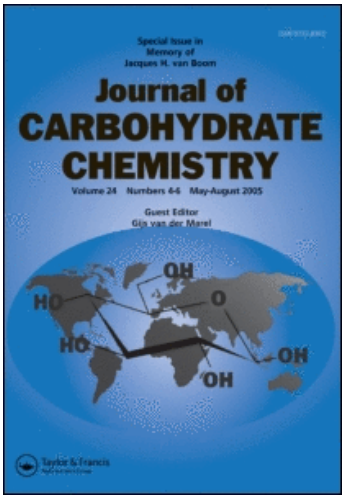

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Convenient Multigram Scale Glycosylations of Scented Alcohols Employing Phase-Transfer Reactions

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Convenient Multigram Scale Glycosylations of Scented Alcohols Employing Phase-Transfer Reactions[†]

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ABSTRACT

Various conditions for glycosylation (Koenigs–Knorr, Helferich, trichloroacetimidate, Fischer–Raske, phase-transfer methods) of 3-ethoxy-4-hydroxybenzaldehyde (ethyl vanillin), 3-hydroxy-2-methyl-4-pyranone (maltol) and 2,5-dimethyl-4-hydroxy-3(2*H*)-furanone (furaneol®) were evaluated, taking into account yields and ease of preparation (e.g., utilized donor, catalyst, conditions). The best results were achieved employing phase transfer catalysis in a two-phase solvent mixture. To increase water solubility for better applicability, the hitherto unknown maltosides of the corresponding alcohols were synthesized, again proving the value of phase-transfer conditions for glycosylation of phenols.

Key Words: Phase-transfer glycosylation; Scented alcohols; Flavorant-release additives.

INTRODUCTION

As non-volatile flavorant-release additives, glycosides of scented alcohols, which release the corresponding volatile alcohol under pyrolytic conditions, (e.g., Scheme 1) are of interest.[1] Such alcohols include 3-ethoxy-4-hydroxybenzaldehyde (ethyl

[†]Dedicated to Professor Dr. Peter Welzel on the occasion of his 65th birthday.

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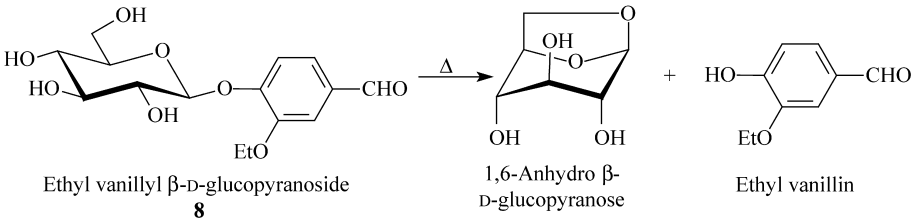


Ethyl vanillyl β-D-glucopyranoside
8

1,6-Anhydro β-D-glucopyranose

Ethyl vanillin

Scheme 1. Pyrolysis of ethyl vanillyl β-D-glucopyranoside (**8**).

vanillin, **1**), 3-hydroxy-2-methyl-4-pyranone (maltol, **2**) and 2,5-dimethyl-4-hydroxy-3(2*H*)-furanone (furaneol®, **3**). Reported syntheses of β-D-glucopyranosides of these alcohols are usually tricky and of unsatisfactory yield requiring an improvement.[2] In addition, syntheses of the respective β-D-maltosides will give products with a higher water solubility and thus a superior application feasibility.

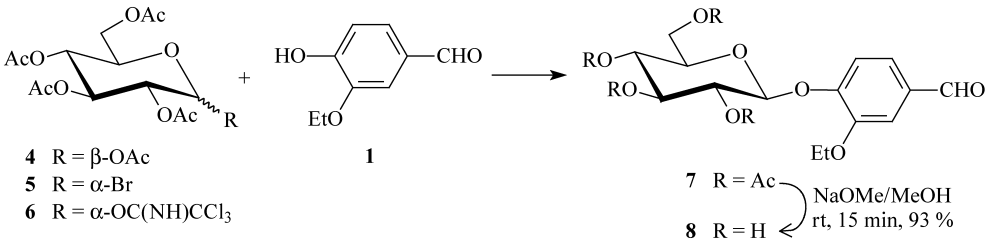
RESULTS

Glycosylation of Ethyl Vanillin

The synthetic ethyl vanillin has a strong vanilla-like odor and finds broad applications in perfumes, pastries and confectioneries having a pleasant aroma. 3-Methoxy-4-hydroxybenzaldehyde (vanillin), the major component of the rather expensive natural vanilla, has a slightly higher odor threshold and is more sensitive to light.

Whereas the glucosylation of ethyl vanillin is reported to proceed in 56% yield by the use of potassium carbonate in THF at 110°C (no pressure mentioned),[1] the application of this method proved not to be successful in our hands in refluxing THF under normal pressure utilizing five equivalents of acceptor. Therefore we decided to evaluate various glycosylation conditions,[3] taking into account yields and ease of preparation (Scheme 2, Table 1).

Helferich conditions (entry 1)[4] employing the donor 1,2,3,4,6-penta-*O*-acetyl-β-D-glucopyranose (**4**) and the promoter tin(IV)-chloride[5] as catalyst in dichlor-



4 R = β-OAc
5 R = α-Br
6 R = α-OC(NH)CCl_3

1

Scheme 2. Synthesis of ethyl vanillyl β-D-glucopyranoside (**8**).

Table 1. Conditions for the glycosylation of ethyl vanillin.

Entry	Donor	Conditions	Yield
1	**4**	$SnCl_4$, DCM, 0 °C, 4 h	–
2	**4**	$BF_3{\cdot}Et_2O$, DCM, 40 °C, 48 h	25%
3	**5**	$Hg(CN)_2$, Tol/$MeNO_2$, rt, 24 h	17%
4	**5**	Ag_2CO_3, MS 4 Å, DCM, rt, 27 h	11%
5	**5**	AgOTf, TMU, DCM, − 30 °C, 3 h	15%
6	**5**	KOH/EtOH, $CHCl_3$, 61 °C, 16 h	27%
7	**5**	KOH/MeOH, DCM, rt, 8 h	37%
8	**5**	Bu_4NBr, 1M NaOH, DCM, rt, 45 min	59%
9	**6**	TMSOTf, DCM, − 20 °C, 2.5 h	39%
10	**6**	$BF_3{\cdot}Et_2O$, DCM, − 18 °C, 2 h	46%

omethane led only to the corresponding α-chloride, which was stable under these reaction conditions. Exchanging the catalyst to boron trifluoride (entry 2)[6] and enforcing reaction conditions resulted in the desired glycosylation product **7** in a poor yield of 25%. Neither tributylstannylation[7] nor trimethylsilylation[8] of the phenolic hydroxy group of acceptor **1** to enhance nucleophilicity were able to improve yields.

Even less satisfying was the use of the expensive and toxic Koenigs–Knorr[9] promoters mercury cyanide (entry 3, hydrogen cyanide is released)[10] in a mixture of toluene and nitromethane, silver carbonate (entry 4, in the presence of molecular sieves 4 Å)[11] and silver triflate (entry 5, addition of an acid scavenger such as tetramethylurea (TMU) is necessary)[12] in dichloromethane utilizing the readily available donor 2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranosyl bromide (**5**). In all cases, the yield was well below 20% and an upscaling would be problematic due to environmental issues.

In contrast, reasonable results were achieved by the Fischer–Raske[13] method utilizing ethanolic potassium hydroxide and the donor **5** in refluxing chloroform (entry 6). As there is no need for exclusion of oxygen or water, the reaction was carried out easily, even on a larger scale, yielding 27% of the product **7**. A further improvement (entry 7) was possible by employing a methanolic solution of potassium hydroxide. In this case we were able to isolate **7** in a yield of 37%, under yet milder reaction conditions.

Comparable reaction conditions were employed by the phase-transfer method.[14] The reaction takes place in an aqueous-organic two-phase-system in the presence of a cheap and non-toxic phase-transfer catalyst, which forms a lipophilic ion-pair together with the deprotonated phenolate, which migrates into the organic phase. In an aprotic nonpolar solvent such as dichloromethane, the ion-pair is not solvated, and the naked phenolate shows enhanced nucleophilicity. Typical phase-transfer catalysts are quaternary ammonium salts or crown ethers, being soluble in both the organic and aqueous phase. Aqueous work-up and crystallization led to product **7** in an excellent yield of 59% on a 30 g scale (entry 8). Side reactions were β-elimination and hydrolysis of the donor.

The trichloroacetimidate method, a widespread and versatile approach for glycosylations,[15] was used in an attempt to improve yields. Thus, the highly reactive *O*-(2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranosyl)trichloroacetimidate (**6**)[16] was condensed with **1**, catalyzed by the Lewis acids trimethylsilyl trifluoromethanesulfonate or boron trifluoride (entries 9 and 10, respectively) under anhydrous conditions in yields of 39 and 46%, respectively.

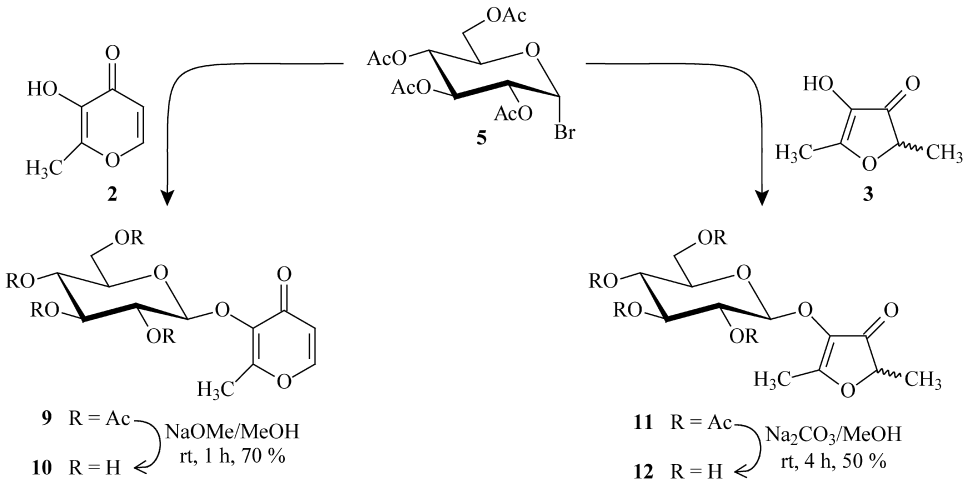
The advantages of the phase-transfer method are obvious: it does not only give improved yields, but further the donor **5** is obtained from glucose in just one step, no toxic or expensive catalysts are required, the reaction is very fast, the conditions are quite mild, and the reaction is carried out easily without exclusion of air or moisture.

Deprotection was achieved with catalytic amounts of sodium methoxide in methanol giving **8** in 93% yield.

Glycosylation of Maltol and Furaneol®

The γ-pyrone 3-hydroxy-2-methyl-4-pyranone (maltol, **2**) is a characteristic aroma compound of caramel and an intermediate of the Maillard reaction, having a sweet scent like cotton candy. Since maltol is sensitive to chelating or oxidizing reagents (e.g., boron trifluoride, silver and mercury salts), attempts to utilize Helferich, trichloroacetimidate or Koenigs–Knorr conditions failed. Therefore we focused on the previously successful Fischer–Raske and phase-transfer methods (Scheme 3, Table 2). This is possible, as maltol has an aromatic character, and the corresponding alcoholate is resonance stabilized.

Glucosylation of **2** with **5** in the presence of ethanolic potassium hydroxide in refluxing chloroform proceeded in only 5% yield (entry 1). Again, methanolic potas-



Scheme 3. Synthesis of maltoyl (**10**) and furaneoyl β-D-glucopyranosides (**12**).

Table 2. Conditions for the glycosylation of maltol and furaneol®.

Entry	Acceptor	Conditions	Yield
1	**2**	KOH/EtOH, $CHCl_3$, 61 °C, 20 h	5%
2	**2**	KOH/MeOH, DCM, rt, 15 h	14%
3	**2**	Bu_4NBr, 1M NaOH, DCM, rt, 3.5 h	20%
4	**2**	Bu_4NBr, 1M NaOH, DCM, 35 °C, 3 h	31%
5	**3**	Bu_4NBr, 1M NaOH, DCM, 35 °C, 45 min	19%

sium hydroxide in dichloromethane at room temperature led to better yields under even milder reaction conditions giving 14% of **9** (entry 2). Looker and Fisher[17] reported this synthesis first, but obtained only 12% of the product in acetone as solvent, the isolated product being contaminated with methyl β-D-glucopyranoside.

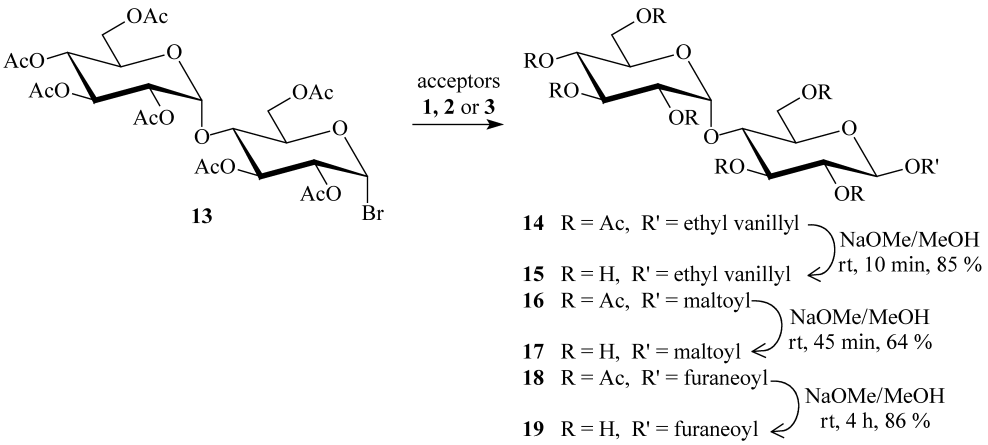
Reaction of **2** and **5** under phase-transfer conditions (entry 3) gave product **9** in 20% yield. Noteworthy is the dramatic improvement caused by elevating the temperature by 10°C to a good yield of 31% (entry 4) after purification by crystallization even on a large scale. The reasons for the lower yield compared to the synthesis of **7** is the superior water solubility of **2**, resulting in a lower concentration of the maltoyl anion in the organic phase. Zemplén deprotection yielded **10** in 70%, due to some decomposition.

2,5-Dimethyl-4-hydroxy-3(2*H*)-furanone (furaneol®, **3**) is an important aroma compound in many fruits and heated up meat, having a sweet caramel-like scent. The odor threshold of furaneol® is only 0.04 ppb, and thus about 10^6 lower than maltol. Mayerl et al.[18] were the first to synthesize the glucoside **11** employing bromide **5** and an ethanolic potassium hydroxide solution in toluene at 80°C; they obtained the product in a yield of only 7%. Zemplén deacetylation was reported to proceed under extensive decomposition, giving after purification by HPLC **12** in 16% yield and a purity of 92%. Thus the total yield over just two steps was only 1%. Due to keto-enol tautomerism, **12** was a mixture of two diastereomers.

Later Roscher et al.[19] utilized silver carbonate in equimolar amounts under Koenigs–Knorr conditions followed by an in situ deprotection with ammonia in methanol. Purification by MLCCC (multilayer coil countercurrent chromatography) followed by HPLC gave **12** in a yield of 2.7%. Both methods are only practicable for very small scale synthesis in the lower milligram range.

For a more convenient and higher-yielding method, phase-transfer conditions proved once again to be the best choice for the glycosylation of aromatic alcohols (Scheme 3, Table 2, entry 5). We were able to isolate **11** in gram quantities in a pleasing yield of 19% after purification by simple flash chromatography. Limitations are the excellent water solubility of furaneol® and its instability.

In our hands the reported deacetylations employing sodium methoxide or ammonia in methanol were not successful, with extensive decomposition observed. Consequently we developed a better method and were able to deprotect **11** to give a high yield of **12** (50%), utilizing sodium carbonate in methanol, releasing only low concentrations of methoxide.



Scheme 4. Synthesis of malto glycosides **15**, **17** and **19**.

Maltosylation of the Alcohols 1, 2, and 3

Since the Fischer–Raske and the phase-transfer methology proved to be the most successful glycosylation conditions for the aforementioned glucosides, these methods were applied for the first reported synthesis of the corresponding maltosides employing the donor 2,3,6-tri-*O*-acetyl-4-*O*-(2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranosyl)-α-D-glucopyranosyl bromide (**13**).

Utilizing ethanolic and methanolic potassium hydroxide in the case of acceptor **1** gave 10% and 22% yield of the maltoside **14,** respectively (Scheme 4, Table 3, entries 1 and 2). Again the phase-transfer catalyzed glycosylation gave the highest yield of 48% within only 60 minutes (entry 3). Deprotection and crystallization furnished the new product **15** in 85% yield.

Maltosylation of maltol and furaneol® was realized under phase-transfer conditions (entries 4 and 5) providing **16** and **18** in good yields of 33% and 22%, respectively. Subsequent Zemplén deacetylation of the protected maltosides gave the novel malto glycosides **17** and **19** in 64% and 86% yield, respectively. Surprisingly, deprotection of **16** with sodium methoxide was accomplished in contrast to the glucoside **11** in rather good yields.

Table 3. Conditions for the glycosylation employing a maltose donor.

Entry	Acceptor	Conditions	Yield
1	**1**	KOH/EtOH, $CHCl_3$, 61 °C, 22 h	10%
2	**1**	KOH/MeOH, DCM, rt, 13 h	22%
3	**1**	Bu_4NBr, 1M NaOH, DCM, rt, 1 h	48%
4	**2**	Bu_4NBr, 1M NaOH, DCM, 35 °C, 3 h	33%
5	**3**	Bu_4NBr, 1M NaOH, DCM, 35 °C, 45 min	22%

EXPERIMENTAL

General methods. TLC was performed on precoated aluminum plates (silica gel 60 F_{254}, Merck 5554) employing UV-adsorption and charring with 20% sulfuric acid/ethanol for visualization. For column chromatography by the flash procedure, silica gel 60 M, 230–400 mesh, 40–63 μm (Macherey–Nagel), was used. ^{1}H NMR and ^{13}C NMR spectra were recorded on Bruker AMX-400 MHz (100.62 MHz for ^{13}C) and Bruker DRX-500 (125.83 MHz for ^{13}C). If necessary, assignments were confirmed by ^{1}H^{1}H- and ^{1}H^{13}C-Cosy experiments. Residual non-deuterated solvent was used as an internal standard for determination of chemical shifts. Melting points were determined with a Büchi apparatus and are not corrected. Optical rotations were measured using a Perkin Elmer 241 instrument at 578 nm and 20°C. MALDI-TOF-MS was performed on a Bruker Biflex III with DHB as a matrix in positive reflector mode. Elemental analysis were performed by the Zentrale Elementanalytik of the Faculty of Chemistry at the University of Hamburg.

(4-Formyl-2-ethoxyphenyl) 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranoside (7). Entry 2 (cf. Table 1): To a solution of **1** (665 mg, 4.0 mmol) and **4**[20] (390 mg, 1.0 mmol) in anhydrous dichloromethane (10 mL) with activated molecular sieves 4 Å (450 mg) at −40°C in a brown glass flask, $BF_3 \cdot Et_2O$ (0.25 mL, 2.0 mmol) was added slowly under argon. The mixture was stirred for 48 h under reflux, and then washed with saturated $NaHCO_3$ and water. The organic phase was dried, concentrated and purified on silica gel employing petrol ether (50–70)/ethyl acetate (1:1) as eluents to yield glycoside **7** (123 mg, 0.25 mmol, 25%) under recovery of **4** (167 mg, 0.43 mmol, 43%).

Entry 3: To a solution of **1** (332 mg, 2.0 mmol) and mercury(II)-cyanide (505 mg, 2.0 mol) in toluene/nitromethane (20 mL, 1:1 v/v), **5**[21] (820 mg, 2.0 mmol) in anhydrous toluene (10 mL) was added over a period of 2 h under argon. After 22 h the mixture was filtered. The organic phase was washed with saturated $NaHCO_3$ and brine, dried and concentrated. The residue was purified by column chromatography using petrol ether (50–70)/ethyl acetate (1:1) to give **7** (172 mg, 0.35 mmol, 17%).

Entry 4: To a solution of **1** (166 mg, 1.0 mmol), silver carbonate (550 mg, 2.0 mmol) and activated molecular sieves 4 Å (220 mg) in anhydrous dichloromethane (3 mL) in a brown glass flask, a solution of **5** (820 mg, 2.0 mmol) in anhydrous dichloromethane (2 mL) was added dropwise under argon. The reaction was left for 27 h at room temperature. After filtration through Celite, the organic phase was neutralized with saturated $NaHCO_3$, washed with water, dried and concentrated. Column chromatography (petrol ether (50–70)/ethyl acetate 1:1) of the residue gave **7** (55 mg, 0.11 mmol, 11%).

Entry 5: The reaction was performed in a brown glass flask under argon. To a solution of **1** (420 mg, 2.5 mmol), tetramethylurea (0.30 mL, 2.5 mmol) and silver trifluoromethanesulfonate (520 mg, 2.0 mmol) in anhydrous dichloromethane (5 mL) at −30°C, a solution of **5** (820 mg, 2.0 mmol) in anhydrous dichloromethane (10 mL)

was added dropwise over a period of 15 min. The reaction was stirred for 30 min at −30°C and additional 3 h at room temperature. Subsequently the mixture was filtered through Celite/Carbon, neutralized and washed. The organic phase was dried, concentrated and purified by flash chromatography on silica gel employing toluene/ethyl acetate (2:1) as eluents to yield **7** (151 mg, 0.30 mmol, 15%).

Entry 6: A solution of potassium hydroxide (4.7 g, 84 mmol) in ethanol (90 mL) was added to **1** (16.3 g, 98 mmol) and **5** (36.4 g, 89 mmol) in chloroform (450 mL) and refluxed for 16 h. The mixture was poured on iced water (800 mL), and the aqueous phase was extracted with chloroform three times. The combined organic phases were dried and concentrated. The crude product was crystallized from ethanol giving pure **7** (11.8 g, 23.8 mmol, 27%).

Entry 7: To a solution of **5** (905 mg, 2.2 mmol) in anhydrous dichloromethane (9 mL), **1** (332 mg, 2.0 mmol) in a 0.45 molar solution of potassium hydroxide in anhydrous methanol (4.4 mL) was added dropwise. The reaction was left for 8 h and subsequently poured on iced water (20 mL). The aqueous phase was extracted with dichloromethane twice and the combined organic phases were dried, concentrated and purified by flash chromatography with the solvent system petrol ether (50–70)/ethyl acetate (1:1) to furnish **7** (366 mg, 0.74 mmol, 37%).

Entry 8: Compounds **1** (33.3 g, 200 mmol), **5** (41.1 g, 100 mmol) and tetrabutylammonium bromide (32.3 g, 100 mmol) were dissolved in dichloromethane (350 mL). A 1 molar sodium hydroxide solution (350 mL) was added, and the mixture was stirred vigorously for 45 min at room temperature. Ethyl acetate (3000 mL) was added, and the organic phase was washed subsequently three times with 1 molar sodium hydroxide, three times with water, once with brine, dried and finally concentrated. The residue was purified twice by crystallization from ethanol to yield **7** (29.3 g, 59 mmol, 59%).

Entry 9: To a solution of **1** (47 mg, 0.28 mmol) and **6** (200 mg, 0.41 mmol) in anhydrous dichloromethane (7 mL) over molecular sieves 4 Å (80 mg) at −20°C, a 0.02 molar solution of trimethylsilyl trifluoromethanesulfonate in anhydrous dichloromethane (1 mL) was added under argon. After 2.5 h the mixture was diluted with dichloromethane, neutralized with saturated $NaHCO_3$ and washed with water. The organic phase was dried, concentrated and purified by column chromatography on silica gel with petrol ether (50–70)/ethyl acetate (1:1) as eluents to yield **7** (54 mg, 0.11 mmol, 39%).

Entry 10: To a solution of **1** (14 mg, 84 μmol) and **6** (56 mg, 110 μmol) in anhydrous dichloromethane (2 mL) over molecular sieves 4 Å (80 mg) at −18°C, $BF_3{\cdot}Et_2O$ (10.6 μL, 84 μmol) was added under argon. After 2 h the mixture was diluted with dichloromethane, neutralized with saturated $NaHCO_3$ and washed with water. The organic phase was dried, concentrated and purified by column chromatography on silica gel with petrol ether (50–70)/ethyl acetate (1:1) as eluents to furnish **7** (14 mg, 28 μmol, 46%) as white crystals: $[\alpha]_D^{20}$ − 50.9° (*c* 1, chloroform); mp 115–117°C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.84 (s, 1 H, CHO), 7.34–7.39 (m, 2 H, $^4J_{ar\text{-}3,ar\text{-}5}$ 1.5 Hz,

$J_{ar\text{-}5,ar\text{-}6}$ 7.6 Hz, aryl H-3, aryl H-5), 7.16 (d, 1 H, aryl H-6), 5.31 (dd, 1 H, $J_{1,2}$ 7.6 Hz, $J_{2,3}$ 9.7 Hz, H-2), 5.27 (dd, 1 H, $J_{3,4}$ 9.2 Hz, H-3), 5.14 (dd, 1 H, $J_{4,5}$ 10.2 Hz, H-4), 5.10 (d, 1 H, H-1), 4.23 (dd, 1 H, $J_{5,6a}$ 5.1 Hz, $J_{6a,6b}$ 12.2 Hz, H-6a), 4.15 (dd, 1 H, $J_{5,6b}$ 2.5 Hz, H-6b), 4.07 (q, 2 H, J_{OEt} 7.1 Hz, O–CH_2–CH_3), 3.83 (ddd, 1 H, H-5), 2.03, 2.02, 2.01, 2.00 (4 × s, 4 × 3 H, 4 × $COCH_3$), 1.40 (t, 3 H, O–CH_2–CH_3) ppm; ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 191.27 (CHO), 170.85, 170.58, 169.74, 169.45 (4 C, 4 × *C*OCH_3), 151.64, 150.55 (2 × C, aryl C-1, aryl C-2), 133.11 (aryl C-4), 125.56 (aryl C-5), 118.43 (aryl C-6), 112.52 (aryl C-3), 99.84 (C-1), 72.84 (C-3), 72.59 (C-5), 71.40 (C-2), 68.69 (C-4), 65.09 (C-6), 62.27 (O–*C*H_2–CH_3), 21.02, 20.99, 20.97, 20.94 (4 C, 4 × CO*C*H_3), 15.04 (O–CH_2–*C*H_3) ppm.[1]

(4-Formyl-2-ethoxyphenyl) β-D-glucopyranoside (8). A solution of **7** (39.6 g, 79.8 mmol) in anhydrous methanol (400 mL) was treated with methanolic sodium methoxide (40 mL, 1%) for 15 min. The mixture was neutralized with Amberlite IR-120 (H^+) and concentrated. Crystallization from ethanol gave **8** (24.3 g, 74.0 mmol, 93%) as a white powder: $[\alpha]_{578}^{20}$ − 14.5° (*c* 1, water); mp 202°C [lit[1] 199–200°C]; MALDI-TOF-MS *m/z* 351.1 $[M + Na]^+$, 367.1 $[M + K]^+$; ^{1}H NMR (400 MHz, d_4-MeOH) δ 9.74 (s, 1 H, CHO), 7.43 (dd, 1 H, $^4J_{ar\text{-}3,ar\text{-}5}$ 1.5 Hz, $J_{ar\text{-}5,ar\text{-}6}$ 8.1 Hz, aryl H-5), 7.40 (d, 1 H, aryl H-3), 7.23 (d, 1 H, aryl H-6), 5.00 (d, 1 H, $J_{1,2}$ 7.1 Hz, H-1), 4.05–4.13 (m, 2H, J_{OEt} 7.1 Hz, O–CH_2–CH_3), 3.79 (dd, 1 H, $J_{5,6a}$ 2.0 Hz, $J_{6a,6b}$ 12.2 Hz, H-6a), 3.61 (dd, 1 H, $J_{5,6b}$ 5.6 Hz, H-6b), 3.30–3.49 (m, 4 H, H-2, H-3, H-4, H-5), 1.36 (t, 3H, O–CH_2–CH_3) ppm; ^{13}C NMR (100.6 MHz, d_4-MeOH) δ 193.38 (CHO), 154.14, 150.92 (2 × C, aryl C-1, aryl C-2), 133.27 (aryl C-4), 127.18 (aryl C-5), 117.31 (aryl C-6), 113.82 (aryl C-3), 102.15 (C-1), 78.79 (C-5), 78.36 (C-3), 75.13 (C-2), 71.61 (C-4), 66.48 (C-6), 62.84 (O–*C*H_2–CH_3), 15.37 (O–CH_2–*C*H_3) ppm.

(2-Methyl-4-oxopyran-3-yl) 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranoside (9). Entry 1 (cf. Table 2): A 1 molar solution of potassium hydroxide in ethanol (0.95 mL) was added to **2** (139 mg, 1.1 mmol) and **5** (411 mg, 1.0 mmol) in chloroform (5 mL) and refluxed for 20 h. The mixture was poured on iced water (10 mL), and the aqueous phase was extracted with chloroform three times. The combined organic phases were dried and concentrated. The crude product was purified on silica gel employing petrol ether (50–70)/ethyl acetate (1:2) as eluents to give **9** (24 mg, 53 μmol, 5%).

Entry 2: To a solution of **5** (905 mg, 2.2 mmol) in anhydrous dichloromethane (9 mL), **2** (252 mg, 2.0 mmol) in a 0.45 molar solution of potassium hydroxide in anhydrous methanol (4.4 mL) was added dropwise. The reaction was left for 15 h and subsequently poured on iced water (20 mL). The aqueous phase was extracted with dichloromethane three times and the combined organic phases were dried, concentrated and purified by flash chromatography with the solvent system petrol ether (50–70)/ethyl acetate (1:2) to furnish **9** (124 mg, 0.27 mmol, 14%).

Entry 3: Compounds **2** (4.03 g, 32 mmol), **5** (6.58 g, 16 mmol) and tetrabutylammonium bromide (5.16 g, 16 mmol) were dissolved in dichloromethane (56 mL). A 1 molar sodium hydroxide solution (56 mL) was added, and the mixture was stirred vigorously for 3.5 h at room temperature. Ethyl acetate (600 mL) was added and the organic phase was washed subsequently twice with 1 molar sodium hydroxide,

twice with water, dried and finally concentrated. The residue was purified by column chromatography employing petrol ether (50–70)/ethyl acetate (1:2) to yield **9** (1.44 g, 3.2 mmol, 20%).

Entry 4: Compounds **2** (48.4 g, 384 mmol), **5** (52.6 g, 128 mmol) and tetrabutylammonium bromide (41.3 g, 128 mmol) were dissolved in dichloromethane (450 mL) and warmed up to 35°C. A 1 molar sodium hydroxide solution (450 mL) was added, and the mixture was stirred vigorously for 3 h at 35°C. Ethyl acetate (3000 mL) was added, and the organic phase was washed subsequently three times with 1 molar sodium hydroxide, twice with water, once with brine, dried and finally concentrated. Dissolving the residue in hot ethanol and precipitation by addition of petrol ether (50–70) gave pure **9** (17.9 g, 39.2 mmol, 31%) as white crystals: $[\alpha]_{578}^{20}$ − 9.9° (*c* 0.1, chloroform); mp 147°C [lit[1] 143–145°C]; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.60 (d, 1 H, $J_{maltyl\ 5,6}$ 5.6 Hz, maltyl H-6), 6.30 (d, 1 H, maltyl H-5), 5.31 (d, 1 H, $J_{1,2}$ 7.6 Hz, H-1), 5.26 (dd, 1 H, $J_{2,3}$ 9.7 Hz, $J_{3,4}$ 9.2 Hz, H-3), 5.16 (dd, 1 H, H-2), 5.09 (dd, 1 H, $J_{4,5}$ 10.2 Hz, H-4), 4.17 (dd, 1 H, $J_{5,6a}$ 4.6 Hz, $J_{6a,6b}$ 12.2 Hz, H-6a), 4.10 (dd, 1 H, $J_{5,6b}$ 2.5 Hz, H-6b), 3.63 (ddd, 1 H, H-5), 2.28 (s, 3 H, maltyl CH_3), 2.11, 2.01, 2.00, 1.99 (4 × s, 4 × 3H, 4 × $COCH_3$) ppm; ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 174.03 (maltyl C-4), 170.80, 170.43, 170.38, 169.88 (4 C, 4 × *C*OCH_3), 161.67 (maltyl C-2), 154.13 (maltyl C-6), 141.62 (maltyl C-3), 117.68 (maltyl C-5), 99.75 (C-1), 72.90 (C-3), 72.17 (C-5), 71.73 (C-2), 68.85 (C-4), 61.94 (C-6), 21.19, 21.07, 20.98, 20.95 (4 C, 4 × CO*C*H_3), 15.58 (maltyl CH_3) ppm.

(2-Methyl-4-oxopyran-3-yl) β-D-glucopyranoside (10). A solution of **9** (1.70 g, 3.72 mmol) in anhydrous methanol (30 mL) was treated with methanolic sodium methoxide (13 mL, 1%) for 1 h. The mixture was neutralized with Amberlite IR-120 (H^+) and concentrated. Column chromatography on silica gel (ethyl acetate/methanol 2:1) gave **10** (746 mg, 2.59 mmol, 70%) as yellowish crystals: $[\alpha]_{578}^{20}$ − 7.0° (*c* 0.1, water); mp 109°C [lit[1] 115–117°C]; MALDI-TOF-MS *m/z* 289.2 $[M + H]^+$, 311.2 $[M + Na]^+$; ^{1}H NMR (400 MHz, D_2O) δ 7.87 (d, 1 H, $J_{maltyl\ 5,6}$ 5.6 Hz, maltyl H-6), 6.36 (d, 1 H, maltyl H-5), 4.72 (m_c, 1 H, $J_{1,2}$ 7.6 Hz, H-1), 3.66 (dd, 1 H, $J_{5,6a}$ 2.0 Hz, $J_{6a,6b}$ 12.7 Hz, H-6a), 3.55 (dd, 1 H, $J_{5,6b}$ 5.1 Hz, H-6b), 3.34–3.38 (m, 2 H, H-2, H-3), 3.27–3.30 (m, 1 H, $J_{4,5}$ 9.7 Hz, H-4), 3.20 (ddd, 1 H, H-5), 2.28 (s, 3 H, CH_3) ppm; ^{13}C NMR (100.6 MHz, D_2O) δ 178.22 (maltyl C-4), 165.98 (maltyl C-6), 158.09 (maltyl C-2), 143.13 (maltyl C-3), 117.30 (maltyl C-5), 104.55 (C-1), 77.70 (C-5), 77.09 (C-3), 74.91 (C-2), 70.93 (C-4), 61.81 (C-6), 16.55 (CH_3) ppm.

(2,5*R*/5*S*-Dimethyl-4-oxofuran-3-yl) 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranoside (11). Compounds **3** (7.93 g, 61.9 mmol), **5** (5.09 g, 12.4 mmol) and tetrabutylammonium bromide (3.99 g, 12.4 mmol) were dissolved in dichloromethane (75 mL) and warmed up to 35°C. A 1 molar sodium hydroxide solution (75 mL) was added, and the mixture was stirred vigorously for 45 min at 35°C. Ethyl acetate (400 mL) was added, and the organic phase was washed subsequently three times with 1 molar sodium hydroxide, twice with water, once with brine, dried and finally concentrated. Flash chromatography on silica gel employing petrol ether (50–70)/ethyl acetate (1:1) as eluents gave the 1:1 diastereomeric mixture **11** (1.09 g, 2.4 mmol, 19%) as an amorphous white solid: $[\alpha]_{578}^{20}$ − 15.3° (*c* 1, chloroform); ^{1}H NMR (400 MHz, $CDCl_3$)

δ 5.17–5.24 (m, 1 H, H-3), 5.04–5.12 (m, 3 H, H-1, H-2, H-4), 4.41, 4.40 (2 × q, 1 H, furaneyl H-5), 4.19 (dd, 1 H, $J_{5,6a}$ 5.6 Hz, $J_{6a,6b}$ 12.2 Hz, H-6a), 4.11 (dd, 1 H, $J_{5,6b}$ 2.5 Hz, H-6b), 3.64–3.71 (m, 1 H, H-5), 2.16, 2.03, 1.99, 1.98 (4 × s, 4 × 3H, 4 × $COCH_3$), 2.09, 2.08 (2 × s, 3 H, furaneyl 2-CH_3), 1.41, 1.40 (2 × d, 3 H, furaneyl 5-CH_3) ppm; ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 196.75, 196.71 (2 C, furaneyl C-4), 181.38, 181.10 (2 C, furaneyl C-2), 170.89, 170.48, 170.23, 169.87 (4 C, 4 × *C*OCH_3), 133.42, 133.32 (2 C, furaneyl C-3), 100.24, 99.92 (2 C, C-1), 81.28, 81.24 (furaneyl C-5), 73.00, 72.97 (2 C, C-3), 72.37, 72.32 (2 C, C-5), 71.50, 71.44 (2 C, C-4), 68.72 (C-2), 62.17, 62.06 (2 C, C-6), 21.18, 21.15, 21.07, 21.00 (4 C, 4 × CO*C*H_3), 16.83, 16.63 (2 C, furaneyl 5-CH_3), 14.20, 14.19 (2 C, furaneyl 5-CH_3) ppm.[18]

(2,5*R*/5*S*-Dimethyl-4-oxofuran-3-yl) β-D-glucopyranoside (12). To a solution of **11** (8.2 g, 17.9 mmol) in anhydrous methanol (150 mL), sodium carbonate (8.2 g, 77.4 mmol) was added. The reaction mixture was left at room temperature for 4 h, filtered and concentrated. Purification on silica gel (ethyl acetate/methanol 5:1) gave **12** (2.60 g, 9.03 mmol, 50%) as an amorphous solid: $[\alpha]_{578}^{20}$ − 34.8° (*c* 0.1, water) [lit[18] $[\alpha]_{589}^{20}$ − 50°]; MALDI-TOF-MS *m/z* 313.1 $[M + Na]^+$, 329.1 $[M + K]^+$; ^{1}H NMR (400 MHz, D_2O) δ 4.82–4.73 (m, 2 H, H-1, furaneyl H-5), 3.87 (dd, 1 H, $J_{6a,6b}$ 12.2 Hz, H-6a), 3.74 (dd, 1 H, $J_{5,6b}$ 5.1 Hz, H-6b), 3.52 (dd, 1 H, $J_{2,3}$ 8.6 Hz, $J_{3,4}$ 8.6 Hz, H-3), 3.49–3.39 (m, 3 H, H-2, H-4, H-5), 2.35 (s, 3 H, furaneyl 2-CH_3), 2.35 (d, 3 H, furaneyl 5-CH_3) ppm; ^{13}C NMR (100.6 MHz, D_2O) δ 203.30 (furaneyl C-4), 188.68 (furaneyl C-2), 136.08 (furaneyl C-3), 106.00 (C-1), 84.71 (furaneyl C-5), 78.88 (C-5), 78.23 (C-3), 75.75 (C-4), 71.95 (C-2), 63.11 (C-6), 18.16, 18.06 (furaneyl 5-CH_3), 16.56 (furaneyl 2-CH_3) ppm.[18]

(4-Formyl-2-ethoxyphenyl) 2,3,6-tri-*O*-acetyl-4-*O*-(2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranosyl)-β-D-glucopyranoside (14). Entry 1 (cf. Table 3): A 1 molar solution of potassium hydroxide in ethanol (4.75 mL) was added to **1** (920 mg, 5.5 mmol) and **13**[22] (3.5 g, 5.0 mmol) in chloroform (25 mL) and refluxed for 16 h. The mixture was poured on iced water (40 mL), and the aqueous phase was extracted with chloroform three times. The combined organic phases were dried and concentrated. The crude product was purified on silica gel employing petrol ether (50–70)/ethyl acetate (1:1) as eluents to give **14** (402 mg, 0.51 mmol, 10%).

Entry 2: To a solution of **13** (1.54 g, 2.2 mmol) in anhydrous dichloromethane (9 mL), **1** (332 mg, 2.0 mmol) in a 0.45 molar solution of potassium hydroxide in anhydrous methanol (4.4 mL) was added dropwise. The reaction was left for 13 h and subsequently poured on iced water (20 mL). The aqueous phase was extracted with dichloromethane twice, and the combined organic phases were dried, concentrated and purified by flash chromatography with the solvent system petrol ether (50–70)/ethyl acetate (1:1) to furnish **14** (341 mg, 0.43 mmol, 22%).

Entry 3: Compunds **1** (665 mg, 4.0 mmol), **13** (1.40 g, 2.0 mmol) and tetrabutylammonium bromide (645 mg, 2.0 mmol) were dissolved in dichloromethane (7 mL). A 1 molar sodium hydroxide solution (7 mL) was added, and the mixture was stirred vigorously for 1 h at room temperature. Ethyl acetate (100 mL) was added, and

the organic phase was washed subsequently three times with 1 molar sodium hydroxide, three times with water, once with brine, dried and finally concentrated. The residue was purified by column chromatography employing petrol ether (50–70)/ethyl acetate (1:1) to yield **14** (749 mg, 0.95 mmol, 48%) as white crystals: $[\alpha]_{578}^{20}$ + 2.1° (*c* 0.1, chloroform); mp 141°C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.86 (s, 1 H, CHO), 7.36–7.41 (m, 2 H, $^4J_{ar\text{-}3,ar\text{-}5}$ 1.5 Hz, $J_{ar\text{-}5,ar\text{-}6}$ 8.7 Hz, aryl H-3, aryl H-5), 7.15 (d, 1 H, aryl H-6), 5.42 (d, 1 H, $J_{1',2'}$ 4.1 Hz, H-1′), 5.35 (dd, 1 H, $J_{2',3'}$ 10.7 Hz, $J_{3',4'}$ 9.7 Hz, H-3′), 5.30 (dd, 1 H, $J_{2,3}$ 7.6 Hz, $J_{3,4}$ 8.6 Hz, H-3), 5.12–5.19 (m, 2 H, H-1, H-2), 5.03 (dd, 1 H, $J_{4',5'}$ 10.2 Hz, H-4′), 4.84 (dd, 1 H, H-2′), 4.49 (dd, 1 H, $J_{5,6a}$ 3.1 Hz, $J_{6a,6b}$ 9.2 Hz, H-6a), 4.20–4.26 (m, 2 H, $J_{5,6b}$ 5.1 Hz, $J_{5',6'a}$ 4.1 Hz, H-6b, H-6′a), 4.02–4.13 (m, 4 H, $J_{5',6'b}$ 2.5 Hz, J_{OEt} 7.1 Hz, H-4, H-6′b, O–CH_2–CH_3), 3.96 (ddd, 1 H, H-5′), 3.85 (ddd, 1 H, $J_{4,5}$ = 9.7, H-5), 2.08, 2.05, 2.03, 2.02, 2.01, 2.00, 1.98 (7 × s, 7 × 3 H, 7 × $COCH_3$), 1.41 (t, 3 H, O–CH_2–CH_3) ppm; ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 190.91 (CHO), 170.52, 170.45, 170.30, 170.16, 169.96, 169.50, 169.41 (7 C, 7 × *C*OCH_3), 151.20, 150.15 (2 × C, aryl C-1, aryl C-2), 132.67 (aryl C-4), 125.34 (aryl C-5), 117.81 (aryl C-6), 112.03 (aryl C-3), 98.77 (C-1), 95.75 (C-1′), 75.00 (C-3), 72.70 (C-4), 71.54 (C-5), 71.86 (C-2), 70.10 (C-2′), 69.34 (C-3′), 68.66 (C-5′), 68.11 (C-4′), 64.70 (O–*C*H_2–CH_3), 62.71 (C-6), 61.60 (C-6′), 20.90, 20.76, 20.71, 20.67, 20.64, 20.61, 20.58 (7 C, 7 × CO*C*H_3), 14.70 (O–CH_2–*C*H_3) ppm.

Anal. Calcd for $C_{35}H_{44}O_{20}$ (784.72): C, 53.57; H, 5.65. Found: C, 53.47; H, 5.75.

(4-Formyl-2-ethoxyphenyl) 4-*O*-(α-D-glucopyranosyl)-β-D-glucopyranoside (15). A solution of **14** (982 mg, 1.25 mmol) in anhydrous methanol (15 mL) was treated with methanolic sodium methoxide (1.5 mL, 1%) for 10 min. The mixture was neutralized with Amberlite IR-120 (H^+) and concentrated. Crystallization from ethanol gave pure **15** (520 mg, 1.06 mmol, 85%) as white solid: $[\alpha]_{578}^{20}$ + 1.2° (*c* 0.1, water); mp 199°C; MALDI-TOF-MS *m/z* 513.2 $[M + Na]^+$, 529.2 $[M + K]^+$; ^{1}H NMR (400 MHz, D_2O) δ 9.67 (s, 1 H, CHO), 7.49 (dd, 1 H, $^4J_{ar\text{-}3,ar\text{-}5}$ 1.5 Hz, $J_{ar\text{-}5,ar\text{-}6}$ 8.1 Hz, aryl H-5), 7.43 (d, 1 H, aryl H-3), 7.21 (d, 1 H, aryl H-6), 5.38 (d, 1 H, $J_{1',2'}$ 4.1 Hz, H-1′), 5.19 (d, 1 H, $J_{1,2}$ 7.6 Hz, H-1), 4.08–4.17 (m, 2H, J_{OEt} 7.1 Hz O–CH_2–CH_3), 3.62–3.89 (m, 10 H, H-2, H-3, H-4, H-5, H-6a, H-6b, H-3′, H-5′, H-6′a, H-6′b), 3.53 (dd, 1 H, $J_{2',3'}$ 9.7 Hz, H-2′), 3.37 (dd, 1 H, $J_{3',4'}$ 9.7 Hz, $J_{4',5'}$ 9.7 Hz, H-4′), 1.36 (t, 3H, O–CH_2–CH_3) ppm; ^{13}C NMR (100.6 MHz, d_4-MeOH) δ 195.11 (CHO), 151.62, 148.36 (2 × C, aryl C-1, aryl C-2), 131.31 (aryl C-4), 126.94 (aryl C-5), 115.34 (aryl C-6), 112.99 (aryl C-3), 100.07 (C-1′), 99.78 (C-1), 76.74 (C-5), 76.21 (C-3), 75.24 (C-4), 73.23 (C-2), 73.11 (C-5′), 72.86 (C-3′), 72.06 (C-2′), 69.69 (C-4′), 65.68 (O–*C*H_2–CH_3), 60.85, 60.80 (2 × C, C-6, C-6′), 15.37 (O–CH_2–*C*H_3) ppm.

Anal. Calcd for $C_{21}H_{30}O_{13}$ (490.46): C, 51.43; H, 6.17. Found: C, 50.97; H, 6.22.

(2-Methyl-4-oxopyran-3-yl) 2,3,6-tri-*O*-acetyl-4-*O*-(2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranosyl)-β-D-glucopyranoside (16). Compounds **2** (3.78 g, 30 mmol), **13** (6.99 g, 10 mmol) and tetrabutylammonium bromide (3.22 g, 10 mmol) were dissolved in dichloromethane (35 mL) and warmed up to 35°C. A 1 molar sodium hydroxide solution (35 mL) was added, and the mixture was stirred vigorously for 3 h at 35°C. Ethyl acetate (400 mL) was added, and the organic phase was washed subsequently twice with 1 molar sodium hydroxide, twice with water, once with brine, dried and finally concentrated. Flash chromatography on silica gel employing petrol ether(50–70)/ethyl acetate (1:3) as eluents gave **16** (2.44 g, 3.27 mmol, 33%) as a white solid:

$[\alpha]_{578}^{20}$ + 3.9° (*c* 0.1, chloroform); mp 85°C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.60 (d, 1 H, $J_{maltyl\ 5,6}$ 5.6 Hz, maltyl H-6), 6.31 (d, 1 H, maltyl H-5), 5.39 (d, 1 H, $J_{1',2'}$ 4.1 Hz, H-1′), 5.27–5.34 (m, 3 H, $J_{3,4}$ 9.2 Hz, $J_{2',3'}$ 10.7 Hz, H-1, H-3, H-3′), 4.96–5.05 (m, 2 H, $J_{4',5'}$ 10.2 Hz, H-2, H-4′), 4.82 (dd, 1 H, H-2′), 4.52 (dd, 1 H, $J_{5,6a}$ 2.5 Hz, $J_{6a,6b}$ 12.2 Hz, H-6a), 4.22 (dd, 1 H, $J_{5',6'a}$ 3.6 Hz, $J_{6'a,6'b}$ 12.2 Hz, H-6′a), 4.14 (dd, 1 H, $J_{5,6b}$ 4.1 Hz, H-6b), 4.02 (dd, 1 H, $J_{5',6'b}$ 2.5 Hz, H-6′b), 4.00 (dd, 1 H, $J_{4,5}$ 9.7 Hz, H-4), 3.90 (ddd, 1 H, H-5′), 3.59 (ddd, 1 H, H-5), 2.24 (s, 1 H, maltyl CH_3), 2.08, 2.07, 2.06, 2.03, 2.00, 1.98, 1.97 (7 × s, 7 × 3 H, 7 × $COCH_3$) ppm; ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 172.57 (maltyl C-4), 169.60, 169.52, 169.34, 169.14, 168.88, 168.85, 168.40 (7 C, 7 × *C*OCH_3), 160.32 (maltyl C-2), 152.71 (maltyl C-6), 140.24 (maltyl C-3), 116.35 (maltyl C-5), 98.09 (C-1), 94.45 (C-1′), 73.83 (C-3), 71.38 (C-4), 71.33 (C-5), 71.12 (C-2), 68.98 (C-2′), 68.31 (C-3′), 67.43 (C-5′), 67.05 (C-4′), 60.98 (C-6), 60.45 (C-6′), 20.03, 19.86, 19.79, 19.70, 19.66, 19.58, 19.57 (7 C, 7 × CO*C*H_3), 14.12 (maltyl CH_3) ppm.

Anal. Calcd for $C_{32}H_{40}O_{20}$ (744.66): C, 51.61; H, 5.41. Found: C, 51.42; H, 5.48.

(2-Methyl-4-oxopyran-3-yl) 4-*O*-(α-D-glucopyranosyl)-β-D-glucopyranoside (17). A solution of **16** (870 mg, 1.17 mmol) in anhydrous methanol (15 mL) was treated with methanolic sodium methoxide (7 mL, 1%) for 45 min. The mixture was neutralized with Amberlite IR-120 (H^+) and concentrated. Column chromatography (methanol/ethyl acetate 2:1) gave **17** (339 mg, 0.75 mmol, 64%) as yellowish solid: $[\alpha]_{578}^{20}$ + 13.5° (*c* 0.1, water); mp 119°C; MALDI-TOF-MS *m/z* 473.1 $[M + Na]^+$; ^{1}H NMR (400 MHz, D_2O) δ 8.04 (d, 1 H, $J_{maltyl\ 5,6}$ 5.6 Hz, maltyl H-6), 6.54 (d, 1 H, maltyl H-5), 5.41 (d, 1 H, $J_{1',2'}$ 3.6 Hz, H-1′), 4.92 (d, 1 H, $J_{1,2}$ 8.1 Hz, H-1), 3.65–3.86 (m, 8 H, H-3, H-4, H-6a, H-6b, H-3′, H-5′, H-6′a, H-6′b), 3.54–3.60 (m, 2 H, H-2, H-2′), 3.47 (ddd, 1 H, $J_{4,5}$ 9.2 Hz, $J_{5,6a}$ 2.6 Hz, H-5), 3.40 (dd, 1 H, H-4′), 2.46 (s, 3H, CH_3) ppm; ^{13}C NMR (100.6 MHz, D_2O) δ 177.22 (maltyl C-4), 164.98 (maltyl C-6), 157.05 (maltyl C-2), 142.02 (maltyl C-3), 116.26 (maltyl C-5), 103.20 (C-1), 99.90 (C-1′), 76.55, 76.46 (2 × C, C-3, C-4), 75.30 (C-5), 73.73 (C-2), 73.19, 73.04 (2 × C, C-3′, C-5′), 72.02 (C-2′), 69.68 (C-4′), 60.85, 60.74 (2 × C, C-6, C-6′), 15.49 (CH_3) ppm.

Anal. Calcd for $C_{18}H_{26}O_{13}$ (450.40): C, 48.00; H, 5.82. Found: C, 47.84; H, 5.91.

(2,5*R*/5*S*-Dimethyl-4-oxofuran-3-yl) 2,3,6-tri-*O*-acetyl-4-*O*-(2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranosyl)-β-D-glucopyranoside (18). Compounds **3** (6.83 g, 53.3 mmol), **13** (7.46 g, 10.7 mmol) and tetrabutylammonium bromide (3.44 g, 10.7 mmol) were dissolved in dichloromethane (65 mL) and warmed up to 35°C. A 1 molar sodium hydroxide solution (65 mL) at 35°C was added, and the mixture was stirred vigorously for 45 min at 35°C. Ethyl acetate (350 mL) was added, and the organic phase was washed subsequently twice with 1 molar sodium hydroxide, twice with water, once with brine, dried and finally concentrated. Flash chromatography on silica gel employing dichloromethane/acetone (8:1) as eluents gave the diastereomeric mixture **18** (1.78 g, 2.38 mmol, 22%) as white crystals: $[\alpha]_{578}^{20}$+ 1.0° (*c* 0.1, chloroform); mp 68°C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.40, 5.39 (2 × d, 1 H, $J_{1',2'}$ 4.1 Hz, H-1′), 5.32 (dd, 1 H, $J_{2',3'}$ 10.7 Hz, $J_{3',4'}$ 9.7 Hz, H-3′), 5.27, 5.26 (2 × dd, 1 H, $J_{2,3}$ 9.1 Hz, $J_{3,4}$ 9.2 Hz, H-3), 5.05, 5.04 (2 × d, 1 H, $J_{1,2}$ 7.6 Hz, H-1), 5.03 (dd, 1 H, $J_{4',5'}$ 10.2 Hz, H-4′), 4.95, 4.94 (2 × dd, 1 H, H-2), 4.82 (dd, 1 H, H-2′), 4.53, 4.52 (2 × dd, 1 H, $J_{5,6a}$ 2.5 Hz, $J_{6a,6b}$ 12.2 Hz, H-6a), 4.42, 4.41 (2 × q, 1 H, $J_{fur\text{-}5,Me}$ 7.6 Hz, furaneyl H-5), 4.23

(dd, 1 H, $J_{5',6'a}$ 3.6 Hz, $J_{6'a,6'b}$ 12.2 Hz, H-6′a), 4.16, 4.15 (2 × dd, 1 H, H-6b), 4.02 (dd, 1 H, $J_{5',6'b}$ 2.5 Hz, H-6′b), 4.00, 3.99 (2 × dd, 1 H, $J_{4,5}$ 9.7 Hz, H-4), 3.91 (ddd, 1 H, H-5′), 3.66, 3.64 (2 × ddd, 1 H, H-5), 2.11, 2.06, 2.04, 1.99, 1.96, 1.95, 1.94 (7 × s, 7 × 3 H, 7 × $COCH_3$), 2.03, 2.02 (2 × s, 3 H, furaneyl 2-CH_3), 1.39, 1.37 (2 × d, 3 H, furaneyl 5-CH_3) ppm; ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 196.77 (furaneyl C-4), 181.56, 181.24 (1 C, furaneyl C-2), 171.00, 170.96, 170.65, 170.55, 170.40, 170.33, 169.84 (7 C, 7 × *C*OCH_3), 133.46 (furaneyl C-3), 100.08, 99.89 (1 C, C-1), 95.95, 95.92 (1 C, C-1′), 81.29 (furaneyl C-5), 75.34 (C-3), 72.87 (C-5), 72.82 (C-4), 72.20 (C-2), 70.41 (C-2′), 69.72 (C-3′), 68.90 (C-5′), 68.42 (C-4′), 62.59 (C-6), 61.88 (C-6′), 21.29, 21.19, 21.17, 21.11, 21.01, 21.00, 20.99 (7 C, 7 × CO*C*H_3), 16.85, 16.65 (1 C, furaneyl 5-CH_3), 14.17 (furaneyl 2-CH_3) ppm.

Anal. Calcd for $C_{32}H_{42}O_{20}$ (746.67): C, 51.48; H, 5.67. Found: C, 51.50; H, 5.88.

(2,5*R*/5*S*-Dimethyl-4-oxofuran-3-yl) 4-*O*-(α-D-glucopyranosyl)-β-D-glucopyranoside (19). A solution of **18** (410 mg, 0.55 mmol) in anhydrous methanol (2 mL) was treated with methanolic sodium methoxide (1.5 mL, 1%) for 4 h. The mixture was neutralized with Amberlite IR-120 (H^+) and concentrated. Column chromatography (methanol/ethyl acetate 2:1) gave **19** (214 mg, 0.74 mmol, 86%) as colorless crystals: $[\alpha]_{578}^{20}$ + 3.2° (*c* 0.1, water); mp 98°C; ^{1}H NMR (400 MHz, D_2O) δ 5.24 (d, 1 H, $J_{1',2'}$ 3.6 Hz, H-1′), 4.56–4.62 (m, 2 H, H-1, $J_{\text{furaneyl 5,Me}}$ 7.1 Hz, furaneyl H-5), 3.48–3.73 (m, 8 H, H-3, H-4, H-6a, H-6b, H-3′, H-5′, H-6′a, H-6′b), 3.35–3.43 (m, 2 H, $J_{5,6a}$ 2.5 Hz, $J_{2',3'}$ 9.7 Hz, H-5, H-2′), 3.32 (dd, 1 H, $J_{1,2}$ 8.1 Hz, $J_{2,3}$ 9.7 Hz, H-2), 3.24 (dd, 1 H, H-4′), 2.18 (s, 3H, furaneyl 2-CH_3), 1.28 (d, 3 H, furaneyl 5-CH_3) ppm; ^{13}C NMR (100.6 MHz, D_2O) δ 200.84 (furaneyl C-4), 186.35, 186.31 (1 C, furaneyl C-2), 133.68, 133.66 (1 C, furaneyl C-3), 103.51, 103.48 (1 C, C-1), 99.96 (C-1′), 82.35 (furaneyl C-5), 76.71, 76.29 (2 C, C-3, C-4), 75.19 (C-5), 73.26, 73.22, 73.06 (3 C, C-2, C-3′, C-5′), 72.04 (C-2′),69.71 (C-4′), 60.89, 60.80 (2 C, C-6, C-6′), 15.87, 15.78 (1 C, furaneyl 5-CH_3), 14.25, 14.24 (1 C, furaneyl 2-CH_3) ppm.

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