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Replacement of an Anomeric Hydroxyl Group by a Halogen Atom Using $PdCl_2/Et_3SiH$/Halogen Source System

by H.H.A.M. Hassan* and A.H.F. El-Husseiny

Chemistry Department, Faculty of Science, Alexandria University, P.O 426 Ibrahimia, 21321-Alexandria, Egypt, E-mail:hassan@safwa.com.eg.

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The anomeric hydroxyl group of perbenzylated and peracetylated carbohydrates can be stereoselectively replaced by a bromine or iodine atom using palladium dichloride, triethylsilane and carbon tetrabromide and/or iodine at room temperature. To illustrate the synthetic potential of this novel method, some models of *O*- and *C*-glycosides are reported. Reduction of sugar halide using excess of triethylsilane was not successful.

Key words: glycosyl donor, palladium, anomers, reduction

Interglycosidic bond formation is one of the most challenging aspects in carbohydrate chemistry, in particular, in the preparation of complex oligosaccharides. The most widely used glycosylation methods utilized glycosyl bromides and chlorides as glycosyl donors [1]. Many other leaving groups at the anomeric centre have been reported [2] as alternatives to the glycosyl halides methodologies. However, the relatively drastic conditions for the generation of glycosyl halide or, on the other hand, the use of either acid or base activation of sugar for the preparation of other leaving groups are still problems to be solved. In connection with this specific point, to date, there is no general applicable method or strategy for oligosaccharides synthesis. Therefore, the development of methods by which glycosidic bonds can be formed under mild, preferable neutral, conditions is highly desirable and of particular interest. In continuation of our recent work in the chemistry of natural glycosides [3] and their analogs [4,5], we wish to report a new efficient method for the generation of glycosyl halide under milder conditions than that previously reported. In order to expand the synthetic potential of this novel method, some models of *O*- and *C*-glycosides are reported.

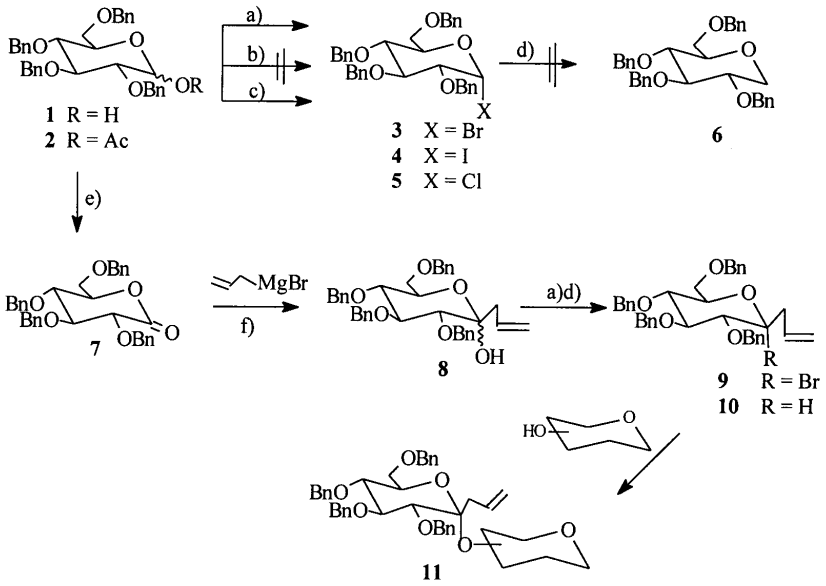
RESULTS AND DISCUSSION

Various model substrates were screened for the present study. As shown in Scheme 1, the known 2,3,4,6-tetra-*O*-benzyl-α-D-glucopyranose (**1**) [6], accessible

*Author for correspondence.

from D-glucose, was chosen as the starting material for the halogenation step. Bromination of **1** (→ **3**) [7] was achieved by subsequent addition of palladium dichloride to a stirred mixture of carbon tetrabromide, triethylsilane and alcohol (**1**) in dry dichloromethane. Analyses of the reaction mixture by ^{1}H NMR and GC/MS revealed the completion of the reaction after 48 hours and the α-bromide **3** ($J_{1,2}$ = 3.7 Hz) was obtained in almost quantitative yield and high purity and therefore it can be used for glycosylation step without further purification. Bromoform ($CHBr_3$, δ 6.79, s, 1H) was the only byproduct observed in ^{1}H NMR spectroscopy of crude (**3**) and no other competitive processes (*i.e* elimination) were detected.

Scheme 1



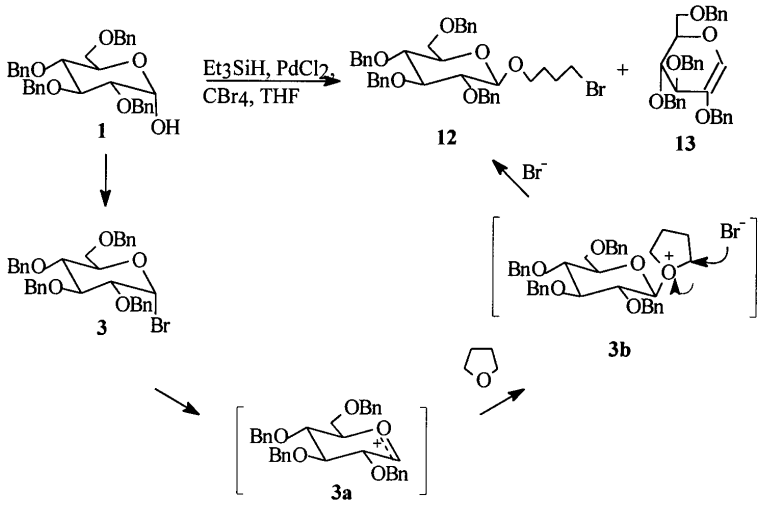
Key: a) Et_3SiH, $PdCl_2$, CBr_4, CH_2Cl_2; b) Et_3SiH, $PdCl_2$, CCl_4; c) Et_3SiH, $PdCl_2$, I_2, CH_2Cl_2; d) Et_3SiH (3 equiv); e) PCC, CH_2Cl_2; f) Et_2O, -78°C.

Other solvents were employed in attempt to increase the reaction rate. In general, halogenated solvents proved to be most suitable. Best results were obtained when dichloromethane and/or chloroform were used and hence both were selected as the solvent of choice for all reactions. Solvents such as acetonitrile and diethyl ether were not suitable to solvate **1**, whereas no reaction was observed in benzene, toluene and dimethylformamide. Surprisingly, when THF was employed as solvent the formation of (4-bromobutyl)-β-glucopyranoside in good yield was observed. Similar product formation was reported upon activation of trichloroacetimidates with air-oxidized samarium diiodide in THF [8]. The formation of **12** can be explained assuming that the anomeric oxocarbenium ion **3a** resulting from activation of the bromide leaving

group can be attacked by a THF solvent molecule from the β-side **3b**, followed by THF ring opening by bromination. The high yielding formation of **12** looked synthetically interesting because of the mild insertion at the anomeric position of an aglycon possessing a versatile functionality at its other end. Compound **12** can be considered as potential building block for the preparation of *O*-linked glycopeptides [9].

The use of glycosyl iodides instead of glycosyl bromides and chlorides is highly desirable since these carbohydrate derivatives display a significantly higher reactivity. However, these halides, in addition to their thermal instability, have to be prepared under drastic conditions [10] and thus they could not be used advantageously in glycoside synthesis. For these reasons, we hoped to improve not only the yields of these halides by carrying out the reaction under milder conditions, but also to avoid the aqueous work up and silica gel purification that strongly effect both yields and stability of the substrate. Thus, glycosyl iodide **4** was obtained from reaction of **1** with $Et_3SiH/PdCl_2/I_2$ mixture after approximately 48 hours at room temperature. The NMR spectrum of 2,3,4,6-tetra-*O*-benzyl-α-D-glucopyranosyl iodide had been reported by Gervay and co-authors [11] and it matched the spectrum of **4**.

Scheme 2



Attempts of chlorination of **1** (→ **5**) (Scheme 1) with a $Et_3SiH/PdCl_2/CCl_4$ system has met with limited success even after mild heating 60–70°C, although this reaction proceeded quite well with a variety of alkyl and aryl alcohols under similar conditions [12].

Trialkylsilanes are known to be poor reducing agents due to their low tendency to donate hydrogen atom or hydride [13]. Nevertheless, application of $Et_3SiH/PdCl_2$ and Et_3SiH/acid mixtures have been reported as an efficient dehalogenation procedure for alkyl and aryl halides [14,15]. Unfortunately, transformation of glycosyl bromide **3** or iodide (**4**) into pyran derivative **6** by adding another portion of Et_3SiH was not successful and afforded only decomposition product.

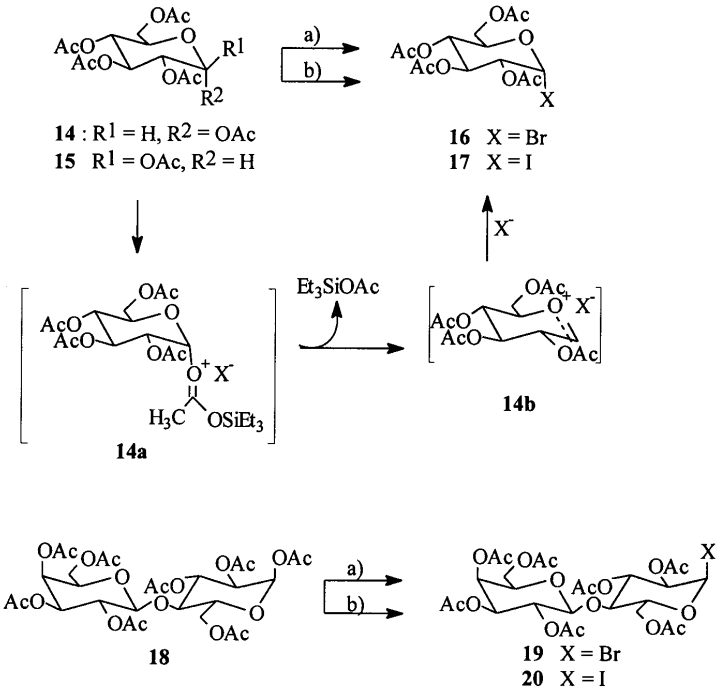
In the next step, we investigated the halogenation/reduction reaction of hemiketal **8** as a useful synthetic intermediate towards oligosaccharide (**11**). Thus, 2,3,4,6-tetra-*O*-benzyl-glucopyranolactone (**7**) was reacted with allyl magnesium bromide in Et_2O providing the corresponding hemiketal **8** in 70% yield. When **8** was treated with $Et_3SiH/PdCl_2/CBr_4$ system, we observed the formation of C-glycoside (**10**) in good yield after 1 h reaction. Although compound **10** is known [15], its NMR spectral data were not reported. ^{13}C NMR showed the carbohydrate carbons signals C(1) to C(6) respectively at δ 73.3, 74.9, 71.6, 75.6, 75.3 and 68.7 ppm, whereas the allyl carbons signals appeared at δ 132.1, 120.1 and 42.8 ppm.

The reaction was then extended to per-*O*-acetylated carbohydrates such as α- and/or β-penta-*O*-acetyl glucose (**14**, **15** respectively) and lactose octaacetate (**18**) (Scheme 3). Thus, when **14**, **15** and/or **18** were treated with $Et_3SiH/PdCl_2/CBr_4$ in CH_2Cl_2, the corresponding glycosyl bromide **16** [16] and α-heptaacetyl lactosyl bromide **19** [17] were obtained in almost quantitative yields after 2 h reaction. The reaction with the disaccharide **18** proceeded smoothly without cleavage of the inter-glycosidic bond. In a similar manner corresponding reactions of **14**, **15** or **18** with $Et_3SiH/PdCl_2/I_2$ mixture afforded the glycosyl iodides **17** and **20** [18], respectively. These results prompted us to examine the reaction of the *in situ* formed Et_3SiBr (in the former process) with 1-*O*-acetyl-2,3,4,6-tetra-*O*-benzyl-α-D-glucopyranoside **2** [19]. After approximately 1 h the glycosyl acetate **2** disappeared and the bromide (**3**) was the only product detected by TLC.

The proposed reaction mechanism of glycosyl acetates **2**, **14** and **15** with Et_3SiX is depicted in Scheme 3 [11]. The carbonyl oxygen atom of the anomeric acetyl group was silylated by Et_3SiX (**14a**), followed by subsequent release of Et_3SiOAc and reaction of the resulting oxocarbenium ion (**14b**) with a halide ion.

To illustrate the synthetic potential of this method, several α-D-glucopyranosides have been prepared following the known procedures. *O*-Glycosides (**21**) and (**22**) (Scheme 4) were obtained by reaction of **3** with MeOH/(+) camphorsulfonic acid and allyl alcohol/$ZnCl_2$. *C*-Glycosides (**23**) and **24** were obtained by a Pd(0) catalysed cross-coupling reaction of, respectively, **3** and **16** with trimethylsilyl acetylene/BuLi and methylcrotonate-4-zinc chloride ($ZnCl\text{-}CH_2\text{-}CH{=}CH\text{-}CO_2Me$) generated *in situ* by successive reaction of the commercial methyl-4-bromocrotonate with BuLi/THF (–78°C) followed by addition of freshly fused $ZnCl_2$. It is interesting to note that stereoselectivities observed for the formation of **21**, **22** and **23** were consistent with the literature data [8,20,21] and favored the formation of α-D-glycosides than its β-counterparts. On the other hand, participation of the acetyl group at C-2 was expected to direct the β-glycoside bond in case of **24**. Nevertheless, **24** was found to be a mixture of ~2:1 β/α anomers. This result led us to believe that the participation of the functionality at C-2 is not the only factor that controls stereoselectivity if we consider the high ratio of α-anomer. Thus, the rational explanation of such stereochemical outcome is that the reaction may proceed *via* the oxonium ion [22] stabilized by complexation with Pd $(Ph_3P)_4$ and not acetoxonium ion, as expected, to give a mixture of anomers.

Scheme 3



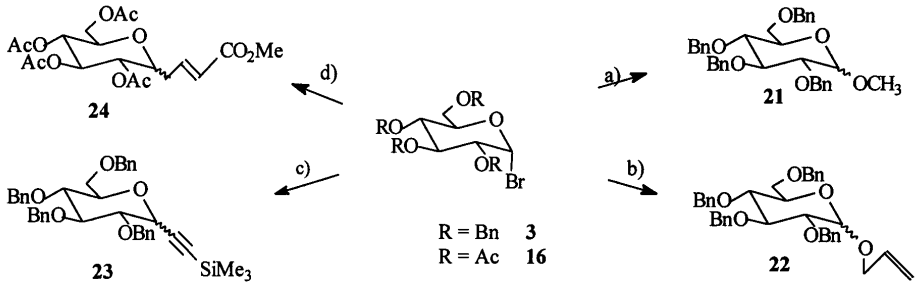
Key: a) Et_3SiH, $PdCl_2$, CBr_4, CH_2Cl_2; b) Et_3SiH, $PdCl_2$, I_2, CH_2Cl_2.

In conclusion, a new efficient method for the generation of glycosyl donors under mild conditions has been developed and applied for various types of substrates [23]. Both benzyl and acetyl protecting groups as well as the interglycosidic bond, in case of disaccharides, are stable under these conditions. The reaction proceeds quantitatively and affords highly pure glycosyl halide that can be used without classical column chromatography purification. The workup requires only simple filtration of the liberated palladium specious followed by removal of the solvent and volatiles under vacuum.

EXPERIMENTAL

General methods: All reactions were performed in closed and pre-heated flasks under N_2 atmosphere. Organic solvents were distilled prior to use. TLC was performed on silica gel 60 F_{254} (*Merck*). For normal column chromatography, silica gel 60 (0.063–0.200 mm, *Merck*) was used. Melting points were determined with an electrothermal melting point apparatus and are not corrected. NMR spectra were recorded for $CDCl_3$ solutions with a *Varian VXR 200* (200 MHz for ^1H NMR and 50 MHz for ^{13}C NMR), while the 400 MHz ^1H NMR and 100 MHz ^{13}C NMR on a *JEOL-400 unity*. GC-MS were performed on a *Finnigan SSQ* 7000 and/or HP-model *MS-5988* operating in the electron impact mode, equipped with a programable injector on a 30 m × 0.32 mm DB-5 column with a fused silica gel (5% phenyl:95% methylsiloxane) stationary phase using N_2 as a carrier gas. Microanalyses were performed on a *Carlo Elba EA* 1108 instrument.

Scheme 4



Key: a) MeOH/(+)-camphorsulfonic acid, b) allyl alcohol, $ZnCl_2$, c) Li-C≡C-$SiMe_3$, $Pd(PPh_3)_2Cl_2$, d) ZnCl-CH_2-CH=CH-CO_2Me, $Pd(PPh_3)_2Cl_2$, THF, -78°C.

2,3,4,6-Tetra-*O*-benzyl-α-D-glucopyranose (**1**) [7]: ^{1}H NMR (400 MHz): 7.33–7.13 (m, 20H, arom.), 5.22 (m, 1H, H-1), 4.94 (d, J = 10.9 Hz, 1H, A_1B_1, PhC$\underline{H}_2$), 4.83 (d, J = 10.9, $A_{1'}B_{1'}$, 1H, PhC$\underline{H}_2$), 4.81 (d, J = 10.9 Hz, 1H, A_2B_2, PhC$\underline{H}_2$), 4.75 (d, J = 11.7 Hz, 1H, A_3B_3, PhC$\underline{H}_2$), 4.68 (d, J = 11.7 Hz, 1H, $A_{3'}B_{3'}$, PhC$\underline{H}_2$), 4.58 (d, J = 12.2 Hz, 1H, A_4B_4, PhC$\underline{H}_2$), 4.47 (d, J = 12.2 Hz, 1H, $A_{4'}B_{4'}$, PhC$\underline{H}_2$), 4.49 (d, J = 10.9 Hz, 1H, $A_{2'}B_{2'}$, 1H, PhC$\underline{H}_2$), 4.03–3.94 (m, 2H), 3.68–3.55 (m, 4H), 3.08 (d, 1H, OH). ^{13}C NMR (100 MHz): 97.4 (C-1, β-isomer), 91.3 (C-1, α- isomer), 81.8, 80.0, 77.7, 70.3 (d, C-2, C-3, C-4 and C-5), 68.6 (C-6), 75.7, 75.0, 73.5, 73.3, (4× $\underline{C}H_2$Ph).

1-Acetoxy-2,3,4,6-tetra-*O*-benzyl-α-D-glucopyranoside (**2**) [19]: ^{1}H NMR (400 MHz): 7.45–7.10 (m, 20H, arom), 6.22 (d, 1H, $J_{1,2}$ = 2.0 Hz, H-C(1)), 4.88 (d, 1H, J_{A1B1} = 10.6 Hz, PhC$\underline{H}_2$), 4.80 (d, 1H, J_{A2B2} = 12.4 Hz, PhC$\underline{H}_2$), 4.72 (d, 1H, J_{A2B2} = 12.4 Hz, PhC$\underline{H}_2$), 4.66 (d, J_{A3B3} = 12.1 Hz, 1H, PhC$\underline{H}_2$), 4.58 (s, 2H, PhC$\underline{H}_2$), 4.53 (d, 1H, J_{A1B1} = 10.6 Hz, PhC$\underline{H}_2$), 4.50 (d, 1H, J_{A3B3} = 12.1 Hz, PhC$\underline{H}_2$), 4.1 (dd, 1H, $J_{3,4}$ = $J_{4,5}$ = 9.5 Hz, H–C(4)), 3.86 (d,1H, $J_{2,3}$ = 3.3 Hz, H-C(3)), 3.84–3.72 (m, 4H, H-C(2), H-C(5), 2× H-C(6)), 2.05 (s, 3H, CH_3). ^{13}C NMR (100 MHz): 170.9, 98.0 (C-1, β-anomer), 91.9 (C-1, α-anomer), 79.2 (C-3), 76.7 (C-2), 75.4, 75.3, 74.5, 73.9 (4× $\underline{C}H_2$Ph), 72.7 (C-5), 69.9 (C-4), 69.6 (C-6), 21.0.

Preparation of glycosyl halides (General procedure): 125 µl (1.075 mmol) of Et_3SiH was treated with 5 mg $PdCl_2$ and (1.1 mmol) of the halogen source. After termination of the exothermic reaction, 500 mg (0.93 mmol) of perprotected glucopyranose **1**, **2**, **14**, **15** or **18** dissolved in 4 ml of CH_2Cl_2 was added dropwise. After 2h stirring at r.t., the reaction mixture was evaporated to dryness to furnish the corresponding glycosyl halide in almost quantitative yield and high purity. The following spectral data are recorded:

2,3,4,6-Tetra-*O*-benzyl-α-D-glucopyranosyl bromide (**3**): ^{1}H NMR (400 MHz): 7.35–7.14 (m, 20H, Aromatic H's), 6.79 (s, 1H, $CHBr_3$), 6.40 (d, J = 3.7 Hz, H–1), 4.95 (d, J = 10.9 Hz, 1H, A_1B_1), 4.82 (d, J = 10.6 Hz, 1H, A_2B_2, PhC$\underline{H}_2$), 4.79 (d, J = 10.9 Hz, 1H, $A_{1'}B_{1'}$, PhC$\underline{H}_2$), 4.54 (d, J = 12.2 Hz, 1H, A_3B_3, PhC$\underline{H}_2$), 4.43 (d, J = 12.2 Hz, 1H, $A_{3'}B_{3'}$, PhC$\underline{H}_2$), 4.51 (d, J = 12.4 Hz, 1H, A_4B_4, PhC$\underline{H}_2$), 4.48 (d, J = 12.4 Hz, 1H, $A_{4'}B_{4'}$, PhC$\underline{H}_2$), 4.67 (dd, J = 9.0, 6.3 Hz, 1H, H-5), 3.69 (dd, J = 10.7, 9.0 Hz, 1H, H-4), 3.60 (dd, J = 6.3, 3.2 Hz, 1H, H-6), 3.59 (dd, J = 6.3, 3.2 Hz, 1H, H-6), 3.50 (dd, J = 9.0, 3.7 Hz, 1H, H-2). ^{13}C NMR (100 MHz, $CDCl_3$): 91.8 (C-1), 82.1, 79.6, 76.0, 75.8 (C-2, C-3, C-4 and C-5), 75.2, 75.2, 73.5 and 72.8 (4× $\underline{C}H_2$Ph), 67.6 (C-6).

2,3,4,6-Tetra-*O*-acetyl-α-D-glucopyranosyl bromide (**16**): GC-MS; 412 (M^+), 331 (M^+ - Br), 289, 271, 242, 228, 211, 199 (base peak), 182, 169, 157, 140, 127, 115, 98, 85, 73, 43. ^{1}H NMR (200 MHz, COSY): 6.32 (d, 1H, $J_{1,2}$ = 3.6 Hz, H-1), 5.46 (2d, $J_{3,4}$ = 9.4 Hz, $J_{3,2}$ = 10.4 Hz, 1H, H-3), 5.15 (dd, $J_{2,3}$ = 10.2 Hz, $J_{2,1}$ = 3.6 Hz, 1H, H-2), 5.09 (dd, $J_{4,3}$ = 10.2, $J_{4,5}$ = 6.2 Hz, 1H, H-4), 4.29–4.22 (m, 1H, H-6), 4.14–4.05 (m, 2H, H-6, H-5), 2.18 (s, 3H, CH_3), 2.09 (s, 3H, CH_3), 2.03 (s, 3H, CH_3), 2.01 (s, 3H, CH_3). ^{13}C NMR (50 MHz): 170.7, 170.3, 169.5, 168.8 (4× $\underline{C}O$), 89.1 (C-1), 69.9 (C-3), 69.3 (C-5), 67.9 (C-4), 61.5 (C-6), 20.9, 20.7, 20.6, 20.5 (4× $\underline{C}H_3$).

2,3,4,6-Tetra-*O*-acetyl-α-D-glucopyranosyl iodide (**17**): GC-MS; 331 (M^+ - I), 317, 287, 271, 259, 242, 228, 211, 199 (base peak), 182, 169, 157, 140, 126, 115, 98, 85, 73, 43. ^{1}H NMR (200 MHz, COSY):

6.32 (d, 1H, $J_{1,2}$ = 3.6 Hz, H-1), 5.10 (m, 3H, H-2, H-3 and H-4), 4.23 (dd, 1H, $J_{6,6'}$ = 12.4, $J_{6,5}$ = 4.4 Hz, 1H, H-6), 4.11 (dd, $J_{6,6'}$ = 12.4, $J_{6',5}$ = 2.2 Hz, 1H, H-6′), 3.83 (m, 1H, H-5), 2.11 (s, 3H, CH_3), 2.08 (s, 3H, CH_3), 2.03 (s, 3H, CH_3), 2.01 (s, 3H, CH_3). ^{13}C NMR (50 MHz): 170.7, 170.2, 169.4, 169.0 (4× $\underline{C}O$), 91.7 (C-1), 72.8 (C-2), 72.8 (C-3), 70.3 (C-5), 67.8 (C-4), 61.5 (C-6), 20.9, 20.8, 20.6 (2C) (4× $\underline{C}H_3$).

4-(2′,3′,4′,6′-Tetra-*O*-acetyl-β-D-galactopyranosyl-1′-yl)-2,3,6-tetra-*O*-acetyl-α-D-glucopyranosyl bromide (**19**): GC-MS: 619 (M^+ - Br), 559, 498, 456, 401, 331, 289, 271, 248, 229, 211, 169 (base peak), 127, 109, 81, 43. ^{1}H-NMR (200 MHz, COSY): 6.53 (d, $J_{1,2}$ = 4.0 Hz, 1H, H-1), 5.55 (t, J = 9.4 Hz, H-3), 5.36 (d, $J_{1',2'}$ = 3.4 Hz, 1H, H-1′), 5.13 (2d, $J_{3',4'}$ = 8.2 Hz, $J_{3',2'}$ = 10.5 Hz, 1H, H-3), 4.96 (dd, $J_{2',3'}$ = 10.5, $J_{2',1'}$ = 3.4 Hz, 1H, H-2′), 4.76 (dd, $J_{2,3}$ = 9.8 Hz, $J_{2,1}$ = 4.0 Hz, 1H, H-2), 4.50 (2d, 2H, $J_{4,3}$ = 8.2 Hz, $J_{6,6}$ = 10.0 Hz, 1H, H-6), 4.22–4.08 (m, 4H, H-5, H-5′, 2× H-6′), 3.92–3.81 (m, 2H, H-4′, H-6), 2.16 (s, 3H, CH_3), 2.14 (s, 3H, CH_3), 2.09 (s, 3H, CH_3), 2.07 (s, 3H, CH_3), 2.06 (s, 3H, CH_3), 2.05 (s, 3H, CH_3), 1.96 (s, 3H, CH_3). ^{13}C NMR (50 MHz): 170.5, 170.3, 170.3, 170.2, 170.1, 169.3, 169.1 (7× $\underline{C}O$), 100.9 (C-1′), 86.5 (C-1), 75.1 (CH), 73.1 (CH), 71.1 (CH), 70.9 (CH), 70.8 (CH), 69.7 (CH), 69.1 (CH), 66.7 (CH), 61.2 (C-6), 60.9 (C-6′), 20.9 (2C), 20.8 (3C), 20.6 (2C) (7× $\underline{C}H_3$).

4-(2′,3′,4′,6′-Tetra-*O*-acetyl-β-D-galactopyranosyl-1′-yl)-2,3,6-tetra-*O*-acetyl-α-D-glucopyranosyl iodide (**20**): GC-MS: 619 (M^+ - I), 559, 498, 456, 401, 347, 331, 289, 271, 248, 229, 211, 169 (base peak), 127, 109, 81, 43. ^{1}H NMR (200 MHz, COSY): 6.36 (d, $J_{1,2}$ = 3.4 Hz, 1H, H–1), 5.66 (d, $J_{1',2'}$ = 8.6 Hz, 1H, H-1′), 5.24 (dd, $J_{2',3'}$ = 9.6 Hz, $J_{2',1'}$ = 8.6 Hz, 1H, H-2′), 5.12 (dd, J = 7.8, 3.8 Hz, 1H), 5.05 (dd, J = 4.0 Hz, 1.4 Hz, 1H), 5.03 (dd, J = 9.2, 5.4 Hz, 1H), 4.93 (dd, $J_{2,3}$ = 10.6 Hz, $J_{2,1}$ = 3.4 Hz, 1H, H-2), 4.42 (dd, J = 4.0, 1.4 Hz, 1H), 4.46 (d, J = 7.8 Hz, 1H), 4.18–4.13 (m, 1H, H-5′), 4.14 (dd,, $J_{6,6}$ = 11.4 Hz, $J_{6,5}$ = 4.8 Hz, 1H, H-6), 4.10 (dd, $J_{6,6}$ = 12.0 Hz, $J_{6,5}$ = 5.4 Hz, 1H, H-6), 3.80–3.75 (m, 1H, H-6′), 3.89–3.86 (m, 1H, H-4′), 3.83 (dd, $J_{5,4}$ = 8.4, $J_{5,6}$ = 5.4 Hz, 1H, H-5), 2.15 (s, 3H, CH_3), 2.11 (s, 3H, CH_3), 2.09 (s, 3H, CH_3), 2.06 (s, 3H, CH_3), 2.04 (s, 3H, CH_3), 2.02 (s, 3H, CH_3), 1.96 (s, 3H, CH_3). ^{13}C NMR (50 MHz): 170.5, 170.4, 170.2, 170.1, 169.7, 169.1, 168.9 (7× $\underline{C}O$), 101.0 (C-1′), 91.6 (C-1), 75.8 (CH), 73.6 (CH), 72.7 (CH), 71.0 (CH), 70.8 (CH), 70.6 (CH), 69.1 (CH), 66.7 (CH), 61.8 (C-6), 60.9 (C-6′), 20.9, 20.9, 20.8, 20.7, 20.7, 20.6 (7× $\underline{C}H_3$).

2,3,4,6-Tetra-*O*-benzyl-D-glucono-1,5-lactone (**7**) [15]: 250 mg (0.46 mmol) of *2,3,4,6-tetra-O-benzyl-D-glucopyranose* (**2**) dissolved in 8.0 ml of anhydrous CH_2Cl_2 was stirred with 460 mg of molecular sieves (powder 4 Å) for 15 min under nitrogen. To this solution 460 mg (2.1 mmol) of PCC was added portionwise and the dark brown solution was allowed to stir at r.t. for additional 1 h. The solution was diluted with Et_2O/hexane mixture (14:7 v/v) and filtered through 2 g of silica gel. The residue was further washed with the same mixture twice. The colorless filtrate was evaporated till dryness to furnish 240 mg (97%, colorless oil) of crude lactone which was pure enough to the next step. A purer sample was obtained by column chromatography using toluene/EtOAc 9:1, R_f 0.4. The following data were recorded: ^{1}H NMR (400 MHz): 7.29–7.08 (m, 20H, arom), 4.89 (d, J = 11.2 Hz, A_1B_1, PhC$\underline{H}_2$), 4.64 (d, J = 10.7 Hz, 1H, A_2B_2, PhC$\underline{H}_2$), 4.61 (d, J = 10.7 Hz, $A_{2'}B_{2'}$, 1H, PhC$\underline{H}_2$), 4.54 (d, J = 11.2 Hz, 1H, $A_{1'}B_{1'}$, PhC$\underline{H}_2$), 4.49 (d, J = 11.9 Hz, 1H, A_3B_3, PhC$\underline{H}_2$), 4.45–4.40 (m, 2H, PhC$\underline{H}_2$), 4.44 (d, J = 6.6 Hz, 1H, H-2), 4.37 (d, J = 11.9 Hz, 1H, $A_{3'}B_{3'}$, PhC$\underline{H}_2$), 4.03 (d, J = 6.3, H-6), 3.88–3.80 (m, 2H, H-4, H-5), 3.64–3.56 (m, 2H, H-3, H-6). ^{13}C NMR (100 MHz): 169.1 (CO), 80.9, 78.1, 76.0 (C-3, C-4, C-5), 73.8, 73.6, 73.6, 73.5 (4× Ph$\underline{C}H_2$), 68.2 (C-6).

3-(1′-Hydroxy-2′,3′,4′,6′-tetra-*O*-benzyl-β-D-glucopyranosyl)prop-1-ene (**8**): 90 mg (0.17 mmol) of lactone (**8**) dissolved in 5.0 ml of dry Et_2O was cooled to –78°C in a two necked round flask under nitrogen atmosphere. To this stirred solution 130 µl (0.2 mmol) of allyl magnesium bromide was added dropwise through the septum by injection. The mixture was allowed to stir for 12 h, then it was quenched with sat. NH_4Cl solution (10 ml) and stirring was continued for 1 h at r.t.. The solution was diluted with CH_2Cl_2 (30 ml) and the organic phase was separated and the aqueous phase was extracted twice with CH_2Cl_2 (2 × 10 ml). The combined extracts were dried ($MgSO_4$) and evaporated till dryness. The crude product was purified on column chromatography using toluene/EtOAc (9:1) mixture to furnish 30 mg (30%) starting material and 60 mg (62%) of the desired product. The following spectral data were recorded: ^{1}H NMR (400 MHz): 7.27–7.11 (m, 20H, arom), 5.82–5.78 (m, 1H, H-2), 5.12 (d, J = 10.3 Hz, 1H, H-1, *cis*-H), 5.06 (d, J = 17.3 Hz, 1H, H-1, *trans*-H), 4.86 (d, J = 10.9 Hz, 1H, A_1B_1, PhC$\underline{H}_2$), 4.84 (d, J = 10.9 Hz, 1H, $A_{1'}B_{1'}$, PhC$\underline{H}_2$), 4.80 (d, J = 10.8 Hz, 1H, A_2B_2, PhC$\underline{H}_2$), 4.76 (d, J = 10.8 Hz, 1H, $A_{2'}B_{2'}$, PhC$\underline{H}_2$), 4.62 (d, J = 11.2 Hz, 1H, A_3B_3, PhC$\underline{H}_2$), 4.55 (d, J = 12.3 Hz, 1H, A_4B_4, PhC$\underline{H}_2$), 4.53 (d, J = 11.2, 1H, $A_{3'}B_{3'}$, PhC$\underline{H}_2$), 4.46 (d, J = 12.3 Hz, 1H, $A_{4'}B_{4'}$, PhC$\underline{H}_2$), 3.95 (t, J = 9.3, 1H, H-3′), 3.9–3.8 (m, 1H,

H-6′), 3.68 (dd, J = 10.9, 3.9 Hz, 1H, H-5′), 3.59 (2d, J = 9.7, 9.3 Hz, 1H, H-4′), 3.37 (d, J = 9.5 Hz, 1H, H-2′), 2.71–2.36 (m, 2H, CH_2). ^{13}C NMR (100 MHz): 132.1 (C-2), 120.1 (C-1), 97.6 (C-4), 83.7, 81.5, 78.4, 71.6 (C-5, C-6, C-7, C-8), 75.6, 75.3, 74.8, 73.3 (4× Ph<u>C</u>H$_2$), 68.7 (C-9), 42.8 (C-3).

3-(2′,3′,4′,6′-Tetra-*O*-benzyl-β-D-glucopyranosyl)prop-1-ene (**10**) [15]: 60 μl (0.516 mmol) of Et_3SiH was treated with 5 mg $PdCl_2$ and 63 mg (0.189 mmol) of the carbon tetrabromide. After termination of the exothermic reaction, 100 mg (0.172 mmol) of glycoside **9** dissolved in 4 ml of CH_2Cl_2 was added dropwise. After 1 h stirring at r.t., the reaction mixture was evaporated till dryness to furnish the titled compound **10** in almost quantitative yield as a mixture of anomers (1:3 α:β) and high purity. The following spectral data are recorded: ^{1}H NMR (400 MHz): 7.45–7.11 (m, 20H, arom), 5.82 (dd, J_{cis} = 10.0 Hz, J_{trans} = 17.3 Hz, 1H, H-2), 5.18 (d, J_{cis} = 10.0 Hz, 1H, H-1), 5.09 (d, J_{trans} = 17.3 Hz, 1H, H-1), 4.87 (d, J_{A1B1} = 10.9 Hz, 1H, PhC<u>H</u>$_2$), 4.84 (d, $J_{A1'B1'}$ = 10.9 Hz, 1H, PhC<u>H</u>$_2$), 4.80 (d, J_{A2B2} = 10.9 Hz, 1H, PhC<u>H</u>$_2$), 4.76 (d, $J_{A2'B2'}$ = 10.9 Hz, 1H, PhC<u>H</u>$_2$), 4.63 (d, J_{A3B3} = 10.7 Hz, 1H, PhC<u>H</u>$_2$), 4.54 (d, $J_{A3'B3'}$ = 10.7 Hz, 1H, PhC<u>H</u>$_2$), 4.50 (d, J_{A4B4} = 12.2 Hz, 1H, PhC<u>H</u>$_2$), 4.46 (d, $J_{A4'B4'}$ = 10.9 Hz, 1H, PhC<u>H</u>$_2$), 3.95 (t, $J_{4',5'} = J_{4',3'}$ = 9.3 Hz, H-4′), 3.92 (dd, $J_{5',4'}$ = 9.3, $J_{5,6}$ = 8.0 Hz, 1H, H-5′), 3.59 (dd, J = 10.3, 9H, 1H), 3.54 (dd, J = 6.1, 3.2 Hz, 1H), 3.37 (d, J = 9.5 Hz, 1H), 2.36 (m, 3H). ^{13}C NMR (100 MHz): 132.1 (C-2), 120.1 (C-1), 83.7, 81.5, 79.6, 78.4 (Ph<u>C</u>H$_2$), 75.6, 75.3, 74.9, 73.3, 71.6 (C-1′→ C-5′), 68.7 (C-6′), 42.8 (C-3).

1-(4′-Bromobutyl)-2,3,4,6-tetra-*O*-benzyl-β-D-glucopyranoside (**12**): In a dry three-necked flask (5 ml) and under oxygen free N_2 atmosphere, 25 μl (0.215 mmol) of Et_3SiH was placed and treated with 15 mg of $PdCl_2$. After termination of the exothermic reaction 75 mg of CBr_4 (0.22 mmol) and 100 mg (0.19 mmol) of **1** dissolved in 5 ml of THF were subsequently added. The progress of the reaction was monitored by TLC that showed the formation of pure single compound after 48 hours. The catalyst was filtered and washed with 5 ml of THF and the combined filtrate was evaporated till dryness to afford 130 mg of the titled compound as colorless oil. The following spectral data were recorded: ^{1}H NMR (400 MHz): 7.36–7.12 (m, 20H, arom), 4.97 (d, $J_{1,2}$ = 10.7 Hz, 1H, H-1), 4.89 (d, J_{A1B1} = 12.9 Hz, 1H, PhC<u>H</u>$_2$), 4.81 (d, J_{A2B2} = 11.9 Hz, 1H, PhC<u>H</u>$_2$), 4.72 (d, $J_{A1'B1'}$ = 12.9 Hz, 1H, PhC<u>H</u>$_2$), 4.69 (d, J_{A3B3} = 11.5 Hz, 1H, PhC<u>H</u>$_2$), 4.67 (d, $J_{A2'B2'}$ = 11.9 Hz, 1H, PhC<u>H</u>$_2$), 4.57 (d, J_{A4B4} = 12.2 Hz, 1H, PhC<u>H</u>$_2$), 4.53 (d, $J_{A4'B4'}$ = 12.2 Hz, 1H, PhC<u>H</u>$_2$), 4.45 (d, $J_{A3'B3'}$ = 11.5 Hz, 1H, PhC<u>H</u>$_2$), 4.01 (dd, $J_{4,3}$ = 9.3, $J_{4,5}$ = 9.0 Hz, 1H, H-4), 3.77 (dt, $J_{5,4}$ = 9.0, $J_{5,6}$ = 6.8 Hz, 1H, H-5), 3.67 (dd, $J_{2,1}$ = 10.7, $J_{2,3}$ = 5.1 Hz, 1H, H-2), 3.61 (dd, $J_{3,4}$ = 9.3, $J_{3,2}$ = 5.1 Hz, 1H, H-3), 3.58–3.55 (m, 2H, 2× H-6), 3.40 (t, J = 6.5 Hz, 2H, H-4′), 2.45 (t, J = 7.5 Hz, 2H, 2× H-1′), 1.46–1.18 (m, 2H, 2× H-3′), 0.93–0.91 (m, 2H, 2× H-2′). ^{13}C NMR (100 MHz, $CDCl_3$): 95.6 (C-1), 82.1 (C-3), 79.9 (C-5), 75.7 (C-2), 73.5 (C-4), 70.4 (C-6), 68.4 (C-1′), 34.2, 28.3, 28.1 (C-2′, C-3′, C-4′).

Methyl 4-(2′,3′,4′,6′-tetra-*O*-acetyl-α-D-glucopyranosyl)-2-butenoate (**24**): 250 mg (1.4 mmol) of methyl 4-bromocrotonate dissolved in dry THF (10 ml) was treated with 800 μl of *t*-BuLi (2.0 mmol, 2.5 M in hexane) followed after 15 min. with 275 mg (2 mmol) of $ZnCl_2$. After approximately 10 min. glucopyranosyl bromide (**16**) (822 mg, 2.0 mmol), dissolved in THF (3 ml), was slowly added followed by addition of 30 mg (0.03 mmol) of $Pd(PPh_3)_4$. The reaction was left to stir to reach room temperature overnight (16 h) and the solvent was removed under vacuum. The residue was subjected to chromatography (EtOAc: hexane 1:4, R_f 0.31) to furnish 600 mg (69%) of **24** as a mixture of 2:1 β/α anomers. ^{1}H NMR (400 MHz): 5.93 (d, J = 12.1 Hz, 1H), 5.89 (dd, J = 12.1, 3.1 Hz, 1H), 5.32–5.22 (m, 2H), 5.09 (dm, J = 9.8 Hz, 1H, H-5), 4.27 (dd, J = 11.4, 11.4 Hz, H-3), 4.21–4.19 (m, 1H, H-1, β-anomer), 4.19 (dd, J = 11.4, 9.8 Hz, 1H, H-4), 4.09–4.07 (m, 1H, H-2), 4.04 (dt, J = 5.0, 2.1 Hz, H-1, α-anomer), 3.74 (s, 3H, CH_3), 2.14 (s, 3H, CH_3), 2.13 (s, 3H, CH_3), 2.11 (s, 3H, CH_3), 2.03–2.01 (m, 2H, CH_2), 2.02 (s, 3H, CH_3). ^{13}C NMR (100 MHz): 170.5, 170.1, 169.7 (4× CO), 134.5, 133.1 (olefinic C's), 90.5 (C-1), 70.5, 68.1, 67.1, 65.5 (C-2, C-3, C-4 and C-5), 62.1 (C-6), 51.7 (OCH_3), 20.6 (OCH_3), 14.1 (CH_2). EI-MS: 331, 242, 169, 158, 145, 140, 115, 103, 98, 86, 84, 73, 43(100). Anal. Cald. for $C_{19}H_{26}O_{11}\cdot H_2O$: C, 50.89; H, 6.25. Found: C, 51.07; H, 6.25.

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