Available online at www.sciencedirect.com
ScienceDirect
Carbohydrate Research 342 (2007) 2546–2556
Carbohydrate RESEARCH

Regioselective synthesis of $1^{I},1^{II},5^{I},5^{II},6^{I},6^{I},6^{II},6^{II}$-$^{2}H_{8}$-cellobiose

Fuyi Zhang and Andrea Vasella*

Laboratorium für Organische Chemie, HCI H 317, ETH Zürich, CH-8093 Zürich, Switzerland

Received 27 June 2007; received in revised form 13 July 2007; accepted 23 July 2007
Available online 2 August 2007

Abstract—Partially deuteriated 1,5,6,6-$^{2}H_{4}$-D-glucose and $1^{I},1^{II},5^{I},5^{II},6^{I},6^{I},6^{II},6^{II}$-$^{2}H_{8}$-D-cellobiose were synthesized in high yields and on a large scale from D-glucose. ^{2}H enrichment at C-5 and C-6 of each glucopyranosyl unit in excess of 85% and 90%, respectively, was realized by ^{1}H–^{2}H exchange in $^{2}H_{2}O$ containing deuteriated Raney Ni. Nucleophilic addition of $LiAlD_{4}$ to 5,6,6-$^{2}H_{3}$-2,3,4,6-tetra-*O*-benzyl-D-gluconolactone led to a 98% ^{2}H enrichment at C-1. Deuteriated cellobiose is of interest as building block for the synthesis of a model compound of cellulose I.

Keywords: 1,5,6,6-$^{2}H_{4}$-D-Glucose; $1^{I},1^{II},5^{I},5^{II},6^{I},6^{I},6^{II},6^{II}$-$^{2}H_{8}$-cellobiose; ^{2}H enrichment; Gluconolactone; Glycosidation; Trichloroacetimidate; Cellulose I

1. Introduction

The structure of cellulose polymorphs was studied by a variety of methods,[1–3] and the solid state structure of cellulose I_{α} and I_{β} and particularly their characteristic H-bond patterns were extensively investigated.[1,2,4–6] The solid state structure of cellotriose and cellotetraose,[7,8] derived from a single crystal X-ray analysis, is sufficiently similar to the one of cellulose II to consider cellotetraose a valuable model of cellulose II.[9–11] We started our search for a similar model compound for cellulose I by synthesizing glycosylated naphthalene-1,8-diethanol-linked cellooligosaccharides.[12] However, the solid state CP/MAS ^{13}C NMR spectrum of the naphthalene-1,8-diethyl bis[cellooctaoside] resembles strongly the spectrum of cellulose II, rather than the one of cellulose I.[12] We assumed that the smaller maximum phase shift characterizing the staggering of the two cellodextrin chains of this model compound (ca. 1.5 Å) as compared to the one for the unit cell of cellulose I (2.7 Å) is responsible for the antiparallel packing of the cellodextrin chains evidenced by the CP/MAS ^{13}C NMR spectrum of the naphthalene-1,8-diethyl bis[cellooctaoside]. We, therefore, designed and synthesized model compounds that implement the correct phase shift by introducing ethynylene and buta-1,3-diynylene linkers between glucopyranosyl, cellobiosyl, cellotetraosyl, and cellooctaosyl moieties and an 1,8-disubstituted anthraquinonyl template.[13] These models are termed T-*n* and T-*n*-*n* (*n* expressing the number of glucosyl units of the cellodextrin chain). The unsymmetric bis-C-glucoside is devoid of interchain H-bonds,[14] suggesting that templated cellodextrins of this type could be useful mimics of cellulose I_{β}. These unsymmetric and symmetric templated cellodextrins are indeed models of cellulose I and II, respectively, with the well-resolved solid-state CP/MAS ^{13}C NMR spectrum of T-8-8 (Chart 1) resembling that of cellulose I_{β}. In contradistinction, the solid-state ^{13}C NMR spectrum of T-8 shows a striking similarity to that of cellulose II, characterizing the cellooctaoside T-8 as a close mimic of cellulose II in the interior of the crystallite. Also the powder-diffraction spectra of T-8-8 and T-8 are very similar to those of cellulose I and II, respectively, confirming that T-8-8 is an oligomeric mimic of cellulose I, and T-8 of cellulose II.[13]

To further analyze the solid state CP/MAS ^{13}C NMR spectrum of T-8-8, we planned to synthesize T-8-8 with

* Corresponding author. Tel.: +41 44 632 51 30; fax: +41 44 632 11 36; e-mail: vasella@org.chem.ethz.ch

0008-6215/$ - see front matter © 2007 Elsevier Ltd. All rights reserved.
doi:10.1016/j.carres.2007.07.017

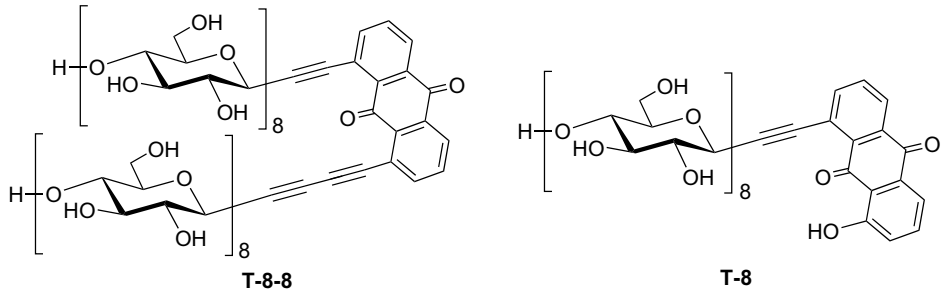


Chart 1. The template-bound single- and double-chained cellodextrins.

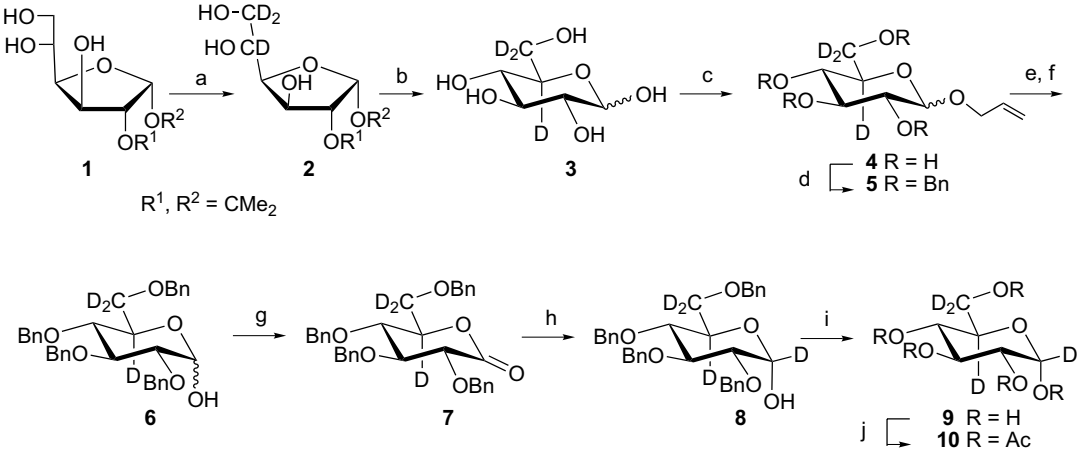
the cellooctaosyl buta-1,3-diyne chain substituted with deuterium at C-1, C-5 and C-6 of each glucose unit. For this, we require fair amounts of $1^{I},1^{II}$, $5^{I},5^{II},6^{I},6^{I},6^{II},6^{II}$-$^{2}H_{8}$-cellobiose. We report the synthesis of this intermediate.

2. Results and discussion

2.1. Synthesis of 1,5,6,6-$^{2}H_{4}$-D-glucose

We planned to introduce deuterium at C-5 and C-6 by following the procedure of Koch and Stuart.[15–17] According to this procedure, multiply deuteriated unprotected glycosides are obtained by proton–deuterium exchange at hydroxymethyl and hydroxymethylene groups upon heating the corresponding alcohols in hot $^{2}H_{2}O$ in the presence of deuteriated Raney Ni. Deuteriation of C-1 was effected by reduction of protected D-glucono-1,5-lactone with deuteriated reagents, such as BD_{3},[17] $LiAlD_{4}$ and $BF_{3}{\cdot}OEt_{2}$,[18,19] or by reduction of aldononitriles in $^{2}H_{2}O$ with $Pd/BaSO_{4}$ and $^{2}H_{2}$.[20] As the synthesis of deuteriated cellobiose and cellooctaosyl-1,3-butadiyne requires sizeable amounts of deuteriated glucose, we planned to develop a large scale economic synthesis of 1,5,6,6-$^{2}H_{4}$-D-glucose (Scheme 1), optimizing the conditions using non-deuteriated chemicals.

We began the synthesis by treating the known isopropylidene glucose **1**[21] with $^{2}H_{2}O$ to deuteriate the hydroxy groups. H-3, H-5, and H-6 were then exchanged with deuterium by boiling the O-deuteriated **1** in $^{2}H_{2}O$ in the presence of deuteriated Raney Ni.[17] No deuteriation of C-3 (or any other ring carbon atom) was observed (the expected deuteriated allofuranose was not isolated). To drive the exchange as far as possible we used a large amount of $^{2}H_{2}O$. This procedure was economical on a scale of a few grams only. We modified it for a 200 g scale by repeating the exchange three times. After each round of exchange we removed Raney Ni by filtration, recuperated excess $^{2}H_{2}O$ and $^{1}H^{2}HO$, and repeated the exchange using recycled deuteriated Raney Ni and fresh $^{2}H_{2}O$. The mixture of $^{1}H^{2}HO$ and $^{2}H_{2}O$ recuperated after each round of exchange was used for the preceding round of equilibration of a new batch of O-deuteriated



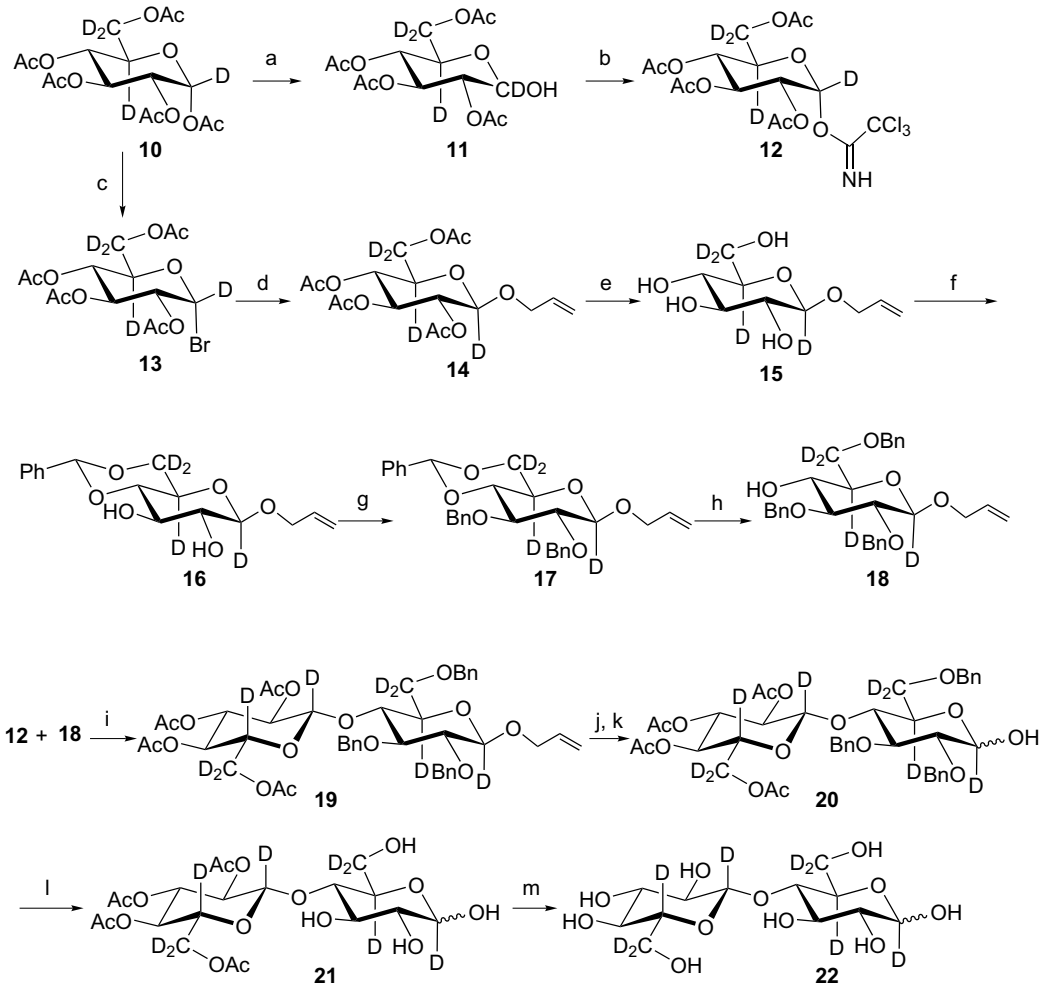
Scheme 1. Reagents and conditions: (a) Raney Ni, $D_{2}O$, reflux, 60%; (b) 0.5% $H_{2}SO_{4}$, 90 °C, 3.5 h, 89%; (c) 0.3 equiv $BF_{3}{\cdot}OEt_{2}$, allyl alcohol, reflux, 8 h; (d) 6 equiv BnBr, 7 equiv NaH, DMF, 0 °C to rt, 16 h, 75%; (e) 1 equiv KO^{t}Bu, DMF, 70 °C, 15 min; (f) 0.1 N HCl, reflux, 1 h, 80%; (g) $Ac_{2}O$, $Me_{2}SO$, rt, overnight, 97%; (h) 1.3 equiv $LiAlD_{4}$, 4.4 equiv $BF_{3}{\cdot}OEt_{2}$, $Et_{2}O$, −10 °C, 83%; (i) 10% Pd/C, H_{2} (6 bar), MeOH, EtOAc, AcOH 96%; (j) Pyridine, $Ac_{2}O$, 0 °C to rt, overnight, 98%.

1. Recrystallization of the crude product in CH_3OH and AcOEt yielded 60% of deuteriated isopropylidene glucose **2**. Its ^1H NMR spectrum shows that around 85% of H-5 and 90% of H-6 were replaced by deuterium. As expected, the proton-decoupled ^{13}C NMR spectrum of **2** was devoid of signals of C-5 and C-6. Hydrolysis of **2** with dilute H_2SO_4 at 90 °C yielded 89% of 5,6,6-trideuteriated glucose **3** ($\alpha/\beta = 45:55$).[22] Fischer glycosylation of deuteriated glucose **3** and allyl alcohol[23] to give an anomeric mixture of trideuteriated allyl glucopyranosides **4** was incomplete on a scale of 50 g, leading to an equilibrium mixture of **3** and **4** containing ca. 20% of **3**. Increasing the amount of allyl alcohol proved beneficial. Boiling a 30:1 mixture of allyl alcohol and **3** for 8 h in the presence of $BF_3{\cdot}OEt_2$ led to almost complete conversion to **4** ($\alpha/\beta = 6:1$). Excess allyl alcohol was recuperated, dried with CaH_2, and recycled. Benzylation[24,25] of crude glucosides **4** provided benzylated allyl glucopyranosides **5** ($\alpha/\beta = 5:1$) in an overall yield of 76% after flash chromatography. Allyl glucosides **5** were isomerized by treatment with KO^{t}Bu in DMF[26] and the resulting prop-1-enyl glucosides were hydrolyzed with 0.1 N of HCl in acetone to provide 80% of crystalline tetra-*O*-benzyl-α-D-glucose **6** on a 99 g scale. Its melting point (145.8–146.3 °C) and specific rotation (+18.3) are slightly lower than those of the corresponding non-deuteriated compound (151–152 °C and +21.7).[27] As expected, the H-5 and H-6 signals in the ^1H NMR spectrum of **6** had almost disappeared, H-4 resonated at 3.62 ppm as a doublet with a coupling constant of 9.0 Hz, and the C-5 and C-6 signals were no longer detected. Swern oxidation of **6**[28] led in a yield of 97% to crude lactone **7**. Reduction of crude **7** with 1.3 equiv of $LiAlD_4$ (98% deuteriated) in the presence of 1.3 equiv of $BF_3{\cdot}OEt_2$ in Et_2O led to little conversion to deuteriated hemiacetal **8**, while an excellent yield of **8** resulted by using up to 4.4 equiv of $BF_3{\cdot}OEt_2$. According to its melting point, specific rotation, and chemical shift of H-3 (3.96 ppm), **8** was obtained as the pure α-D-anomer. Its H-2 signal appeared as a doublet at 3.58 ppm with a coupling constant of 9.6 Hz. The signal of C-1 disappeared from the ^{13}C NMR-spectrum. Hydrogenolytic debenzylation of **8**, catalyzed by 10% Pd/C in a mixture of MeOH and AcOH, yielded 96% of deuteriated D-glucose **9** with a degree of deuteriation at C(1) in excess of 98%. Crystallization gave a pure sample as a mixture of anomers ($\alpha/\beta = 11:9$), while the crude product was mostly the α-D-anomer, as evidenced by its acetylation with acetic anhydride/pyridine[29] to provide the α-D-pentaacetate **10** in a yield of 98% on a 50 g scale.

2.2. Synthesis of $1^{I},1^{II},5^{I},5^{II},6^{I},6^{II},6^{I},6^{II}$-$^2H_8$-cellobiose

For the synthesis of the deuteriated cellobiose we required deuteriated trichloroacetimidate **12** as glycosyl donor and the selectively O-benzylated, tetradeuteriated glucopyranoside **18** as acceptor (Scheme 2). Both were prepared from 1,5,6,6-$^2H_4$-α-D-glucose pentaacetate **10**. To obtain trichloroacetimidate **12** we first examined the selective 1-O-deacetylation of crystalline **10**, treating it with benzylamine,[30] hydrazine acetate,[31] $(NH_4)_2CO_3$,[32] and ammonia.[33] Complete conversion occurred in an ammonia soln at 0 °C on a milligram scale, but proceeded slowly on a multigram scale, leading to a mixture. The procedure was improved by bubbling ammonia gas through the stirred reaction mixture at −10 °C. Under these conditions, 1-O-deacetylation occurred cleanly on a 40 g scale. Crude tetraacetate **11** ($\alpha/\beta = 7:3$) was treated with trichloroacetonitrile in the presence of DBU. Purification of the product by flash chromatography gave deuteriated α-D-trichloroacetimidate **12** in an overall yield of 82% and on a scale of about 20 g from crude **10**.

Acceptor **18** was synthesized on a gram scale from the crude pentaacetate **10** (Scheme 2). Bromination of **10** with HBr in AcOH[34] gave **13** in a yield of 85% on a scale of 30 g and in a yield of 95% on a scale of 60 g. Glucosidation of allyl alcohol[35] by **13** in the presence of $Hg(CN)_2$ occurred very cleanly on a scale of 50 g, yielding 85% of pure, crystalline β-D-glucopyranoside **14**. Zemplen deacetylation of **14** generated the tetradeuteriated allyl β-D-glucoside **15** in a high yield. The crude product was benzylidenated with benzaldehyde dimethyl acetal in the presence of *p*-toluenesulfonic acid. Performing this acetalization in acetonitrile rather than in DMF,[36] or in 1,4-dioxane[37] led to a much cleaner transformation, resulting in 90% of benzylidene acetal **16**. Benzylation of crude **16** with benzyl bromide according to the procedure of Ogawa et al.[36] yielded 82% of the fully protected benzylated acetal **17**. Purification of the acidic sensitive **17** by column chromatography on silica gel was improved by adding 1% of triethylamine to the eluent. The 1,3-dioxane ring was regioselectively cleaved by treating **17** with Et_3SiH and $BF_3{\cdot}OEt_2$[38] to give a mixture that was separated by flash chromatography to yield 70% of the desired isomer **18** and 16% of starting material. Somewhat lower yields of **18** (after purification by flash chromatography) resulted by treating **17** with either $BH_3{\cdot}Me_2NH/BF_3{\cdot}OEt_2$[39] (60%), or with $NaBH_3(CN)$ and $HCl{\cdot}OEt_2$[38] (63% of **18** besides 15% of starting material). The concentration of HCl in the reduction with $NaBH_3(CN)$ had a strong effect on the conversion. The conditions chosen involved bubbling HCl gas through a stirred soln of **17** in THF at 0 °C. The reduction was slow for the first 20 min and became faster once the soln was saturated by HCl, the starting material disappearing within 30 min. The crude product was purified by flash chromatography to yield 73% of the benzylated allyl glycoside **18** on a scale of 3.7 g. The regioisomeric monoalcohol was not obtained.



Scheme 2. Reagents and conditions: (a) NH_3 (g), THF, MeOH, −10 °C, 2 h; (b) CCl_3CN, DBU, 0 °C, 2 h, 82%; (c) 33% HBr in AcOH; CH_2Cl_2, 0 °C, 3 h, 95%; (d) $Hg(CN)_2$, allyl alcohol, rt, overnight, 85%; (e) MeONa, MeOH; (f) $PhCH(OCH_3)_2$, TsOH, CH_3CN, 80 °C, 1 h, 90%; (g) BnBr, NaH, DMF, 0 °C to rt, 8 h, 82%; (h) $NaB(CN)H_3$, THF, HCl (g), 0 °C, 50 min, 73%; (i) TMSOTf, CH_2Cl_2, −50 °C, 2 h, 88%; (j) $[Ir(MePh_2P)_2(C_8H_{12})]PF_6$, H_2, THF, rt, 1 h; (k) I_2, H_2O, rt, 1 h, 83%; (l) 20% $Pd(OH)_2$/C, H_2 (6 bar), MeOH, rt, 3 days, 90%; (m) MeONa, MeOH, 91%.

Glycosidation of **18** with 1.2 equiv of trichloroacetimidate **12** in CH_2Cl_2 at −50 °C gave the desired cellobioside **19**, but as its chromatographic separation from excess **12** was inconvenient it proved advantageous to only use 0.9 equiv of **12**. Trichloroacetimidate **12** was consumed, and excess **18** was readily separated from **19** that was obtained in a yield of 88% on a scale of 13 g. Isomerization to the corresponding prop-1-enyl glycosides according to the procedure of Baudry et al.[40] and hydrolysis (I_2 in THF–water) led to the protected cellobiose **20** in a yield of 83% on a scale of 2.36 g. Hydrogenolytic debenzylation of **20** with H_2 under a pressure of 6 bar and in the presence of 20% $Pd(OH)_2$/C yielded 90% of tetraacetate **21**. It was deacetylated with MeONa in MeOH to the desired $1^I,1^{II},5^I,5^{II},6^I,6^{II},6^I$, 6^{II}-$^2H_8$-cellobiose **22** (α/β = 7:43) that was obtained in a yield of 91% on a scale of 0.61 g. Its ^{13}C NMR spectrum differs from the one of non-deuteriated cellobiose by the absence of the C-1^I, C-1^{II}, C-5^I, C-5^{II}, C-6^I, and C-6^{II} signals.

3. Experimental

3.1. General methods

Sixty percent NaH in oil was washed with dry hexane and dried in high vacuum. Melting points are uncorrected. TLC was performed on silica gel (60F-254 E. Merck), detected by heating with mostain (400 mL of 10% H_2SO_4 soln, 20 g of $(NH_4)_6Mo_7O_{24}{\cdot}6H_2O$, 0.4 g of $Ce(SO_4)_2$). Silica gel (0.063–0.200 mm, E. Merck) was used for flash column chromatography. IR spectra were recorded with a Perkin–Elmer FT-IR-spectrometer. ^1H and ^{13}C NMR spectra chemical shifts are given in ppm and coupling constants (J) in Hertz. The signals were assigned by homo- and heteronuclear two-dimensional techniques. Optical rotations were measured on soln with JASCO P-1030 polarimeter. HRMALDIMS was measured in a gentisic acid (2,5-dihydroxybenzoic acid, DHB) matrix.

3.2. 5,6,6-$^2H_3$-1,2-*O*-Isopropylidene-α-D-glucofuranose (2)

A suspension of 1,2-*O*-isopropylidene-α-D-glucofuranose (**1**, 200 g, 0.91 mol) was heated in D_2O (200 mL) to 85 °C until formation of a clear soln. After coevaporation, a soln of the residue in D_2O (240 mL) was heated with Raney nickel (120 mL),[17] and boiled under reflux. Nickel was filtered off, and washed with D_2O. The combined filtrate and washings were taken to dryness to give a solid residue. The deuteriation was repeated three times. ^1H NMR spectroscopy indicated that more than 85% of H-5 and 90% of H-6 were exchanged. The crude product was recrystallized in MeOH–EtOAc (6:1) to afford colorless crystals of **2** (122.8 g, 60%): mp 156–159 °C; R_f 0.65 (1:1 EtOAc–MeOH); $[\alpha]_D^{25}$ −12.1 (*c* 1.0, H_2O); IR (ATR): 3425w, 2978w, 2916w, 2535m, 2465m, 2109w, 1463w, 1388m, 1378m, 1318w, 1289w, 1264m, 1214m, 1161m, 1119m, 1081s, 1056s, 1022s, 961s, 941s, 907w, 884w, 863w, 850s, 804w, 775m, 756m, 661w, 649w; ^1H NMR (300 MHz, D_2O): δ 6.02 (d, 1H, $J_{1,2}$ 3.6 Hz, H-1), 4.70 (d, 1H, $J_{2,1}$ 3.6 Hz, H-2), 4.32 (d, 1H, $J_{3,4}$ 2.4 Hz, H-3), 4.09 (d, 1H, $J_{4,3}$ 2.4 Hz, H-4), 1.52, 1.36 (2s, 6H, Me_2C); ^{13}C NMR (75 MHz, D_2O):[17,22] δ 112.38 (Me_2C), 104.42 (C-1), 84.15 (C-2), 79.43 (C-4), 73.33 (C-3), 25.39, 24.96 (Me_2C); HRMALDIMS (*m*/*z*): $[M+Na]^+$ calcd for $C_9H_{13}D_3NaO_6^+$, 246.1033; found, 246.1032. Anal. Calcd for $C_9H_{13.37}D_{2.63}O_6$: C, 48.50; H, 7.32. Found: C, 48.54; H, 7.33.

3.3. 5,6,6-$^2H_3$-D-Glucopyranose (3)

A soln of **2** (100 g, 448 mmol) in water (1000 mL) and concd H_2SO_4 (2.5 mL, 46.6 mmol) was heated at 90 °C for 2 h, cooled to room temperature, and neutralized with Amberlite IR 93 resin (OH^- form). The mixture was filtered, and the residue washed with water. After evaporation of the combined filtrate and washings, the residue was dissolved in water (30 mL), and treated with 2-propanol (20 mL), leading to a precipitate. The solid was filtered off, washed with 2-propanol, and dried to give **3** as a colorless solid (73.0 g, 89%, α/β = 9:11): mp 141.4–142.0 °C; $[\alpha]_D^{25}$ +49.5 (*c* 1.0, water). IR (ATR): 3244m, 2946w, 2912w, 2217w, 2113w, 1441w, 1374w, 1286w, 1210w, 1138m, 1150m, 1118s, 1092m, 1052s, 1026s, 1008s, 979s, 936m, 913w, 896m, 765w, 734w, 626w; ^1H NMR (300 MHz, D_2O):[22] δ 5.22 (d, 0.45H, $J_{1\alpha,2\alpha}$ 3.9 Hz, H-1α), 4.63 (d, 0.55H, $J_{1\beta,2\beta}$ 8.1 Hz, H-1β), 3.71 (t, 0.45H, $J_{3\alpha,2\alpha} = J_{3\alpha,4\alpha}$ 9.3 Hz, H-3α), 3.52 (dd, 0.45H, $J_{2\alpha,3\alpha}$ 9.6, $J_{2\alpha,1\alpha}$ 3.9 Hz, H-2α), 3.48 (t, 0.55H, $J_{3\beta,2\beta} = J_{3\beta,4\beta}$ 9.3 Hz, H-3β), 3.39 (d, 0.45H, $J_{4\alpha,3\alpha}$ 9.0 Hz, H-4α), 3.38 (d, 0.55H, $J_{4\beta,3\beta}$ 9.0 Hz, H-4β), 3.23 (dd, 0.55H, $J_{2\beta,3\beta}$ 9.0, $J_{2\beta,1\beta}$ 7.8 Hz, H-2β); ^{13}C NMR (75 MHz, D_2O): δ 95.70 (C-1β), 91.91 (C-1α), 75.60 (C-3β), 73.99 (C-2β), 72.62 (C-3α), 71.34 (C-2α), 69.43, 69.38 (C-4β, C-4α); ESIMS (*m*/*z*): $[M+Na]^+$ calcd for $C_6H_9D_3NaO_6^+$, 206.1; found, 206.2. Anal. Calcd for $C_6H_{9.37}D_{2.63}O_6$: C, 39.42; H, 6.71. Found: C, 39.26; H, 6.50.

3.4. Allyl 5,6,6-$^2H_3$-2,3,4,6-tetra-*O*-benzyl-D-glucopyranoside (5)

A suspension of **3** (50 g, 273 mmol) in anhyd allyl alcohol (1500 mL) was treated with $BF_3{\cdot}OEt_2$ (10 mL, 81.5 mmol), heated under reflux for 10 h, cooled to room temperature, and neutralized with Et_3N. Solvents were evaporated and the oily residue was dried in high vacuum. A soln of this residue in DMF (400 mL) was cooled to 0 °C, and treated dropwise with a suspension of NaH (76.5 g, 191.0 mmol) in dry DMF (400 mL). BnBr (163 mL, 136.2 mmol) was added dropwise for 1.5 h. The mixture was stirred at room temperature for 16 h, and poured onto ice. After extraction with Et_2O (4 × 200 mL), the combined organic layers were washed with brine, dried over Na_2SO_4, and evaporated. Flash chromatography (1:0→8:1 cyclohexane/EtOAc) gave **5** as a colorless syrup (120 g, 75.5%, α/β = 5:1): R_f 0.60 (5:1 cyclohexane/EtOAc); $[\alpha]_D^{25}$ +25.6 (*c* 1.0, $CHCl_3$); IR ($CHCl_3$): 3067w, 3033w, 3010m, 2928w, 2868w, 2189w, 2088w, 1951w, 1872w, 1807w, 1730w, 1603w, 1496w, 1454w, 1360w, 1221w, 1158m, 1069s, 1028s, 932w; ^1H NMR (500 MHz, $CDCl_3$):[24,25] δ 8.45–7.21 (m, 20H), 6.09–5.95 (m, 1H, C*H*=CH_2), 5.44–5.35 (m, 1H, CH=C*H*H), 5.29–5.25 (m, 1H, CH=CH*H*), 5.08–4.50 (m, 9H, 4 × PhC*H*$_2$, H-1α, H-1β), 4.48 (ddt, 0.2H, J_1 13.0, J_2 6.5, J_3 1.5 Hz, CH_2=CHC*H*H(β)), 4.24–4.18 (m, 1H, CH_2=CHCH*H*), 4.10–4.03 (m, 1.6H, CH_2=CHCH*H*(α), H-3α), 3.71–3.61 (m, 2H, H-4, H-3β, H-2α), 3.54 (t, 0.2H, $J_{2\beta,1\beta} = J_{2\beta,3\beta}$ 10.0 Hz, H-2β); ^{13}C NMR (75 MHz, $CDCl_3$): δ 138.82–138.08 (aromatic C), 134.02 (CH_2=*C*H(β)), 133.73 (CH_2=*C*H(α)), 128.33–127.46 (aromatic *C*H), 118.05 (*C*H_2=CH(α)), 117.13 (*C*H_2=CH(β)), 102.63 (1β), 95.67 (1α), 84.63 (3β), 82.22 (2β), 82.03 (3α), 79.86 (2α), 77.75 (4β), 77.60 (4α), 75.62 (PhCH_2(α)), 75.59 (PhCH_2(β)), 74.97 (PhCH_2(α), PhCH_2(β)), 74.89 (PhCH_2(β)), 74.79 (PhCH_2(β)), 73.33 (PhCH_2(α)), 73.11 (PhCH_2(α)), 70.21 (CH_2=CHCH_2(β)), 68.14 (CH_2=CHCH_2(α)); HRMALDIMS (*m*/*z*): $[M+Na]^+$ calcd for $C_{37}H_{37}D_3NaO_6^+$, 606.2911; found, 606.2894. Anal. Calcd for $C_{37}H_{37.37}D_{2.63}O_6$: C, 76.18; H, 6.94. Found: C, 76.08; H, 7.17.

3.5. 5,6,6-$^2H_3$-2,3,4,6-Tetra-*O*-benzyl-α-D-glucopyranose (6)

A soln of **5** (134 g, 229.5 mmol) in dry DMF (1300 mL) was treated with KO^{t}Bu (25.6 g, 229.5 mmol), and heated at 70 °C for 15 min. Solvents were evaporated at 50 °C under 15 mbar, the residue was poured onto

ice, and neutralized with HCl soln (6 N). The soln was extracted with Et_2O (5 × 150 mL), the combined organic layers were washed with brine, and evaporated to give a syrup (133 g) of crude prop-1-enyl glycosides. A soln of this crude in acetone (800 mL) was treated with 0.1 N HCl (100 mL, 10 mmol), heated under reflux for 1 h, and taken to dryness. A soln of the residue in EtOAc (400 mL) was washed with brine, dried with Na_2SO_4, and evaporated to yield crude **6** as a solid. Recrystallization in EtOAc and cyclohexane (5:1) afforded pure **6** (99.2 g, 80%): R_f 0.42 (2:1 cyclohexane/EtOAc); mp 145.8–146.3 °C; $[\alpha]_D^{25}$ +18.3 (*c* 1.0, $CHCl_3$); IR ($CHCl_3$): 3593w, 3067w, 3034w, 3009w, 2929w, 2866w, 2193w, 2083w, 1951w, 1875w, 1807w, 1604w, 1496w, 1454w, 1363w, 1213w, 1145m, 1028m, 912w, 849w, 695w, 613w; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.36–7.12 (m, 20H), 5.23 (dd, 1H, $J_{1,2}$ 3.3 Hz, $J_{1,OH}$ 2.7 Hz, H-1), 4.91 (d, B of AB, 1H, *J* 10.8 Hz, PhCH_B), 4.84 (d, A of AB, 1H, *J* 10.8 Hz, PhCH_A), 4.82 (d, 1H, *J* 10.8 Hz, PhC*H*), 4.78 (d, B′ of AB′, 1H, *J* 11.8 Hz, PhC$H_{B'}$), 4.69 (d, A′ of AB′, 1H, *J* 11.8 Hz, PhC$H_{A'}$), 4.60 (d, B″ of AB″, 1H, *J* 12.2 Hz, PhC$H_{B''}$), 4.48 (d, A″ of AB″, 1H, *J* 12.2 Hz, PhC$H_{A''}$), 4.49 (d, 1H, *J* 10.8 Hz, PhC*H*), 3.97 (t, 1H, $J_{3,2} = J_{3,4}$ 9.3 Hz, H-3), 3.62 (d, 1H, $J_{4,3}$ 9.0 Hz, H-4), 3.58 (dd, 1H, $J_{2,3}$ 9.3, $J_{2,1}$ 3.6 Hz, H-2), 2.90 (d, $J_{OH,1}$ 2.1 Hz, OH); ^{13}C NMR (75 MHz, $CDCl_3$): δ 138.64, 138.16, 137.81 (4 aromatic C), 128.50, 128.36, 128.05, 127.94, 127.85, 127.69, 127.62 (20 aromatic *C*H); 91.31 (C-1), 81.71 (C-3), 79.95 (C-2), 77.55 (C-4), 75.69, 75.00, 73.41, 73.26 (4 × Ph*C*H$_2$); HRMALDIMS (*m*/*z*): $[M+Na]^+$ calcd for $C_{34}H_{33}D_3NaO_6^+$, 566.2598; found, 566.2590. Anal. Calcd for $C_{34}H_{33.37}D_{2.63}O_6$: C, 75.17; H, 6.71. Found: C, 75.13; H, 6.64.

3.6. 5,6,6-^{2}H$_3$-2,3,4,6-Tetra-*O*-benzyl-D-gluconolactone (7)

A soln of **6** (100 g, 5.35 mol) in Me_2SO (380 mL) and Ac_2O (170 mL) was stirred at room temperature overnight and poured into cold water. The precipitate was filtered off, and the aqueous layer was extracted with Et_2O (4 × 100 mL). The combined organic layers and precipitate were washed with satd aq $NaHCO_3$ soln and brine, dried over Na_2SO_4, and evaporated. Drying of the residue under high vacuum gave crude **7** (96.6 g, 97%) as pale brownish syrup, which was used for the next step without further purification. A small sample was purified by flash chromatography (6:1 cyclohexane–EtOAc) to afford an analytical sample of **7**: R_f 0.55 (2:1 cyclohexane–EtOAc); $[\alpha]_D^{25}$ +76.1 (*c* 1.0, $CHCl_3$); IR ($CHCl_3$): 3067w, 3021s, 2869w, 2189w, 2089w, 1951w, 1754m, 1603w, 1497w, 1454w, 1364w, 1218w, 1158w, 1075m, 1028w, 912w, 834w, 685w, 605w; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.38–7.14 (m, 20H), 4.97 (d, 1H, *J* 11.4 Hz, PhC*H*), 4.73–4.43 (m, 7H, 7PhC*H*), 4.10 (d, 1H, $J_{2,3}$ 6.3 Hz, H-2), 3.94–3.86 (m, 2H, H-3, H-4); ^{13}C NMR (75 MHz, $CDCl_3$): δ 169.17 (C=O), 137.46, 137.36, 136.78 (4 aromatic C); 128.33, 128.00, 127.88, 127.71 (20 aromatic *C*H), 80.88 (C-3), 75.94 (C-4), 77.34 (C-2), 73.91, 73.71 (2C), 73.49 (4 × Ph*C*H$_2$); HRMALDIMS (*m*/*z*): $[M+Na]^+$ calcd for $C_{34}H_{31}D_3O_6^+$, 564.2441; found, 564.2426. Anal. Calcd for $C_{34}H_{31.37}D_{2.63}O_6$: C, 75.45; H, 6.36. Found: C, 75.16; H, 6.45.

3.7. 1,5,6,6-^{2}H$_4$-2,3,4,6-Tetra-*O*-benzyl-α-D-glucopyranose (8)

A suspension of $LiAlD_4$ (3.0 g, 71.6 mmol) in dry Et_2O (500 mL) at 0 °C was treated dropwise with a soln of **7** (30.0 g, 55.4 mmol) and $BF_3{\cdot}Et_2O$ (30 mL, 244.5 mmol) in dry Et_2O (500 mL), and stirred for 3 h. Excess $LiAlD_4$ was destroyed by dropwise addition of MeOH. The soln was washed with H_2O (3 × 30 mL), satd aq $NaHCO_3$, and brine, dried over Na_2SO_4, and evaporated to yield a colorless solid. Recrystallization in cyclohexane–EtOH (3:1) gave pure **8** (25.0 g, 83%): R_f 0.42 (4:1 cyclohexane–EtOAc); mp 153.6–153.9 °C; $[\alpha]_D^{25}$ +20.4 (*c* 1.0, $CHCl_3$); IR ($CHCl_3$): 3595w, 3067w, 3033w, 3010w, 2867w, 2192w, 2087w, 1949w, 1870w, 1809w, 1604w, 1496w, 1454w, 1360w, 1070s, 1028m, 911w, 780w, 681w, 609w; ^{1}H NMR (300 MHz, $CDCl_3$):[19] δ 7.32–7.13 (m, 20H), 4.95 (d, B of AB, 1H, *J* 10.6 Hz, PhCH_B), 4.84 (d, A of AB, 1H, *J* 10.6 Hz, PhCH_A), 4.82 (d, 1H, *J* 11.1 Hz, PhC*H*), 4.78 (d, B′ of AB′, 1H, *J* 11.7 Hz, PhC$H_{B'}$), 4.69 (d, A′ of AB′, 1H, *J* 11.7 Hz, PhC$H_{A'}$), 4.60 (d, B″ of AB″, 1H, *J* 12.2 Hz, PhC$H_{B''}$), 4.48 (d, A″ of AB″, 1H, *J* 12.2 Hz, PhC$H_{A''}$), 4.48 (d, 1H, *J* 10.8 Hz, PhC*H*), 3.96 (t, 1H, $J_{3,2} = J_{3,4}$ 9.3 Hz, H-3), 3.62 (d, 1H, $J_{4,3}$ 9.3 Hz, H-4), 3.58 (d, 1H, $J_{2,3}$ 9.3 Hz, H-2), 2.89 (br, OH); ^{13}C NMR (75 MHz, $CDCl_3$): δ 138.64, 138.15, 137.82 (4 aromatic C); 128.48–127.61 (20 aromatic C); 81.69 (C-3), 79.85 (C-2), 77.57 (C-4), 75.69, 74.98, 73.40, 73.22 (4 × Ph*C*H$_2$); HRMALDIMS (*m*/*z*): $[M+Na]^+$ calcd for $C_{34}H_{32}D_4NaO_6^+$, 567.2661; found, 567.2646. Anal. Calcd for $C_{34}H_{32.39}D_{3.61}O_6$: C, 75.03; H, 6.71. Found: C, 75.75, H, 7.05.

3.8. 1,5,6,6-^{2}H$_4$-D-Glucose (9)

A suspension of **8** (30 g, 55.1 mmol), 10% Pd/C (2.7 g) in 10:3:3 MeOH–EtOAc–HOAc (575 mL) was stirred under 6 bar of H_2 for 3 days, and filtered through Celite (washing with 1 L of MeOH). The combined filtrate and washings were evaporated and co-evaporated with toluene to give crude **9** (9.7 g, 96%,) as a white solid, which was used for the next step without further purification. Recrystallization of a small sample in water and 2-propanol (3:2) gave pure **9** ($\alpha/\beta = 11:9$): R_f 0.35 (2:1 MeOH/CH_2Cl_2); mp 145.2–146.1 °C; $[\alpha]_D^{\alpha}$ +91.5 (*c* 1.0, water); IR (ATR): 3242m, 2912w, 2215w, 2113w,

1416w, 1370w, 1278w, 1214m, 1166m, 1124s, 1085m, 1035s, 1009s, 979s, 960s, 929m, 884m, 872m, 751m, 716m, 615s; ^{1}H NMR (300 MHz, D_2O):[22] δ 3.69 (t, 0.55H, $J_{3\alpha,2\alpha} = J_{3\alpha,4\alpha}$ 9.0 Hz, H-3α), 3.52–3.36 (m, 2H, H-2α, H-3β, H-4), 3.22 (d, 0.45H, $J_{2\beta,3\beta}$ 9.0 Hz, H-2β); ^{13}C NMR (75 MHz, D_2O): δ 75.61 (C-3β), 73.93 (C-2β), 72.63 (C-3α), 71.26 (C-2α), 69.45 (C-4); ESIMS (*m*/*z*): $[M+Na]^+$ calcd for $C_6H_8D_4NaO_6^+$, 207.1; found, 207.3. Anal. Calcd for $C_6H_{8.26}D_{3.74}O_6$: C, 39.18; H, 6.71. Found: C, 38.88; H, 6.64.

3.9. 1,5,6,6-$^2H_4$-1,2,3,4,6-Penta-*O*-acetyl-α-D-glucopyranose (10)

A soln of Ac_2O (150 mL) and dry pyridine (150 mL) was cooled to 0 °C, and treated with crude **9** (25 g, 135.7 mmol). The suspension was stirred at 0 °C overnight, and the resulting soln of **9** was concentrated. The residue was poured into stirred ice water (100 mL). The precipitate was filtered off and washed with water to give **10** (50.0 g, 98%) as a colorless solid, which was used for the next step without further purification. Recrystallization in EtOH of a small sample gave pure **10**: R_f 0.50 (2:1 CH_2Cl_2–EtOAc); mp 108.0–109.4 °C; $[\alpha]_D^{25}$ +119.2 (*c* 1.0, $CHCl_3$); IR (ATR): 3032w, 2446w, 2129w, 1755s, 1420w, 1371m, 1233m, 1102m, 1069m, 1038m, 1015w, 932w, 737m; ^{1}H NMR (300 MHz, $CDCl_3$): δ 5.47 (t, 1H, $J_{3,2} = J_{3,4}$ 9.9 Hz, H-3), 5.14 (d, 1H, $J_{4,3}$ 9.9 Hz, H-4), 5.09 (d, 1H, $J_{2,3}$ 9.9 Hz, H-2), 2.18, 2.09, 2.04, 2.03, 2.02 (5s, 15H, 5Ac); ^{13}C NMR (75 MHz, $CDCl_3$): δ 170.61, 170.19, 169.62, 169.36, 168.72 (5 × C=O), 69.75 (C-3), 69.06 (C-2), 67.76 (C-4), 20.84, 20.66, 20.53 (2C), 20.41 (5 × Me); HRMALDIMS (*m*/*z*): $[M+Na]^+$ calcd for $C_{16}H_{18}D_4NaO_6^+$, 417.1311; found, 417.1309. Anal. Calcd for $C_{16}H_{18.26}D_{3.74}O_{11}$: C, 48.73; H, 5.68. Found: C, 48.60; H 5.50.

3.10. 1,5,6,6-$^2H_4$-2,3,4,6-Tetra-*O*-acetyl-D-glucopyranose (11)

A soln of crude **10** (40 g, 50.7 mmol) in 7:1 THF–MeOH was cooled to −10 °C and treated with gaseous NH_3 for 2 h. The soln was evaporated and co-evaporated with toluene to give crude **11**, which was directly used for the next step without further purification. Flash chromatography (2:1 cyclohexane–EtOAc) gave a sample of pure **11** (α/β = 71:29) for microanalysis and optical rotation: R_f 0.30 (1:1 cyclohexane–EtOAc). $[\alpha]_D^{25}$ +79.8 (*c* 1.0, $CHCl_3$); IR ($CHCl_3$): 3595w, 3334w, 3032w, 3009w, 2962w, 2131w, 1751s, 1712m, 1429w, 1370m, 1249s, 1063s, 1038s, 981w, 909w, 796w, 600w; ^{1}H NMR (300 MHz, $CDCl_3$):[33] δ 5.47 (t, 0.71H, $J_{3\alpha,2\alpha} = J_{3\alpha,4\alpha}$ 9.9 Hz, H-3α), 5.18 (t, 0.29H, $J_{3\beta,2\beta} = J_{3\beta,4\beta}$ 9.6 Hz, H-3β), 5.01 (d, 1H, $J_{4,3}$ 9.9 Hz, H-4), 4.84 (d, 0.29H, $J_{2\beta,3\beta}$ 9.6 Hz, H-2β), 4.81 (d, 0.71H, $J_{2\alpha,3\alpha}$ 10.2 Hz, H-2α), 2.04, 2.02, 2.00, 1.98, 1.96 (5s, 12H, 4 × Ac); ^{13}C NMR (75 MHz, $CDCl_3$): δ 170.75, 170.02, 169.47 (4 × C=O), 72.59 (C-2β), 72.09 (C-3β), 70.78 (C-2α), 69.58 (C-3α), 68.13, 68.01 (C-4α, C-4β), 20.35, 20.27 (4 × Me); HRMALDIMS (*m*/*z*): $[M+Na]^+$ calcd for $C_{14}H_{16}D_4NaO_{10}^+$, 375.1206; found, 375.1202.

3.11. 1,5,6,6-$^2H_4$-2,3,4,6-Tetra-*O*-acetyl-α-D-glucopyranosyl trichloroacetimidate (12)

A mixture of crude **11** (17.6 g, 49.9 mmol) and molecular sieves 4 Å (30 g) in CH_2Cl_2 (170 mL) at 0 °C was treated with CCl_3CN (50.2 mL, 0.5 mol) and 1,8-diazabicyclo[5.4.0]undec-7-ene (1.5 mL, 10 mmol), stirred for 2 h, diluted with CH_2Cl_2, and filtered. After evaporation of the filtrate, flash chromatography (2:1 cyclohexane–EtOAc) of the residue gave **12** as a foam (20.3 g, 82%): R_f 0.60 (1:1 cyclohexane–EtOAc); $[\alpha]_D^{25}$ +98.4 (*c* 1.0, $CHCl_3$); IR ($CHCl_3$): 3347w, 3032w, 3007w, 2961w, 2250w, 2127w, 1754s, 1675m, 1430w, 1371m, 1309w, 1242s, 1100m, 1052s, 963m, 901w, 851w, 824w, 639w; ^{1}H NMR (300 MHz, $CDCl_3$):[41] δ 8.68 (s, 1H, NH), 5.56 (t, 1H, $J_{3,2} = J_{3,4}$ 9.7 Hz, H-3), 5.17 (d, 1H, $J_{4,3}$ 9.7 Hz, H-4), 5.12 (d, 1H, $J_{2,3}$ 9.7 Hz, H-2), 2.07, 2.04, 2.03, 2.01 (4s, 12H, 4 × Ac); ^{13}C NMR (75 MHz, $CDCl_3$): δ 170.38, 169.81, 169.66, 169.31 (4 × C=O); 160.51 (C=N), 90.61 (CCl_3), 69.82 (C-2), 69.62 (C-3), 67.69 (C-4), 20.76 (2C), 20.67, 20.53 (4 × Me); HRMALDIMS (*m*/*z*): $[M+Na]^+$ calcd for $C_{16}H_{16}D_4Cl_3NNaO_{10}^+$, 518.0302; found, 518.0301. Anal. Calcd for $C_{16}H_{16.28}D_{3.72}NCl_3O_{10}$: C, 38.71; H, 4.09; N, 2.82; Cl, 21.42. Found: C, 38.98; H, 4.21; N, 2.84; Cl, 21.42.

3.12. 1,5,6,6-$^2H_4$-2,3,4,6-Tetra-*O*-acetyl-α-D-glucopyranosyl bromide (13)

A soln of crude **10** (60 g, 152.2 mmol) in dry CH_2Cl_2 (200 mL) at 0 °C was treated with 33% HBr in AcOH (200 mL), stirred for 3 h, and diluted with CH_2Cl_2. The soln was washed in water (4 × 60 mL), and the aqueous layers were extracted with CH_2Cl_2 (3 × 40 mL). The combined organic layers were washed with brine, dried over Na_2SO_4, and evaporated. Crystallization from hexane gave **13** as a colorless solid (60 g, 95%): R_f 0.70 (2:1 CH_2Cl_2–EtOAc); mp 85.5–86.0 °C; $[\alpha]_D^{25}$ +190.1 (*c* 1.0, $CHCl_3$); IR ($CHCl_3$): 3489w, 3013w, 3032w, 2123w, 1752s, 1429w, 1372m, 1251m, 1162w, 1104m, 1054m, 1035m, 973w, 911w, 765w; ^{1}H NMR (300 MHz, $CDCl_3$): δ 5.56 (t, 1H, $J_{3,2} = J_{3,4}$ 9.9 Hz, H-3), 5.15 (d, 1H, $J_{4,3}$ 9.9 Hz, H-4), 4.83 (d, 1H, $J_{2,3}$ 9.9 Hz, H-2), 2.10, 2.09, 2.05, 2.04 (4s, 12H, 4Ac); ^{13}C NMR (75 MHz, $CDCl_3$, assignments based on a HSQC spectrum): δ 170.33, 169.66, 169.60, 169.27 (4 × C=O), 69.75 (C-2), 69.06 (C-3), 67.76 (C-4), 20.84 (2C), 20.66, 20.53, 20.41 (5 × Me); ESIMS (*m*/*z*): $[M+Na]^+$ calcd for

$C_{14}H_{15}D_4BrNaO_9^+$, 437.0; found, 437.2. Anal. Calcd for $C_{14}H_{15.28}D_{3.72}BrO_9$: C, 40.50; H, 4.66; Br, 19.24. Found: C, 40.55; H, 4.95; Br, 19.00.

3.13. Allyl 1,5,6,6-$^2H_4$-2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranoside (14)

A mixture of $Hg(CN)_2$ (39.0 g, 154.4 mmol) and molecular sieves 4 Å (10 g) in allyl alcohol (300 mL) was stirred at room temperature for 30 min, treated with **13** (53.0 g, 127.6 mmol), stirred at room temperature overnight, and filtered. After evaporation of the filtrate, a suspension of the residue in $CHCl_3$ (200 mL) was filtered and the filtrate was washed with $CHCl_3$ (50 mL). The combined organic layers were washed with saturated KI soln (3 × 30 mL) and brine, dried over Na_2SO_4 and taken to dryness to give crude **14** as a white solid (42.6 g, 85%), which was directly used for the next step. Recrystallization of a small sample in Et_2O gave an analytical sample of **14**: R_f 0.70 (2:1 cyclohexane–EtOAc); mp 87.3–87.9 °C; $[\alpha]_D^{25}$ −20.2 (*c* 1.0, $CHCl_3$); IR ($CHCl_3$): 3006w, 3032w, 2945w, 2871w, 2126w, 1754s, 1427w, 1372m, 1249s, 1100m, 1062s, 1037m, 986w, 938w, 906w, 599w, 576w; ^1H NMR (300 MHz, $CDCl_3$):[25] δ 5.91–5.78 (m, 1H, C*H*=CH_2), 5.30–5.18 (m, 3H, CH=CH_2, H-3), 5.08 (d, 1H, $J_{4,3}$ 9.3 Hz, H-4), 5.03 (d, 1H, $J_{2,3}$ 9.6 Hz, H-2), 4.37–4.30 (m, 1H, C*H*CH=CH_2), 4.13–4.06 (m, 1H, C*H*CH=CH_2), 2.09, 2.04, 2.02, 2.00 (4s, 12H, 4 × Ac); ^{13}C NMR (75 MHz, $CDCl_3$): δ 170.49, 170.09, 169.20, 169.02 (4 × C=O), 133.14 (*C*H=CH_2), 117.55 (CH=*C*H_2), 72.79 (C-3), 71.17 (C-2), 69.93 (*C*H_2CH=CH_2), 68.32 (C-4), 20.81, 20.75, 20.69, 20.67 (4 × Me); HRMALDIMS (*m*/*z*): $[M+Na]^+$ calcd for $C_{17}H_{20}D_4NaO_{10}^+$, 415.1518; found, 415.1510. Anal. Calcd for $C_{17}H_{20.28}D_{3.72}O_6$: C, 52.04; H, 6.23. Found: C, 51.86, H, 6.35.

3.14. Allyl 1,5,6,6-$^2H_4$-β-D-glucopyranoside (15)

A soln of **14** (50 g, 127.4 mmol) in MeOH (700 mL) was treated with NaOMe (0.68 g, 12.6 mmol), stirred at room temperature for 2 h, and neutralized with Amberlite-120 (H^+-form). Filtration through Celite and evaporation gave **15** as a colorless syrup (28.0 g, 98%) that was used for the next step. An analytical sample of **15** was obtained by deacetylating pure **14**. R_f 0.50 (5:1 CH_2Cl_2–MeOH); $[\alpha]_D^{25}$ −28.6 (*c* 1.0, H_2O); IR (ATR): 3341m, 2912w, 2111w, 1646w, 1422w, 1330w, 1271w, 1221w, 1186m, 1162m, 1051s, 992s, 938s; ^1H NMR (300 MHz, D_2O): δ 6.03–5.90 (m, 1H, C*H*=CH_2), 5.36 (br. d, 1H, *J* 17.4 Hz, CH=C*H*H), 5.27 (br d, 1H, *J* 10.5 Hz, CH=CH*H*), 4.38 (br dd, 1H, J_1 12.6, J_2 5.4 Hz, allylic H), 4.21 (br dd, 1H, J_1 12.9, J_2 6.6 Hz, allylic H); 3.47 (t, 1H, $J_{3,2} = J_{3,4}$ 9.1 Hz, H-3), 3.36 (d, 1H, $J_{4,3}$ 9.1 Hz, H-4), 3.26 (d, $J_{2,3}$ 9.1 Hz, H-2); ^{13}C NMR (75 MHz, D_2O; assignments based on a HSQC spectrum): δ 133.97 (*C*H=CH_2), 119.32 (CH=*C*H_2), 76.46 (C-3), 73.72 (C-2), 71.20 (*C*H_2CH=CH_2), 70.25 (C-4); HRMALDIMS (*m*/*z*): $[M+Na]^+$ calcd for $C_9H_{12}D_4NaO_6^+$, 247.1096; found, 247.1088.

3.15. Allyl 1,5,6,6-$^2H_4$-4,6-*O*-benzylidene-β-D-glucopyranoside (16)

A mixture of crude **15** (16.8 g, 74.9 mmol), benzaldehyde dimethyl acetal (32 mL, 210.2 mmol), and TsOH (0.8 g, 4.65 mmol) in dry MeCN (160 mL) was heated to 80 °C for 1 h. The soln was neutralized with satd aq $NaHCO_3$ soln, and MeCN was evaporated. A soln of the residue in EtOAc was washed with brine, dried with Na_2SO_4, and evaporated to afford **16** as a colorless solid (35.8 g, 90%) that was used for the next step. A small sample was purified by flash chromatography (3:1 CH_2Cl_2–EtOAc) and recrystallized in 1:2 EtOAc–cyclohexane (1:2) to give an analytical sample of **16**: R_f 0.60 (10:1 CH_2Cl_2/MeOH); mp 150.3–150.7 °C; $[\alpha]_D^{25}$ −53.8 (*c* 1.0, $CHCl_3$); IR (ATR): 3590m, 3033w, 3011w, 2928w, 2853w, 2106w, 1603w, 1457w, 1378w, 1314w, 1063s, 1020s, 974m, 854w, 680w; ^1H NMR (300 MHz, $CDCl_3$):[36,42] 7.51–7.34 (m, 5H); 5.94 (m, 1H, C*H*=CH_2), 5.53 (s, 1H, PhC*H*), 5.34 (dq, 1H, J_1 17.1, J_2 1.3 Hz, CH=C*H*H), 5.24 (dq, 1H, J_1 10.4, J_2 1.3 Hz, CH=CH*H*), 4.38 (ddt, 1H, J_1 12.8, J_2 5.4, J_3 1.3 Hz, allylic H), 4.14 (ddt, 1H, J_1 12.8, J_2 6.3, J_3 1.3 Hz, allylic H); 3.81 (br t, 1H, $J_{3,2} = J_{3,4}$ 9.0 Hz, H-3), 3.55 (d, 1H, $J_{4,3}$ 9.0 Hz, H-4), 3.52 (dd, 1H, $J_{2,3}$ 9.0, $J_{2,OH}$ 1.5 Hz, H-2), 2.96 (br s, 1H, HO-3), 2.82 (br s, 1H, HO-2); ^{13}C NMR (75 MHz, $CDCl_3$): δ 136.80 (*C*H=CH_2), 138.29 (aromatic C), 129.18, 128.24, 126.16 (5 × aromatic *C*H), 118.31 (CH=*C*H_2), 101.79 (Ph*C*H), 80.38 (C-4), 74.39 (C-2), 73.12 (C-3), 70.59 (*C*H_2CH=CH_2); HRMALDIMS (*m*/*z*): $[M+Na]^+$ calcd for $C_{16}H_{16}D_4NaO_6^+$, 335.1409; found, 335.1408.

3.16. Allyl 1,5,6,6-$^2H_4$-2,3-di-*O*-benzyl-4,6-*O*-benzylidene-β-D-glucopyranoside (17)

A stirred suspension in dry DMF (150 mL) of 50% NaH in mineral oil (22.3 g, 557.5 mmol) was treated dropwise with a soln of crude **16** (24.0 g, 76.8 mmol) in dry DMF (150 mL) for 30 min, treated dropwise with BnBr (36 mL, 301.1 mmol), stirred for 8 h at room temperature, and poured onto ice. After extraction with Et_2O (5 × 100 mL) the combined organic layers were washed with brine, dried over Na_2SO_4, and evaporated. Flash chromatography (cyclohexane, then 20:1 cyclohexane–EtOAc, containing 1% Et_3N) gave **17** as an oil (31.0 g, 82%): R_f 0.45 (10:1 cyclohexane–EtOAc); $[\alpha]_D^{25}$ −33.3 (*c* 1.0, $CHCl_3$); IR ($CHCl_3$): 3067w, 3034w, 3010w, 2872w, 2237w, 2105w, 1951w, 1809w, 1604w, 1497w, 1454w, 1367w, 1301w, 1263w, 1162w, 1090s, 1074s, 1028m, 855w, 686w; ^1H NMR (300 MHz, $CDCl_3$):[36] δ

7.53–7.27 (m, 15H); 6.04-5.91 (m, 1H, C*H*=CH_2); 5.59 (s, 1H, PhC*H*), 5.38 (dq, 1H, J_1 17.4, J_2 1.5 Hz, CH=C*H*H), 5.25 (dq, 1H, J_1 10.2, J_2 1.5 Hz, CH=CH*H*), 4.94 (d, 2B of 2AB, 2H, J 11.1 Hz, 2 × PhCH_B), 4.82 (d, A of AB, 1H, J 11.1 Hz, PhCH_A), 4.80 (d, A′ of AB′, 1H, J 11.1 Hz, PhC$H_{A'}$), 4.43 (ddt, 1H, J_1 12.7, J_2 5.1, J_3 1.5 Hz, allylic H), 4.19 (ddt, 1H, J_1 12.6, J_2 6.0, J_3 1.5 Hz, allylic H), 3.78 (dd, 1H, $J_{3,2}$ 9.6, $J_{3,4}$ 9.2 Hz, H-3), 3.74 (d, 1H, $J_{4,3}$ 9.0 Hz, H-4), 3.52 (d, 1H, $J_{2,3}$ 9.2 Hz, H-2); ^{13}C NMR (75 MHz, $CDCl_3$): δ 138.48, 138.29, 137.30 (3 × aromatic C), 133.69 (*C*H=CH_2), 128.91, 128.31, 128.26, 128.21, 128.14, 127.99, 127.70, 127.59, 125.96 (15 × aromatic *C*H), 117.63 (CH=*C*H_2), 101.03 (Ph*C*H), 82.03 (C-2), 81.32 (C-4), 80.85 (C-3), 75.39, 75.10 (2 × Ph*C*H_2), 70.65 (*C*H_2CH=CH_2); HRMALDIMS (*m*/*z*): $[M+Na]^+$ calcd for $C_{30}H_{28}D_4NaO_6^+$, 515.2450; found, 515.2351. Anal. Calcd for $C_{30}H_{28.28}D_{3.72}O_6$: C, 73.19; H, 6.60. Found: C, 73.08; H, 6.74.

3.17. Allyl 1,5,6,6-$^2H_4$-2,3,6-tri-*O*-benzyl-β-D-glucopyranoside (18)

A mixture of **17** (5.0 g, 10.1 mmol), $NaB(CN)H_3$ (6.5 g, 103.5 mmol) and molecular sieves 4 Å (6 g) in dry THF (300 mL) was stirred at room temperature for 50 min, cooled to 0 °C, treated with gaseous HCl for 50 min, and filtered. The filtrate was neutralized with satd aq $NaHCO_3$ soln. After evaporation of THF, a soln of the residue in CH_2Cl_2 (80 mL) was washed with H_2O and brine, dried over Na_2SO_4, and evaporated. Flash chromatography (8:1 cyclohexane–EtOAc) gave **18** as a colorless syrup (3.7 g, 73%): R_f 0.40 (4:1 cyclohexane–EtOAc); $[\alpha]_D^{25}$ −24.8 (*c* 1.0, $CHCl_3$); IR ($CHCl_3$): 3579w, 3067w, 3033w, 3010w, 2868w, 2193w, 2092w, 1951w, 1870w, 1809w, 1604w, 1497w, 1454w, 1355w, 1307w, 1071s, 1028m, 994w, 935w; ^{1}H NMR (300 MHz, $CDCl_3$): 7.39–7.27 (m, 15H); 6.01–5.90 (m, 1H, C*H*=CH_2); 5.35 (dq, 1H, J_1 17.4, J_2 1.5 Hz, CH=C*H*H), 5.22 (dq, 1H, J_1 10.5, J_2 1.5 Hz, CH=CH*H*), 4.97 (d, B of AB, 1H, J 10.8 Hz, PhCH_B), 4.95 (d, B′ of AB′, 1H, J 11.2 Hz, PhC$H_{B'}$), 4.74 (d, A′ of AB′, 1H, J 11.2 Hz, PhC$H_{A'}$), 4.73 (d, A of AB, 1H, J 10.8 Hz, PhCH_A), 4.62 (d, B″ of AB″, 1H, J 12.1 Hz, PhC$H_{B''}$), 4.57 (d, A″ of AB″, 1H, J 12.1 Hz, PhC$H_{A''}$), 4.43 (ddt, 1H, J_1 12.6, J_2 4.8, J_3 1.5 Hz, allylic H), 4.15 (ddt, 1H, J_1 12.9, J_2 6.0, J_3 1.5 Hz, allylic H), 3.62–3.57 (m, 1H, H-4), 3.50–3.42 (m, 2H, H-2, H-3); ^{13}C NMR (75 MHz, $CDCl_3$): δ 138.58, 138.35, 137.93 (3 aromatic C), 133.94 (*C*H=CH_2), 128.52–127.67 (15 aromatic *C*H), 117.34 (CH=*C*H_2), 83.98 (C-3), 81.63 (C-2), 75.26, 74.78, 73.57 (3 × Ph*C*H_2), 71.44 (C-4), 70.28 (*C*H_2CH=CH_2); HRMALDIMS (*m*/*z*): $[M+Na]^+$ calcd for $C_{30}H_{30}D_4NaO_6^+$, 517.2504; found, 517.2495. Anal. Calcd for $C_{30}H_{30.28}D_{3.72}O_6$: C, 72.89; H, 6.99. Found: C, 72.72; H, 7.03.

3.18. Allyl 1,5,6,6-$^2H_4$-2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl-(1→4)-1,5,6,6-$^2H_4$-2,3,6-tri-*O*-benzyl-β-D-glucopyranoside (19)

A mixture of **18** (9.7 g, 19.6 mmol), **12** (8.9 g, 17.9 mmol) and molecular sieves 4 Å (10 g) in dry CH_2Cl_2 (350 mL) was stirred at room temperature for 30 min, cooled to −50 °C, treated with TMSOTf (0.89 mL, 4.95 mmol), stirred for 2 h, diluted with CH_2Cl_2, allowed to reach room temperature, and filtered through Celite. The filtrate was washed with satd aq $NaHCO_3$ soln and brine, dried over Na_2SO_4, and evaporated. Flash chromatography (4:1 → 3:1 cyclohexane–EtOAc) gave **19** as an oil (13.1 g, 88%): R_f 0.50 (1:1 cyclohexane–EtOAc); $[\alpha]_D^{25}$ −9.4 (*c* 1.0, $CHCl_3$); IR ($CHCl_3$): 3033w, 3010w, 2868w, 2094w, 1754s, 1604w, 1497w, 1454w, 1426w, 1372m, 1245m, 1067s, 1036m, 995w, 936w, 908w; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.42–7.24 (m, 15H); 6.01–5.88 (m, 1H, C*H*=CH_2), 5.33 (dq, 1H, J_1 17.2, J_2 1.5 Hz, CH=C*H*H), 5.20 (dq, 1H, J_1 11.2, J_1 1.5 Hz, CH=CH*H*), 5.04-4.99 (m, 2H, H-3^{II}, H-4^{II}), 4.95 (d, B of AB, 1H, J 10.6 Hz, PhCH_B), 4.90 (d, 1H, $J_{2^{II},3^{II}}$ 9.6 Hz, H-2^{II}), 4.87 (d, 1H, J 11.0 Hz, PhC*H*), 4.76 (d, B′ of AB′, 1H, J 12.1 Hz, PhC$H_{B'}$), 4.75 (d, A of AB, 1H, J 10.6 Hz, Ph*C*H_A), 4.66 (d, 1H, J 11.0 Hz, PhC*H*), 4.50 (d, A′ of AB′, 1H, J 12.1 Hz, PhC$H_{A'}$), 4.40 (ddt, 1H, J_1 12.9, J_2 5.1, J_3 1.5 Hz, allylic H), 4.12 (ddt, 1H, J_1 12.9, J_2 6.3, J_3 1.5 Hz, allylic H), 3.92 (d, 1H, $J_{4^I,3^I}$ 8.7 Hz, H-4^I), 3.56 (t, 1H, $J_{3^I,2^I} = J_{3^I,4^I}$ 9.0 Hz, H-3^I), 3.42 (d, 1H, $J_{2^I,3^I}$ 9.6 Hz, H-2^I), 1.99, 1.98, 1.96, 1.95 (4s, 12H, 4 × Ac); ^{13}C NMR (75 MHz, $CDCl_3$): δ 170.46, 170.05, 169.17, 168.94 (4 × C=O), 138.94, 138.25, 137.84 (3 × aromatic C), 133.88 (*C*H=CH_2), 128.44–127.16 (15 × aromatic *C*H), 117.19 (CH=*C*H_2), 82.58 (C-3^I), 81.59 (C-2^I); 77.29 (C-4^I), 75.02, 74.88, 73.54 (3 × Ph*C*H_2), 73.11 (C-3^{II}), 71.87 (C-2^{II}), 70.21 (*C*H_2CH=CH_2), 67.94 (C-4^{II}), 20.71 (4 × Me); HRMALDIMS (*m*/*z*): $[M+Na]^+$ calcd for $C_{44}H_{44}D_8NaO_{15}^+$, 851.3706; found, 851.3714. Anal. Calcd for $C_{44}H_{44.54}D_{7.46}O_{15}$: C, 63.80; H, 6.38. Found: C, 63.86; H, 6.78.

3.19. 1^{II},5^{II},6^{II},6^{II}-$^2H_4$-2,3,4,6-Tetra-*O*-acetyl-β-D-glucopyranosyl-(1→4)-1^I,5^I,6^I,6^I-$^2H_4$-2,3,6-tri-*O*-benzyl-D-glucopyranose (20)

A stirred suspension of bis[methyl(diphenyl)phosphine](cycloocta-1,5-diene)iridium(I) hexafluorophosphate (246 mg, 0.289 mmol) in dry THF (24 mL) was degassed at room temperature for 30 min, and stirred under H_2 until the red suspension turned into a pale yellow soln. It was flushed with Ar, treated with a soln of **19** (3.0 g, 3.62 mmol) in dry THF (60 mL), water stirred for 1 h. The mixture was treated with H_2O (36 mL) and I_2 (1.92 g, 7.56 mmol), stirred for 1 h, and

treated with aq $Na_2S_2O_3$ soln until the color of the mixture turned to pale yellow. The layers were separated, and the aq layer was extracted with CH_2Cl_2 (4 × 25 mL). The combined organic layers were washed with brine, dried over Na_2SO_4, and evaporated. Flash chromatography (2:1 cyclohexane–EtOAc) gave **20** as a foam (2.36 g, 83%, α/β = 57:43): R_f 0.50 (1:1 cyclohexane–EtOAc); mp 56–58 °C; $[\alpha]_D^{25}$ −5.2 (*c* 1.0, $CHCl_3$); IR ($CHCl_3$): 3592w, 3032w, 3011w, 2943w, 2864w, 2184w, 2094w, 1754s, 1602w, 1497w, 1454w, 1372m, 1243m, 1066s, 1036m, 908w, 791w, 701w, 597w; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.42–7.23 (m, 15H), 5.00–4.93 (3H, H-3^{II}, H-4^{II}, PhC*H*), 4.89–4.86 (m, 1H, H-2^{II}), 4.80 (d, B of AB, 0.43H, *J* 11.0 Hz, PhCH_B), 4.75–4.67 (m, 3H, 3 × PhC*H*), 4.58 (d, A′ of AB′, 0.57H, *J* 11.5 Hz, PhC$H_{A'}$), 4.44 (d, 0.43H, *J* 12.5 Hz, PhC*H*), 4.40 (d, 0.57H, *J* 12.5 Hz, PhC*H*), 3.94 (d, 0.43H, $J_{4\beta^I,3\beta^I}$ 8.5 Hz, H-4β^I), 3.88 (d, 0.57H, $J_{4\alpha^I,3\alpha^I}$ 9.0 Hz, H-4α^I), 3.78 (t, 0.57H, $J_{3\alpha^I,2\alpha^I} = J_{3\alpha^I,4\alpha^I}$ 9.5 Hz, H-3α^I), 3.55 (t, 0.43H, $J_{3\beta^I,2\beta^I} = J_{3\beta^I,4\beta^I}$ 9.0 Hz, H-3β^I), 3.47 (d, 0.57H, $J_{2\alpha^I,3\alpha^I}$ 9.5 Hz, H-2α^I), 3.29 (d, 0.43H, $J_{2\beta^I,3\beta^I}$ 9.0 Hz, H-2β^I), 3.17 (s, 0.43H, OH-1β^I), 2.98 (s, 0.57H, OH-1α^I), 1.95–1.89 (7s, 12H, 4 × Ac); ^{13}C NMR (125 MHz, $CDCl_3$): δ 170.64–169.02 (4 × C=O), 139.14, 138.97, 138.20, 137.77, 137.69, 137.71 (3 × aromatic C), 128.67–127.28 (15 × aromatic *C*H), 82.49 (C-3β^I), 82.45 (C-2β^I), 79.61 (C-3α^I), 78.94 (C-2α^I), 76.70 (C-4), 75.16, 74.95, 74.71, 73.70, 73.64, 73.50 (3 × Ph*C*H$_2$), 73.11 (C-3α^{II}), 73.09 (C-3β^{II}), 71.86 (C-2β^{II}), 71.76 (C-2α^{II}), 68.13 (C-4α^{II}), 68.01 (C-4β^{II}), 20.61–20.53 (4 × Me); HRMALDIMS (*m*/*z*): $[M+Na]^+$ calcd for $C_{41}H_{40}D_8NaO_{15}^+$, 811.3393; found, 811.3375. Anal. Calcd for $C_{41}H_{40.54}D_{7.46}O_{15}$: C, 62.47; H, 6.20. Found: C, 62.13; H, 6.41.

3.20. 1^{II},5^{II},6^{II},6^{II}-^{2}H$_4$-2,3,4,6-Tetra-*O*-acetyl-β-D-glucopyranosyl-(1→4)-1^I,5^I,6^I,6^I-^{2}H$_4$-D-glucopyranose (21)

A soln of **20** (3.0 g, 3.8 mmol) in 1:1 acetone–MeOH (100 mL) was treated with 20% $Pd(OH)_2$/C (1.0 g), stirred under 6 bar of H_2 for 3 days, and filtered through Celite (washing with 50 mL of MeOH). The combined filtrate and washings were evaporated. Flash chromatography (20:1 cyclohexane–MeOH) gave **21** as a foam (1.77 g, 90%, α/β = 57:43): R_f 0.60 (10:1 CH_2Cl_2/MeOH); mp 90–95 °C; $[\alpha]_D^{25}$ +27.1 (*c* 1, water); IR (ATR): 3474w, 2941w, 2115w, 1743s, 1431w, 1370m, 1213s, 1187m, 1035s, 983m, 903m, 739w; ^{1}H NMR (300 MHz, D_2O): δ 5.37 (t, 1H, $J_{3^{II},2^{II}} = J_{3^{II},4^{II}}$ 9.6 Hz, H-3^{II}), 5.13 (d, 1H, $J_{4^{II},3^{II}}$ 9.3 Hz, H-4^{II}), 5.01 (d, 0.57H, $J_{2^{II},3^{II}}$ 9.6 Hz, H-2α^{II}), 5.00 (d, 0.43H, $J_{2\beta^{II},3\beta^{II}}$ 9.6 Hz, H-2β^{II}), 3.81 (t, 0.57H, $J_{3\alpha^I,2\alpha^I} = J_{3\alpha^I,4\alpha^I}$ 9.0 Hz, H-3α^I), 3.63–3.60 (m, 1.43H, H-3β^I, H-4), 3.54 (d, 0.57H, $J_{2\alpha^I,3\alpha^I}$ 9.6 Hz, H-2α^I), 3.25 (dd, 0.43H, J_1 7.5, J_2 1.8 Hz, H-2β^I), 2.13, 2.09, 2.05 (3s, 12H, 4 × Ac); HRMALDIMS (*m*/*z*): $[M+Na]^+$ calcd for $C_{20}H_{22}D_8NaO_{15}^+$, 541.1985; found, 541.1973.

3.21. 1^I,1^{II},5^I,5^{II},6^I,6^I,6^{II}6^{II}-^{2}H$_8$-Cellobiose (22)

A soln of **21** (1.0 g, 1.93 mmol) and NaOMe (50 mg, 0.92 mmol) in MeOH (15 mL) was stirred at room temperature for 2 h. The precipitate was filtered off, and washed with MeOH (5 mL). The filtrate was neutralized with Amberlite IR-120 (H^+-form), and filtered. The filtrate was taken to dryness to give a colorless solid. The combined solids were recrystallized in water to give **22** (0.61 g, 91%, α/β = 7:43): mp 228–240 °C (dec.); $[\alpha]_D^{25}$ +26.4 (*c* 1.0, H_2O); IR (ATR): 3417m, 3353m, 2895w, 2107w, 1481w, 1425w, 1393w, 1362w, 1318w, 1278w, 1219w, 1194w, 1164m, 1040s, 980s, 967w, 957w, 943m, 907m, 769m, 739m, 610s; ^{1}H NMR (500 MHz, D_2O;): δ 3.86 (dd, 0.14H, $J_{3\alpha^I,2\alpha^I}$ 12.5, $J_{3\alpha^I,4\alpha^I}$ 12.0 Hz, H-3α^I), 3.71–3.65 (m, 1.86H, H-4^I, H-3β^I), 3.61 (d, 0.14H, $J_{2\alpha^I,3\alpha^I}$ 12.5 Hz, H-2α^I), 3.55 (t, 1H, $J_{3^{II},2^{II}} = J_{3^{II},4^{II}}$ 11.3 Hz, H-3^{II}), 3.44 (d, 1H, $J_{4^{II},3^{II}}$ 11.3 Hz, H-4^{II}), 3.37–3.29 (m, 1.86H, H-2β^I, H-2^{II}); ^{13}C NMR (125 MHz, D_2O):[43–45] δ 79.40 (C-4α^I), 79.26 (C-4β^I), 76.29 (C-3^{II}), 75.08 (C-3β^I), 74.64 (C-2β^I), 73.91 (C-2^{II}), 72.14 (C-3α^I), 71.96 (C-2α^I), 70.20 (C-4^{II}); HRESIMS (*m*/*z*): $[M+Na]^+$ calcd for $C_{12}H_{14}D_8NaO_{11}^+$, 373.1562; found, 373.1555. Anal. Calcd for $C_{12}H_{14.54}D_{7.46}O_{11}$: C, 41.20; H, 5.92. Found: C, 41.02; H, 6.50.

Acknowledgements

We thank the Swiss National Science Foundation for generous support of this work and Dr. Bruno Bernet for checking the manuscript.

References

1. Nishiyama, Y.; Langan, P.; Chanzy, H. *J. Am. Chem. Soc.* **2002**, *124*, 9074–9082.
2. Nishiyama, Y.; Sugiyama, J.; Chanzy, H.; Langan, P. *J. Am. Chem. Soc.* **2003**, *125*, 14300–14306.
3. Heiner, A. P.; Sugiyama, J.; Teleman, O. *Carbohydr. Res.* **1995**, *273*, 207–223.
4. Sugiyama, J.; Vuong, R.; Chanzy, H. *Macromolecules* **1991**, *24*, 4168–4175.
5. Jarvis, M. *Nature* **2003**, *426*, 611–612.
6. Langan, P.; Sukumar, N.; Nishiyama, Y.; Chanzy, H. *Cellulose* **2005**, *12*, 551–562.
7. Raymond, S.; Henrissat, B.; Qui, D. T.; Kvick, A.; Chanzy, H. *Carbohydr. Res.* **1995**, *277*, 209–229.
8. Raymond, S.; Heyraud, A.; Qui, D. T.; Kvick, A.; Chanzy, H. *Macromolecules* **1995**, *28*, 2096–2100.
9. Gessler, K.; Krauss, N.; Steiner, T.; Betzel, C.; Sarko, A.; Saenger, W. *J. Am. Chem. Soc.* **1995**, *117*, 11397–11406.
10. Gessler, K.; Krauss, N.; Steiner, T.; Betzel, C.; Sandmann, C.; Saenger, W. *Science* **1994**, *266*, 1027–1029.

11. Poppleton, B. J.; Mathieson, A. M. *Nature* **1968**, *219*, 1046.
12. Xu, J.; Vasella, A. *Helv. Chim. Acta* **1999**, *82*, 1728–1752; Bernet, B.; Xu, J.; Vasella, A. *Helv. Chim. Acta* **2000**, *83*, 2072–2114.
13. Murty, K. V. S. N.; Xie, T.; Bernet, B.; Vasella, A. *Helv. Chim. Acta* **2006**, *89*, 675–730.
14. Murty, K. V. S. N.; Vasella, A. *Helv. Chim. Acta* **2001**, *84*, 939–963.
15. Koch, H. J.; Stuart, R. S. *Carbohydr. Res.* **1977**, *59*, C1–C6.
16. Koch, H. J.; Stuart, R. S. *Carbohydr. Res.* **1978**, *67*, 341–348.
17. Koch, H. J.; Stuart, R. S. *Carbohydr. Res.* **1978**, *64*, 127–134.
18. Funabashi, M.; Yoshioka, S. *Chem. Lett.* **1984**, 677–680.
19. Funabashi, M.; Hasegawa, T. *Bull. Chem. Soc. Jpn.* **1991**, *64*, 2528–2531.
20. Serianni, A. S.; Barker, R. *Can. J. Chem.* **1979**, *57*, 3160–3167.
21. Schmidt, O. T. *Methods Carbohydr. Chem.* **1963**, *II*, 320–323.
22. Hardick, D. J.; Hutchinson, D. W. *Tetrahedron* **1993**, *49*, 6707–6716.
23. Tronchet, J. M. J.; Zsely, M.; Geoffroy, M. *Carbohydr. Res.* **1995**, *275*, 245–258.
24. Lehmann, J.; Ziser, L. *Carbohydr. Res.* **1992**, *225*, 83–97.
25. Rodebaugh, R.; Fraser-Reid, B. *Tetrahedron* **1996**, *52*, 7663–7678.
26. Hu, Y. J.; Dominique, R.; Das, S.; Roy, R. *Can. J. Chem.* **2000**, *78*, 838–845.
27. Perrine, T. D.; Glaudemans, C. P. J.; Ness, R. K.; Kyle, J.; Fletcher, H. G. *J. Org. Chem.* **1967**, *32*, 664–669.
28. Kuzuhara, H.; Fletcher, H. G. *J. Org. Chem.* **1967**, *32*, 2531–2534.
29. Wolfrom, M. L.; Thompson, A. *Methods Carbohydr. Chem.* **1963**, *II*, 211–212.
30. Sim, M. M.; Kondo, H.; Wong, C. H. *J. Am. Chem. Soc.* **1993**, *115*, 2260–2267.
31. Excoffier, G.; Gagnaire, D.; Utille, J. P. *Carbohydr. Res.* **1975**, *39*, 368–373.
32. Mikamo, M. *Carbohydr. Res.* **1989**, *191*, 150–153.
33. Fiandor, J.; García-López, M. T.; De Las Heras, F. G.; Méndez-Castrillón, P. P. *Synthesis* **1985**, 1121–1123.
34. Zemplen, G.; Csuros, Z.; Bruckner, Z. *Ber. Dtsch. Chem. Ges.* **1928**, *61*, 927–937.
35. Lee, R. T.; Lee, Y. C. *Carbohydr. Res.* **1974**, *37*, 193–201.
36. Sugawara, F.; Nakayama, H.; Strobel, G. A.; Ogawa, T. *Agric. Biol. Chem.* **1986**, *50*, 2251–2259.
37. Yoneda, Y.; Kawada, T.; Rosenau, T.; Kosma, P. *Carbohydr. Res.* **2005**, *340*, 2428–2435.
38. Garegg, P. J.; Hultberg, H.; Wallin, S. *Carbohydr. Res.* **1982**, *108*, 97–101.
39. Oikawa, M.; Liu, W.-C.; Nakai, Y.; Koshida, S.; Fukase, K.; Kusumoto, S. *Synlett* **1996**, 1179–1180.
40. Baudry, D.; Ephritikhine, M.; Felkin, H. J. *Chem. Soc. Chem. Commun.* **1978**, 694–695.
41. Duclos, R. I. *Chem. Phys. Lipids* **2001**, *111*, 111–138.
42. Khan, S. H.; Abbas, S. A.; Matta, K. L. *Carbohydr. Res.* **1989**, *193*, 125–139.
43. Gast, J. C.; Atalla, R. H.; Mckelvey, R. D. *Carbohydr. Res.* **1980**, *84*, 137–146.
44. Pfeffer, P. E.; Valentine, K. M.; Parrish, F. W. *J. Am. Chem. Soc.* **1979**, *101*, 1265–1274.
45. Heyraud, A.; Rinaudo, M.; Vignon, M. *Biopolymers* **1979**, *18*, 167–185.