n-Pentenyl Glycoside Based Methodology for Determining the Relative Reactivities of Variously Protected Pairs of Glycosides

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The relative rate of hydrolysis of an α/β anomeric pair of glycosides is generally considered to provide insight into various factors that influence anomeric reactivity. However the fact that such hydrolyses are usually carried out with aqueous acids severely limits the range of substrates that can studied. This limitation is overcome with n-pentenyl glycosides (NPGs) which are hydrolyzed under neutral, oxidative conditions. A procedure is described in which a pair (e.g. α_1/β_1, α_1/β_2, β_1/β_2, etc.) of NPGs is made to compete for an insufficient amount of *N*-bromosuccinimide, the relative rates of reaction being determined from HPLC peak heights of the unreacted starting materials. Some commonly used acid labile protecting groups, e.g. cyclic acetals and acetyl, are shown to exert profound effects upon relative and absolute rates of anomeric activation.

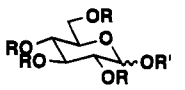
The relative rate of hydrolysis of an α/β pair of glycoside anomers provides insight into steric, torsional, and electronic forces that influence anomeric reactivity, and a number of mechanistic rationalizations have been based upon this concept.[1] However as far as we are aware, the only compilation of such relative rates is the oft-cited 1965 paper of Feather and Harris[2] in which the authors tabulate data from several investigators[3] who had studied the acid-catalyzed hydrolyses of methyl glycopyranosides. In these studies, the hydrolyses had been carried out separately on each member of a given anomeric pair under conditions that varied widely between investigators, in terms of reaction temperatures, mineral acid used, acid strengths, mode of monitoring reaction progress, etc.

Nevertheless, trends in the data[2,3a] suggest an β/α ratio of ~2 ± 0.5 for hydrolysis of a pair of hexopyranoside anomers.

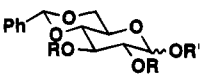
The use of aqueous acid for these hydrolyses clearly precluded studying of the vast array of substrates carrying protecting groups, such as acetal and acetyl, that would not survive the conditions. Into this category fall many useful synthetic intermediates, knowledge of whose relative β/α reactivities might be advantageously incorporated into synthetic planning. n-Pentenyl glycosides (NPGs) are hydrolyzed under neutral conditions[4] and are therefore amenable to investigation of such substrates. In this manuscript we describe a procedure which we have developed for this purpose.

Procedure

Separate hydrolyses of the individual anomers, as was done in the studies cited above[2,3] require extreme caution in order to ensure that a standard set of reaction conditions is maintained. Such demands could be obviated by carrying out one-pot hydrolyses in which equivalent amounts of each NPG anomer are allowed to compete for an insufficient quantity of the oxidizing agent.



1 R = H R' = Pent
3 R = Bn R' = Pent
4 R = Ac R' = Pent
7 R = Bn R' = H
8 R = Ac R' = H



2 R = H R' = Pent
5 R = Bn R' = Pent
6 R = Ac R' = Pent
9 R = Bn R' = H
10 R = Ac R' = H

Pentenyl glucosides **3** → **6** were chosen for study, and the typical procedure used was as follows:

(i) Accurately weighed, and approximately equal, amounts of each anomer were placed in a flask and dissolved in dry dichloromethane. A portion of the solution was injected into the HPLC to obtain relative β/α ratios from the peak heights at time zero (t_0).

(ii) The solvent was removed on a rotary evaporator and the residue was dried overnight *in vacuo*.

(iii) *N*-Bromosuccinimide (NBS) that had been recently recrystallized from water, dried, and stored *in vacuo* in the dark was dissolved in 1% water in redistilled acetonitrile so that 80 mL of the solution contained 1 mmol of NBS.

(iv) An aliquot of the solution in iii containing 1 equiv of NBS was measured into the flask in ii.

(v) The reaction was allowed to progress at room temperature until a negative test was obtained with potassium iodide–starch paper.

(vi) The mixture was processed in the usual way by pouring into 10% aqueous sodium thiosulfate solution, followed by standard workup procedures.

For each anomeric pair of compounds **3** → **6**, the HPLC revealed residual starting materials as well as one new product, the latter being identified as a corresponding

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hemiacetal, **7** → **10**, by comparison with an independently prepared authentic sample (see Experimental Section).

The relative β/α ratio of the unreacted anomers was determined from the HPLC chromatogram, and comparison with the ratio obtained in i allowed us to determine the percentage change.

Each analysis was carried out twice and the results are reported in Table 1.

Calculation of Relative Rates

A system of equations was derived to calculate the relative rate ratios from the HPLC data. The equations for NBS-induced hydrolysis of two pentenyl glycosides, S_1 and S_2, are the following:

$$S_1 + NBS \rightarrow S_1\text{-OH} \qquad \frac{-d[S_1]}{dt} = k_1[S_1][NBS]$$

$$S_2 + NBS \rightarrow S_2\text{-OH} \qquad \frac{-d[S_2]}{dt} = k_2[S_2][NBS]$$

Since both anomers are in the same reaction medium, the NBS terms cancel out, and rearrangement gives

$$\frac{d[S_1]}{[S_1]} = \frac{k_1}{k_2}\frac{d[S_2]}{[S_2]}$$

Further rearrangement and integrating from times zero (t_0) to time final (t_f) gives eq 1 in which the zero time concentrations are known, and three unknowns, $[S_1]_f$, and $[S_2]_f$, and k_1/k_2 need to be determined.

If one assumes (a) that all of the NBS is consumed during the reaction and, (b) that the glycosides are present in excess, then the relationship in eq 2 holds.

$$\int_0^f \frac{d[S_1]}{[S_1]} = \frac{k_1}{k_2}\int_0^f \frac{d[S_2]}{[S_2]} \qquad \ln\frac{[S_1]_f}{[S_1]_0} = \frac{k_1}{k_2}\ln\frac{[S_2]_f}{[S_2]_0} \quad (1)$$

$$([S_1]_0 - [S_1]_f) + ([S_2]_0 - [S_2]_f) = [NBS]_0 \quad (2)$$

The HPLC product chromatogram gives the ratio of unreacted anomers, x in eq 3, which upon substitution into eq 2 gives eq 4 and thence eq 5 from which the unreacted amounts of one anomer, e.g. S_1, can be determined. The residual amount of the other anomer, S_2, may then be calculated from eq 3, and the relative ratio, k_1/k_2, from eq 1.

$$\frac{[S_2]_f}{[S_1]_f} = x \quad (3)$$

$$([S_1]_0 - [S_1]_f) + ([S_2]_0 - x[S_1]_f) = [NBS]_0 \quad (4)$$

$$[S_1]_f = \frac{-[NBS]_0 + [S_1]_0 + [S_2]_0}{x + 1} \quad (5)$$

The validity of eq 2 is crucial to the above analysis. The classic potassium iodide–starch indicator test paper proved adequate for confirming the presence of NBS down to 0.2 mmol, or 1.6% of the amount present at the start of the reaction.

Discussion

The results in Table 1 show that the above noted value of ~2 ± 0.5 for the β/α relative hydrolysis rates[2,3] is supported in entries a and c, but not in entries b and d. Since the substrates chosen for this initial study are all glucose derivatives, the results emphasize the profound effect that "protecting groups" can have on relative as well as absolute reactivities. For example the relative β/α reactivities of compounds **3** and **5** (entries a and c) are "of the same order"; however, their "absolute" rates differ by a factor of 5.

Table 1. Relative Rates of Oxidative Hydrolysis for Some n-Pentenyl Glycosides

entry	anomeric substrates	k_β/k_α (run 1, run 2) avg	reaction times[a]
a	**3** (α,β)[b]	1.68, 1.72, 1.70	6 h
b	**4** (α,β)[c]	4.84, 5.54, 5.19	7 d
c	**5** (α,β)[d]	1.44, 1.45, 1.45	31 h
d	**6** (α,β)[e]	3.35, 4.07, 3.71	14 d
e	**3**β,**5**β[f]	$k_{3\beta}/k_{5\beta}$: 1.57, 1.61, 1.59	6 h
f	**4**β,**6**β[g]	$k_{4\beta}/k_{6\beta}$: 10.3, 10.4, 10.4	7 d

[a] Time required for disappearance of NBS as determined by potassium iodide–starch indicator. HPLC conditions. [b] 10 → 50% ethyl acetate/hexane over 50 min. [c] 35% ethyl acetate/hexane over 20 min. [d] 15 → 55% ethyl acetate/hexane over 50 min. [e] 25 → 35% ethyl acetate/hexane over 15 min, then 35 → 75% ethyl acetate/hexane over 35 min. [f] 5 → 55% ethyl acetate/hexane over 50 min. [g] 30% ethyl acetate/hexane over 20 min.

The procedure described above can also be employed to determine the relative reaction rates of any pair of substrates, not just an anomeric pair. For example in entries e and f the relative reactivities of pairs of β-pyranosides have been evaluated.

That cyclic acetal protecting groups impose severe restraint on hydrolysis rates have been clearly demonstrated by experimental[5] and theoretical[6] studies, and this conclusion is further borne out by the above mentioned six-fold reactivity difference between compounds **3** and **5** (entries a and c). However, comparison of entries e and f shows that the effect of the restraining ring is highly substrate dependent, being much more exaggerated in the case of diacetate **6** than with the dibenzyl ether **5** (i.e entry f *vs* e).

This procedure should greatly facilitate the development of a comprehensive table of reactivities for a large variety of substrates, and studies aimed at providing these data are currently underway.

Experimental Section

General Procedures. Elemental analyses were performed by Atlantic Microlab, Inc., P. O. Box 2288, Norcross, GA 30091-2288. Melting points were determined in capillary tubes and are uncorrected. Optical rotations were determined at the sodium D line. For ^1H (300 MHz) and ^{13}C (75 MHz) NMR spectra, $CHCl_3$ was used the internal standard. Coupling constants were determined from double irradiation experiments. High performance liquid chromatography was performed with a Rainin Dynamax system interfaced with a Macintosh computer. Compounds were separated on a Rainin Dynamax column of 250 mm length, 4.6 mm internal diameter, and 8 mm particle size by elution with ethyl acetate/hexane solutions supplied by an HPLX solvent delivery system. In the competition experiments involving the acetylated derivatives **4** (α,β) and **6** (α,β), final concentration ratios were calculated from peak areas as measured by a Rainin Dynamax Refractive Index Detector Model RI-1. All other compounds, benzyl or benzylidene derivatives, were detected by a Rainin

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Dynamax UV-1 Variable Wavelength Absorbance Detector set to 265 nm. Dichloromethane was distilled from phosphorus pentoxide. DMF was dried over calcium hydride. Pyridine was dried over potassium hydroxide. Solvents were removed under vacuum with a rotovapor. NBS was recrystallized from water and stored in the dark under vacuum over phosphorus pentoxide. Reactions were monitored by TLC on aluminum plates precoated with silica gel HF-254 (0.2 mm layers) containing a fluorescent indicator (Merck, 5554). TLC plates were visualized by charring with a solution of ammonium molybdate(VI) tetrahydrate (12.5 g) and cerium(IV) sulfate tetrahydrate (5.0 g) in 10% aqueous sulfuric acid (500 mL). Flash chromatography was performed using Kieselgel 60 (230–400 mesh, E. Merck).

Pent-4-enyl 2,3,4,6-tetra-*O*-benzyl-α- and β-D-glucopyranoside (3α,3β). Camphorsulfonic acid (440 mg) was added to a mixture of D-glucose (20.02 g, 0.1111 mol) and 4-penten-1-ol (140 mL, 1.15 mol). The mixture was refluxed under argon in an oil bath for three days. The pentenyl alcohol was distilled under vacuum using a dry ice condenser and the residue was purified by flash chromatography (15 → 30% methanol/ethyl acetate) to yield the pentenyl glucoside, **1α,β**, as a dark orange oil (14.53 g, 0.0585 mol, 52.7%). The material was dissolved in DMF (300 mL) under argon cooled to 0 °C, and the solution was treated with sodium hydride (13.91g, of a 60% suspension in mineral oil, 0.3478 mol) and benzyl bromide (43.5 mL, 0.366 mol), and allowed to warm to room temperature while stirring overnight. The reaction was quenched with methanol, diluted with ether (225 mL), and washed with water (1 × 200 mL). The organic phase was washed with saturated aqueous ammonium chloride (1 × 200 mL), brine (1 × 200 mL), dried (Na_2SO_4), filtered, and concentrated. The crude residue was purified by flash chromatography (10 → 15% ethyl acetate/petroleum ether) to give the α anomer as a colorless oil (7.97 g, 22.4%), the β anomer as a white solid (1.82 g, 5.11%), and a mixture (~2:1 α:β) of anomers (13.36 g, 37.50%). The β-anomer was recrystallized from ethanol to yield white crystals. **3α**: $[\alpha]^{21}_D$ +32.3° (*c* 1.80, $CHCl_3$). ^1H NMR δ 7.42–7.12 (m, aromatic, 20H), 5.83 (ddt, 1H), 5.09–4.97 (m, 3H), 4.77–4.69 (m, 4H), 4.65 (m, 2H), 4.49 (m, 2H), 4.01 (m, 1H), 3.83–3.56 (m, 6H), 3.46 (ddd, 1H), 2.16 (m, 2H), 1.77 (m, 2H). ^{13}C NMR δ 138.93, 138.34, 138.26, 138.11, 137.96, 128.43, 128.23, 128.19, 127.98, 127.74, 127.65, 114.94 (aromatics and olefin), 97.02 (C-1), 82.14, 80.10, 77.76, 75.76, 75.16, 73.51, 73.23, 70.14, 68.50, 67.53 (ring, benzyl, and OPent), 30.33, 28.58 (alkane). Anal. Calcd for $C_{39}H_{44}O_6$: C, 76.95; H, 7.28. Found: C, 76.83; H, 7.26.

3β: mp = 71 °C. $[\alpha]^{21}_D$ +5.50° (*c* 3.42, $CHCl_3$). ^1H NMR δ 7.38–7.12 (m, aromatic, 20H), 5.82 (ddt, 1H), 5.06–4.89 (m, 4H), 4.83–4.69 (m, 3H), 4.62–4.49 (m, 3H), 4.38 (d, $J_{1,2}$ = 7.76 Hz, H-1), 3.95 (ddd, 1H), 3.75–3.40 (m, 7H), 2.17 (m, 2H), 1.76 (m, 2H). ^{13}C NMR δ 138.65, 138.50, 138.23, 138.12, 128.44, 128.21, 128.05, 127.94, 127.83, 127.66, 115.10 (aromatics and olefin), 103.69 (C-1), 89.8, 84.76, 82.30, 77.94, 75.77, 75.08, 74.91,73.53, 69.42 (ring, benzyl, and O-Pent), 30.32, 29.04 (alkane). Anal. Calcd for $C_{39}H_{44}O_6$: C, 76.95; H, 7.28. Found: C, 76.74; H, 7.33.

Pent-4-enyl 2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranoside (4α). The *n*-pentenyl glucoside **1α,β** (9.14 g, 0.0368 mol) was dissolved in pyridine (70 mL) under argon, acetic anhydride (38 mL, 0.40 mol) was added, and the solution was stirred overnight. The solution was then concentrated and the crude residue partitioned between dichloromethane and water. The organic phase was washed with saturated aqueous sodium bicarbonate (3 × 100 mL), brine (1 × 100 mL), dried (Na_2SO_4), and concentrated. The crude product was flash chromatographed (25 → 60% ethyl acetate/petroleum ether) to yield **4α** (7.50 g, 48.9%) and **4β** (1.93 g, 12.6%) and a mixture (~2:1 β:α) of anomers (4.25 g, 27.7%). For **4α**: mp = 62–64 °C (petroleum ether, ethyl ether). $[\alpha]^{21}_D$ +127° (*c* 1.07, $CHCl_3$). ^1H NMR δ 5.78 (ddt, 1 H), 5.45 (t, $J_{3,4} = J_{2,3}$ = 9.98 Hz, H-3), 5.10–4.92 (m, 4 H, H-1, H-4), 4.83 (dd, $J_{1,2}$ = 3.72 Hz, H-2), 4.23 (dd, $J_{6,6'}$ = 12.30 Hz, H-6), 4.07 (dd, H-6'), 3.99 (m, $J_{5,6}$ = 4.49 Hz, $J_{5,6'}$ = 2.32 Hz, H-5), 3.68 (ddd, 1 H), 3.41 (ddd, 1 H), 2.11 (m, 2H), 2.10–2.00 (four singlets for four acetates, 12H), 1.68 (m, 2H). ^{13}C NMR δ 170.56, 170.07, 169.55 (four carbonyls), 137.65, 115.28 (olefins), 95.63 (C-1), 70.83, 70.15, 68.54, 67.78, 67.11, 61.87 (ring and O-Pent), 30.03, 28.34 (alkane), 20.98, 20.64 (four acetates). Anal. Calcd for $C_{19}H_{28}O_{10}$: C, 54.80; H, 6.78. Found: C, 54.88; H, 6.82.

Pent-4-enyl 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranoside (4β). 2,3,4,6-Tetra-*O*-acetyl-α,D-glucopyranosyl bromide[7] (9.00 g, 0.0219 mol) and a mixture of freshly activated, powdered molecular sieves 4 Å (12.9 g) in dichloromethane (50 mL) were stirred under argon. After 10 min, 4-penten-1-ol (16.6 mL, 0.161 mol) and silver carbonate (12.0 g, 0.0435 mol) were added and the mixture refluxed. After two days, the mixture was filtered through Celite. The filtrate was washed with saturated aqueous sodium bicarbonate (2 × 50 mL) and the combined aqueous washes were extracted with dichloromethane (10 mL). The organic phases were combined and washed with brine (50 mL), dried (Na_2SO_4), filtered, and concentrated. The crude residue was flash chromatographed (25 → 35% ethyl acetate/petroleum ether) to afford the product as a clear solid (3.03 g, 30.4%) which was recrystallized. Mp = 47–48 °C (ether/hexane). $[\alpha]^{21}_D$ −19.5° (*c* 1.52, $CHCl_3$) [lit. -19.4° (*c* 1.0, $CHCl_3$)].[8] ^1H NMR δ 5.77 (ddt, 1 H), 5.18 (t, $J_{2,3} = J_{3,4}$ = 9.55 Hz, H-3), 5.10–4.92 (m, 4 H, H-2, H-4), 4.46 (d, $J_{1,2}$ = 7.92 Hz, H-1), 4.24 (dd, $J_{5,6}$ = 4.69 Hz, $J_{6,6'}$ = 12.24 Hz, H-6), 4.09 (dd, $J_{5,6'}$ = 2.44 Hz, H-6'), 3.85 (ddd, 1 H), 3.67 (m, H-5), 3.48 (ddd, 1 H), 2.08 (m, 2H), 2.05–1.97 (four singlets for four acetates, 12H), 1.65 (m, 2H). ^{13}C NMR δ 170.69, 170.32, 169.04, 169.28 (four carbonyls), 137.77, 115.09 (olefins), 100.81 (C-1), 72.85, 71.66, 71.35, 69.33, 68.39, 61.96 (ring and O-Pent), 29.81, 28.54 (alkane), 20.77, 20.69, 20.64, 20.58 (four acetates). Anal. Calcd for $C_{19}H_{28}O_{10}$: C, 54.80: H, 6.78. Found: C, 54.80; H, 6.80.

Pent-4-enyl 4,6-*O*-benzylidene-α- and β-D-glucopyranoside (2α,β). Benzaldehyde dimethyl acetal (75.0 mL, 0.500 mol) and *p*-toluenesulfonic acid monohydrate (1.82 g) were added to a solution of the pentenyl glucoside **1α,β** (17.97 g, 0.07238 mol) dissolved in acetonitrile (400 mL). The solution was stirred at 70 °C. After 1 h, TLC showed no remaining starting material. The reaction was quenched with triethylamine and the solution concentrated. The crude residue was partitioned between ethyl acetate and water. The organic phase was washed with saturated aqueous sodium bicarbonate (1 × 100 mL) and brine (1 × 100 mL), dried (Na_2SO_4), filtered, and concentrated. The crude residue was flash chromatographed (55 → 70% ethyl acetate/hexane) to yield the β anomer (1.62 g, 6.67%) and the α anomer (6.11 g, 25.1%). For **2β**: mp = 144–145 °C (ethanol). $[\alpha]^{21}_D$ −43.7° (*c* 1.01, $CHCl_3$). ^1H NMR δ 7.50–7.31 (m, aromatics, 5H), 5.79 (ddt, 1H), 5.49 (s, H-7), 5.10–4.93 (m, 2H), 4.36–4.25 (m, $J_{1,2}$ = 7.62Hz, $J_{5,6}$ = 4.82 Hz, H-1, H-6), 3.88 (ddd, 1H), 3.74 (m, 2H), 3.60–3.35 (m, 4H), 3.20 (s, 1H), 3.02 (s, 1H), 2.11 (m, 2H), 1.71 (m, 2H). ^{13}C NMR δ 137.98, 137.00, 129.29, 128.36, 126.32, 115.09 (aromatics and olefins), 103.19 (C-1), 101.90 (C-7), 80.57, 74.53, 73.10, 69.88, 68.68, 66.35 (ring and O-Pent), 30.12, 28.71 (alkane). Anal. Calcd for $C_{18}H_{24}O_6$: C, 64.27; H, 7.19. Found: C, 64.10; H, 7.23.

2α: mp = 89 °C (ethyl acetate/hexane). $[\alpha]^{21}_D$ +96.0° (*c* 1.22, $CHCl_3$). ^1H NMR δ 7.50–7.31 (m, aromatic, 5H), 5.79 (ddt, 1H), 5.49 (s, H-7), 5.08–4.96 (m, 2H), 4.83 (d, $J_{1,2}$= 3.91 Hz, H-1), 4.23 (dd, $J_{6,6'}$ = 9.49 Hz, H-6), 3.89 (t, $J_{2,3} = J_{3,4}$ = 9.25 Hz, H-3), 3.86–3.67 (m, 4H, H-5), 3.56 (dd, H-2), 3.44 (m, 2H), 2.90–2.30 (broad s, 2H), 2.12 (m, 2H), 1.73 (m, 2H). ^{13}C NMR δ 137.84, 137.05, 129.26, 128.35, 126.33, 115.27 (aromatics and olefin), 101.90 (C-7), 98.75 (C-1), 80.92, 72.90, 71.83, 68.93, 67.96, 62.62 (ring and O-Pent), 30.34, 28.56 (alkane). Anal. Calcd for $C_{18}H_{24}O_6$: C, 64.27; H, 7.19. Found: C, 64.07; H, 7.17.

Pent-4-enyl 2,3-Di-*O*-acetyl-4,6-*O*-benzylidene-α-D-glucopyranoside (6α). To a solution of pent-4-enyl 4,6-*O*-benzylidene-α-D-glucopyranoside (**2α**) (2.49 g, 7.40 mmol) dissolved in pyridine (55 mL) was added acetic anhydride (2.1 mL, 22 mmol) and 4-(dimethylamino)pyridine (198 mg, 1.62

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mmol). The solution was stirred overnight. The solution was concentrated, azeotroped with toluene three times, and flash chromatographed (20 → 25% ethyl acetate/hexane) to afford **6α** as a white solid (2.29 g, 73.4%). mp = 133–134 °C (ethyl acetate/hexane). $[\alpha]^{21}_D$ +85.8° (*c* 1.03, $CHCl_3$). ^1H NMR δ 7.47–7.29 (m, aromatics, 5H), 5.78 (ddt, 1H), 5.68 (t, $J_{2,3}$ = $J_{3,4}$ = 9.86Hz, H-3), 5.48 (s, H-7), 5.05–4.95 (m, 3H, H-1), 4.84 (dd, $J_{1,2}$ = 3.80 Hz, H-2), 4.27 (dd, $J_{5,6}$ = 4.70 Hz, $J_{6,6'}$ = 10.18 Hz, H-6), 3.94 (ddd, H-5), 3.78–3.58 (m, 3H, H-4, H-6), 3.39 (ddd, 1H), 2.11 (m, 2H), 2.05- 2.00 (two singlets for two acetates, 6H), 1.69 (m, 2H). ^{13}C NMR δ 170.39, 169.77 (two carbonyls), 137.71, 136.90, 128.98, 128.16, 126.06, 115.13 (aromatics and olefin), 101.44 (C-7), 96.48 (C-1), 79.28, 71.66, 68.99, 68.81, 67.68, 62.32 (ring and O-Pent), 30.02, 28.39 (alkane), 20.82, 20.67 (two acetates). Anal. Calcd for $C_{22}H_{28}O_8$: C, 62.85; H, 6.71. Found: C, 62.71; H, 6.74.

Pent-4-enyl 2,3-Di-*O*-acetyl-4,6-*O*-benzylidene-β-D-glucopyranoside (6β). Pent-4-enyl 4,6-*O*-benzylidene-β-D-glucopyranoside (**2β**) (1.37 g, 4.08 mmol) was acetylated as described for **6α**. The crude product was flash chromatographed (20% ethyl acetate/hexane) to yield **6β** as a white solid (978 mg, 57.1%). Mp = 130–131 °C (ethanol). $[\alpha]^{21}_D$ −76.8° (*c* 1.10, $CHCl_3$). ^1H NMR δ 7.46–7.31 (m, aromatics, 5H), 5.77 (ddt, 1H), 5.49 (s, H-7), 5.30 (t, $J_{2,3}$ = $J_{3,4}$ = 9.52 Hz, H-3), 5.03–4.92 (m, 3H, H-2), 4.55 (d, $J_{1,2}$ = 7.87 Hz, H-1), 4.34 (dd, $J_{5,6}$ = 4.93 Hz, $J_{6,6'}$ = 10.52 Hz, H-6), 3.80–3.77 (m, 2H, H-5), 3.68 (t, $J_{4,5}$ = 9.52 Hz, H-4), 3.49 (m, 2H, H-6'), 2.11–2.01 (m, two acetates, 8H), 1.66 (m, 2H). ^{13}C NMR δ 170.17, 169.52 (two carbonyls), 137.73, 136.78, 129.10, 128.22, 126.10, 115.01 (aromatics and olefin), 101.43 (C-7), 101.38 (C-1), 78.35, 72.30, 71.79, 69.50, 68.55, 66.30 (ring and O-Pent), 29.79, 28.58 (alkane), 20.79, 20.68 (two acetates). Anal. Calcd for $C_{22}H_{28}O_8$: C, 62.85; H, 6.71. Found: C, 62.76; H, 6.69.

Pent-4-enyl 2,3-Di-*O*-benzyl-4,6-*O*-benzylidene-α-D-glucopyranoside (5α). Pent-4-enyl 4,6-*O*-benzylidene-α-D-glucopyranoside (**2α**) (2.46 g, 7.31 mmol) was dissolved in DMF (60 mL) and chilled to 0 °C under argon. Sodium hydride (2.50 g of a 60% suspension in mineral oil, 0.0625 mmol) was added in portions after which time benzyl bromide (6.99 mL, 58.8 mmol) was added. The solution was stirred overnight gradually warming to room temperature. The reaction was quenched with methanol and the solution concentrated under high vacuum. The crude residue was taken up in dichloromethane, washed with water (2 × 100 mL), and saturated aqueous ammonium chloride (2 × 100 mL), brine (1 × 100 mL), dried (Na_2SO_4), filtered, and concentrated. The crude product was flash chromatographed (0 → 5% ethyl acetate/hexanes) to yield **5α** as a white solid (2.60 g, 69.0%). mp = 81–82 °C (ethanol). $[\alpha]^{21}_D$ +0.65° (*c* 9.41, $CHCl_3$). ^1H NMR δ 7.52–7.25 (m, aromatics, 15H), 5.82 (ddt, 1H), 5.55 (s, H-7), 5.09–4.78 (m, 5H), 4.70 (m, 2H, $J_{1,2}$ = 3.77 Hz, H-1), 4.27 (dd, $J_{5,6}$ = 4.64 Hz, $J_{6,6'}$ = 10.01 Hz, H-6), 4.05 (t, $J_{2,3}$ = $J_{3,4}$ = 9.28 Hz, H-3), 3.87 (ddd, $J_{5,6'}$ = $J_{4,5}$ = 9.89 Hz, H-5), 3.76–3.50 (m, 4H, H-2, H-4, H-6), 3.44 (ddd, 1H), 2.16 (m, 2H), 1.76 (m, 2H). ^{13}C NMR δ 138.80, 138.28, 137.92, 137.38, 128.85, 128.38, 128.26, 128.19, 127.93, 127.80, 127.51, 125.97, 115.00 (aromatics and olefin), 101.16 (C-7), 98.02 (C-1), 82.22, 79.37, 78.59, 75.28, 73.50, 69.04, 67.67, 62.40 (ring, benzyl, and O-Pent), 30.20, 28.50 (alkane). Anal. Calcd for $C_{32}H_{36}O_6$: C, 74.39; H, 7.02. Found: C, 74.15; H, 7.06.

Pent-4-enyl 2,3-Di-*O*-benzyl-4,6-*O*-benzylidene-β-D-glucopyranoside (5β). Pent-4-enyl 4,6-*O*-benzylidene-β-D-glucopyranoside (**2β**) was benzylated as described above for **5α**. The crude product was flash chromatographed (5 → 10% ethyl acetate/hexane) to yield **5β** as a clear oil that crystallized overnight under vacuum (1.39 g, 75.2%). Mp = 76 °C (ethanol). $[\alpha]^{21}_D$ −36.5° (*c* 1.02, $CHCl_3$). ^1H NMR δ 7.50–7.21 (m, aromatics, 15H), 5.80 (ddt, 1H), 5.56 (s, H-7), 5.06–4.87 (m, 4H), 4.78 (m, 2H), 4.49 (d, $J_{1,2}$= 7.76 Hz, H-1), 4.34 (dd, $J_{5,6}$ = 4.91 Hz, $J_{6,6'}$ = 10.47 Hz, H-6), 3.93 (ddd, 1H), 3.81–3.64 (m, H-3, H-4, H-5), 3.58 (ddd, 1H), 3.48–3.36 (m, H-2, H-6), 2.16 (m, 2H), 1.75 (m, 2H). ^{13}C NMR δ 138.54, 138.36, 137.94, 137.36, 128.98, 128.37, 128.33, 128.15, 128.10, 127.77, 127.68, 126.05, 115.11 (aromatic and olefin), 104.15 (C-1), 101.13 (C-7), 82.17, 81.54, 80.93, 75.44, 75.19, 69.86, 68.85, 66.04 (ring, benzyl, and O-Pent), 30.22, 28.99 (alkane). Anal. Calcd for $C_{32}H_{36}O_6$: C, 74.39; H, 7.02. Found: C, 74.35; H, 7.02.

Oxidative Hydrolysis of NPGs to give 7 → 10. A standard procedure was as follows: *N*-Bromosuccinimide (3 equiv) was added to a solution of the NPG (1 equiv) in 1% aqueous MeCN (40 mL/mmol of glycoside). Upon completion (TLC), the reaction was quenched by addition of 10% aqueous $Na_2S_2O_3$. Most of the solvent was removed *in vacuo*, and the residue was diluted with water and extracted with Et_2O. The ethereal extract was dried (Na_2SO_4), filtered, and evaporated *in vacuo*. Column chromatography of the resulting material afforded the pyranoses **7** → **10**.

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