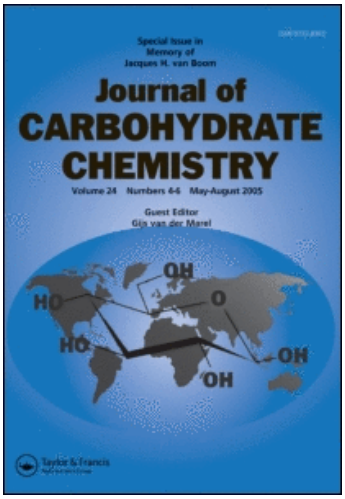

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Synthesis of Acetylated Ranunculin Diastereoisomers and δ-Glucosyloxy-γ-Oxo Esters from α or β Glucosylmethylfurfural

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The α and β acetylated (5-formyl-2-furyl)methyl-D-glucopyranosides were synthesized and converted into acetylated ranunculin diastereoisomers and δ-glucosyloxy-γ-oxo esters.

Keywords Synthesis, Glycosylation, Furanic compounds, Photooxygenation

INTRODUCTION

Ten years ago, we were interested in the synthesis of 5-hydroxymethylfurfural (HMF) obtained from fructose or disaccharides[1,2] and its conversion into hydroxybutenolides, γ-oxo acids, γ-oxo esters, and 5-aminolevulinic acid hydrochlororide.[3,4] More recently, we applied our methodology[3] to the synthesis of the diastereoisomers **1*α*** and **2*β*** of [(2S)-5-oxo-2,5-dihydro-2-furanyl]methyl 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranoside (ranunculin tetraacetate) [**2*β***(S)] (Schs. 1 and 3). Ranunculin tetracetate is a precursor of (−)-ranunculin (**3*β***)

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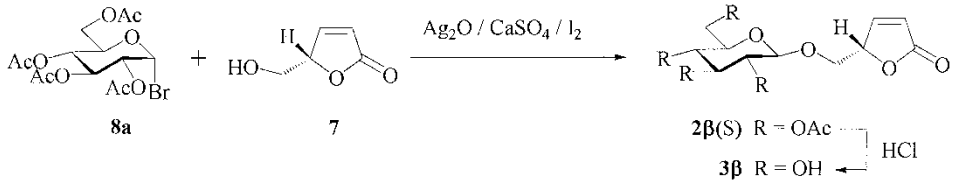
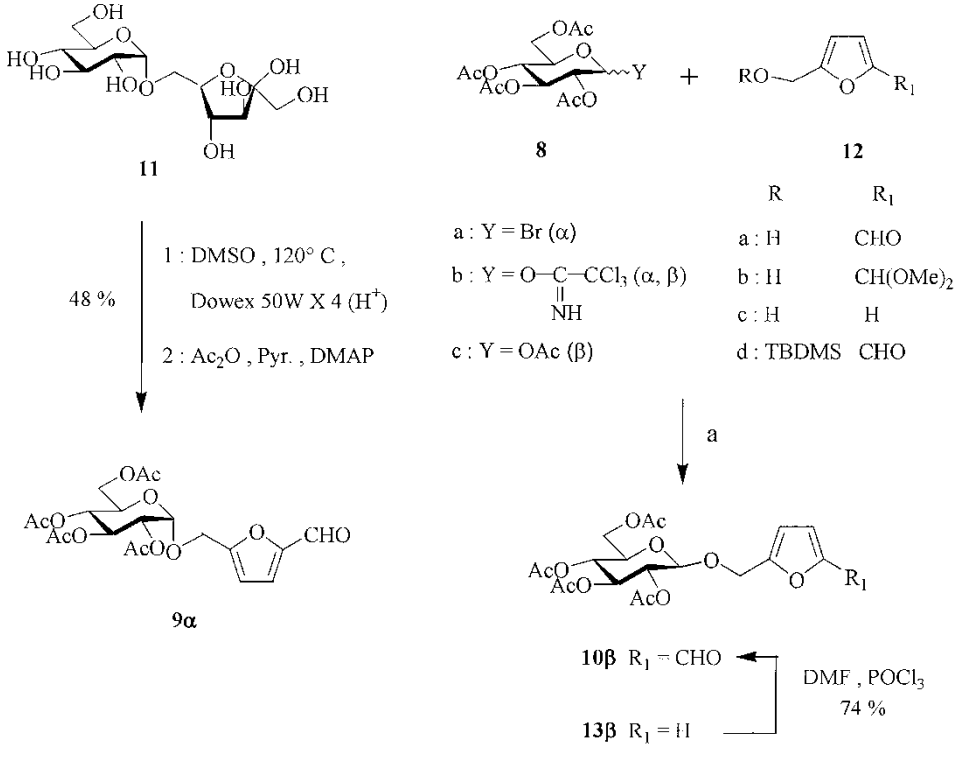
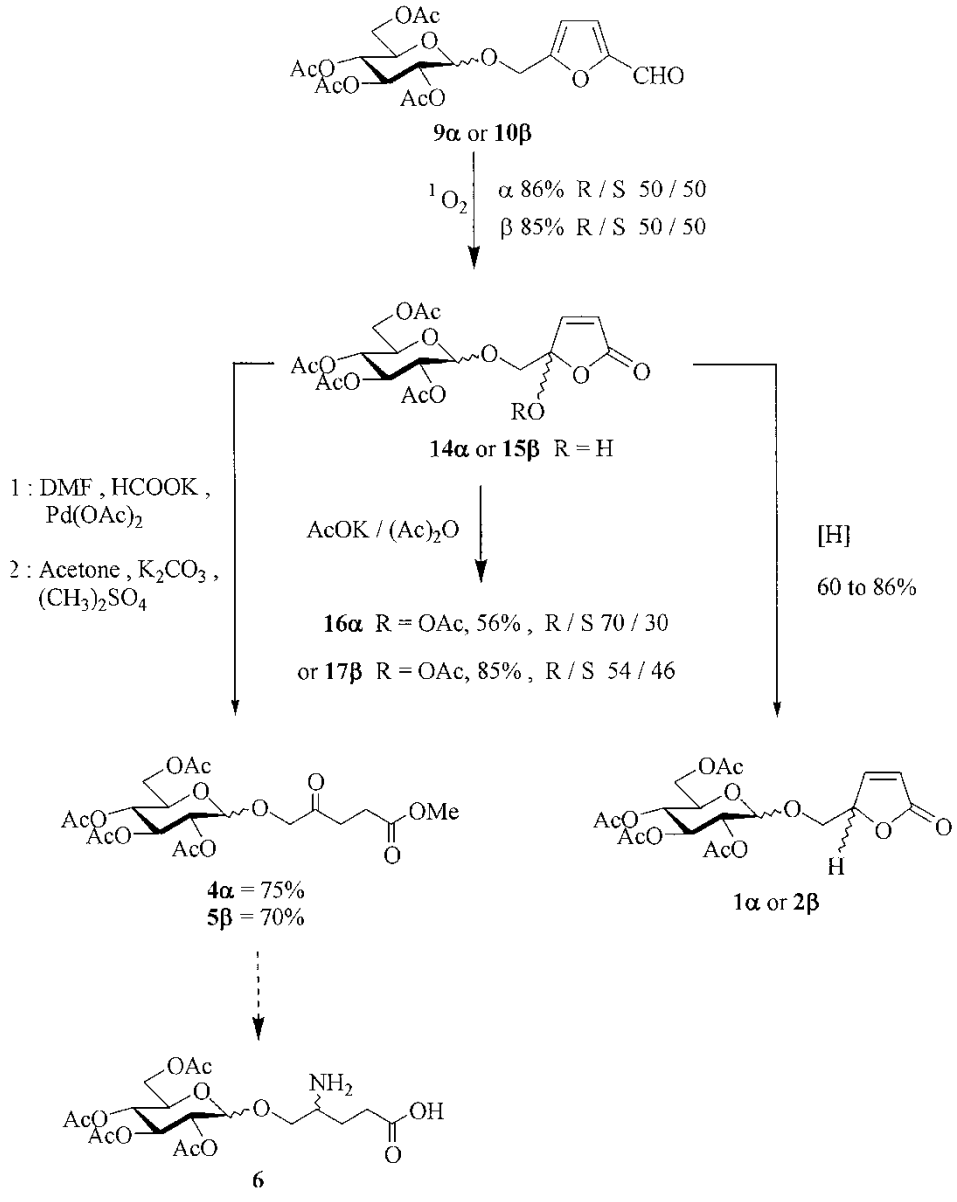


Scheme 1

having cytotoxic and antimutagenic activities.[5,6] We also extended our methodology to the preparation of the δ-glucosyloxy-γ-oxo esters **4α** and **5β**, precursors of GABA derivative **6** bearing a glucosyloxymethyl moiety (Sch. 3). This work is in line with the recent publications of Lichtenthaler et al.[7,8] on the synthesis of heterocycles from carbohydrate feedstocks. The structure of (−)-ranunculin (**3β**) was established to be a β-glucoside of a γ-hydroxymethyl-α, β-butenolide.[9–11] The first total synthesis of **3β** was described by Cardellach et al.[12,13] using a Koenigs-Knorr reaction between (5S)-5-(hydroxymethyl)-2(5H)-furanone (**7**) and the tetra-*O*-acetyl-α-D-glucopyranosyl bromide (**8a**) in the presence of silver oxide (Ag_2O), followed by acidic hydrolysis. In the first



Scheme 2



Scheme 3

publication,[12] the peracetate of ranunculin **2*β*** was obtained as a mixture of epimers, while in a second publication,[13] a compound **3*β*** identical with the natural product was synthesized (Sch. 1). However, a large excess of both Ag_2O and **8a** was used, which may appear somewhat limiting.

Some years later, Fang et al.[14] published the preparation of (−)-ranunculin **3*β*** from mannitol in six steps and a rather low 15% overall yield. Moreover,

the α-anomer of the per-*O*-benzoyl ranunculin derivative was obtained from isomaltulose[15] in four steps. Indeed, the oxidative degradation of isomaltulose in alkaline medium, followed by product conversion into lactones, subsequent benzoylation, and samarium diiodide mediated elimination, led to the per-*O*-benzoylester with an overall yield of 36%. In this paper, we describe the preparation of acetylated ranunculin diastereoisomers **1α** and **2β** from the furanyl glucopyranosides **9α** or **10β** (α and β GMF), respectively (Sch. 3), via the photooxygenation of the furanic ring. This new approach to the various diastereoisomeric targets should help the study of their biologic activities.

RESULTS AND DISCUSSION

The acetylated GMF (**9α**) was obtained from isomaltulose (**11**) according to Lichtenthaler's procedure[15] in 48% yield after peracetylation (Sch. 2). However, the preparation of the corresponding anomer **10β** via the condensation between a glycosyl donor **8a–c** and an alcohol furanic acceptor **12a–d** was more difficult (Table 1).

The first coupling attempt of **8a** and HMF (**12a**) in the presence of Ag_2O led to **10β** in poor yield, probably due to the electron withdrawing effect of the aldehyde moiety decreasing the nucleophilicity of the hydroxyl group (Sch. 2). The transformation of the aldehyde function into an acetal moiety, to give **12b**, did not improve the yield. The substitution of HMF by furfuryl alcohol (**12c**) led to the glucoside **13β** in a higher yield (80%). The latter was easily converted into **10β** by a Vilsmeier-Haack formylation (74% yield). Two other alternatives to prepare **10β** were also studied. The method of Schmidt[16] using imidate **8b** and HMF (**12a**) gave **10β** in moderate yield (32%). Analogously, the reaction between glucose pentaacetate (**8c**) and the

Table 1: Condensation between glucose derivatives **8** and the furanic alcohols **12**.

Compounds		Experimental conditions[a]	(%) Products	
8	**12**		**10β**	**13β**
a	**a**	Ag_2O, rt	11	
a	**b**	Ag_2O, I_2, $CaSO_4$, rt	8	
a	**c**	Ag_2O, I_2, $CaSO_4$, rt		80
b	**a**[b]	$BF_3.Et_2O$, $-20^\circ C$ then rt	32	
b	**d**	$BF_3.Et_2O$, $-20^\circ C$ then rt	0	
c	**c**	$BF_3.Et_2O$, $-20^\circ C$ then rt	trace	
c	**d**	$BF_3.Et_2O$, $-20^\circ C$ then rt	33	

[a]Solvent: CH_2Cl_2.
[b]Solvent CH_3CN.

silylated HMF derivative **12d** according to Nair and Joseph[17] yielded **10β** in a similar yield. Since glucose pentaacetate is cheaper and more stable than the corresponding glucosyl bromide, and since the silylated **12d** is more stable than HMF **12a**, the latter strategy appeared more convenient.

The photooxygenation of GMF **9α** with singlet oxygen[3] led to the corresponding hydroxy-Δ^2-butenolide **14α** as a 1/1 diastereoisomeric mixture (Sch. 3). These compounds are very unstable and easily decomposed on column chromatography.

Due to their poor stability during column chromatography, the 1/1 mixture of diastereoisomers **14α** was acetylated (acetic anhydride and sodium acetate)[18] to give the corresponding isomers **16α**, which were not separated. However, NMR data of the crude mixture of **16α** showed the presence of a major epimer (70%). The increased proportion of one epimer was attributed to the kinetically esterification of the corresponding hydroxy-Δ^2-butenolide diastereoisomer **14α**. Under identical conditions, the acetylated isomers **17β** were prepared as a 54/46 R/S mixture, from **10β**. In this case, the diastereoisomers were separated by chromatography.

As a hemiacetalic cyclic compound is in equilibrium with the alicyclic tautomeric form, the compounds **14α** or **15β** were reduced to the corresponding acetylated (5′-oxo-2′,5′-dihydrofuran-2′-yl)methyl-α or β-D-glucopyranoside (**1α**) or (**2β**). Unfortunately, the sugar moiety did not induce any stereoselectivity (Table 2, entry 1). Even the addition of ceric chloride, which, according to Kumar et al.,[19] favors the stereospecific reduction of 7-oxocholesterylacetate, did not improve significantly the stereoselectivity, whatever the temperature used (Table 2, entries 2 and 3). Besides, attempted reduction with 9-BBN failed (Table 2, entry 4).

An X-ray analysis of first eluted epimer **17β**, showing an R configuration for carbon C-2′, allowed the possibility to assign the configuration R or S at this carbon for each of the epimers **17β**. The synthesis of pure **2β**(S), identical

Table 2: Reduction of hemiacetals **14α** and **15β**.

		Compounds, products	
Entry	**Experimental conditions**[a]	**14α, 1α (Yields %, R/S %)**	**15β, 2β (Yields %, R/S %)**
1	$NaBH_4$, MeOH, rt	80, 50/50	81, 50/50
2	$NaBH_4$, $CeCl_3$, $7H_2O$ (0.4M) MeOH, rt	80, 40/60	82, 60/40
3	$NaBH_4$, $CeCl_3$, $7H_2O$ (0.4M) MeOH, −78°C then rt	80, 40/60	80, 60/40
4	9-BBN, THF, 0°C then rt	Trace	Trace

[a]After the total reduction, the pH of the solution was adjusted to 1 with HCl (5N).

to (−) ranunculin tetraacetate according to Camps et al.[13] and its epimerisation into **1α**(S) with $TiCl_4$ according to Dasgupta et al.,[20] allowed to assign the chemical shift of protons and carbons of the other stereoisomers **1α**(R) and **2β**(R), and to estimate the epimers ratio. The R/S configuration of carbon C-2′ in epimers **16α** was attributed by comparing their NMR spectra and those of **17β**, **1α**(R or S) and **2β** (R or S).

The hydroxy-Δ^2-butenolides **14α** and **15β** were easily transformed into the corresponding γ-oxo esters **4α** and **5β** respectively, via the corresponding γ-oxo acids (Sch. 3). Some years ago, γ-oxo acids and γ-oxo esters were obtained by photooxygenation of furanic compounds and reduction under ultrasound with Zn in acetic acid.[3] As Misiti et al.[21] described the chemoselective catalytic hydrogenation of α,β unsaturated esters using Pd/C, the isomers **14α** and **15β** were selectively reduced via a hydrogen transfer reaction in the presence of the potassium formate/palladium(II) acetate system.[22] The γ-keto acids intermediates were not isolated but transformed into γ-keto esters **4α** and **5β**.

CONCLUSION

Several methods of synthesis of α- and β-GMF **9α** and **10β** were compared. If the synthesis of α-GMF **9α** is easy from isomaltulose, the preparation of β-GMF **10β** is more difficult. The best yield was obtained via the condensation of tetra-*O*-acetyl-α-D-glucopyranosyl bromide (**8a**) with furfuryl alcohol (**12c**) followed by a formylation reaction. The direct condensation of HMF (**12a**) with a glucosyl donor gave a moderate yield (32%) of **10β**. The photooxygenation of the furanic moiety of α and β GMF, and subsequent reduction, led to the acetylated diastereoisomers of ranunculin **1α** and **2β** in moderate yield. However, this methodology gave the possibility to prepare both acetylated epimers **1α** and **2β** of α and β ranunculin in two steps from α and β GMF. The selective reduction of the intermediate hydroxy butenolides **14α** and **15β**, via a hydrogen transfer reaction, gave access to γ-keto esters **4α** and **5β**, precursors of GABA derivatives with a glycosyl moiety having an α or β configuration.

EXPERIMENTAL

Isomaltulose was kindly provided by Südzucker AG Company (Germany). Melting points were determined on a Buchi melting point apparatus and are uncorrected. Optical rotations were measured with a Perkin Elmer Model 241 polarimeter. The 200 MHz or 300 MHz ^{1}H-NMR and 50 or 75 MHz ^{13}C-NMR were recorded with a Bruker AC 200 or AM 300 spectrometer with TMS as an internal standard. In the ^{1}H- and ^{13}C-NMR spectra, the chemical shift of the protons or the carbons of each enantiomer **14α** and **15β** was

assigned using the COSY and HSQC procedures. Mass Spectra were recorded with a Finnigan Mat 95 XL spectrometer. Thin layer chromatography (TLC) was carried out on plates coated with silica gel 60. Column chromatography was carried out on silica gel Si 60; the ratio of solvents were measured in volume.

(5′S) (5′-Oxo-2′,5′-dihydrofuran-2′-yl)methyl-2,3,4,6-tetra-O-acetyl-β-D-glucopyranoside (2β)

The compound **2β**(S) was prepared according to Camps et al.[13] 0.5 g (4.38 mmol) of butenolide **7** in dichloromethane with silver oxide (3 × 1.12 g, 4.8 mmol) and bromide **8a** (3 × 1.93 g, 4.38 mmol) led to **2β**(S) (0.44 g, 1.0 mmol) in 23% yield after purifying by column chromatography (dichloromethane/ethyl acetate: 70/30). **2β**(S): white solid; mp 135–136°C lit[13] mp 136–138°C; $[\alpha]_D^{20}$ −22.6 (*c* 1.1, CH_2Cl_2) lit[13] $[\alpha]_D^{20}$ −24.2 (*c* 1.1, $CHCl_3$); ^{1}H-NMR (200 MHz, $CDCl_3$): δ 2.02–2.09 (4s, 12H, $-OCOCH_3$), 3.70 (m, 1H, H-5), 3.80 (dd, 1H, J_{CH_a}, $H_{2'} = 4.8$, $J_{gemCH_2} = 11.0$ Hz, -OCH_2), 4.08 (dd, 1H, J_{CH_b}, $H'_2 = 4.80$, $J_{gemCH_2} = 11.0$ Hz, -OCH_2), 4.12 (dd, 1H, $J_{5,6a} = 2.2$, $J_{6a,6b} = 12.4$ Hz, H-6_a), 4.23 (dd, 1H, $J_{5,6b} = 4.5$, $J_{6a,6b} = 12.4$ Hz, H-6_b), 4.60 (d, 1H, $J_{1,2} = 7.9$ Hz, H-1), 5.08 (dd, 1H, $J_{1,2} = 7.9$, $J_{2,3} = 9.2$ Hz, H-2), 5.15 (t, 1H, $J_{3,4} = J_{4,5} = 9.2$ Hz, H-4), 5.15 (m, 1H, H-2′), 5.22 (t, H, $J_{2,3} = J_{3,4} = 9.2$ Hz, H-3), 6.20 (dd, 1H, $J_{2',4'} = 2.0$, $J_{3',4'} = 5.7$ Hz, H-4′), 7.47 (dd, 1H, $J_{2',3'} = 1.5$, $J_{3',4'} = 5.7$ Hz, H-3′) similar to literature data;[13] ^{13}C-NMR (75 MHz, $CDCl_3$): δ 20.6–20.7 (4 CH_3), 61.7 (C-6), 68.3 (C-4), 69.3 (CH_2), 70.8 (C-2), 72.0 (C-5), 72.5 (C-3), 81.4 (C-2′), 100.9 (C-1), 122.8 (C-4′), 153.0 (C-3′), 169.5–170.1 (4 CO_2), 172.4 (C-5′).

(5-(Dimethoxymethyl)-2-furyl)methanol (12b)

To a solution of **12a** (0.3 g, 2.4 mmol) in methanol (7 mL) maintained at 0°C were added 0.1 g (0.23 mmol of Ytterbium) of Ytterbium sulfate supported on Amberlite 15[23] and trimethyl orthoformate (0.3 mL, 2.78 mmol). The mixture was allowed to warm to rt and stirred for 2 hr. Then trimethyl orthoformate (1 mL, 9.15 mmol) was added and the solution was stirred for 2 hr more. The solution was filtered using a glass apparatus previously washed with alcaline solution. Volatiles were evaporated under vacuum. **12b** (0.33 g, 1.92 mmol, 80%) was obtained pure as a yellow oil. **12b**: ^{1}H-NMR (200 MHz, $CDCl_3$): δ 2.88 (s broad, 1H, OH), 3.33 (s, 6H, $-OCH_3$), 4.56 (s, 2H, $-OCH_2$), 5.38 (s, 1H, $CH(OCH_3)_2$), 6.24 (d, 1H, $J_{3,4} = 3.1$ Hz, H-3), 6.34 (d, 1H, $J_{3,4} = 3.1$ Hz, H-4); ^{13}C-NMR (75 MHz, $CDCl_3$): δ 52.8, 57.8 (2 $-OCH_3$), 66.3 ($-OCH_2$), 109.1 (C–3), 109.7 (C–4), 151.1 (C–2), 151.8 (C–5).

Anal. Calcd for $C_8H_{12}O_4$ (172.18): C, 55.80; H, 7.02. Found: C, 55.67; H, 6.99.

5-({{*Tert*-butyl(dimethyl)silyl)oxy}methyl)-2-furaldehyde (12d)

To a solution of **12a** (6.3 g, 50 mmol) in dimethylformamide (12.6 mL) were added imidazole (8.5 g, 125 mmol) and *ter*-butyldimethylsilyl chloride (8.9 g, 59 mmol). The solution was stirred for 24 hr. The silylated compound was extracted with petroleum ether (5 × 25 mL). After washing with brine, drying, and evaporating the solvent, the remaining oil was distillated (132°C/1.5 Torr) giving **12d** (9 g, 3.7 mmol, 74%) as a light yellow liquid. **12d**: ^{1}H-NMR: similar to literature data.[24]

(5′-Formyl-2′-furyl)methyl-2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranoside (9α)

To a solution of isomaltulose monohydrate **11** (4.5 g, 11.5 mmol) in dimethyl sulfoxide (45 mL), heated to 120°C, was added 0.4 g of strongly acidic sulfonic acid-type ion-exchange resin (Dowex 50-WX4, H^+ form, dried) and stirred at 120°C for 7 hr. After filtration, the filtrate was removed under reduced pressure at 80°C and the residual brown syrup was dissolved in water (25 mL). This solution was extracted with dichloromethane (2 × 10 mL). The aq. phase was evaporated under reduced pressure giving an oil (7.6 g), which was dissolved in pyridine (380 mL). After adding acetic anhydride, this new solution was stirred for 24 hr. Cold water (150 mL) was added, and the mixture was treated with sulfuric acid (2N, 1 mL), neutralized with aq. sodium hydrogenocarbonate (5 mL), washed with water, and dried. After filtration and evaporation, the raw material was purified by column chromatography (petroleum ether/ethyl acetate: 50/50) giving **9*α*** (2.75 g, 6 mmol, 48%) as a yellow oil. **9*α***: $[\alpha]_D^{20}$ +132 (*c* 1.7, $CHCl_3$) lit.[15] +133 (*c* 1.7, $CHCl_3$); ^{1}H-NMR and ^{13}C-NMR: similar to literature data.[15]

(5′-Formyl-2′-furyl)methyl-2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranoside (10β)

(a) Koenigs-Knorr method: To a solution of HMF **12a** (0.9 g, 2.2 mmol) in dry dichloromethane (15 mL) were added **8a** (0.9 g, 2.2 mmol) and silver oxide (0.41 g, 17.6 mmol). After stirring for 5 hr at rt, the mixture was filtered and the solvent evaporated. The residue was chromatographed through silica gel (dichloromethane/ethyl acetate: 80/20) giving pure product **10*β*** (0.11 g, 0.24 mmol, 11%) as a yellow solid. **10*β***: mp 130°C; $[\alpha]_D^{20}$ −39 (*c* 1, CH_2Cl_2); ^{1}H-NMR (200 MHz, $CDCl_3$): δ2.03–2.09 (4s, 12H, $-OCOCH_3$), 3.75 (m, 1H, H-5), 4.18 (dd, 1H, $J_{5,6a} = 3.2$, $J_{6a,6b} = 12.8$ Hz, H–6_a), 4.25 (dd, 1H, $J_{5,6b} = 6.5$, $J_{6a,6b} = 12.8$ Hz, H–6_b), 4.62 (d, 1H, $J_{1,2} = 7.8$ Hz, H–1), 4.70 (d, 1H, $J_{\text{gem } CH_2} = 13.7$ Hz, CH_2), 4.84 (d, 1H, $J_{\text{gem } CH_2} = 13.7$ Hz, CH_2), 5.00

(dd, 1H, $J_{1,2} = 7.8$, $J_{2,3} = 9.2$ Hz, H–2), 5.10 (dd, 1H, $J_{3,4} = J_{4,5} = 9.2$ Hz, H–4), 5.20 (dd, 1H, $J_{2,3} = J_{3,4} = 9.2$ Hz, H–3), 6.53 (d, 1H, $J_{3',4'} = 3.5$ Hz, H–3′), 7.22 (d, 1H, $J_{3',4'} = 3.5$ Hz, H–4′), 9.63 (s, 1H, CHO); ^{13}C-NMR (75 MHz, $CDCl_3$): δ 20.7–20.9 (4 CH_3), 61.8 (C–6), 68.2 (C–4), 71.0 (C–2), 72.0 (C–5), 72.6 (C–3), 99.8 (C–1), 111.8 (C–3′), 122.1 (C–4′), 152.8 (C–5′), 156.7 (C–2′), 169.5–170.0 (4 $COCH_3$),177.6 (CHO).

Anal. Calcd for $C_{20}H_{24}O_{12}$ (456): C, 52.63; H, 5.30. Found: C, 52.42; H, 5.16.

(b) According to Schmidt et al.[16]: Under argon, **12a** (0.14 g, 1.1 mmol) and **8b** (1.08 g, 2.2 mmol) were dissolved in a mixture of acetonitrile (22 mL) and dry dichloromethane (10 mL). After addition of molecular sieve (1 g), boron trifluoride diethyl etherate (0.6 mL, 4.4 mmol) was added to the solution, cooled to 0°C. The mixture was stirred for 2 hr at rt, and then diluted with dichloromethane (10 mL), neutralized with sodium hydrogenocarbonate, washed with water, and dried. After filtration, the solvent was evaporated. The residue was chromatographed through column silica gel (dichloromethane/ethyl acetate: 80/20) giving pure **10*β*** (0.16 g, 0.35 mmol, 32%).

(c) According to Nair and Joseph:[17] The compound **12d** (0.25 g, 2 mmol) then boron trifluoride diethyl etherate (4 mL) were added at −20°C to a solution of **8c** (0.86 g, 2.2 mmol) in dry dichloromethane (15 mL). After stirring for 5 hr at −20°C, the mixture was neutralized with sodium hydrogenocarbonate and diluted with diethyl ether (75 mL). The organic phase was washed with water (2 × 15 mL) and then brine (10 mL), and dried. After filtration, the solvent was evaporated. The raw product was purified by column chromatography (dichloromethane/ethyl acetate: 80/20) giving pure **10*β*** (0.302 g, 0.66 mmol, 33%).

(d) From **13*β***: A solution of phosphorus oxychloride in dimethylformamide (0.7 mL) was previously prepared by adding phosphorus oxychloride (0.9 mL, 9.2 mmol) in dimethylformamide maintained below 20°C. This orange solution, cooled to 0°C, was dropped in a cooled solution of **13*β*** (1.96 g, 4.5 mmol) in 1,2-dichloroethane (4.5 mL). This mixture was allowed to warm to rt, stirred for 8 hr, and then neutralized with an aq. solution of sodium acetate (3.1 g in 14 mL) and diluted with diethyl ether (80 mL). The organic solution was washed with brine (2 × 10 mL), dried, and evaporated. The crude product was purified by column chromatographed with an elution gradient (dichloromethane then dichloromethane/ethyl acetate until, 80/20) giving **10*β*** (1.52 g, 3.3 mmol, 74%).

2′-Furylmethyl-2,3,4,6-tetra-*O*-acetyl-*β*-D-glucopyranoside (13*β*)

To a solution of **12c** (9.6 g, 0.1 mmol) in dichloromethane (40 mL) were added dry calcium sulfate (4 g) and silver carbonate (5.5 g, 20 mmol). After stirring for 30 min, iodine (1.52 g, 6.2 mmol) was added and then was

dropped **8a** (8.22 g, 20 mmol) dissolved in dichloromethane (30 mL). The mixture was stirred at room temperature for 3 hr and then centrifugated to eliminate the mineral salts. The organic phase was washed with sodium thiosulfate (2 × 10 mL) and with brine, and dried. The solvent was evaporated, and the raw solid was recrystallized (petroleum ether/ethyl acetate) giving **13*β*** pure (6.9 g, 15.6 mmol, 80%). **13*β***: mp 110–111°C; $[\alpha]_D^{20}$ +47 (*c* 1, $CHCl_3$); ^{1}H-NMR (200 MHz, $CDCl_3$): δ 2.00–2.10 (4s, 12H, $-OCOCH_3$), 3.68 (ddd, 1H, $J_{4,5} = 9.7$, $J_{5,6a} = 2.5$, $J_{5,6b} = 4.6$ Hz, H–5), 4.13 (dd, 1H, $J_{5,6a} = 2.5$, $J_{6a,6b} = 12.3$ Hz, H–6a), 4.26 (dd, 1H, $J_{5,6b} = 2.5$, $J_{6a,6b} = 4.6$ Hz, H–6b), 4.56 (d, 1H, $J_{1,2} = 7.9$ Hz, H–1) 4.61 (d, 1H, $J_{\text{gem } CH_2} = 13.2$ Hz, CH_2), 4.74 (d, 1H, $J_{\text{gem } CH_2} = 13.2$ Hz, CH_2), 4.98 (dd, 1H, $J_{1,2} = 7.9$, $J_{2,3} = 9.3$ Hz, H–2), 5.08 (dd, 1H, $J_{3,4} = J_{4,5} = 9.3$ Hz, H–4), 5.17 (dd, 1H, $J_{2,3} = J_{3,4} = 9.3$ Hz, H–3), 6.33 (dd, 1H, $J_{3',4'} = 3.3$, $J_{3',5'} = 0.8$ Hz, H–3′), 6.35 (dd, 1H, $J_{3',4'} = 3.3$, $J_{4',5'} = 1.8$ Hz, H–4′), 7.40 (dd, 1H, $J_{3',5'} = 0.8$, $J_{4',5'} = 1.8$ Hz, H–5′); ^{13}C-NMR (75 MHz, $CDCl_3$): δ 20.5–20.8 (4 CH_3), 62.2 (C–6), 63.0 (CH_2), 68.8 (C–4), 71.4 (C–2), 72.2 (C–5), 73.1 (C–3), 99.3 (C–1), 110.6 (C–3′), 110.8 (C–4′), 143.0 (C–5′), 150.6 (C–2′), 169.3–170.6 (4 $COCH_3$).

Anal. Calcd for $C_{19}H_{24}O_{11}$ (428.38): C, 53.27; H, 5.65. Found: C, 53.23; H, 5.63.

(2′-Hydroxy-5′-oxo-2′,5′-dihydrofuran-2′-yl)methyl-2,3,4,6-tetra-*O*-acetyl-*α*-D-glucopyranoside (14*α* R+S)

Rose Bengal-Sephadex resin[25] (109 mg) was added to **9α** (302 mg, 0.66 mmol) dissolved in a mixture of dichloromethane (4 mL) and ethyl alcohol (9 mL). The mixture, under a low pressure of dioxygen, was quickly stirred and irradiated for 6 hr with a halogen lamp (150 W). After filtration and evaporation of the solvents, the residue was chromatographed on a preparative TLC plate (dichloromethane/ethyl acetate: 50/50) giving **14*α*** (0.261 mg, 0.57 mmol, 86%) as a mixture of epimers (R/S: 1/1). A second preparative plate chromatography with a little amount led to two fractions I and II having one of both epimers in a bigger amount. **14*α*** (R+S), solid; mp 45–46°C; fraction I: ^{1}H-NMR (200 MHz, $CDCl_3$): δ 2.00–2.10 (4s, 12H, $-OCOCH_3$), 2.20 (s, 1H, OH); 3.70 (d, 1H, $J_{\text{gem } CH_2} = 11.0$ Hz, CH_2), 3.90 (d, 1H, $J_{\text{gem } CH_2} = 11.0$ Hz, CH_2), 4.05 (m, 2H, H–5, H–6_b), 4.25 (dd, 1H, $J_{5,6a} = 4.4$, $J_{6a,6b} = 12.5$ Hz, H–6_a), 4.86 (dd, 1H, $J_{1,2} = 3.7$, $J_{2,3} = 9.6$ Hz, H–2), 5.01 (dd, 1H, $J_{3,4} = J_{4,5} = 9.6$ Hz, H–4), 5.10 (d, 1H, $J_{1,2} = 3.7$ Hz, H–1), 5.41 (dd, 1H, $J_{2,3} = J_{3,4} = 9.6$ Hz, H–3), 6.19 (d, 1H, $J_{3',4'} = 5.6$ Hz, H–4′), 7.22 (d, 1H, $J_{3',4'} = 5.6$ Hz, H–3′); ^{13}C-NMR (75 MHz, $CDCl_3$): δ 20.6–20.7 (4 CH_3), 61.8 (C–6), 67.8 (CH_2), 68.0 (C–5), 68.4 (C–4), 70.1 (C–3), 70.4 (C–2), 96.9 (C–1), 105.6 (C–2′), 125.2 (C–4′), 147.9 (C–3′)), 169.2–170.8 (4 $COCH_3$), 170.1 (C–5′); fraction II: ^{1}H-NMR (200 MHz, $CDCl_3$): δ 2.00–2.10 (4s, 12H, $-OCOCH_3$), 2.20 (s, 1H, OH), 3.68 (d, 1H, $J_{\text{gem } CH_2} = 11.0$ Hz, CH_2),

3.87 (d, 1H, $J_{\text{gem CH}_2} = 11.0$ Hz, CH_2), 4.05 (m, 2H, H–5, H–6_a), 4.23 (dd, 1H, $J_{5,6b} = 4.4$, $J_{6a,6b} = 12.5$ Hz, H–6_b), 4.92 (dd, 1H, $J_{1,2} = 3.7$, $J_{2,3} = 9.6$ Hz, H–2), 5.02 (dd, 1H, $J_{3,4} = J_{4,5} = 9.6$ Hz, H–4), 5.13 (d, 1H, $J_{1,2} = 3.7$ Hz, H–1), 5.39 (dd, 1H, $J_{2,3} = J_{3,4} = 9.6$ Hz, H–3), 6.23 (d, 1H, $J_{3',4'} = 5.6$ Hz, H–4′), 7.24 (d, 1H, $J_{3',4'} = 5.6$ Hz, H–3′); ^{13}C-NMR (75 MHz, $CDCl_3$): δ 20.6–20.7 (4 CH_3), 61.8 (C–6), 67.9 (CH_2), 68.1 (C–5), 68.3 (C–4), 70.0 (C–3), 70.4 (C–2), 96.8 (C–1), 105.6 (C–2′), 125.1 (C–4′), 148.0 (C–3′), 169.2–170.8 (4 $COCH_3$), 170.1 (C–5′).

(2′-Hydroxy-5′-oxo-2′,5′-dihydrofuran-2′-yl)methyl-2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranoside (15β R+S)

Compound **15β** was prepared analogously to the same method than **14α** Compound **10β** (302 mg, 0.26 mmol) was irradiated as **9α** leading to **15β** (260 mg, 0.57 mmol, 86%) as a mixture of diastereoisomers (R/S: 1/1). A second preparative plate chromatography (dichloromethane/ethyl acetate: 50/50) led to two fractions I and II having one of both epimers in a bigger amount. **15β** (R+S): solid; mp 137°C; fraction I: ^{1}H-NMR (200 MHz, $CDCl_3$): δ2.00–2.10 (4s, 12H, –$OCOCH_3$), 2.08 (s, 1H, OH); 3.78 (m, 1H, H–5), 3.91 (d, 1H, $J_{\text{gem CH}_2} = 11.2$ Hz, CH_2), 4.08 (d, 1H, $J_{\text{gem CH}_2} = 11.2$ Hz, CH_2), 4.16 (dd, 1H, $J_{5,6a} = 2.4$, $J_{6a,6b} = 12.5$ Hz, H–6_a), 4.26 (dd, 1H, $J_{5,6b} = 4.6$, $J_{6a,6b} = 12.5$ Hz, H–6_b), 4.63 (d, 1H, $J_{1,2} = 7.9$ Hz, H–1), 4.93 (dd, 1H, $J_{1,2} = 7.9$, $J_{2,3} = 9.4$ Hz, H–2), 5.05 (dd, 1H, $J_{3,4} = J_{4,5} = 9.4$ Hz, H–4), 5.20 (dd, 1H, $J_{2,3} = J_{3,4} = 9.4$ Hz, H–3), 6.15 (d, 1H, $J_{3',4'} = 5.7$ Hz, H–4′), 7.23 (d, 1H, $J_{3',4'} = 5.7$ Hz, H–3′); ^{13}C-NMR (75 MHz, $CDCl_3$): δ20.6–20.7 (4 CH_3), 62.0 (C–6), 68.3 (C–4), 70.4 (CH_2), 71.2 (C–2), 71.8 (C–5), 72.5 (C–3), 101.3 (C–1), 105.9 (C–2′), 125.5 (C–4′), 152.4 (C–3′), 169.2–170.8 (4 $COCH_3$), 170 (C–5′); fraction II: ^{1}H NMR (200 MHz, $CDCl_3$): δ2.00–2.10 (4s, 12H, –$OCOCH_3$), 2.08 (s, 1H, OH); 3.78 (m, 1H, H–5), 3.87 (d, 1H, $J_{\text{gem CH}_2} = 11.2$ Hz, CH_2), 3.94 (d, 1H, $J_{\text{gem CH}_2} = 11.2$ Hz, CH_2), 4.16 (dd, 1H, $J_{5,6a} = 2.4$, $J_{6a,6b} = 12.5$ Hz, H–6_a), 4.26 (dd, 1H, $J_{5,6b} = 4.4$, $J_{6a,6b} = 12.5$ Hz, H–6_b), 4.68 (d, 1H, $J_{1,2} = 7.9$ Hz, H–1), 4.96 (dd, 1H, $J_{1,2} = 7.9$, $J_{2,3} = 9.6$ Hz, H–2), 5.02 (dd, 1H, $J_{3,4} = J_{4,5} = 9.6$ Hz, H–4), 5.23 (dd, 1H, $J_{2,3} = J_{3,4} = 9.6$ Hz, H–3), 6.19 (d, 1H, $J_{3',4'} = 5.6$ Hz, H–4′), 7.27 (d, 1H, $J_{3',4'} = 5.6$ Hz, H–3′); ^{13}C-NMR (75 MHz, $CDCl_3$): δ20.6–20.7 (4 CH_3), 61.8 (C–6), 68.2 (C–4), 70.9 (C–2), 71.8 (C–5), 72 (CH_2), 72.4 (C–3), 100.9 (C–1), 105.6 (C–2′), 125.2 (C–4′), 152.9 (C–3′), 169.2–170.8 (4 $COCH_3$), 170.0 (C–5′).

(2′-Acetoxy-5′-oxo-2′,5′-dihydrofuran-2′-yl)methyl-2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranoside (16α)

Dry potassium acetate (417 mg, 4.25 mmol) and acetic anhydride (2.8 mL, 29.75 mmol) were added to a cooled solution of alcohol **14α** (394 mg,

0.85 mmol) in dry dichloromethane (4.5 mL). The mixture was allowed to warm to rt and stirred until TLC (petroleum ether/ethyl acetate/ethyl alcohol: 48/47/5) indicated completed conversion (4 hr). After filtration on a pad of Celite, the organic solution was concentrated. The crude product was chromatographed twice through silica gel (petroleum ether/ethyl acetate/ethyl alcohol: 48/47/5), and then (petroleum ether/dichloromethane/diethyl ether: 33/33/33) giving **16*α*** (240 mg, 0.48 mmol, 56%) as mixture of epimers (R + S) in a ratio of 70/30 according to NMR data; white solid, mp 68–70°C; major epimer **16*α*** (R): ^{1}H-NMR (200 MHz, $CDCl_3$): δ2.00–2.10 (5s, 15H, CH_3), 3.83 (d, 1H, $J_{gem\ CH_2} = 11.1$ Hz, CH_2), 4.03 (m, 1H, H–5), 4.11 (d, 1H, $J_{gem\ CH_2} = 11.1$ Hz, CH_2), 4.14 (dd, 1H, $J_{5,6a} = 3.9$, $J_{6a,6b} = 12.5$ Hz, H–6_a), 4.23 (dd, 1H, $J_{5,6b} = 4.3$, $J_{6a,6b} = 12.5$ Hz, H–6_b), 4.91 (dd, 1H, $J_{1,2} = 3.7$, $J_{2,3} = 9.8$ Hz, H–2), 5.07 (dd, 1H, $J_{3,4} = J_{4,5} = 9.8$ Hz, H–4), 5.09 (d, 1H, $J_{1,2} = 3.7$ Hz, H–1), 5.36 (dd, 1H, $J_{2,3} = J_{3,4} = 9.8$ Hz, H–3), 6.31 (d, 1H, $J_{3',4'} = 6.0$ Hz, H–4′), 7.56 (d, 1H, $J_{3',4'} = 6.0$ Hz, H–3′); ^{13}C-NMR (75 MHz, $CDCl_3$): δ20.5–21.3 (5 CH_3), 61.7 (C–6), 67.8 (CH_2), 68.0 (C–4), 68.7 (C–2), 70.1 (C–5), 70.6 (C–3) 97.0 (C–1), 105.7 (C–2′), 124.8 (C–4′), 150.5 (C–3′), 168.3–170.0 (5 $COCH_3$), 170.6 (C–5′); minor epimer **16*α*** (S): ^{1}H-NMR (200 MHz, $CDCl_3$): δ2.00–2.10 (5s, 15H, CH_3), 3.83 (d, 1H, $J_{gem\ CH_2} = 11.1$ Hz, CH_2), 4.03 (m, 1H, H–5), 4.08 (dd, 1H, $J_{5,6a} = 3.9$, $J_{6a,6b} = 12.5$ Hz, H–6_a), 4.11 (d, 1H, $J_{gem\ CH_2} = 11.1$ Hz, CH_2), 4.27 (dd, 1H, $J_{5,6b} = 4.3$, $J_{6a,6b} = 12.5$ Hz, H–6_b), 4.88 (dd, 1H, $J_{1,2} = 3.7$, $J_{2,3} = 9.8$ Hz, H–2), 5.07 (dd, 1H, $J_{3,4} = J_{4,5} = 9.8$ Hz, H–4), 5.08 (d, 1H, $J_{1,2} = 3.7$ Hz, H–1), 5.48 (dd, 1H, $J_{2,3} = J_{3,4} = 9.8$ Hz, H–3), 6.31 (d, 1H, $J_{3',4'} = 6.0$ Hz, H–4′), 7.58 (d, 1H, $J_{3',4'} = 6.0$ Hz, H–3′); ^{13}C-NMR (75 MHz, $CDCl_3$): δ20.5–21.3 (5 CH_3), 62.1 (C–6), 68.7 (CH_2), 68.4 (C–4), 69.7 (C–2), 69.9 (C–5), 70.7 (C–3) 96.4 (C–1), 105.4 (C–2′), 124.4 (C–4′), 151.1 (C–3′), 168.3–170.0 (5 $COCH_3$), 170.6 (C–5′).

Anal. Calcd for $C_{21}H_{26}O_{14}$ (502.43) (R + S): C, 50.20; H, 5.21. Found: C, 50.52; H, 5.25.

(2′-Acetoxy-5′-oxo-2′,5′-dihydrofuran-2′-yl)methyl-2,3,4,6-tetra-*O*-acetyl-*β*-D-glucopyranoside (17*β*)

The peracetylated compound **17*β*** was prepared as **16*α***. **15*β*** (395 mg, 0.85 mmol) led to **17*β*** (R+S) (400 mg), the epimers of which were separated by column chromatography (petroleum ether/dichloromethane/ethyl acetate: 25/25/50). The first eluted compound corresponded to the epimer **17*β*** (R) (196 mg, 0.39 mmol, 46%), while the second corresponded to **17*β*** (S) (167 mg, 0.33 mmol, 39%); (R/S) = 54/36; compound **17*β*** (R): white solid, mp 172–173°C; $[\alpha]_D^{20}$ –111 (*c* 1, $CHCl_3$); ^{1}H-NMR (200 MHz, $CDCl_3$): δ2.00–2.10 (5s, 15H, CH_3), 3.74 (m, 1H, H–5), 3.94 (d, 1H, $J_{gem\ CH_2} = 10.9$ Hz, CH_2), 4.13 (dd, 1H, $J_{5,6a} = 2.3$, $J_{6a,6b} = 12.4$ Hz, H–6_a), 4.26 (dd, 1H, $J_{5,6b} = 4.6$,

$J_{6a,6b} = 12.4$ Hz, H−6_b), 4.28 (d, 1H, $J_{gem\ CH_2} = 10.9$ Hz, CH_2), 4.57 (d, 1H, $J_{1,2} = 7.9$ Hz, H−1), 4.93 (dd, 1H, $J_{1,2} = 7.9$, $J_{2,3} = 9.3$ Hz, H−2), 5.05 (dd, 1H, $J_{3,4} = J_{4,5} = 9.3$ Hz, H−4), 5.18 (dd, 1H, $J_{2,3} = J_{3,4} = 9.3$ Hz, H−3), 6.23 (d, 1H, $J_{3',4'} = 5.7$ Hz, H−4′), 7.45 (d, 1H, $J_{3',4'} = 5.7$ Hz, H−3′); ^{13}C-NMR (75 MHz, $CDCl_3$): δ20.5−21.3 (5 CH_3), 61.7 (C−6), 68.2 (C−4), 68.6 (CH_2), 70.8 (C−2), 72 (C−5), 72.5 (C−3), 101.0 (C−1), 105.6 (C−2′), 124.3 (C−4′), 151.0 (C−3′), 168.1−170.1 (5 $COCH_3$), 170.6 (C−5′); minor epimer **17*β*** (S): white solid, mp 153°C; $[\alpha_D^{20}]$-18 (*c* 1, $CHCl_3$); ^{1}H-NMR (200 MHz, $CDCl_3$): δ2.00−2.10 (5s, 15H, CH_3), 3.77 (m, 1H, H−5), 3.94 (d, 1H, $J_{gem\ CH_2} = 10.8$ Hz, CH_2), 4.12 (dd, 1H, $J_{5,6a} = 2.0$, $J_{6a,6b} = 12.0$ Hz, H−6_a), 4.27 (dd, 1H, $J_{5,6b} = 4.4$, $J_{6a,6b} = 12.0$ Hz, H−6_b), 4.28 (d, 1H, $J_{gem\ CH_2} = 10.8$ Hz, CH_2), 4.58 (d, 1H, $J_{1,2} = 7.6$ Hz, H−1), 4.94 (dd, 1H, $J_{1,2} = 7.6$, $J_{2,3} = 9.3$ Hz, H−2), 5.06 (dd, 1H, $J_{3,4} = J_{4,5} = 9.3$ Hz, H−4), 5.20 (dd, 1H, $J_{2,3} = J_{3,4} = 9.3$ Hz, H−3), 6.25 (d, 1H, $J_{3',4'} = 5.7$ Hz, H−4′), 7.58 (d, 1H, $J_{3',4'} = 5.7$ Hz, H−3′); ^{13}C-NMR (75 MHz, $CDCl_3$): δ20.5−21.3 (3 CH_3), 61.6 (C−6), 68.1(C−4), 69.9 (CH_2), 70.1 (C−2), 72.1 (C−5), 72.5 (C−3), 101.0 (C−1), 105.4 (C−2′), 124.2 (C−4′), 151.3 (C−3′), 168.1−170.2 (5 $COCH_3$), 170.6 (C−5′).

Anal. Calcd for $C_{21}H_{26}O_{14}$ (502.43) (R): C, 50.20; H, 5.21. Found: C, 50.18; H, 5.22.

Anal. Calcd for $C_{21}H_{26}O_{14}$ (502.43) (S): C, 50.20; H, 5.21. Found: C, 50.20; H, 5.25.

(5′-Oxo-2′,5′-dihydrofuran-2′-yl)methyl-2,3,4,6-tetra-*O*-acetyl-*α*-D-glucopyranoside (1*α*)

Sodium borohydride (8.7 mg, 0.23 mmol) was added by little portion to a solution of **14*α*** (106 mg, 0.23 mmol) in dry methanol (10 mL) at rt. The mixture was stirred until TLC (dichloromethane/ethyl acetate: 66/34) indicated completed conversion (1 hr) at rt. Then pH of the solution was reached up to 1 by adding aq. hydrogen chloride (5N). After stirring for 1 hr, water (10 mL) and dichloromethane (3 mL) were added. The organic phase was treated with aq. sodium hydrogenocarbonate solution, dried, and evaporated. The crude product was purified on column chromatography (dichloromethane/ethyl acetate: 66/34) giving **1*α*** (R + S) (8.1 mg, 0.184 mmol, 80%) as a colorless oil. The reduction in the presence of cesium sulfate led to **1*α*** (S) in a smaller amount, allowing to attribute the NMR data of each epimer. Epimer **1*α*** (R): ^{1}H-NMR (200 MHz, $CDCl_3$): δ2.00−2.10 (4s, 12H, CH_3), 3.87 (dd, 1H, $J_{CH_a,H_{2'}} = 4.3$, $J_{gem\ CH_2} = 12.2$ Hz, −OCH_2), 3.95 (m, 1H, H−5), 4.07 (dd, 1H, $J_{CH_b,H_{2'}} = 2.2$, $J_{gem\ CH_2} = 12.2$ Hz, −OCH_2), 4.10 (dd, 1H, $J_{5,6a} = 2.2$, $J_{6a,6b} = 12.2$ Hz, H−6_a), 4.22 (dd, 1H, $J_{5,6b} = 4.2$, $J_{6a,6b} = 12.2$ Hz, H−6_b), 4.90 (dd, 1H, $J_{1,2} = 3.6$, $J_{2,3} = 10.0$ Hz, H−2), 5.06 (dd, 1H, $J_{3,4} = J_{4,5} = 10.0$ Hz, H−4), 5.14 (d, 1H, $J_{1,2} = 3.6$ Hz, H−1), 5.21 (m, 1H, H−2′),

5.43 (dd, 1H, $J_{2,3} = J_{3,4} = 10.0$ Hz, H–3), 6.25 (dd, 1H, $J_{2',4'} = 2.0$, $J_{3',4'} = 5.5$ Hz, H–4′), 7.51 (dd, 1H, $J_{2',3'} = 1.5$, $J_{3',4'} = 5.5$ Hz, H–3′); ^{13}C-NMR (75 MHz, $CDCl_3$): δ 20.7–20.8 (4 CH_3), 61.9 (C–6), 67.5 (CH_2), 67.9 (C–5), 68.4 (C–4), 69.9 (C–3), 70.7 (C–2), 81.6 (C–2′), 96.7 (C–1), 123.5 (C–4′), 152.6 (C–3′), 170.1–170.6 (4 $COCH_3$), 172.2 (C–5′); epimer **1**$\boldsymbol{\alpha}$ (S): ^{1}H-NMR (200 MHz, $CDCl_3$): δ 2.00–2.10 (4s, 12H, CH_3), 3.93 (dd, 1H, $J_{CH_a,H2'} = 4.3$, $J_{gem\ CH_2} = 12.2$ Hz, $-OCH_2$), 3.95(m, 1H, H–5), 4.07 (dd, 1H, $J_{CH_b,H2'} = 2.2$, $J_{gem\ CH_2} = 12.2$ Hz, $-OCH_2$), 4.10 (dd, 1H, $J_{5,6b} = 2.2$, $J_{6a,6b} = 12.2$ Hz, H–6_b), 4.29 (dd, 1H, $J_{5,6a} = 4.2$, $J_{6a,6b} = 12.2$ Hz, H–6_a), 4.85 (dd, 1H, $J_{1,2} = 3.5$, $J_{2,3} = 10.0$ Hz, H–2), 5.06 (dd, 1H, $J_{3,4} = J_{4,5} = 10.0$ Hz, H–4), 5.07 (d, 1H, $J_{1,2} = 3.5$ Hz, H–1), 5.23 (m, 1H, H–2′), 5.41 (dd, 1H, $J_{2,3} = J_{3,4} = 10.0$ Hz, H–3), 6.23 (dd, 1H, $J_{2',4'} = 2.0$, $J_{3',4'} = 5.5$ Hz, H–4′), 7.49 (dd, 1H, $J_{2',3'} = 1.5$, $J_{3',4'} = 5.5$ Hz, H–3′); ^{13}C-NMR (75 MHz, $CDCl_3$): δ 20.7–20.8 (4 CH_3), 61.8 (C–6), 67.5 (CH_2), 67.7 (C–5), 68.5 (C–4), 70.0 (C–3), 70.4 (C–2), 81.4 (C–2′), 96.6 (C–1), 123.5 (C–4′), 152.5 (C–3′), 169.6–170.4 (4 $COCH_3$), 172.3 (C–5′); a fraction of chromatography contained pure **1**$\boldsymbol{\alpha}$ (R) in very little amount; HRMS calcd for $C_{19}H_{25}O_{12}$ $[M + H]^+$: 445.1346. Found: 445.1343.

The compound **1**$\boldsymbol{\alpha}$ (S) was also obtained *via* the anomerisation of **2**$\boldsymbol{\beta}$ (S), according to Dasgupta's procedure[20] in nitromethane as solvent and titane tetrachloride as catalyst. The conversion rate was equal to 80% but was adequate to determine the NMR data of **1**$\boldsymbol{\alpha}$ (S) obtained from the reduction of **14**$\boldsymbol{\alpha}$.

(5′-Oxo-2′,5′-dihydrofuran-2′-yl)methyl-2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranoside (2β)

This dihydrofuranone **2**$\boldsymbol{\beta}$ was prepared as **1**$\boldsymbol{\alpha}$. The same amount of **15**$\boldsymbol{\beta}$ afforded after purification by column chromatography (dichloromethane/ethyl acetate: 65/35) **2**$\boldsymbol{\beta}$ (83 mg, 0.187 mmol, 81%) as a mixture of epimers (R/S: 1/1) while in the presence of cerium sulfate the epimer (R) was slightly major. **2**$\boldsymbol{\beta}$ colorless oil; epimer **2**$\boldsymbol{\beta}$ (R): ^{1}H-NMR (200 MHz, $CDCl_3$): δ 2.00–2.10(4s, 12H, CH_3), 3.70 (m, 1H, H–5), 3.75 (dd, 1H, $J_{CH_a,H_{2'}} = 4.6$, $J_{gemCH_2} = 11$ Hz, $-OCH_2$), 4.08 (dd, 1H, $J_{CH_b,H_{2'}} = 4.9$, $J_{gemCH_2} = 11.0$ Hz, $-OCH_2$), 4.16 (dd, 1H, $J_{5,6a} = 2.2$, $J_{6a,6b} = 12.4$ Hz, H–6_a), 4.26 (dd, 1H, $J_{5,6b} = 4.2$, $J_{6a,6b} = 12.4$ Hz, H–6_b), 4.53 (d, 1H, $J_{1,2} = 7.9$ Hz, H–1), 5.03 (dd, 1H, $J_{1,2} = 7.9$, $J_{2,3} = 9.3$ Hz, H–2), 5.10 (m, 1H, H–2′), 5.15 (dd, 1H, $J_{3,4} = J_{4,5} = 9.3$ Hz, H–4), 5.24 (dd, 1H, $J_{2,3} = J_{3,4} = 9.3$ Hz, H–3), 6.17 (dd, 1H, $J_{2',4'} = 2.0$, $J_{3',4'} = 5.7$ Hz, H–4′), 7.47 (dd, 1H, $J_{2',3'} = 1.5$, $J_{3',4'} = 5.7$ Hz, H–3′); ^{13}C-NMR (75 MHz, $CDCl_3$): δ 20.7–20.8 (4 CH_3), 61.8 (C–6), 68.1 (CH_2), 68.2 (C–4), 71.0 (C–2), 72.5 (C–5), 72.6 (C–3), 81.8 (C–2′), 101.3 (C–1), 123.1 (C–4′), 153.0 (C–3′), 170.2–170.6 (4 $COCH_3$), 172.5 (C–5′); epimer **2**$\boldsymbol{\beta}$ (S): ^{1}H-NMR (200 MHz, $CDCl_3$): δ 2.00–2.10 (4s, 12H, CH_3), 3.70 (m, 1H, H–5), 3.81 (dd, 1H, $J_{CH_a,H_{2'}} = 4.6$, $J_{gem\ CH_2} = 11.0$ Hz, $-OCH_2$), 4.08 (dd, 1H,

$J_{CH_b},H_{2'} = 4.6$, $J_{gem\ CH_2} = 11.0$ Hz, $-OCH_2$), 4.12 (dd, 1H, $J_{5,6a} = 2.2$, $J_{6a,6b} = 12.4$ Hz, H–6_a), 4.23 (dd, 1H, $J_{5,6b} = 4.5$, $J_{6a,6b} = 12.4$ Hz, H–6_b), 4.60 (d, 1H, $J_{1,2} = 7.9$ Hz, H–1), 5.08 (dd, 1H, $J_{1,2} = 7.9$, $J_{2,3} = 9.2$ Hz, H–2), 5.15 (dd, 1H, $J_{3,4} = J_{4,5} = 9.2$ Hz, H–4), 5.15 (m, 1H, H–2′), 5.24 (dd, 1H, $J_{2,3} = J_{3,4} = 10.0$ Hz, H–3), 6.20 (dd, 1H, $J_{2',4'} = 2$, $J_{3',4'} = 5.57$ Hz, H–4′), 7.49 (dd, 1H, $J_{2',3'} = 1.5$Hz, $J_{3',4'} = 5.7$ Hz, H–3′); ^{13}C-NMR (75 MHz, $CDCl_3$): δ20.6–20.7 (4 CH_3), 61.7 (C–6), 68.3 (C–4), 69.3 (CH_2), 70.8 (C–2), 72.0 (C–5), 72.5 (C–3), 81.3 (C–2′), 100.9 (C–1), 122.7 (C–4′), 153.5 (C–3′), 169.5–170.1 (4 $COCH_3$), 172.4 (C–5′) similar to **2*β*** (S) NMR data.

Methyl 4-Oxo-5((2′,3′,4′,6′-tetra-*O*-acetyl-*α*-D-glucopyranosyl)oxy)pentanoate (4*α*)

To a solution of **14*α*** (460 mg, 1 mmol) in dimethylformamide (2 mL), maintained under argon, were added potassium formate (217 mg, 2.64 mmol) and palladium acetate (6 mg, 0.03 mmol). The mixture was stirred at 60°C until TLC (dichloromethane/ethyl acetate: 88/12) indicated completed conversion (2 hr 30 min). The cooled mixture was diluted with diethyl ether (20 mL). The solid was filtered off and the solvent was evaporated. To the remaining oil, dissolved in dried acetone (64 mL) and stirred at rt, were added dimethyl sulfate (0.6 mL) and potassium carbonate (4 × 0.52 mg, each 15 min). The mixture was stirred until TLC (dichloromethane/ethyl acetate: 88/12) indicated completed conversion (4 hr). The solid was filtered off and the solvent was evaporated. The crude product was purified by column chromatography (dichloromethane/ethyl acetate: 88/12) giving **4*α*** (357 mg, 0.75 mmol, 75%), which was recrystallized in ethyl alcohol. **4*α***: white solid, mp 48°C; $[\alpha]_D^{20} + 158$ (*c* 0.1, $CHCl_3$); ^{1}H-NMR (200 MHz, $CDCl_3$): δ2.00–2.10 (4s, 12H, CH_3), 2.75 (m, 4H, $J_{2a,3a} = J_{2b3a} = 4.8$, $J_{2a,2b} = J_{3a,3b} = 12.0$ Hz, H–2, H–3), 3.66 (s, 3H, $-OCH_3$), 4.07 (dd, 1H, $J_{5',6'a} = 2.2$, $J_{6'a,6'b} = 10.5$ Hz, H–$6'_a$), 4.15 (m, 2H, H–5′, H–$6'_b$), 4.26 (s, 2H, H–5), 4.90 (dd, 1H, $J_{1',2'} = 3.7$, $J_{2',3'} = 10.2$ Hz, H–2′), 5.07 (dd, 1H, $J_{3',4'} = J_{4',5'} = 9.6$ Hz, H–4′), 5.09 (d, 1H, $J_{1',2'} = 3.7$ Hz, H–1), 5.51 (dd, 1H, $J_{2',3'} = 10.2$, $J_{3',4'} = 9.6$ Hz, H–3); ^{13}C-NMR (75 MHz, $CDCl_3$): δ20.6–20.7 (4 CH_3), 27.3 (C–2), 33.5 (C–3), 51.9 ($-OCH_3$), 61.8 (C–6′), 67.9 (C–4′), 68.4 (C–5′), 69.9 (C–2′), 70.5 (C–3′), 72.2 (C–5), 96.2 (C–1′), 169.6–170.6 (4 $COCH_3$), 172.8 (C–4), 204.9 (C–1).

Anal. Calcd for $C_{20}H_{28}O_{13}$ (472.42): C, 50.42; H, 5.92. Found: C, 50.20; H, 5.85.

Methyl 4-Oxo-5((2′,3′,4′,6′-tetra-*O*-acetyl-*β*-D-glucopyranosyl)oxy)pentanoate (5*β*)

The *β* ceto ester **5*β*** was prepared as **4*α***. The same amount of **15*β*** (460 mg, 1 mmol) gave **5*β*** (330 mg, 0.7 mmol, 70%) as a white solid, which was

recrystallized in ethyl alcohol. **5β**: mp 89°C; $[\alpha]_D^{20}$ −29 (*c* 0.8, $CHCl_3$); ^{1}H-NMR (200 MHz, $CDCl_3$): δ 2.00–2.10 (4s, 12H, CH_3), 2.57 (m,2H, $J_{2a,3} = 4.3$, $J_{2b,3a} = 6.0$, $J_{2a,2b} = 12.0$ Hz, H–2), 2.75 (m, 2H, $J_{2,3a} = 4.3$, $J_{2,3b} = 6.0$, $J_{3a,3} = 12.0$ Hz, H–3), 3.65 (s, 3H, $-OCH_3$), 3.73–3.78 (m, 2H, H–5′, H–6′$_a$), 4.13 (dd, 1H, $J_{5',6'b} = 6.6$, $J_{6'a,6'b} = 12.3$ Hz, H–6′$_b$), 4.21 (d, 1H, $J_{5a,5b} = 12.0$ Hz, H–5a), 4.25 (d, 1H, $J_{5a,5b} = 12.0$ Hz, H–5b), 4.56 (d, 1H, $J_{1',2'} = 7.6$ Hz, H–1′), 5.06 (dd, 1H, $J_{1',2'} = 7.6$, $J_{2',3'} = 9.3$ Hz, H–2′), 5.10 (dd, 1H, $J_{3',4'} = J_{4',5'} = 9.3$ Hz, H–4′), 5.21 (dd, 1H, $J_{2',3'} = J_{3',4'} = 9.3$ Hz, H–3′); ^{13}C-NMR (75 MHz, $CDCl_3$): δ 20.6–20.7 (4 CH_3), 27.2 (C–2), 33.7 (C–3), 51.8 ($-OCH_3$), 61.7 (C–6′), 68.3 (C–4′), 71.1 (C–5′), 72.0 (C–2′), 72.6 (C–3′), 73.7 (C–5), 100.7 (C–1′), 169.4–170.6 (4 $COCH_3$), 173.0 (C–4), 206.2 (C–1).

Anal. Calcd for $C_{20}H_{28}O_{13}$ (472.42): C, 50.42; H, 5.92. Found: C, 50.70; H, 5.95.

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