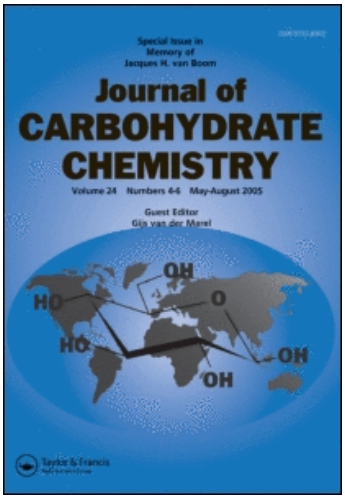

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ALKYLIDENATION OF SUGAR LACTONES AND FURTHER TRANSFORMATION TO *C*-GLYCOSIDES[1]

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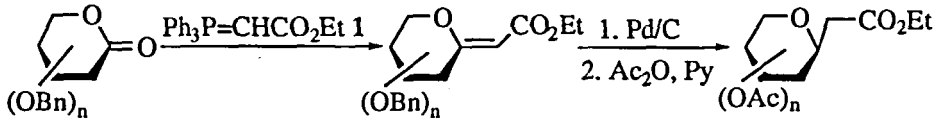
ABSTRACT

The Wittig reaction of (carbethoxymethylene)triphenylphosphorane with perbenzylated sugar δ-lactones and their 2-acetamido-2-deoxy derivatives is described. It is shown that this olefination occurred readily with the *galacto* and *gluco* derivatives, leading stereoselectively to *Z*-*C*-glycosylidenes in good yields. However, the same reaction with the perbenzylated 2-deoxy-D-*arabino*-hexono-1,5-lactone and the mannonolactones worked poorly. Reduction over Pd/C followed by acetylation of the obtained *C*-glycosylidenes led stereoselectively to peracetylated β-*C*-glycosides and amino β-*C*-glycosides. The olefin function could also be reduced selectively by Raney nickel or $NiCl_2/NaBH_4$, affording the perbenzylated *C*-glycosides and amino β-*C*-glycosides. Other transformation of the enol ether function is also reported.

INTRODUCTION

The *C*-glycosylidenes are of potential synthetic interest since such compounds could be used as substrates for glycosidases to elucidate the enzymatic mechanism,[2,3] and as interesting intermediates in the synthesis of more complex *C*-glycosidic structures.[4] The introduction of an enol ether function on sugars can be achieved either by the Wittig reaction[5] or by titanium-based reagents.[6] To date, several preparations of

C-glycosylidenes by the Wittig olefination have been described.[7] However, these examples are limited mainly to the five-membered furanoside rings. In a previous communication,[8] we reported a stereocontrolled alkylidenation of perbenzylated glycono-1,5-lactones with (carbethoxymethylene) triphenylphosphorane **1** and their further transformation to the peracetylated β-*C*-glycosides and amino β-*C*-glycosides:



This process can be considered as an alternative and easy access to β-*C*-glycosides and amino β-*C*-glycosides.

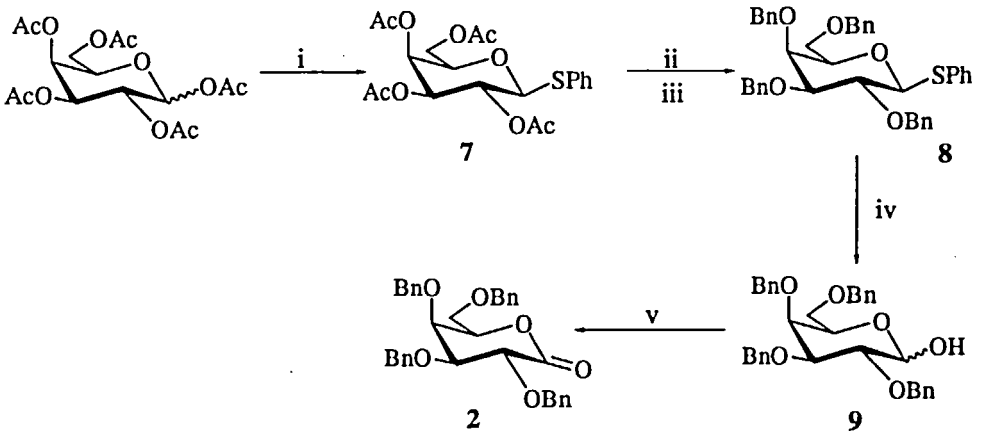
In this work, we investigate: 1) the preparation of several sugar lactones used as starting materials, 2) the scope and limitations of this olefination reaction and 3) our special efforts in the transformation of *C*-glycosylidenes to other *C*-glycoside derivatives.

RESULTS AND DISCUSSION

Preparation of the perbenzylated glyconolactones 2, 4, 5 and 12.

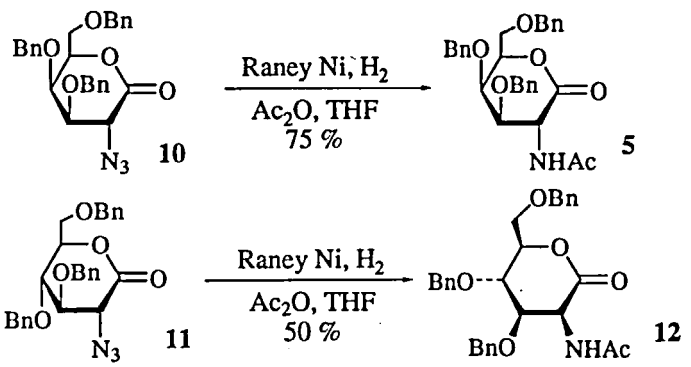
Perbenzylated D-galactono and D-mannono-1,5-lactones (**2** and **4**) were obtained in good yields (> 90 %) by oxidation of 2,3,4,6-tetra-*O*-benzyl-D-galactopyranose and -D-mannopyranose with tetra-*n*-propylammonium perruthenate (VII) (TPAP) in the presence of 4-methylmorpholine-*N*-oxide (NMO).[9] Although the preparation of **9** has already been described from 2,3,4,6-tetra-*O*-acetyl-D-galactopyranosyl bromide[10] or methyl β-D-galactopyranoside,[11] the reported overall yield was relatively low (less than 45 %). We propose here an alternative approach to **9** from peracetylated D-galactopyranose (Scheme 1). D-Galactose pentaacetate was first transformed to phenyl β-thiogalactopyranoside **7** with thiophenol catalyzed by $BF_3{\cdot}Et_2O$. Compound **7** was then deacetylated by Zemplen's method and benzylated (BrBn, NaH in DMF). Hydrolysis of the thiogalactoside **8** with $Hg(CF_3COO)_2$ afforded **9** in 67 % overall yield.

The known 2-acetamido-2-deoxy-D-galactono-1,5-lactone **5**[12] could equally be obtained by hydrogenation of 2-azido-2-deoxy-D-galactono-1,5-lactone **10** over Raney nickel in the presence of Ac_2O in THF (75 % yield, Scheme 2). Surprisingly, reduction of the 2-azido-2-deoxy-D-glucono-1,5-lactone **11**[12] under the same conditions resulted in a total epimerization at position 2, affording 2-acetamido-2-deoxy-D-



Reagents and Conditions: i) PhSH, $BF_3.Et_2O$, CH_2Cl_2, rt under Ar, 1 h, 90 %; ii) MeONa, MeOH, 3 h at rt, 96 %; iii) NaH, $PhCH_2Br$, DMF, 0 °C to rt under Ar, 1 h, 87 %; iv) $Hg(CF_3COO)_2$, THF/H_2O, rt, 10 min, 90 %; v) TPAP, NMO, molecular sieves 3 Å, CH_2Cl_2, rt under Ar, 15 h, 91 %.

Scheme 1



Scheme 2

mannono-1,5-lactone **12** in 50 % yield. In the light of this result, we reexamined the oxidation of 2-acetamido-3,4,6-tri-*O*-benzyl-2-deoxy-D-glucopyranose and -D-mannopyranose by TPAP/NMO.[12] In fact, no epimerization at C-2 position occurred for the *manno* derivative. However, a prolonged reaction (more than 2 h) could induce partial epimerization of 2-acetamido-2-deoxy-D-glucono-1,5-lactone **6** to mannono-1,5-lactone **12**. This is in contradiction with previous conclusions[12] which we believe to be a mistake. Similarly, Pravdic and Fletcher[13] have observed the epimerization of lactone **6** caused by an amine.

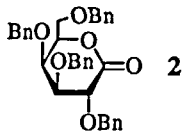
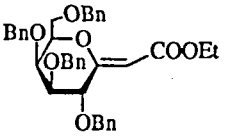
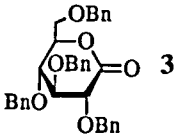
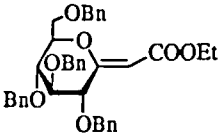
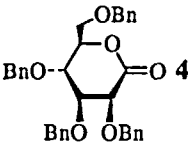
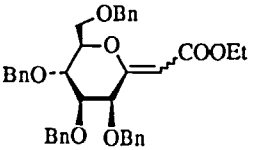
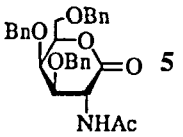
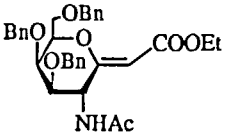
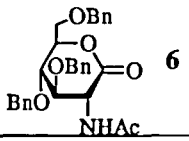
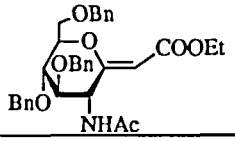
Alkylidenation of sugar lactones

The reaction of ylide **1** with the lactones **2** and **3** in refluxing toluene afforded the corresponding *Z*-*C*-glycosylidenes **13** and **14** as unique isomers in good yields (Scheme 3). The *Z* geometry of the newly formed double bond was established by X-ray diffraction analysis of **13**.[8] The observed excellent stereochemical outcome in these two cases is explicable as a result of the bulky C_2 benzyl group favouring the formation of less hindered betain (**A** or **C** compared to **B** or **D**, Scheme 4), leading to the *Z* isomer. This preference to the formation of *Z*-*C*-glycosylidene has also been noted by Nakai[14] in the asymmetric [2,3]-Wittig rearrangement of a perbenzylated glucose derivative. Otherwise, no isomerization of *galactono* or *glucono* lactones has been detected under these reaction conditions.[15]

However, the reaction of mannono-1,5-lactone **4** with the ylide **1** did not go to completion even in the presence of a large excess of **1**. Prolonged heating led to the decomposition of the starting material by β-elimination to the known 2,4,6-tri-*O*-benzyl-3-deoxy-D-*erythro*-hex-2-enono-1,5-lactone. The use of xylene as solvent afforded a mixture of several products. After 15 h reflux in toluene, the condensation product **15** was isolated in 28 % yield as a mixture of two isomers in a ratio of 9 to 1, for which we could not establish the configuration of the double bond of the major product from ^1H and ^{13}C NMR data. In a recent communication, Chapleur[7c] has shown that the reaction of 2,3:4,6-di-*O*-isopropylidene-D-mannono-1,5-lactone with (carbomethoxymethylene) triphenylphosphorane in toluene at 140 °C gave a 3:1 mixture of olefins *E* and *Z*. The better stereoselectivity observed in our case clearly indicated that the nature of the protecting groups played a striking role in stereocontrol during reaction.

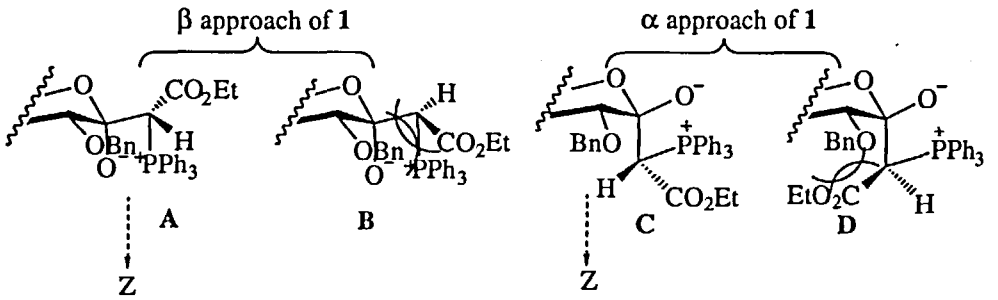
Application of these Wittig reaction conditions to 3,4,6-tri-*O*-benzyl-2-deoxy-D-*arabino*-hexono-1,5-lactone led to a total decomposition of the starting lactone in refluxing toluene. No reaction was observed in THF.

The condensation of ylide **1** with the 2-acetamido-2-deoxylactones **5** and **6** went to completion only after one to two hours, leading to compounds **16** and **17**. Here the ylide **1** should be washed throughly until neutral before use. Otherwise, a partial epimerization of the glucono-1,5-lactone **6** occurs, with the formation of the mannono-1,5-lactone **12** as byproduct. A similar result has also been noted by Vyplel.[16] The Z configuration of compound **17** was established by the observed NOE between NHAc and H-2: irradiation of NH enhanced the signal of H-2 (9.6 %); irradiation of H-2 increased both signals of NH (3.4 %) and acetyl H (10.6 %). Unfortunately, the compound **16** was contaminated with some triphenylphosphine oxide and it was impossible for us to isolate the pure product.

Lactones	C-Glycosylidenes		Solvent reaction time	Yield %
 2		13	toluene, 15 h	90
 3		14	toluene, 15 h	87
 4		15[a]	toluene, 15 h	28
 5		16	toluene, 2 h	70
 6		17	THF, 1 h	70

a. Compound **15** was obtained as a mixture of two *C*-glycosylidenes in a ratio of 9/1.

Scheme 3 The reaction of lactones **2 - 6** with the ylide **1** under reflux.



Scheme 4

In contrast to *galacto* and *gluco* derivatives, treatment of the 2-acetamido-2-deoxy-D-mannono-1,5-lactone **12** with the ylide **1** in refluxing toluene led to a total decomposition. On the other hand, the lactone **12** remained unchanged in THF.

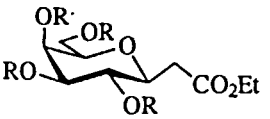
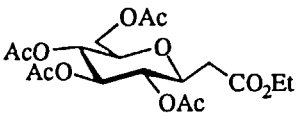
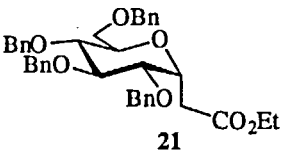
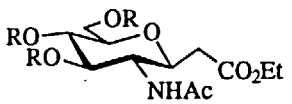
Thus, the alkylidenation of perbenzylated sugar lactones with ylide occurred readily with the *galacto* and *gluco* derivarives. The same reaction with the 2-deoxy-D-*arabino*-hexono-1,5-lactone and the mannono-1,5-lactones appeared more complex, leading to a mixture of several products or total decomposition.

Transformation to *C*-glycosides

The reduction of the double bond of *C*-glycosylidenes represents a direct access to *C*-glycosides.[7a] The hydrogenation of compounds **13-17** was achieved at room temperature in THF over 10 % Pd/C as catalyst (Method A, Scheme 5). Under these conditions, the benzylic ethers were cleaved so further acetylation was performed as usual. The corresponding peracetylated β-*C*-glycosides were obtained in ~ 75 % yield, except the *manno* derivative **15** and the impure *galacto* derivative **16** where hydrogenation gave a mixture of several compounds. The reduction conducted stereospecifically for the compounds **13** and **14**: no α-isomer was detected by ^{1}H NMR. An excellent diastereoselectivity has equally been observed for the amino derivative **22**[17] with β/α in 93/7 ratio.

Attempts to selectively reduce the double bond with Raney nickel (Method B, Scheme 5) failed in the case of the *galacto* derivative **13**. Only partial reduction could be observed for the compound **14**. The best result was obtained with the amino derivative **17**: the amino β-*C*-glucoside **23** was isolated in 40 % yield in a β:α ratio of 95 to 5. Finally the protocol described by Dondoni[18] using $NiCl_2/NaBH_4$ (Method C, Scheme 5) proved to be more efficient, leading to **23** in a better yield (53 %). The same treatment with the *C*-glycosylidene **13** gave the perbenzylated β-*C*-galactoside **19** in 72 % yield (β/α : 95/5). Consequently this procedure represents an alternative access to **19** from the lactone **2** compared to Kishi's approach[19] (by addition of a organometallic reagent on **2** and subsequent reduction). We also noted an inverse diastereoselectivity for the compound **14**: the reduction with $NiCl_2/NaBH_4$ afforded mainly the perbenzylated α-*C*-glucoside **21**[15] (α/β: 80/20).

Assignment of the β configuration for compounds **18, 20, 22** and **23** was based on the large coupling constants between H_1 and H_2 ($J_{1,2}$ = 9.3 to 10.3 Hz) observed in the ^{1}H NMR spectra. It has been shown that the chemical shifts of the signals for C-1' are at higher field (33-34 ppm) in the α isomers and at lower field (37-38 ppm) in the β isomers.[20] Examination of C-1' δ values of β-*C*-glycosides **18** (37.5 ppm), **19** (38.3

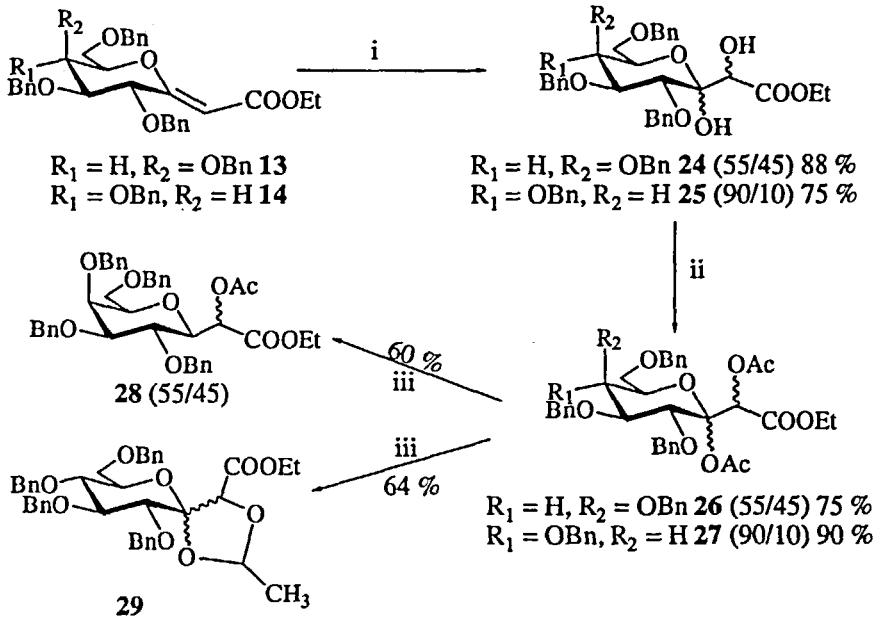
C-Glycosylidenes	Method[a]	*C*-Glycosides	Diastereoselectivity β : α	Yield %
13				
	A	R = Ac **18**	100 : 0	75
	C	R = Bn **19**	95 : 5	72
14	A	 **20**	100 : 0	76
	C	 **21**	20 : 80	65
17				
	A	R = Ac **22**	93 : 7	76
	B	R = Bn **23**	95 : 5	40
	C	**23**	95 : 5	53

a. Method A: i) Pd/C, H_2, MeOH; ii) Ac_2O, Pyr; Method B: Raney Ni, H_2, THF; Method C: $NiCl_2 \cdot 6H_2O$, $NaBH_4$, MeOH.

Scheme 5 Transformation of *C*-glycosylidenes to *C*-glycosides.

ppm), **20** (38.2 ppm), **22** (37.5 ppm), **23** (38.9 ppm) showed that these values fit quite well in the range from 37.5 to 38.9 ppm. On the other hand, the C-1' appeared at 32.6 ppm for compound **21**, confirming the α configuration.

Introduction of a hydroxy function at the C-1' position of β-*C*-glycosides such as **19** may provide a useful synthon for the preparation of natural nucleoside antibiotics as for example ezomycin and octosylic acid. For this purpose, the *C*-glycosylidenes **13** and **14** were treated with OsO_4 and NMO (Scheme 6). A poor diastereoselectivity was noted for the *galacto* derivative: a mixture of two diols **24** was obtained in 55/45 ratio. The selectivity was better for the *gluco* derivative **14**: the compound **25** was obtained in 90/10 ratio. Direct deoxygenation of **24** and **25** to the corresponding *C*-glycosides with an excess of $BF_3 \cdot Et_2O/Et_3SiH$ failed: starting materials were recovered. Thus, we



Reagents and conditions: i) OsO_4 cat, NMO, acetone/H_2O, rt, 15 h; ii) Ac_2O, Pyr, DMAP, rt, 15 h; iii) TMSOTf (4.8 eq), Et_3SiH (10 eq), CH_2Cl_2, molecular sieves 4 Å, rt, 30 min.

Scheme 6

acetylated the diols **24** and **25** and tried to reduce the tertiary acetate according to Dondoni.[21] Treatment of the compound **26** with an excess of TMSOTf/Et_3SiH led to the corresponding β-*C*-galactoside **28** in 60 % yield. However, the same reaction with the *gluco* derivative **27** afforded the cyclic ketal **29**. The formation of this latter compound may rely on the "participation" of the neighboring acyloxy group. A different conformation may be adopted by the *gluco* derivative compared to the *galacto* one, leading to different reactivities.

In summary, the alkylidenation of sugar lactones complements the usual approach[22] to *C*-glycosides and amino-*C*-glycosides after reduction. The high reactivity of *C*-glycosylidenes might be used to access a variety of highly functionnalized *C*-glycosides or natural products.

EXPERIMENTAL

General methods Melting points were measured with a Thomas-Hoover apparatus. IR spectra were recorded with a Unicam spectrometer. ^1H NMR and ^{13}C

NMR spectra were recorded on a Bruker AGH 250 spectrometer in $CDCl_3$ solutions. Optical rotations were measured using a Perkin-Elmer 141 polarimeter and a 10-cm cell. Analytical TLC were performed on Merck aluminum precoated plates of silica gel 60 F-254 with detection by UV and by spraying with 6 N H_2SO_4 and heating about 2 min at 300 °C. For flash chromatography, Merck silica gel 60 (230-400 mesh) was employed. Microanalyses were performed at the service de Microanalyse de l'Université Pierre et Marie Curie.

Phenyl 2,3,4,6-tetra-*O*-acetyl-1-thio-β-D-galactopyranoside (7). To a stirred solution of D-galactose pentaacetate (10 g, 25.6 mmol) and thiophenol (3.2 mL, 31.2 mmol) in dry CH_2Cl_2 (44 mL) were added BF_3-Et_2O (16 mL, 130 mmol). The mixture was stirred at room temperature for 1 h under argon atmosphere and then 40 mL of CH_2Cl_2 were added. The resulting solution was washed with 5% $NaHCO_3$ (3 x 50 mL), H_2O (50 mL) until neutral pH, dried ($MgSO_4$) and concentrated. Crystallization in a mixture of Et_2O/hexane of the obtained residue gave 10.15 g of **7** (90%) as a white solid: mp 74 °C lit.[23] mp 73-76 °C; Rf 0.3 (hexane /AcOEt 3/1); $[\alpha]_D$ + 7.83 (*c* 1.06, CH_2Cl_2); ^1H NMR δ 1.94 (s, 3H, OAc), 2.00 (s, 3H, OAc), 2.06 (s, 3H, OAc), 2.08 (s, 3H, OAc) 3.90 (ddd, 1H, $J_{5,6}$= 6.1, $J_{5,6'}$= 7.1, $J_{5,4}$ = 1.0 Hz, H-5), 4.04-4.16 (2 dd, 2H, $J_{6,6'}$= 11,3, $J_{6,5}$= 6.1, $J_{6',5}$= 7.1 Hz, H-6,6'), 4.68 (d, 1H, $J_{1,2}$= 10.0 Hz, H-1), 5.01 (dd, 1H, $J_{3,2}$= 9.9, $J_{3,4}$= 3.3 Hz, H-3), 5.21 (dd, 1H, $J_{2,1}$= 10.0, $J_{2,3}$= 9.9 Hz, H-2), 5.38 (dd, 1H, $J_{4,3}$= 3.3, $J_{4,5}$= 1.0 Hz, H-4), 7.22-7.29 (m, 3H, Arom), 7.46-7.49 (m, 2H, Arom).

Phenyl 2,3,4,6-tetra-*O*-benzyl-1-thio-β-D-galactopyranoside (8). To a solution of compound **7** (10.15 g, 23 mmol) in MeOH (80 mL) was added NaOMe (1M solution in MeOH, 1.3 mL). The mixture was stirred at room temperature for 3 h and neutralized by Amberlite Resin (IR-120 H^+). After filtration, the solution was concentrated to give phenyl 1-thio-β-D-galactopyranoside (6.04 g, 96%) as white crystals.[24] This crude thiogalactopyranoside was dissolved in dry DMF (40 mL) and the solution added dropwise to a suspension of NaH (3.99 g, 0.133 mol) in dry DMF (60 mL) under argon atmosphere at 0 °C. The mixture was stirred for 2 h and then benzyl bromide (16.5 mL, 0.136 mol) was added dropwise at 0 °C. After an additional 1 h at room temperature the excess of NaH was destroyed by treatment with MeOH. After concentration, the residue was dissolved in Et_2O (100 mL) and washed with H_2O (3 x 50 mL). The aqueous layer was extracted with Et_2O (3 x 50 mL). The combined organic layers were dried (Na_2SO_4) and concentrated. Recrystallization of the crude yellow solid from hot EtOH (100 mL) gave 12.23 g (87%) of the thiogalactoside **8** as white crystals: mp 70 °C, Rf 0.6 (hexane/AcOEt 1/3); $[\alpha]_D$ + 16.5 (*c* 1, CH_2Cl_2); ^1H NMR δ 3.20-3.30 (m, 3H, H-5,6,6'), 3.50 (dd, 1H, $J_{3,2}$= 9.0, $J_{3,4}$= 5.6 Hz, H-3); 3.60 (t, 1H, $J_{2,1}$= 7.4, $J_{2,3}$= 9.0 Hz,

H-2), 3.71 (d, 1H, $J_{4,5}$= 2.5 Hz, H-4), 4.50 (d, 1H, $J_{1,2}$= 7.3 Hz, H-1), 4.65-4.95 (m, 8H, 4 CH_2 benzyl), 6.80-7.70 (m, 25H, Arom).

Anal. Calcd for $C_{40}H_{40}O_5S$: C, 75.92; H, 6.37; Found: C, 75.88; H, 6.34.

2,3,4,6-Tetra-*O*-benzyl-D-galactopyranose (9).[10,11] To a solution of phenyl thiogalactoside **8** (4.74 g, 7.5 mmol) in THF (10 mL), H_2O (10 mL) and $Hg(CF_3COO)_2$ (3.9 g, 9.1 mmol) were added. After 10 min stirring at room temperature, CH_2Cl_2 (100 mL) and Na_2S 5% (50 mL) were added to the mixture. After separation, the organic layer was washed with brine (2 x 50 mL), dried ($MgSO_4$) and concentrated. Flash chromatography (hexane/Et_2O 6/4) of the residue gave **9** as a mixture of α/β anomers (3.66 g, 90%): oil, Rf 0.3 (hexane/AcOEt 3/1); ^1H NMR δ 2.90 (s, 1H, OH), 3.35-3.53 (m, 3H, H-3,6,6'), 3.68 (dd, 0.24H, $J_{2,1}$= 7.5, $J_{2,3}$= 9.6 Hz, H-2β), 3.79-3.86 (m, 1H, J= 2.7, 4.8 Hz, H-4), 3.95 (dd, 0.76H, $J_{2,1}$= 3.6, $J_{2,3}$= 9.6 Hz, H-2α), 4.05-4.10 (m, 1H, H-5), 4.29-4.48 (m, 8.24H, $J_{1,2}$= 7.5 Hz, H-1β, 4 CH_2 benzyl), 5.19 (d, 0.76H, $J_{1,2}$= 3.6 Hz, H-1α), 7.16-7.28 (m, 20H, Arom).

2,3,4,6-Tetra-*O*-benzyl-D-galactono-1,5-lactone (2). To a solution of 2,3,4,6-tetra-*O*-benzyl-D-galactopyranose (**9**) (1.01 g, 1.86 mmol) in dry CH_2Cl_2 (15 mL) under argon atmosphere, were added 3Å molecular sieves (1 g) and 4-methylmorpholine-*N*-oxide (0.5 g, 4.26 mmol). After stirring at room temperature for 10 min, tetra-*n*-propylammonium perruthenate (VII) (TPAP) (64 mg, 0.18 mmol) was added. After one night stirring at room temperature, the suspension was filtered through florisil/silica gel (50/50) and concentrated. The residue was diluted with CH_2Cl_2 (10 mL), washed successively with 5% Na_2SO_3 (10 mL), brine (10 mL) and saturated $CuSO_4$ (10 mL), dried ($MgSO_4$) and concentrated under reduced pressure to give **2** as an oil (904 mg, 90%): Rf 0.5 (hexane/AcOEt 3/1); $[\alpha]_D$ + 73 (*c* 1, $CHCl_3$), lit.[21] $[\alpha]_D$ + 75.2 (*c* 1, $CHCl_3$); ^1H NMR δ 3.61-3.71 (m, 2H, H-6,6'), 3.85 (dd, 1H, $J_{3,4}$= 2.1, $J_{3,2}$= 9.6 Hz, H-3), 4.13 (dd, 1H, $J_{4,5}$= 1.8, $J_{4,3}$= 1.9 Hz, H-4), 4.40-4.51 (ddd, 1H, $J_{5,4}$= 1.8, $J_{5,6}$= 5.8, $J_{5,6'}$ = 7.7 Hz, H-5), 4.27-5.18 (m, 8H, 4 CH_2 benzyl), 4.44 (d, 1H, $J_{2,3}$= 9.6 Hz, H-2), 7.33-7.54 (m, 20H, Arom); ^{13}C NMR δ 67.2, 72.2, 72.5, 73.3, 74.4, 74.9, 76.2, 79.8, 127.2, 127.7, 128.0, 128.1, 137.0, 137.2, 137.5, 169.7.

2,3,4,6-Tetra-*O*-benzyl-D-mannono-1,5-lactone (4). 2,3,4,6-Tetra-*O*-benzyl-D-mannopyranose (Sigma) (1.01g, 1.86 mmol) was oxidized as for **9** to afford **4** as white crystals (954 mg, 95%): mp 83 °C, Rf 0.6 (hexane/AcOEt 3/1), $[\alpha]_D$ + 13.0 (*c* 1.0, CH_2Cl_2); lit.[25] mp 83.5-85 °C, $[\alpha]_D$ - 0.5 (*c* 10.5, $CHCl_3$); ^1H NMR δ 3.55 (d, 2H, J= 4.5 Hz, H-6,6'), 3.70 (dd, 1H, $J_{4,5}$ = 7.2, $J_{3,4}$= 1.5 Hz, H-4), 3.97 (dd, $J_{3,4}$= 1.6, $J_{3,2}$= 2.5 Hz, H-3), 4.15 (m, 1H, H-5), 4.18 (t, 2H, J= 11.5 Hz, OCH_2), 4.27 (d, 1H, $J_{2,3}$= 2.5 Hz, H-2), 4.45 (s, 2H, OCH_2), 4.51 (d, 1H, J= 11.7 Hz, OCH), 4.55 (d, 1H, J= 12.0 Hz, OCH), 4.75 (d, 1H, J= 12.2 Hz, OCH), 4.98 (d, 1H, J= 12.0 Hz, OCH), 7.00-7.31 (m,

20H, Ph); ^{13}C NMR δ 69.1 (C-6), 71.8, 72.9, 73.4 (3 OCH_2), 75.4 (C-2), 76.0 (C-4), 76.6 (C-3), 78.5 (C-5), 127.7, 127.8, 127.9, 128.1, 128.3, 128.4 (CH-Arom), 136.7, 137.2, 137.6 (C-ipso), 169.3 (C-1).

2-Acetamido-3,4,6-tri-*O*-benzyl-2-deoxy-D-galactono-1,5-lactone (5). A solution of 2-azido-3,4,6-tri-*O*-benzyl-2-deoxy-D-galactono-1,5-lactone **10** (312 mg, 0.66 mmol) in distilled THF (2 mL) and acetic anydride (124 μL, 1.32 mmol) was hydrogenated at atmospheric pressure over Raney nickel (one spatula) for 2 h at room temperature. The catalyst was filtered off and washed with THF. The concentration of the filtrate afforded 241 mg (75 %) of **5** as a white solid. One portion of **5** was recrystallized from hot EtOH to give an analytically pure compound: mp 145-146 °C; $[\alpha]_D$ + 123.8 (*c* 0.78, CH_2Cl_2); lit.[12] mp 138-141 °C; $[\alpha]_D$ + 89.0 (*c* 1, CH_2Cl_2).

2-Acetamido-3,4,6-tri-*O*-benzyl-2-deoxy-D-mannono-1,5-lactone (12). A solution of 2-azido-3,4,6-tri-*O*-benzyl-2-deoxy-D-glucono-1,5-lactone **11** (100 mg, 0.212 mmol) was treated with Raney nickel as for **10** to afford the title compound after recrystallization from hot EtOH (52 mg, 50 %): Rf 0.56 (CH_2Cl_2/MeOH 30/1), mp 105 °C, $[\alpha]_D$ + 112.3 (*c* 0.6, CH_2Cl_2); IR 1648, 1780, 3296 cm^{-1}; ^1H NMR δ 1.91 (s, 3 H, CH_3), 3.62-3.64 (m, 2H, H-6,6'), 3.83 (dd, 1H, $J_{3,4}$= 0.8, $J_{4,5}$= 7.7 Hz, H-4), 4.10 (dd, 1H, $J_{2,3}$= 3.2, $J_{3,4}$= 0.8 Hz, H-3), 4.30-4.35 (m, 1H, H-5), 4.26-4.55 (m, 6H, 3 CH_2 benzyl), 4.95 (dd, $J_{2,3}$= 3.2, $J_{2,NH}$= 7.1 Hz, H-2), 6.20 (d, 1H, J= 7.1 Hz, NH), 7.16-7.29 (m, 15H, Arom); ^{13}C NMR ($CDCl_3$) δ 23.0 (CH_3), 51.2 (C-2), 68.4 (C-6), 72.0, 72.2, 73.5 (3 CH_2 benzyl), 74.1 (C-5), 77.2 (C-4), 78.9 (C-3), 127.9, 128.0, 128.2, 128.3, 128.5, 128.6, 128.6, 128.7 (CH-Arom), 136.8, 137.1, 137.7 (C-ipso), 169.6, 170.1 (C=O).

Anal. Calcd for $C_{29}H_{31}O_6$: C, 71.15; H, 6.38; N, 2.86; Found: C, 70.02; H, 6.33; N, 2.93.

3,7-Anhydro-4,5,6,8-tetra-*O*-benzyl-2-deoxy-D-*galacto*-oct-1-ethoxycarbonyl-2-*Z*-enitol (13). To a solution of lactone **2** (245 mg, 0.402 mmol) in toluene (4 mL), was added (carbethoxymethylene)triphenylphosphorane **1** (304 mg, 0.804 mmol). The mixture was heated under reflux for 15 h, concentrated and purified by flash chromatography with hexane-AcOEt (9:1) as eluent to give **13** as white crystals (250 mg, 90 %): R_f 0.5 (hexane/AcOEt 3/1); mp 83-85 °C, $[\alpha]_D$ + 81.6 (*c* 1.0, CH_2Cl_2); ^1H NMR δ 1.20 (t, 3H, J= 7.1 Hz, CH_3), 3.70 (dd, 1H, $J_{5,4}$= 9.3, $J_{5,6}$= 2.7 Hz, H-5), 3.73-3.77 (m, 2H, H-8,8'), 3.95 (td, 1H, J= 1.3, 6.9 Hz, H-7), 4.05-4.13 (m, 3H, OCH_2, H-6), 4.41 (dd, 1H, $J_{4,5}$= 9.3, $J_{4,2}$= 1.5 Hz, H-4), 4.43-4.95 (m, 8H, 4 CH_2 benzyl), 5.56 (d, 1H, $J_{2,4}$= 1.6 Hz, H-2), 7.22-7.33 (m, 20H, Arom); ^{13}C NMR δ 14.0 (CH_3), 59.3, 67.6, 72.2, 73.1, 73.3 (5 CH_2), 74.1; 74.3 (CH_2), 76.1, 78.1, 81.4; 99.6 (C-2), 127.2, 127.3,

127.5, 127.7, 127.9, 128.1, 129.5 (CH-Arom), 137.3, 137.4, 137.7, 138.0 (C-ipso), 164.7 (C-3), 164.8 (C=O).

Anal. Calcd for $C_{38}H_{40}O_7$: C, 74.98; H, 6.62; Found: C, 74.67; H, 6.52.

3,7-Anhydro-4,5,6,8-tetra-*O*-benzyl-2-deoxy-D-*gluco*-oct-1-ethoxycarbonyl-2-*Z*-enitol (14). The lactone **3** was treated with Ph_3P=CHCOOEt (2 eq) as for **2** to give **14** as an oil (87%): R_f 0.50 (hexane/AcOEt 3/1); $[\alpha]_D$ + 46.0 (*c* 1.0, CH_2Cl_2); ^1H NMR δ 1.27 (t, 3H, J= 7.1 Hz, CH_3), 3.79-3.92 (m, 5H), 4.17 (q, 2H, J= 7.1 Hz, OCH_2), 4.32 (td, 1H, J= 2.4, 9.0 Hz, H-7), 4.48-4.78 (m, 8H, 4 CH_2 benzyl), 5.20 (s, 1H, H-2), 7.16-7.37 (m, 20H, Arom); ^{13}C NMR δ 14.9 (CH_3), 60.2, 68.8, 71.9, 73.3, 74.0, 74.2 (6 CH_2), 77.8, 77.9, 78.2, 83.2; 100.3 (C-2), 127.4, 128.0, 128.3, 128.4, 128.8, 129.9, 129.0 (CH-Arom), 137.6, 138.0, 138.3, 138.7 (C-ipso), 162.4 (C-3), 165.3 (C=O).

Anal. Calcd for $C_{38}H_{40}O_7$: C, 74.98; H, 6.62; Found: C, 75.23; H, 6.69.

3,7-Anhydro-4,5,6,8-tetra-*O*-benzyl-2-deoxy-D-*manno*-oct-1-ethoxycarbonyl-2-enitol (15). The lactone **4** was treated with Ph_3P=CHCOOEt (2 eq) as for **2**. The title compound **15** was obtained in 28 % yield after chromatography on a column of silica gel with hexane-AcOEt (4:1) as eluent: oil, R_f 0.56 (hexane/AcOEt 3/1), $[\alpha]_D$ + 30.5 (*c* 0.2, CH_2Cl_2); ^1H NMR δ 1.25 (t, 3H, J= 7.1 Hz, CH_3), 3.76-3.89 (m, 5H), 4.15 (q, 2H, J= 7.1 Hz, OCH_2), 4.24-4.34 (m, 1H), 4.46-4.76 (m, 8H, 4 CH_2 benzyl), 5.18 (s, 1H, H-2), 7.12-7.31 (m, 20H, Arom); ^{13}C NMR δ 14.8 (CH_3), 60.1 (CH_2), 68.8 (C-8), 71.5, 72.8, 73.5, 73.7 (4 CH_2), 77.3, 77.4, 77.8 (C-5,6,7); 82.8 (C-4), 99.9 (C-2), 127.5, 127.7, 127.8, 127.9, 128.0, 128.2, 128.3, 128.4, 128.5 (CH-Arom); 137.1, 137.6, 137.8, 138.3 (C-ipso), 161.8 (C-3), 164.7 (C=O).

Anal. Calcd for $C_{38}H_{40}O_7$: C, 74.98; H, 6.62; Found: C, 74.73; H, 6.65.

4-Acetamido-3,7-anhydro-5,6,8-tri-*O*-benzyl-2,4-dideoxy-D-*galacto*-oct-1-ethoxycarbonyl-2-*Z*-enitol (16). The Wittig reaction of **5** (292 mg, 0.597 mmol) at refluxing toluene during 2 h as described for **2** followed by chromatography on silica gel (hexane/AcOEt 1/1) gave **16** contaminated with Ph_3P=O (286 mg, 70 %): oil, R_f 0.31 (hexane/AcOEt 2/3); ^1H NMR δ 1.15 (t, 3H, J= 7.1 Hz, CH_3), 1.92 (s, 3H, CH_3), 3.66 (dd, 1H, $J_{5,4}$= 10.8, $J_{5,6}$= 2.3 Hz, H-5), 3.70-3.82 (m, 2H, H-8,8'), 3.97-4.08 (m, 1H, H-7), 4.06 (q, 2H, J= 7.1 Hz, OCH_2), 4.16 (m, 1H, H-6), 4.39 (d, 1H, J= 12.2 Hz, OCH), 4.46 (d, 1H, J= 11.6 Hz, OCH), 4.50 (d, 1H, J= 11.5 Hz, OCH), 4.59 (d, 1H, J= 12.1 Hz, OCH), 4.71 (d, 1H, J= 11.2 Hz, OCH), 4.86-5.01 (m, 1H, H-4), 4.90 (d, 1H, J= 11.5 Hz, OCH), 5.14 (d, 1H, J= 1.8 Hz, H-2), 5.45 (d, 1H, $J_{4,NH}$= 8.4 Hz, NH), 7.23-7.67 (m, 22H, Arom + Ph_3P=O); ^{13}C NMR δ 14.4 (CH_3), 23.2 (CH_3), 50.1 (C-4), 59.4 (CH_2), 68.1 (C-8), 71.8, 73.5, 74.4 (3 CH_2 benzyl), 71.7, 78.2, 78.8 (C-5,6,7), 97.7 (C-2), 127.6, 128.0, 128.3, 128.4, 128.5, 128.7 (CH-Arom); 137.9, 138.1, 138.3 (C-ipso); 165.2 (C-3), 165.9, 170.7 (C=O).

4-Acetamido-3,7-anhydro-5,6,8-tri-*O*-benzyl-2,4-dideoxy-D-*gluco*-oct-1-ethoxycarbonyl-2-*Z*-enitol (17). The Wittig reaction of **6** (100 mg, 0.204 mmol) with Ph_3P=CHCOOEt (2 eq) at refluxing THF during 1 h and chromatography on silica gel (hexane/AcOEt 1/1) furnished **17** as a white solid (80 mg, 70 %): R_f 0.5 (hexane/AcOEt 2/3); mp 125-126 °C; $[\alpha]_D$ + 52.0 (*c* 1.0, CH_2Cl_2); ^1H NMR δ 1.42 (t, 3H, J= 7.1 Hz, CH_3), 2.04 (s, 3H, CH_3), 3.63 (dd, 1H, J= 6.1, 6.2 Hz, H-5), 3.80 (m, 2H, H-8,8'), 3.93 (dd, 1H, J= 6.2, 6.3 Hz, H-6), 4.08 (q, 2H, J= 7.1 Hz, OCH_2), 4.14-4.20 (m, 1H, H-7), 4.49-4.70 (m, 7H, 3 CH_2 benzyl, H-4), 5.24 (s, 1H, H-2), 5.97 (d, 1H, J= 8.5 Hz, NH), 7.35-7.51 (m, 15H, Arom); ^{13}C NMR δ 14.2 (CH_3), 23.2 (CH_3), 50.9 (C-4), 59.6 (CH_2), 68.6 (C-8), 72.9, 73.4, 73.5 (3 CH_2 benzyl), 75.3 (C-6), 77.9 (C-5), 79.0 (C-7), 101.0 (C-2), 127.6, 127.7, 127.9, 128.0, 128.3, 128.5 (CH-Arom); 137.2, 137.5, 137.9 (C-ipso); 162.5 (C-3), 164.7, 169.3 (C=O).

Anal. Calcd for $C_{33}H_{37}NO_7$: C, 70.82; H, 6.66; N, 2.50; Found: C, 69.11; H, 6.89; N, 2.41.

Ethyl (2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl)ethanoate (18). Method A: A solution of **13** (90 mg, 0.15 mmol) in a mixture of THF/MeOH (2:7, 0.9 mL) was hydrogenated at atmospheric pressure over 10 % palladium on charcoal (20 mg) for 15 h at room temperature. The catalyst was filtered off on Celite and the filtrate concentrated. The crude product was treated with acetic anhydride (0.3 mL) and pyridine (1 mL) under N_2 atmosphere at room temperature. After 15 h, pyridine was evaporated and the residue purified on a column of silica gel using hexane-AcOEt (3:2) as eluent to give 46 mg (75 %) of the title compound as an oil: R_f 0.3 (hexane/AcOEt 3/2), $[\alpha]_D$ + 13.8 (*c* 1.5, CH_2Cl_2); ^1H NMR δ 1.21 (t, 3H, J= 7.1 Hz, CH_3), 1.92 (s, 3H, CH_3), 1.97 (s, 3H, CH_3), 1.98 (s, 3H, CH_3), 2.09 (s, 3H, CH_3), 2.46-2.52 (m, 2H, CH_2), 3.83-3.93 (m, 2H), 4.00-4.04 (m, 2H), 4.11 (q, 2H, J= 7.1 Hz, OCH_2), 4.99 (dd, 1H, $J_{3,4}$= 3.2, $J_{3,2}$= 10.0 Hz, H-3), 5.07 (dd, 1H, $J_{2,3}$= 10.0, $J_{2,1}$= 9.3 Hz, H-2), 5.37 (dd, 1H, $J_{4,5}$= 1.0, $J_{4,3}$= 3.2 Hz, H-4); ^{13}C NMR δ 14.1(CH_3), 20.5, 20.6, 20.7, 20.8 (4 CH_3), 37.5 (CH_2), 60.8, 61.4 (OCH_2, C-6), 67.6, 68.9, 71.9, 74.2, 75.0; 169.8, 170.0, 170.1, 170.2, 170.3 (5 C=O).

Anal. Calcd for $C_{18}H_{26}O_{10}$: C, 53.73; H, 6.51; Found: C, 53.66; H, 6.41.

Ethyl (2,3,4,6-tetra-*O*-benzyl-β-D-galactopyranosyl)ethanoate (19). Method C: To a cold solution of **13** (200 mg, 0.329 mmol) in dry MeOH (4 mL) were added 7 mL of a 0.4% MeOH solution of $NiCl_2 \cdot 6H_2O$ (0.118 mmol). The solution was stirred for 30 min at 0 °C and then treated with $NaBH_4$ (100 mg, 2.63 mmol). The resulting black mixture was stirred for 1 h at 0 °C and 18 h at room temperature, treated with AcOH (2-3 drops), filtered through Celite and concentrated. The residue was partitioned between saturated $NaHCO_3$ solution (10 mL) and CH_2Cl_2 (3 x 10 mL). The combined organic layers were dried ($MgSO_4$), concentrated and chromatographed with hexane-

AcOEt (9:1) as eluent to give the title compound as an oil: 145 mg (72 %), R_f 0.5 (hexane/AcOEt 3/1), $[\alpha]_D$ + 3.45 (*c* 1.1, $CHCl_3$); ^1H NMR δ 1.14 (t, 3H, J= 7.1 Hz, CH_3), 2.45 (dd, 1H, J= 7.9, 15.3 Hz, CH-COO), 2.74 (dd, 1H, J= 2.8, 15.3 Hz, CH-COO), 3.50-3.74 (m, 6H), 3.98 (d, 1H, J= 2.4 Hz), 4.02 (q, 2H, J= 7.1 Hz, OCH_2), 4.34-4.97 (m, 8H, 4 CH_2 benzyl), 7.21-7.33 (m, 20H, Arom); ^{13}C NMR δ 14.6 (CH_3), 38.3 (CH_2), 60.9, 69.1, 72.6, 74.0 (4 CH_2), 74.3; 74.9, 75.7 (2 CH_2), 76.9, 77.7, 78.6, 85.2; 128.0, 128.1, 128.2, 128.3, 128.4, 128.6, 128.7, 128.8, 128.9 (CH-Arom); 138.1, 138.4, 138.7, 138.8, 139.3 (C-ipso); 171.7 (C=O).

Anal. Calcd for $C_{38}H_{42}O_7$: C, 74.73; H, 6.93; Found: C, 75.06; H, 6.97.

Ethyl (2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl)ethanoate (20). A solution of **14** (147 mg, 0.24 mmol) in MeOH (1 mL) was hydrogenated, acetylated and purified as for **13** (Method A) to afford **20** as an oil (77 mg, 76 %): R_f 0.3 (hexane/AcOEt 3/2); $[\alpha]_D$ - 0.6 (*c* 3.8, CH_2Cl_2); ^1H NMR δ 1.22 (t, 3H, J= 7.1 Hz, CH_3), 1.95 (s, 3H, CH_3), 1.98 (s, 3H, CH_3), 1.99 (s, 3H, CH_3), 2.02 (s, 3H, CH_3), 2.45-2.49 (m, 2H, CH_2), 3.65 (m, 1H, H-5), 3.92 (ddd, 1H, J= 4.5, 7.4, $J_{1,2}$= 9.9 Hz, H-1), 4.01 (dd, 1H, $J_{6,6'}$= 12.4, $J_{6,5}$= 1.7 Hz, H-6), 4.11 (q, 2H, J= 7.1 Hz, OCH_2), 4.20 (dd, 1H, $J_{6,6'}$= 12.4, $J_{6',5}$= 4.8 Hz, H-6'), 4.88 (dd, 1H, J= 9.5, 9.6 Hz, H-2), 5.02 (dd, 1H, J= 9.5, 9.7 Hz, H-4), 5.16 (dd, 1H, J= 9.3, 9.4 Hz, H-3); ^{13}C NMR δ 15.1 (CH_3), 21.6, 21.7 (CH_3), 38.2 (CH_2); 61.9, 63.1 (OCH_2, C-6); 69.4, 72.4, 75.1, 75.5, 76.8; 170.5, 170.6, 171.0, 171.3, 171.6 (5 C=O).

Anal. Calcd for $C_{18}H_{26}O_{10}$: C, 53.73; H, 6.51; Found: C, 53.66; H, 6.41.

Ethyl (2,3,4,6-tetra-*O*-benzyl-α-D-glucopyranosyl)ethanoate (21). Compound **14** (100 mg, 0.164 mmol) in dry MeOH (1.7 mL) was treated with $NiCl_2 \cdot 6H_2O$ (0.4 % solution in MeOH, 1.64 mL, 0.028 mmol) and $NaBH_4$ (24 mg, 0.632 mmol) as for **13** (Method C). After purification by preparative thin-layer chromatography using hexane-AcOEt (3:1) as eluent, the title compound was obtained as an oil (65 mg, 65 %): R_f 0.66 (hexane/AcOEt 4/1); $[\alpha]_D$ + 36.9 (*c* 1.2, $CHCl_3$), lit.[15] $[\alpha]_D$ + 35.1 (*c* 1, $CHCl_3$) ; ^1H NMR δ 1.21 (t, 3H, J= 7.0 Hz, CH_3), 2.70-2.79 (m, 2H, CH_2COO), 3.64-3.76 (m, 6H), 4.10 (q, 2H, J= 7.1 Hz, OCH_2), 4.44-4.94 (m, 9H, H-1, 4 CH_2 benzyl), 7.12-7.36 (m, 20H, Arom); ^{13}C NMR δ 14.2 (CH_3), 32.6 (CH_2), 60.7, 68.8 (2 CH_2), 71.6, 72.2; 73.2, 73.5, 75.1, 75.5 (4 CH_2), 77.8, 79.3, 82.2; 127.6, 127.7, 127.8, 127.9, 128.0, 128.1, 128.4, 128.5, 128.6 (CH-Arom); 138.0, 138.1, 138.2, 138.7 (C-ipso); 171.3 (C=O).

Ethyl (2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-β-D-glucopyranosyl)ethanoate (22). A solution of **17** (40 mg, 0.071 mmol) in MeOH (1 mL) was hydrogenated and acetylated as for **13** (Method A). The title compound was obtained after chromatography on silica gel with CH_2Cl_2-MeOH (98:2) as eluent (white solid, 23 mg, 77 %): R_f 0.56 (hexane/AcOEt 2/3); mp 118-120 °C; $[\alpha]_D$ - 6.4 (*c* 1, $CHCl_3$); lit.[17]

$[\alpha]_D$ - 1.94 (*c* 0.09, $CHCl_3$); ^1H NMR δ 1.19 (t, 3H, J= 7.1 Hz, CH_3), 1.87 (s, 3H, CH_3), 1.97 (s, 6H, 2 CH_3), 2.01 (s, 3H, CH_3), 2.54 (d, 2H, J= 5.8 Hz, CH_2), 3.57-3.62 (m, 1H, J= 2.3 Hz, H-5), 3.76 (td, 1H, J= 5.8 Hz, $J_{1,2}$= 10.3 Hz, H-1), 3.94-4.22 (m, 6H, OCH_2, H-2,3,4,5); 4.93-5.06 (m, 2H, H-6,6'); 5.75 (d, 1H, J= 9.4 Hz, NH); ^{13}C NMR δ 14.1 (CH_3), 20.6, 20.7, 23.1 (3 CH_3), 37.5 (CH_2), 53.4 (C-2), 60.6, 62.2 (CH_2, C-6); 68.3, 72.5, 74.2, 74.8 (C-1,3,4,5); 169.3, 170.3, 170.7, 171.1, 171.6 (5 C=O).

Ethyl (2-acetamido-3,4,6-tri-*O*-benzyl-2-deoxy-β-D-glucopyranosyl)ethanoate (23). Method B: A solution of **17** (40 mg, 0.071 mmol) in THF (2 mL) was hydrogenated at atmospheric pressure over Raney nickel at room temperature for 18 h. The catalyst was filtered off and the filtrate concentrated and purified by preparative layer chromatography using CH_2Cl_2-MeOH (95:5) as eluent to give 16 mg (40 %) of **23** as a white solid.

Method C: Compound **17** (66 mg, 0.118 mmol) in dry MeOH (1.2 mL) was treated with $NiCl_2 \cdot 6H_2O$ (0.4 % solution in MeOH, 1.2 mL, 0.020 mmol) and $NaBH_4$ (17 mg, 0.447 mmol) as for **13**. After purification by preparative thin-layer chromatography using CH_2Cl_2-MeOH (95:5) as eluent, the title compound was obtained as a white solid (35 mg, 53 %): R_f 0.43 (CH_2Cl_2/MeOH 95/5); mp 103-104 °C; $[\alpha]_D$ + 30.8 (*c* 0.6, $CHCl_3$); ^1H NMR δ 1.18 (t, 3H, J= 7.1 Hz, CH_3), 1.73 (s, 3H, CH_3), 2.55 (m, 2H, CH_2), 3.39-3.45 (m, 1H, H-5), 3.47 (dd, 1H, $J_{2,3}$= 9.9 Hz, $J_{3,4}$= 8.8 Hz, H-3), 3.63-3.71 (m, 4H, H-1,4,6,6'), 3.85 (q, 1H, J= 9.9 Hz, H-2), 4.07 (dd, 2H, J= 7.1 Hz, CH_2), 4.47-4.84 (m, 6H, 3 CH_2 benzyl), 5.00 (d, 1H, $J_{2,NH}$= 9.1 Hz, NH), 7.17-7.36 (m, 15H, Arom); ^{13}C NMR δ 14.9 (CH_3), 24.1 (CH_3), 38.9 (CH_2), 55.2 (C-2), 61.4 (C-6), 69.5, 74.2, 75.1, 75.6 (4 CH_2); 76.7, 79.5 (C-1,4); 80.0, 83.7 (C-3,5); 128.3, 128.5, 128.8, 129.1, 129.2, 129.3 (CH-Arom), 138.7, 138.9, 139.1 (C-ipso), 170.9, 172.5 (C=O).

Anal. Calcd for $C_{33}H_{39}NO_7$: C, 70.57; H, 7.00; N, 2.49; Found: C, 70.44; H, 6.85; N, 2.67.

Ethyl (2,3,4,6-tetra-*O*-benzyl-1-hydroxy-D-galactopyranosyl) hydroxyethanoate (24). To a solution of **13** (250 mg, 0.411 mmol) in a mixture of acetone-H_2O (8:1, 8.5 mL), was added NMO (96.3 mg, 0.822 mmol) and a solution of OsO_4 (4 % solution in water, 353 μL, 0.041 mmol). After stirring at room temperature for 15 h, CH_2Cl_2 (10 mL) and a solution of $NaHSO_3$ (40 % in water, 10 mL) were added. The organic layer was washed with brine (10 mL), dried ($MgSO_4$) and concentrated. The crude product was purified by chromatography on silica gel with hexane/AcOEt (3:1) as eluent to afford **24** (232 mg, 88 %) as a mixture of two isomers (55/45): oil, R_f 0.4 (hexane/AcOEt 3/2); ^1H NMR δ 0.94 (t, 3H, J= 7.1 Hz, CH_3), 3.28 (d, 1H, J= 7.8 Hz, OH), 3.42 (dd, 1H, $J_{6,5}$= 5.8, $J_{6,6'}$= 9.1 Hz, H-6), 3.52 (dd, 1H, $J_{6',5}$= 7.8, $J_{6',6}$= 9.1 Hz, H-6'), 3.92-4.09 (m, 6H), 4.25 (d, 1H, J= 7.6 Hz, CH-OH), 4.36 (dd,

1H, $J_{2,3}$= 9.9, J= 1.1 Hz, H-2), 4.43-5.01 (m, 8H, 4 CH_2 benzyl), 7.21-7.35 (m, 20H, Arom); ^{13}C NMR δ 13.6 (CH_3), 62.2, 68.4 (2 CH_2); 70.3, 71.4, 72.4, 73.4, 74.6, 74.7, 75.1, 80.9; 97.4 (Cq); 127.4, 127.5, 127.7, 127.8, 128.0, 128.2, 128.4 (CH-Arom); 137.9, 138.3, 138.5, 138.9 (C-ipso); 170.6 (C=O).

Anal. Calcd for $C_{38}H_{42}O_9$: C, 71.01; H, 6.59; Found: C, 71.26; H, 6.59.

Ethyl (2,3,4,6-tetra-*O*-benzyl-1-hydroxy-D-glucopyranosyl)hydroxyethanoate (25). Compound **14** (250 mg, 0.411 mmol) was oxidized and purified as for **13** to afford the title compound (oil, 210 mg, 75 %) as a mixture of two diols (90/10): R_f 0.4 (hexane/AcOEt 3/2); ^1H NMR δ 1.19 (t, 3H, J= 7.1 Hz, CH_3), 3.42 (d, 1H, J= 7.9 Hz, OH), 3.60 (dd, 1H, $J_{6,5}$= 1.8, $J_{6,6'}$= 11.2 Hz, H-6), 3.66 (dd, 1H, J= 9.5, 9.8 Hz, H-4), 3.74 (dd, 1H, $J_{6',5}$= 3.7, $J_{6',6}$= 11.2 Hz, H-6'), 3.89 (dd, 1H, J= 9.5, 1.2 Hz, H-2), 3.96 (ddd, 1H, $J_{5,6}$= 1.8, $J_{5,6'}$= 3.6, $J_{5,4}$= 10.0 Hz, H-5), 4.08-4.21 (m, 4H), 4.30 (d, 1H, J= 8.0 Hz, CH-OH), 4.43-5.05 (m, 8H, 4 CH_2 benzyl), 7.25-7.34 (m, 20H, Arom); ^{13}C NMR δ 14.1 (CH_3), 62.2, 68.4, 71.5, 71.9, 73.0, 74.9, 75.1, 75.7, 78.4, 78.8, 83.4; 97.1 (Cq); 127.3, 127.4, 127.6, 127.7, 127.8, 127.9, 128.0, 128.2, 128.3, 128.4, 128.5 (CH-Arom); 138.0, 138.2, 138.3, 138.4 (C-ipso); 170.4 (C=O).

Anal. Calcd for $C_{38}H_{42}O_9$: C, 71.01; H, 6.59; Found: C, 71.36; H, 6.62.

Ethyl acetoxy(1-acetoxy-2,3,4,6-tetra-*O*-benzyl-D-galactopyranosyl)ethanoate (26). Compound **24** (470 mg, 0.732 mmol) was acetylated under an argon atmosphere with acetic anhydride (0.5 mL) and pyridine (7 mL) in the presence of DMAP (180 mg, 1.47 mmol) at room temperature. After 15 h, the mixture was concentrated and chromatographed on silica gel with hexane/AcOEt (9:1) as eluent to give **26** (400 mg, 75 %) as a mixture of two isomers (55/45): oil, Rf 0.5 (hexane/ AcOEt 7/3); ^1H NMR δ 0.98 (t, 1.35H, J= 7.2 Hz, CH_3), 1.05 (t, 1.65H, J= 7.2 Hz, CH_3), 1.95 (s, 1.65H, CH_3), 2.07 (s, 1.65H, CH_3), 2.08 (s, 1.35H, CH_3), 2.09 (s, 1.35H, CH_3), 3.49-4.16 (m, 5H), 4.04 (q, 2H, J= 7.2 Hz, CH_2), 4.36-4.98 (m, 9H), 6.06 (s, 0.55H, CH-OAc), 6.23 (s, 0.45H, CH-OAc), 7.22-7.36 (m, 20H, Arom).

Anal. Calcd for $C_{42}H_{46}O_{11}$: C, 69.41; H, 6.38; Found: C, 69.28; H, 6.42.

Ethyl acetoxy(1-acetoxy-2,3,4,6-tetra-*O*-benzyl-D-glucopyranosyl)ethanoate (27). Compound **25** was acetylated and purified as for **24** to afford **27** as an oil with a ratio of 90/10 for two isomers: Rf 0.5 (hexane/ AcOEt 7/3); ^1H NMR δ 1.01 (t, 3H, J= 7.2 Hz, CH_3), 2.08 (s, 3H, CH_3), 2.12 (s, 3H, CH_3), 3.65-3.90 (m, 6H), 3.93 (d, 1H, $J_{2,3}$= 9.5 Hz, H-2), 4.04 (dd, 1H, J= 9.1, 9.2 Hz), 4.46-4.89 (m, 8H, 4 CH_2 benzyl), 6.30 (s, 1H, CH-OAc), 7.18-7.31 (m, 20H, Arom); ^{13}C NMR δ 13.7 (CH_3), 20.5, 21.9 (2 CH_3); 67.7 (CH_2), 69.5 (C-6), 73.2 (CH_2), 73.8; 74.2, 75.3, 75.7 (3 CH_2), 77.4, 77.6, 83.1; 102.1 (C-1); 127.1, 127.2, 127.4, 127.5, 127.6, 127.7, 127.8, 127.9, 128.0, 128.1,

128.2, 128.3, 128.4, 128.5 (CH-Arom); 137.8, 138.0, 138.1, 138.3 (C-ipso); 167.7, 168.3, 169.0 (3 C=O).

Anal. Calcd for $C_{42}H_{46}O_{11}$: C, 69.41; H, 6.38; Found: C, 69.35; H, 6.43.

Ethyl acetoxy(2,3,4,6-tetra-*O*-benzyl-β-D-galactopyranosyl)ethanoate (28). To a solution of **26** (85 mg, 0.117 mmol) in CH_2Cl_2 (0.5 mL), was added molecular sieves 4 Å (85 mg), Et_3SiH (187 µL, 1.17 mmol) and TMSOTf (113 µL, 0.569 mmol). After 30 min stirring at room temperature, the mixture was neutralized with Et_3N, diluted with CH_2Cl_2 and filtered on Celite. The mixture was then concentrated and purified by chromatography over silica gel (eluent: hexane/AcOEt 3:1) to give **28** as a mixture of two diastereoisomers in a ratio of 55/45: oil, Rf 0.7 (hexane/ AcOEt 7/3); ^1H NMR δ 0.90 (t, 1.65H, J= 7.1 Hz, CH_3), 1.04 (t, 1.35H, J= 7.1 Hz, CH_3), 2.00 and 2.02 (2s, 3H, CH_3), 3.49-3.66 (m, 3H), 3.75 (dd, 0.45H, J = 1.3, $J_{1,2}$= 9.9 Hz, H-1), 3.84 (dd, 0.55H, J= 2.3, $J_{1,2}$= 9.9 Hz, H-1), 3.90-4.26 (m, 5H), 4.37-4.98 (m, 8H, 4 CH_2 benzyl), 5.38 (d, 0.45H, J= 1.3 Hz, CH-OAc), 5.48 (d, 0.55H, J= 2.3 Hz, CH-OAc), 7.21-7.34 (m, 20H, Arom); ^{13}C NMR δ 13.7, 14.0 (CH_3), 20.6, 20.7 (CH_3); 61.4 (CH_2); 68.4, 68.5 (C-6); 70.5; 71.9; 72.0, 72.1 (CH_2), 72.3; 73.4, 73.6 (CH_2); 73.7; 74.0; 74.3, 74.8, 75.2 (CH_2); 77.1, 77.9, 78.4, 78.9, 84.8; 127.4, 127.5, 127.7, 127.8, 127.9, 128.1, 128.2, 128.4, 129.0 (CH-Arom); 137.8, 138.0, 138.2, 138.8 (C-ipso); 166.8, 167.8, 170.2, 170.3 (C=O).

Anal. Calcd for $C_{40}H_{44}O_9$: C, 71.84; H, 6.63; Found: C, 71.92; H, 6.72.

Ethyl 2-(2',3',4,'6'-tetra-*O*-benzyl-1'-hydroxy-D-glucopyranosyl)-2,1'-*O*-ethylidene-2-hydroxyethanoate (29). Compound **27** was treated in the same condition as for **26** to give the title compound as an oil: 64 %, Rf 0.7 (hexane/ AcOEt 7/3), ^1H NMR δ 1.09 (t, 3H, J= 7.2 Hz, CH_3), 1.44 (d, 3H, J= 4.9 Hz, CH_3), 3.59 (dd, 1H, $J_{6',6''}$= 11.1, $J_{6',5'}$= 1.5 Hz, H-6'), 3.68-3.82 (m, 4H, H-3',4',5',6''), 4.00 (d, 1H, $J_{2',3'}$= 9.0 Hz, H-2'), 4.08 (q, 2H, J= 7.1 Hz, CH_2), 4.37-5.03 (m, 8H, 4 CH_2 benzyl), 4.43 (s, 1H, H-2), 5.28 (q, 1H, J= 4.9 Hz, CH-CH_3), 7.19-7.31 (m, 20H, Arom); ^{13}C NMR δ 14.1, 19.5 (2 CH_3), 61.0 (CH_2); 68.3 (C-6'), 72.8; 73.2, 75.0, 75.5, 75.7 (4 CH_2 benzyl); 77.7, 78.0, 78.6, 83.8; 102.6 (CH ethylidene), 105.4 (C-1'); 127.4, 127.7, 127.8, 127.9, 128.3, 128.4, 128.5 (CH-Arom); 137.7, 138.1, 138.2, 138.3 (C-ipso); 167.8 (C=O).

Anal. Calcd for $C_{40}H_{44}O_9$: C, 71.84; H, 6.63; Found: C, 71.77; H, 6.56.

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