$ Hz, H-1), 7.40–7.25 (m, 15H, 3Ph), 4.69 and 4.61 (2d, 2H, $J=11.8$ Hz, PhCH_2), 4.67 and 4.61 (2d, 2H, $J=12.0$ Hz, PhCH_2), 4.58 (dd, 1H, $J_{2,3}=6.2$, $J_{3,4}=4.4$ Hz, H-3), 4.54 (s, 2H, PhCH_2), 4.44 (d, 1H, H-2), 4.33 (ddd, 1H, $J_{4,5}=5.2$, $J_{5,6a}=3.8$, $J_{5,6b}=4.7$ Hz, H-5), 4.11 (dd, 1H, H-4), 3.64 (dd, 1H, $J_{6a,6b}=11.0$ Hz, H-6a), 3.59 (dd, 1H, H-6b).

1.1.10. 2,5-Anhydro-3,4,6-tri-*O*-benzyl-*aldehydo*-D-*allo*-hexofuranose (β-4c). Thiazolyl glycoside β-**3c** (292 mg, 0.60 mmol) was treated as described for the preparation of α-**4c** to give, after the same workup, the aldehyde β-**4c** (246 mg, 95%, ca. 90% pure by ^1H NMR analysis) identical to the product obtained using mercury(II) chloride.[1] ^1H NMR (300 MHz, DMSO-d_6, 140°C): $\delta=9.58$ (d, 1H, $J_{1,2}=1.5$ Hz, H-1), 7.40–7.20 (m, 15H, 3Ph), 4.64 and 4.56 (2d, 2H, $J=11.7$ Hz, PhCH_2), 4.63 (s, 2H, PhCH_2), 4.54 (s, 2H, PhCH_2), 4.36 (dd, 1H, $J_{2,3}=4.8$ Hz, H-2), 4.27 (dd, 1H, $J_{3,4}=5.2$ Hz, H-3), 4.24 (ddd, 1H, $J_{4,5}=4.9$, $J_{5,6a}=3.6$, $J_{5,6b}=4.7$ Hz, H-5), 3.97 (dd, 1H, H-4), 3.66 (dd, 1H, $J_{6a,6b}=11.0$ Hz, H-6a), 3.60 (dd, 1H, H-6b).

1.1.11. Epimerization of α-4c. A solution of formyl *C*-riboside α-**4c** (43 mg, ca. 0.1 mmol) in CH_2Cl_2 (1 mL), isopropanol (0.8 mL), and triethylamine (0.2 mL) was kept at room temperature for 24 h, then concentrated. Since the NMR analysis of the residue revealed the presence of diastereomeric isopropyl hemiacetals, the products were reduced to the corresponding alcohols. To a stirred solution of the crude reaction mixture in 1:1 Et_2O–MeOH (2 mL) was added $NaBH_4$ (5.5 mg, 0.15 mmol). The mixture was stirred at room temperature for an additional 10 min, diluted with acetone, and concentrated. The residue was suspended in CH_2Cl_2 (20 mL), washed with H_2O (2×5 mL), dried (Na_2SO_3), and concentrated to give almost pure **15** (NMR analysis, see Section1.1.13).

1.1.12. 2,5-Anhydro-1,6-di-*O*-benzyl-3,4-*O*-isopropylidene-D-altritol (14). Formyl *C*-glycoside α-**4b** was prepared from α-**3b** (70 mg, 0.20 mmol) as described for the synthesis of α-**4c**. To a stirred solution of the crude aldehyde in 1:1 Et_2O–MeOH (2 mL) was added $NaBH_4$ (11 mg, 0.30 mmol). The mixture was stirred at room temperature for an additional 10 min, diluted with acetone, and concentrated. The residue was suspended in CH_2Cl_2 (40 mL), washed with H_2O (2×10 mL), dried (Na_2SO_3), and concentrated to give syrupy 2,5-anhydro-6-*O*-benzyl-3,4-*O*-isopropylidene-D-altritol (**13**). ^1H NMR (300 MHz, $CDCl_3$): $\delta=7.41$–7.29 (m, 5H, Ph), 4.85–4.81 (m, 2H, H-3, H-4), 4.57 and 4.50 (2d, 2H, $J=12.0$ Hz, PhCH_2), 4.28 (ddd, 1H, $J_{4,5}=0.4$, $J_{5,6a}=3.7$, $J_{5,6b}=4.0$ Hz, H-5), 4.27–4.22 (m, 1H, H-2), 3.92 (ddd, 1H, $J_{1a,1b}=12.0$, $J_{1a,OH}=J_{1a,2}=5.5$ Hz, H-1a), 3.87 (ddd, 1H, $J_{1b,2}=5.5$, $J_{1b,OH}=7.4$ Hz, H-1b), 3.63 (dd, 1H, $J_{6a,6b}=10.2$ Hz, H-6a), 3.58 (dd, 1H, H-6b), 2.24 (dd, 1H, OH), 1.53 and 1.35 (2s, 6H, 2CH_3). To a stirred solution of the crude alcohol in

DMF (1 mL) was added NaH (12 mg, 0.30 mmol, of a 60% dispersion in oil) and, after 10 min, benzyl bromide (30 μL, 0.25 mmol). The mixture was stirred at room temperature for 30 min, then treated with CH_3OH (0.5 mL), stirred for an additional 10 min, diluted with H_2O (5 mL), and extracted with Et_2O (2×20 mL). The combined organic phases were dried (Na_2SO_4) and concentrated. The residue was eluted from a column of silica gel with 7:1 cyclohexane–AcOEt to give **14** (54 mg, 70% from α-**3b**) as a syrup; $[\alpha]_D=-34.8$ ($c=1.1$, $CHCl_3$). IR: 2980, 2940, 2915, 2860, 1450, 1380, 1370, 1090, 1020, 900, 870, 860 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): $\delta=7.41–7.27$ (m, 10H, 2Ph), 4.83 (dd, 1H, $J_{3,4}=6.0$, $J_{4,5}=0.8$ Hz, H-4), 4.77 (dd, 1H, $J_{2,3}=4.0$ Hz, H-3), 4.69 and 4.56 (2d, 2H, $J=12.1$ Hz, PhCH_2), 4.57 and 4.49 (2d, 2H, $J=12.0$ Hz, PhCH_2), 4.34 (ddd, 1H, $J_{1a,2}=4.3$, $J_{1b,2}=7.4$ Hz, H-2), 4.26 (ddd, 1H, $J_{5,6a}=4.0$, $J_{5,6b}=3.9$ Hz, H-5), 3.78 (dd, 1H, $J_{1a,1b}=10.2$ Hz, H-1a), 3.66 (dd, 1H, H-1b), 3.64 (dd, 1H, $J_{6a,6b}=10.3$ Hz, H-6a), 3.58 (dd, 1H, H-6b). ^{13}C NMR ($CDCl_3$): $\delta=138.2$, 137.8, and 128.3–127.4 (Ph), 112.2 (OCO), 83.1 (C-4), 83.0 (C-5), 81.6 (C-3), 81.2 (C-2), 73.4 (2PhCH_2), 71.4 (C-6), 69.2 (C-1), 26.2 and 24.9 (CH_3). MALDI-TOF MS (384.5): 407.8 (M+Na), 423.4 (M+K). Anal. Calcd for $C_{23}H_{28}O_5$: C, 71.85; H, 7.34. Found: C, 71.98; H, 7.39.

1.1.13. 2,5-Anhydro-3,4,6-tri-*O*-benzyl-D-allitol (15). To a cooled (0°C), stirred solution of aldehyde β-**4c** (150 mg, 0.35 mmol) in CH_3OH (4 mL) was added $NaBH_4$ (16 mg, 0.42 mmol). The mixture was stirred at 0°C for an additional 10 min, then diluted with acetone (0.5 mL), warmed to room temperature, and concentrated. The residue was suspended in CH_2Cl_2 (20 mL), washed with H_2O (2×5 mL), dried (Na_2SO_4), concentrated, and eluted from a column of silica gel with 2:1 cyclohexane–AcOEt to give **15** (143 mg, 95%) as a white foam; $[\alpha]_D=+25.4$ ($c=0.9$, $CHCl_3$). IR: 3440, 2920, 2860, 1730, 1355, 1110, 1085, 1025 cm^{-1}. ^1H NMR (300 MHz, $C_6D_6+D_2O$): $\delta=7.40–7.00$ (m, 15H, 3Ph), 4.45 and 4.29 (2d, 2H, $J=12.0$ Hz, PhCH_2), 4.41 and 4.35 (2d, 2H, $J=12.2$ Hz, PhCH_2), 4.32 (ddd, 1H, $J_{4,5}=6.5$, $J_{5,6a}=3.0$, $J_{5,6b}=2.2$ Hz, H-5), 4.23 (ddd, 1H, $J_{1a,2}=2.9$, $J_{1b,2}=2.2$, $J_{2,3}=4.2$ Hz, H-2), 4.22 (dd, 1H, $J_{3,4}=4.0$ Hz, H-4), 4.21 and 4.10 (2d, 2H, $J=11.9$ Hz, PhCH_2), 4.02 (dd, 1H, H-3), 3.78 (dd, 1H, $J_{1a,1b}=12.0$ Hz, H-1a), 3.50 (dd, 1H, $J_{6a,6b}=10.5$ Hz, H-6a), 3.44 (dd, 1H, H-1b), 3.31 (dd, 1H, H-6b). ^{13}C NMR (C_6D_6): $\delta=138.9$ and 128.6–127.8 (Ph), 83.5 (C-2), 81.3 (C-5), 79.0 (C-3), 78.8 (C-4), 73.4, 72.2, and 72.1 (PhCH_2), 69.9 (C-6), 63.4 (C-1). MALDI-TOF MS (434.5): 457.7 (M+Na), 473.9 (M+K). Anal. Calcd for $C_{27}H_{30}O_5$: C, 74.63; H, 6.96. Found: C, 74.50; H, 7.10.

1.1.14. 2,5-Anhydro-1,3,4,6-tetra-*O*-benzyl-*meso*-allitol (16). To a cooled (0°C), stirred solution of **15** (100 mg, 0.23 mmol) in DMF (2 mL) was added NaH (11 mg, 0.28 mmol, of a 60% dispersion in oil) and, after 30 min, benzyl bromide (41 μL, 0.35 mmol). The mixture was stirred at room temperature for 30 min, then treated with CH_3OH (0.5 mL), stirred for an additional 10 min, diluted with H_2O (5 mL), and extracted with Et_2O (2×20 mL). The combined organic phases were dried (Na_2SO_4) and concentrated. The residue was eluted from a column of silica gel with 6:1 cyclohexane–AcOEt to give **16** (111 mg, 92%) as a white solid; mp below 55°C (from AcOEt–cyclohexane); $[\alpha]_D=0.0$ ($c=0.3$ and 0.8, $CHCl_3$). IR: 2910, 2860, 1440, 1355, 1110, 1085, 1040, 1020 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): $\delta=7.50–7.20$ (m, 20H, 4Ph), 4.61 and 4.54 (2d, 4H, $J=11.9$ Hz, 2PhCH_2), 4.59 and 4.55 (2d, 4H, $J=11.2$ Hz, 2PhCH_2), 4.28 (dd, 2H, $J_{2,3}=8.8$, $J_{3,4}=4.1$ Hz, H-3=H-4), 3.93 (ddd, 2H, $J_{1a,2}=4.0$, $J_{1b,2}=4.9$ Hz, H-2=H-5), 3.61 (dd, 2H, $J_{1a,1b}=10.0$ Hz, H-1a=H-6a), 3.57 (dd, 2H, H-1b=H-6b). ^{13}C NMR ($CDCl_3$): $\delta=138.2$, 137.8, and 128.3–127.5 (Ph), 80.9 (C-3=C-4), 77.4 (C-2=C-5), 73.3 and 71.8 (PhCH_2), 70.3 (C-1=C-6). MALDI-TOF MS (524.7): 547.6 (M+Na), 563.8 (M+K). Anal. Calcd for $C_{34}H_{36}O_5$: C, 77.84; H, 6.92. Found: C, 78.00; H, 7.10.

1.1.15. (*E*,*Z*)-8,11-Anhydro-9,10,12-tri-*O*-benzyl-6,7-dideoxy-1,2:3,4-di-*O*-isopropylidene-α-D-*allo*-D-*galacto*-tridec-6-eno-1,5-pyranose (18). A mixture of phosphonium salt **17** (253 mg, 0.40 mmol), activated 4 Å powdered molecular sieves (0.40 g), anhydrous THF (2 mL), and anhydrous HMPA (1 mL) was stirred at room temperature for 10 min, then cooled to −30°C. To the stirred mixture was added dropwise, *n*-butyllithium (250 μL, 0.40 mmol, of a 1.6 M solution in hexanes) and, after 5 min, a solution of β-**4c** (173 mg, 0.40 mmol) in anhydrous THF (1 mL) over a 10 min period. The mixture was stirred at −30°C for an additional 30 min, then allowed to reach −10°C in 1.5 h, diluted with Et_2O (100 mL), and filtered through a pad of Celite. The ethereal solution was washed with 1 M phosphate buffer at pH 7 (10 mL), dried (Na_2SO_4), and concentrated. Column chromatography (from 7:1 to 4:1 cyclohexane–AcOEt) of the residue afforded **18** (198 mg, 75%) as a 4:1 *Z*/*E* mixture of isomers identical to the products described in an earlier publication.[6]

1.1.16. 9,10,12-Tri-*O*-acetyl-8,11-anhydro-6,7-dideoxy-1,2:3,4-di-*O*-isopropylidene-α-D-*allo*-D-*galacto*-trideco-1,5-pyranose (19b). For NMR studies a sample of triol **19a** was acetylated at room temperature in 1:1 acetic anhydride–pyridine, concentrated, and used without further purifications. ^1H NMR (500 MHz, acetone-d_6): $\delta=5.47$ (d, 1H, $J_{1,2}=5.1$ Hz, H-1), 5.17 (dd, 1H, $J_{9,10}=5.9$, $J_{10,11}=4.7$ Hz, H-10), 4.95 (dd, 1H, $J_{8,9}=6.2$ Hz, H-9), 4.60 (dd, 1H, $J_{2,3}=2.3$, $J_{3,4}=7.8$ Hz, H-3), 4.32 (dd, 1H, H-2), 4.30 (dd, 1H, $J_{11,12a}=4.9$, $J_{12a,12b}=13.3$ Hz, H-12a), 4.17 (dd, 1H, $J_{4,5}=2.0$ Hz, H-4), 4.14–4.10 (m, 2H, H-11, H-12b), 3.98 (ddd, 1H, $J_{7a,8}=4.9$, $J_{7b,8}=7.6$ Hz, H-8), 3.75 (ddd, 1H, $J_{5,6a}=5.0$, $J_{5,6b}=8.0$ Hz, H-5), 2.05 (s, 9H, 3Ac), 1.88–1.82 and 1.72–1.58 (2m, 4H, 2H-6, 2H-7), 1.50, 1.39, and 1.34 (3s, 12H, 4CH_3). MALDI-TOF MS (516.5): 539.7 (M+Na), 556.0 (M+K).

1.1.17. (*Z*)-8,11-Anhydro-12-*O*-benzyl-6,7-dideoxy-1,2:3,4:9,10-tri-*O*-isopropylidene-α-D-*altro*-D-*galacto*-tridec-6-eno-1,5-pyranose (21). A mixture of phosphonium salt **17** (253 mg, 0.40 mmol), activated 4 Å powdered molecular sieves (0.40 g), anhydrous THF (2 mL), and anhydrous HMPA (1 mL) was stirred at room temperature for 10 min, then cooled to −30°C. To the stirred mixture was added dropwise *n*-butyllithium (250 μL, 0.40 mmol, of a 1.6 M solution in hexanes) and, after 5 min, a solution of α-**4b** (117 mg, 0.40 mmol) in anhydrous THF (1 mL) over a 10 min period. The mixture was stirred at −30°C for an additional 30 min, then allowed to reach −10°C in 1.5 h,

diluted with Et_2O (100 mL), and filtered through a pad of Celite. The ethereal solution was washed with 1 M phosphate buffer at pH 7 (10 mL), dried (Na_2SO_4), and concentrated. The residue was eluted from a column of silica gel with 2:1 cyclohexane–AcOEt (containing 0.3% of Et_3N) to give **21** (176 mg, 85%) as a syrup; $[\alpha]_D=-99.0$ ($c=1.0$, $CHCl_3$). IR: 2990, 2940, 2910, 2860, 1450, 1380, 1160, 1060, 995, 900, 855 cm^{-1}. ^1H NMR (300 MHz, C_6D_6): $\delta=7.20$–7.03 (m, 5H, Ph), 6.28 (dd, 1H, $J_{5,6}=6.7$, $J_{6,7}=11.5$ Hz, H-6), 6.23 (dd, 1H, $J_{7,8}=6.2$ Hz, H-7), 5.54 (d, 1H, $J_{1,2}=5.1$ Hz, H-1), 4.98 (dd, 1H, $J_{8,9}=3.8$ Hz, H-8), 4.92 (dd, 1H, $J_{4,5}=1.6$ Hz, H-5), 4.71 (dd, 1H, $J_{9,10}=6.2$, $J_{10,11}=0.7$ Hz, H-10), 4.66 (dd, 1H, H-9), 4.51 (dd, 1H, $J_{2,3}=2.3$, $J_{3,4}=7.9$ Hz, H-3), 4.35 (ddd, 1H, $J_{11,12a}=4.9$, $J_{11,12b}=4.3$ Hz, H-11), 4.22 and 4.14 (2d, 2H, $J=12.5$ Hz, PhCH_2), 4.18 (dd, 1H, H-2), 4.17 (dd, 1H, H-4), 3.34 (dd, 1H, $J_{12a,12b}=10.0$ Hz, H-12a), 3.19 (dd, 1H, H-12b), 1.50, 1.48, 1.42, 1.19, 1.12, and 1.04 (6s, 18H, $6CH_3$). ^{13}C NMR (C_6D_6): $\delta=138.5$, 128.6, 127.7 and 127.6 (Ph), 130.0 (C-6), 129.5 (C-7), 112.3, 109.1, and 108.0 (OCO), 83.8 (C-10), 83.5 (C-9), 83.4 (C-11), 78.8 (C-8), 73.9 (C-4), 73.4 (PhCH_2), 71.4 (C-3, C-12), 70.7 (C-2), 65.0 (C-5), 26.7, 26.3, 25.2, 24.9, and 24.4 (CH_3). MALDI-TOF MS (518.6): 541.4 (M+Na), 557.7 (M+K). Anal. Calcd for $C_{23}H_{28}O_5$: C, 64.85; H, 7.39. Found: C, 65.08; H, 7.47.

1.1.18. 8,11-Anhydro-6,7-dideoxy-1,2:3,4:9,10-tri-*O*-isopropylidene-α-D-*altro*-D-*galacto*-trideco-1,5-pyranose (22). A vigorously stirred mixture of **21** (155 mg, 0.30 mmol), 20% palladium hydroxide on carbon (80 mg), and 1:1 MeOH–AcOEt (9 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 **22** (129 mg, 100%) as a colorless syrup; $[\alpha]_D=-42.0$ ($c=0.9$, $CHCl_3$). IR: 3600, 2990, 2940, 2870, 1710, 1600, 1450, 1380, 1305, 1160, 1065, 1030, 1000, 895 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): $\delta=5.53$ (d, 1H, $J_{1,2}=5.1$ Hz, H-1), 4.65 (dd, 1H, $J_{8,9}=3.8$, $J_{9,10}=6.2$ Hz, H-9), 4.59 (dd, 1H, $J_{2,3}=2.3$, $J_{3,4}=7.9$ Hz, H-3), 4.57 (dd, 1H, $J_{10,11}=1.4$ Hz, H-10), 4.29 (dd, 1H, H-2), 4.17 (dd, 1H, $J_{4,5}=1.8$ Hz, H-4), 4.12 (ddd, 1H, $J_{11,12a}=J_{11,12b}=6.2$ Hz, H-11), 3.93 (ddd, 1H, $J_{7a,8}=5.8$, $J_{7b,8}=7.7$ Hz, H-8), 3.78 (ddd, 1H, $J_{5,6a}=4.5$, $J_{5,6b}=8.2$ Hz, H-5), 3.56 (d, 2H, 2H-12), 1.97–1.67 (m, 4H, 2H-6, 2H-7), 1.52, 1.50, 1.46, 1.35, and 1.33 (5s, 18H, $6CH_3$). ^{13}C NMR ($CDCl_3$): $\delta=112.4$, 108.9, and 108.3 (OCO), 96.5 (C-1), 84.0 (C-11), 82.3 (C-10), 81.6 (C-9), 80.3 (C-8), 72.8 (C-4), 70.9 (C-3), 70.5 (C-2), 67.3 (C-5), 61.5 (C-12), 26.7 and 25.4 (C-6, C-7), 26.3, 26.0, 25.0, 24.9, and 24.3 (CH_3). MALDI-TOF MS (430.5): 453.8 (M+Na), 469.8 (M+K). Anal. Calcd for $C_{21}H_{34}O_9$: C, 58.59; H, 7.96. Found: C, 58.40; H, 8.09.

1.1.19. 8,11-Anhydro-6,7-dideoxy-D-*altro*-D-*galacto*-tridecose (α-20). A mixture of **22** (86 mg, 0.20 mmol), H_2O (4 mL), and Amberlite IR120 (0.40 g, activated immediately before the use) was gently stirred at 70°C for 3 h, then cooled to room temperature, filtered through a plug of cotton, and concentrated to give α-**20** (61 mg, 98%) as a white foam; $[\alpha]_D=+41.0$ ($c=0.9$, H_2O). ^1H NMR (500 MHz, D_2O): $\delta=5.10$ (d, 0.4H, $J_{1,2}=3.8$ Hz, H-1α), 4.44 (d, 0.6H, $J_{1,2}=7.9$ Hz, H-1β), 4.12 (dd, 1H, $J_{9,10}=4.4$, $J_{10,11}=8.3$ Hz, H-10αβ), 4.02 (dd, 1H, $J_{8,9}=2.7$ Hz, H-9αβ), 3.97–3.88 (m, 1.4H, H-8αβ, H-5α), 3.78 (dd, 0.4H, $J_{3,4}=3.5$, $J_{4,5}=1.0$ Hz, H-4α), 3.76 (ddd, 1H, $J_{11,12a}=2.9$, $J_{11,12b}=5.2$ Hz, H-11αβ), 3.74 (dd, 0.4H, $J_{2,3}=10.5$ Hz, H-3α), 3.72 (dd, 0.6H, $J_{3,4}=3.5$, $J_{4,5}=1.0$ Hz, H-4β), 3.69 (dd, 1H, $J_{12a,12b}=12.3$ Hz, H-12aαβ), 3.66 (dd, 0.4H, H-2α), 3.54 (dd, 1H, H-12bαβ), 3.54–3.51 (m, 0.6H, H-5β), 3.52 (dd, 0.6H, $J_{2,3}=9.9$ Hz, H-3β), 3.35 (dd, 0.6H, H-2β), 1.65–1.45 (m, 4H, 2H-6αβ, 2H-7αβ). MALDI-TOF MS (310.3): 333.8 (M+Na), 349.5 (M+K). Anal. Calcd for $C_{12}H_{22}O_9\cdot H_2O$: C, 43.90; H, 7.37. Found: C, 43.78; H, 7.44.

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References

1. Dondoni, A.; Scherrmann, M.-C. *J. Org. Chem.* **1994**, *59*, 6404.
2. For orthogonally protected formyl *C*-glycosides for *C*-oligosaccharide synthesis by an iterative methodology, see: Dondoni, A.; Kleban, M.; Zuurmond, H. M.; Marra, A. *Tetrahedron Lett.* **1998**, *39*, 7991. Dondoni, A.; Mizuno, M.; Marra, A. *Tetrahedron Lett.* **2000**, *41*, 6657.
3. For a review see: Dondoni, A.; Marra, A. *Chem. Commun.* **1999**, 2133.
4. Hanessian, S.; Girard, C. *Synlett* **1994**, 863.
5. For a review on SmI_2-promoted reactions, see: Molander, G. A. *Chem. Rev.* **1992**, *92*, 29.
6. This result was succinctly reported in a note of an earlier publication from our group. See: Dondoni, A.; Zuurmond, H. M.; Boscarato, A. *J. Org. Chem.* **1997**, *62*, 8114.
7. The reaction can be followed by the disappearance of the deep blue color of the SmI_2 solution which is added dropwise to the mixture of **2** and ethylene glycol.
8. It is worth recalling here that the exceptional stability towards β-elimination displayed by 2-alkoxy- and 2-silyloxy-glycosyl samarium intermediates is the key point of the SmI_2-based *C*-glycosidation method developed by Sinaÿ and later on by Skrydstrup and Beau. See: (a) de Pouilly, P.; Chénedé, A.; Mallet, J.-M.; Sinaÿ, P. *Tetrahedron Lett.* **1992**, *33*, 8065. (b) de Pouilly, P.; Chénedé, A.; Mallet, J.-M.; Sinaÿ, P. *Bull. Soc. Chim. Fr.* **1993**, *130*, 256. (c) Mazéas, D.; Skrydstrup, T.; Doumeix, O.; Beau, J.-M. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 1383. (d) Mazéas, D.; Skrydstrup, T.; Beau, J.-M. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 909.
9. The quantitative glycal formation upon samariation of 2-azido-3,4,5-tri-*O*-benzyl-2-deoxy-galactosyl pyridyl sulfone has been reported: Urban, D.; Skrydstrup, T.; Riche, C.; Chiaroni, A.; Beau, J.-M. *Chem. Commun.* **1996**, 1883.
10. Kusuda, K.; Inanaga, J.; Yamaguchi, M. *Tetrahedron Lett.* **1989**, *30*, 2945.
11. Vlahov, I. R.; Vlahova, P. I.; Linhardt, R. J. *J. Am. Chem. Soc.* **1997**, *119*, 1480.
12. Dondoni, A.; Marra, A.; Perrone, D. *J. Org. Chem.* **1993**, *58*, 275.
13. This improvement in the thiazole to aldehyde synthesis has been recently exploited for the preparation of linear and cyclic

oligoketosides, see: Dondoni, A.; Marra, A.; Scherrmann, M.-C.; Bertolasi, V. *Chem. Eur. J.* **2001**, *7*, 1371.
14. The facile epimerization of α-linked formyl *C*-pyranosides into the corresponding β-anomers under basic conditions has been reported (see Ref. 1).
15. See compound α-**6g** in Ref. 1.
16. See compound **34** in Ref. 6.
17. The α-D configuration of the formyl *C*-ribofuranoside α-**4b** was confirmed by reduction to alcohol followed by benzylation to give the non-symmetrical (NMR analysis) and optically active alditol **14**.
18. Armarego, W. L. F.; Perrin, D. D. *Purification of Laboratory Chemicals*; 4th ed.; Butterworth-Heinemann: Oxford, 1996.
19. Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923.
20. Molander, G. A.; McKie, J. A. *J. Org. Chem.* **1994**, *59*, 3186.
21. Dondoni, A.; Zuurmond, H., to be published.
22. Dondoni, A.; Marra, A.; Rojo, I.; Scherrmann, M.-C. *Tetrahedron* **1996**, *52*, 3057.