Notes

New and Easy Access to C-Glycosides of Glucosamine and Mannosamine†

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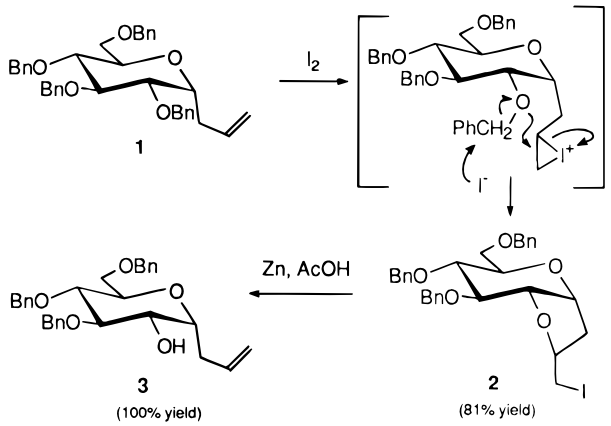
Introduction

The significant roles that cell surface-associated carbohydrates exert in most cell−cell and cell−pathogen recognition phenomena have recently stimulated the interest in molecules that could interfere in these processes. Analogues of cell surface-associated carbohydrates, which compete in the adhesion processes, or inhibitors of carbohydrate-processing enzymes, which interfere in the biosynthesis of specific cell surface carbohydrates, are of great pharmaceutical interest. Therefore many synthetic efforts have been devoted to this class of molecules,[1] and in particular to C-glycosides,[1,2] where the glycosidic oxygen is substituted by a carbon atom.

During the last decade many C-glycosylation procedures have been reported, and ambitious syntheses of C-glycosidically linked oligosaccharides and glycoconjugates have been performed. However, despite these successes, only few examples of C-glycosylations of aminosugars have been proposed,[3] although these compounds, particularly glucosamine and mannosamine, are involved in important biological processes such as the biosynthesis of the bacterial cell wall. As far as we know, no examples of C-glycosylation of mannosamino derivatives have been reported until now.

In our studies devoted to glycomimetics of glucosamino derivatives, we experienced that the amino group strongly interferes in the manipulation of the C-glycosidic appendage, in particular when the C-glycosidic carbon must be transformed into an electrophile. For example, in the synthesis of the phosphono analogue of α-D-glucosamine 1-phosphate,[4] any attempt to convert the C-glycosidic carbon of a glucosamino or *N*-acetylglucosamino derivative in an electrophile failed. These observations convinced us that a general procedure to synthesize C-glucosaminosides requires the easy introduction of the amino function at the end of the synthesis. This can be done by proper manipulation of the selectively deprotected C-2 hydroxyl group of a C-glucosidic intermediate, a procedure that can afford also C-mannosaminosides.

Scheme 1



We have previously described an easy method to synthesize C-glucosides with a free hydroxyl group at C-2.[5] Now, we describe a new and easy method to deprotect regioselectively the hydroxyl group at C-2 of α- and β-C-glucosyl-2-propenes, and its application in the synthesis of α- and β-C-glycosides of glucosamine and mannosamine.

Results and Discussion

In our opinion, one of the best methods for the synthesis of C-glucosides is the Lewis acid catalyzed allylation of methyl 2,3,4,6-tetra-*O*-benzyl-α-D-glucopyranoside with allyltrimethylsilane,[6] which affords 1-(2′,3′,4′,6′-tetra-*O*-benzyl-α-D-glucopyranosyl)-2-propene (**1**)[7] in excellent yield and stereoselection. To obtain α-C-glucosides with the hydroxyl group at C-2 selectively deprotected, the possibility to exploit the double bond of the allylic appendage of **1** was explored. The idea is based on the observation that the oxygen of a benzyl ether can act as a nucleophile on a iodonium ion, with subsequent loss of the benzyl cation, in a intramolecular process.[8] The reaction affords a cyclic iodoether which on reductive elimination restores the double bond and a free hydroxyl group, the entire process resulting in a debenzylation. In the case of **1**, the benzyloxy group at C-2 is the only one that can undergo this intramolecular reaction. It reacted with the iodonium ion, in a 5-*exo* type cyclization, affording the cyclic iodoether **2** (Scheme 1). Treatment of **2** with Zn and AcOH resulted in the formation of 1-(3′,4′,6′-tri-*O*-benzyl-α-D-glucopyranosyl)-

† Dedicated to Professor Dr. Hans Paulsen on the occasion of his 75th birthday.

(1) *Topics in Current Chemistry*; Driguez, H., Thiem, J., Eds., Springer: Berlin, 1997, Vol 187.

(2) For a comprehensive description of C-glycosides see: (a) Postema, M. H. D. *C-Glycoside Synthesis*; CRC Press: Boca Raton, 1995. (b) Levy D. E.; Tang, C. *The Chemistry of C-Glycosides*, Tetrahedron Organic Chemistry Series Volume 13, Pergamon: New York, 1995.

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(5) Boschetti, A.; Nicotra, F.; Panza, L.; Russo, G. *J. Org. Chem.* **1988**, *53*, 4181.

(6) Lewis, M. D.; Kun Cha, J.; Kishi, Y. *J. Am. Chem. Soc.* **1982**, *104*, 4976.

(7) We named C-glycosides by semisistematic names generally accepted for this class of compounds; this allows an easier comparison with the parent sugar.

(8) (a) Rychnovsky, S. D.; Bartlett, P. A. *J. Am. Chem. Soc.* **1981**, *103*, 3963. (b) Nicotra, F.; Panza, L.; Russo, G. *J. Org. Chem.* **1987**, *52*, 5627.

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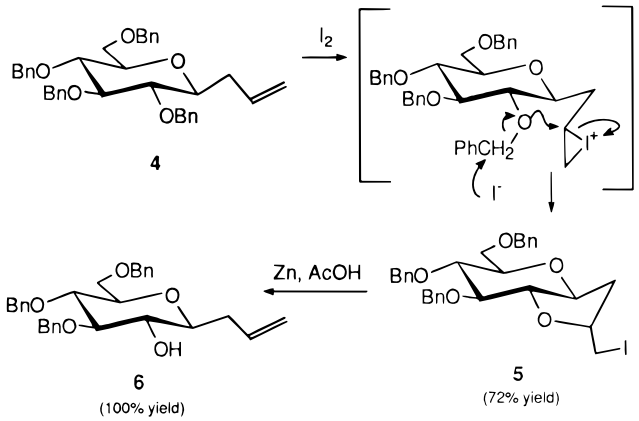
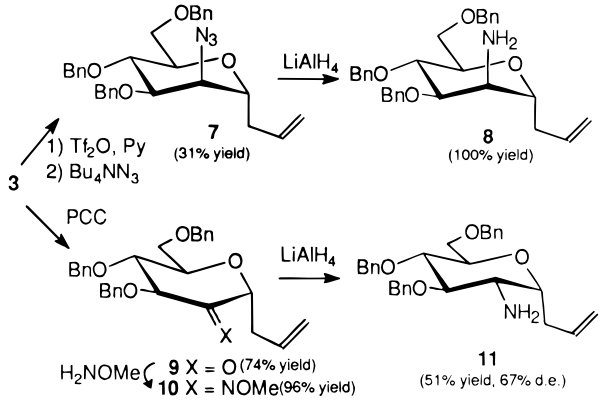
Scheme 2



Scheme 3



Scheme 4

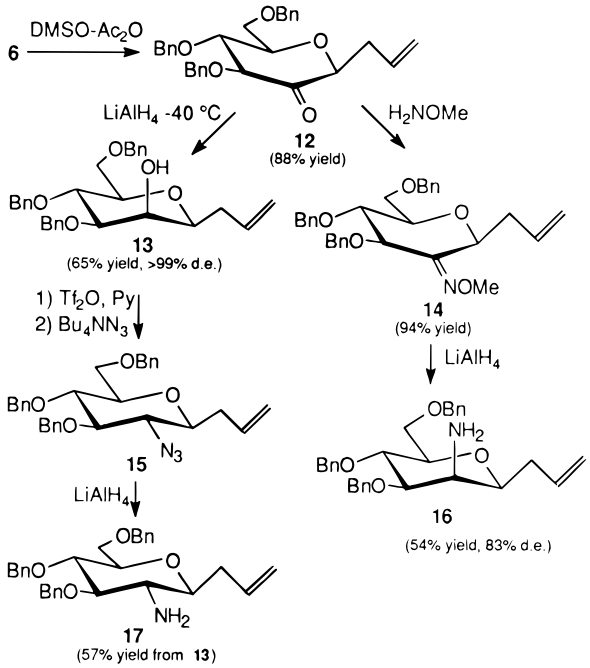
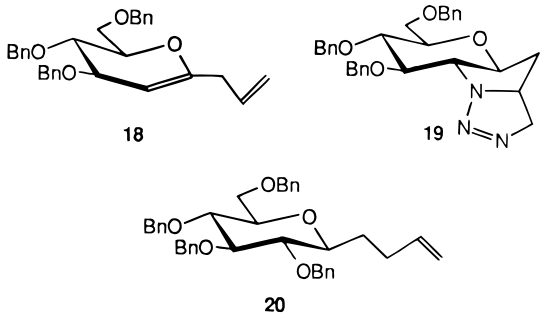


Chart 1



2-propene (**3**),[9] the regioselective deprotection process occurring in 81% yield.

The process can also be applied to 1-(2′,3′,4′,6′-tetra-*O*-benzyl-*β*-D-glucopyranosyl)-2-propene (**4**)[6] (Scheme 2), although more controlled experimental conditions are required to obtain the cyclic iodoether **5** in good yields. The reductive elimination of **5** with Zn and AcOH afforded 1-(3′,4′,6′-tri-*O*-benzyl-*β*-D-glucopyranosyl)-2-propene (**6**) in 72% overall yield (from **4**).

The conversion of the free hydroxyl group of **3** and **6** into an amino function was accomplished alternatively with retention and with inversion of the configuration, so affording all the possible α and *β*, *gluco* and *manno* 2-amino-2-deoxy-C-glycopyranosides (Schemes 3 and 4).

The α-*manno* isomer, 1-(2′-amino-3′,4′,6′-tri-*O*-benzyl-2′-deoxy-α-D-mannopyranosyl)-2-propene (**8**), was obtained by converting **3** into the triflate, treating the triflate with Bu_4NN_3, and reducing the obtained 1-(2′-azido-3′,4′,6′-tri-*O*-benzyl-2′-deoxy-α-D-mannopyranosyl)-2-propene (**7**) with $LiAlH_4$. The triflate intermediate was very labile, undergoing spontaneous elimination at room temperature with formation of the glucal **18**. Direct treatment of the crude triflate with the azide was then required. The *manno* configuration of **8** was confirmed by a 3.2 Hz coupling constant between H-2′ and H-3′ (see Experimental Section).

The α-*gluco* isomer, 1-(2′-amino-3′,4′,6′-tri-*O*-benzyl-2′-deoxy-α-D-glucopyranosyl)-2-propene (**11**), was obtained by oxidation of **3** to the corresponding ketone **9**, conversion of the ketone into the methyloxime **10**, and reduction of the methyloxime with $LiAlH_4$. This reduction was stereoselective (5:1, *gluco*/*manno*), the hydride approaching from the less hindered *β*-face of the α-glycoside.[10] The *gluco* isomer **11** was easily separated from the *manno* isomer **8** by flash chromatography.

To obtain the *β*-*gluco* isomer, 1-(2′-amino-3′,4′,6′-tri-*O*-benzyl-2′-deoxy-*β*-D-glucopyranosyl)-2-propene (**17**), **6** was oxidized with DMSO−Ac_2O to afford the ketone **12**, which was stereoselectively[10] reduced with $LiAlH_4$ in THF at −40 °C affording only the *manno* isomer **13** (according with the $J_{2,3} = 3.4$ Hz). Finally, the hydroxyl group of **13** was converted into an amino group, with inversion of the configuration, by treatment with Tf_2O in Py and reaction of the obtained triflate with Bu_4NN_3. The obtained 1-(2′-azido-3′,4′,6′-tri-*O*-benzyl-2′-deoxy-*β*-D-glucopyranosyl)-2-propene (**15**) underwent a spontaneous cycloaddition, as reported for its α-epimer,[11] to afford **19**; so immediate reduction with $LiAlH_4$ to 1-(2′-amino-3′,4′,6′-tri-*O*-benzyl-2′-deoxy-*β*-D-glucopyranosyl)-2-propene (**17**) was required.

The synthesis of *β*-mannosides is in general disfavored. In our case the attempts to convert the hydroxyl group of **6** into an azide with inversion of configuration failed, the triflate intermediate undergoing spontaneous elimination to glucal **18**. In the light of the excellent stereoselection in favor of the *β*-*manno* isomer, obtained in the

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(11) Bertozzi, C. R.; Bednarski, M. D. *Tetrahedron Lett.* **1992**, *33*, 3109.

reduction of the ketone **12** at −40 °C with $LiAlH_4$, to prepare the *β*-C-mannosamino derivative **16** the reduction of the methyloxime **14** was tested. The reduction does not occur at temperatures lower than 20 °C, and at 20 °C the stereoselection in favor of the *β-manno* isomer **16** was very low (50% de). Different reducing agents, such as $LiEt_3BH$ or catalytic hydrogenation with Raney-Ni, gave worst results. Surprisingly, increasing the temperature to 40 °C the reduction of **14** with $LiAlH_4$ became more stereoselective, affording the *β-manno* isomer **16** in 83% de, which was isolated in pure form by flash chromatography. The *manno* configuration of **16** was confirmed by the 3.8 Hz coupling constant between H-2′ and H-3′.

The described regioselective debenzylation procedure is limited to the propenyl derivatives. In fact 1-(2′,3′,4′,6′-tetra-*O*-benzyl-*β*-D-glucopyranosyl)-3-butene (**20**), treated with iodine in different experimental conditions, gave unsatisfactory results even if the 6-*exo*-type cyclization is allowed as well.

In conclusion, the "late amination" of C-glucosides with the hydroxyl group at C-2 selectively deprotected is a useful procedure to obtain different α- and *β*-C-glycosides of glucosamine and mannosamine. We have previously reported a C-glycosylation procedure that affords α-C-glucosides with a free hydroxyl group at C-2.[5] Now we have described a procedure that allows the regioselective deprotection at C-2 of the easily available α- and *β*-1-(2′,3′,4′,6′-tetra-*O*-benzyl-D-glucopyranosyl)-2-propenes (**1** and **4**) and their conversion into α- and *β*-C-glycosides of glucosamine and mannosamine. It is worthy of note that the procedure can be exploited in general to obtain α- and *β*-C-glycosides differently functionalized at C-2.

Experimental Section

General. ^1H NMR and ^{13}C NMR spectra were recorded with TMS as internal reference. The signals of the aromatic carbons in the ^{13}C NMR spectra are not reported. $[\alpha]_D$ values were measured at 20 °C and are given in units of 10^{-1} deg cm^2 g^{-1}. Chromatographic purifications were performed with the flash procedure using silica gel 60 (230−400 mesh). TLC were performed on silica gel 60 F_{254} plates and visualized by spraying with a solution containing H_2SO_4 (31 mL), ammonium molybdate (21 g), and $Ce(SO_4)_2$ (1 g) in water (500 mL) and then heating at 110 °C for 5 min. Usual workup refers to dilution with an organic solvent, washing with water to neutrality (pH test paper), drying with Na_2SO_4, filtration, and evaporation under reduced pressure.

1-(3′,4′,6′-Tri-*O*-benzyl-α-D-glucopyranosyl)-2-propene (3). To a solution of **1** (1.00 g, 1.77 mmol) in dry THF (4 mL) was added iodine (2.3 g, 9 mmol) at 0 °C, under N_2 atmosphere. After 1 h 30 min, the reaction mixture was diluted with EtOAc, aqueous $Na_2S_2O_3$ was added, and the mixture was stirred till the organic layer became colorless. Usual workup and chromatography (9:1, hexane−EtOAc) afforded **2** (876 mg, 81%) as a colorless oil (mixture of diastereomers). ^{13}C NMR (50.29 MHz, $CDCl_3$) of the major isomer: *δ* 85.2 (d), 83.8 (d), 82.4 (d), 76.1 (d), 75.9 (d), 75.6 (d), 75.0 (t), 74.0 (t), 73.5 (t), 70.4 (t), 38.8 (t), 10.8 (t). Product **2** (870 mg, 1.45 mmol) was dissolved in a 1:1 mixture of Et_2O−MeOH (15 mL), and powdered zinc (872 mg, 13.2 mmol) and glacial acetic acid (152 *μ*L, 2.72 mmol) were sequentially added. The suspension was stirred overnight and then filtered over a Celite pad. The filtrate was evaporated, and the residue was submitted to usual workup and filtration over a short column of silica gel (8:2, hexane−EtOAc), affording **3** (687 mg, quantitative yield) as a white solid. $[\alpha]_D$ +33.3° (*c* 1, $CHCl_3$); mp 69−71 °C; ^1H NMR (300 MHz, $CDCl_3$) *δ* 7.42−7.28 (m, 15 H), 5.95−5.78 (m, 1 H), 5.15 (broad dd, 1 H, *J* = 16.0, 3.2 Hz), 5.07 (broad dd, 1 H, *J* = 9.6, 3.2 Hz), 4.68−4.46 (m, 6 H), 4.11−4.04 (m, 1 H), 3.93 (ddd, 1 H, *J* = 8.0, 5.8, 3.5 Hz), 3.82 (t, 1 H, *J* = 9.3 Hz), 3.79 (t, 1 H, *J* = 9.3 Hz), 3.76−3.62 (m, 3 H), 2.93 (d, 1 H, *J* = 8.0 Hz), 2.53−2.35 (m, 2 H); ^{13}C NMR (75.43 MHz, $CDCl_3$) *δ* 135.4 (d), 117.5 (t), 78.2 (d), 75.47 (d), 74.2 (d), 73.9 (2t), 73.4 (t), 71.7 (d), 69.7 (d), 68.8 (t), 33.9 (t). Anal. Calcd for $C_{30}H_{34}O_5$: C, 75.92%; H, 7.22%. Found: C, 76.08%; H, 7.08%.

1-(3′,4′,6′-Tri-*O*-benzyl-*β*-D-glucopyranosyl)-2-propene (6). To a solution of **4** (1.00 g, 1.77 mmol) in dry CH_2Cl_2 (50 mL) was added iodine (4.5 g, 17.7 mmol) at 0 °C under N_2 atmosphere. The reaction mixture was allowed to warm to room temperature and stirred for 5 h. The reaction was then quenched with aqueous $Na_2S_2O_3$ till the organic phase became colorless. Usual workup and chromatography (85:15, hexane−EtOAc) afforded **5** (765 mg, 72%) as a colorless oil (mixture of diastereomers). ^{13}C NMR (75.43 MHz, $CDCl_3$) of the major isomer: *δ* 83.9 (d), 83.8 (d), 80.9 (d), 78.0 (d), 77.6 (d), 77.5 (d), 75.3 (t), 73.5 (t), 73.0 (t), 69.3 (t), 34.3 (t), 11.2 (t). The cyclic iodoether **5** (600 mg), treated with Zn and AcOH as described for the preparation of **3,** afforded **6** as a white solid (473 mg, quantitative yield) which crystallizes from Et_2O−hexane. $[\alpha]_D$ +37.5° (*c* 0.9, $CHCl_3$); mp 63−65 °C; ^1H NMR (300 MHz, $CDCl_3$) *δ* 7.45−7.25 (m, 15 H), 6.05−5.88 (m, 1 H), 5.14 (broad dd, 1 H, *J* = 16.0, 2.0 Hz), 5.08 (broad d, 1 H, *J* = 10.0 Hz), 4.97, 4.63 (Abq, 2 H, *J* = 11.4 Hz), 4.83, 4.75 (Abq, 2 H, *J* = 10.4 Hz), 4.65, 4.58 (Abq, 2 H, *J* = 11.8 Hz), 3.79−3.67 (m, 2 H), 3.64 (t, 1 H, *J* = 9.0 Hz), 3.51 (t, 1 H, *J* = 9.0 Hz), 3.47−3.43 (m, 1H), 3.38 (t, 1 H, *J* = 9.0 Hz), 3.27 (ddd, 1 H, *J* = 9.0, 6.4, 2.4 Hz), 2.59 (ddd, 1 H, *J* = 15.0, 6.4, 2.4 Hz), 2.32 (dt, 1 H, *J* = 15.0, 6.4 Hz), 2.05 (s, 1 H); ^{13}C NMR (75.43 MHz, $CDCl_3$) *δ* 134.6 (d), 117.1 (t), 86.8 (d), 79.2 (d), 78.8 (d), 78.5 (d), 75.2 (t), 74.9 (t), 74.8 (t), 73.5 (t), 69.0 (t), 36.2 (t). Anal. Calcd for $C_{30}H_{34}O_5$: C, 75.92%; H, 7.22%. Found: C, 75.80%; H, 7.31%.

1-(2′-Azido-3′,4′,6′-tri-*O*-benzyl-2′-deoxy-α-D-mannopyranosyl)-2-propene (7). To a solution of **3** (100 mg, 0.21 mmol) in dry CH_2Cl_2 (2 mL) were added dry pyridine (68 *μ*L, 0.84 mmol) and Tf_2O (69 *μ*L, 0.42 mmol) at 0 °C under N_2. After 1 h the reaction was complete. Usual workup afforded the crude triflate (150 mg), which was dissolved in dry toluene (2 mL), under N_2 atmosphere, and stirred overnight with a solution of Bu_4NN_3 (120 mg) in dry toluene (2 mL). Evaporation of the solvent to dryness, and chromatographic purification (9.5:0.5, hexane−EtOAc) afforded **7** (32 mg, 31%) as a white amorphous solid. $[\alpha]_D$ +13.0° (*c* 0.8, $CHCl_3$); IR (film) *ν* 2096 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) *δ* 7.38−7.28 (m, 15 H), 5.85−5.71 (m, 1 H), 5.08 (d, 1 H, *J* = 9.5 Hz), 5.06 (d, 1 H, *J* = 17.9 Hz), 4.72, 4.55 (ABq, 2 H, *J* = 11.4 Hz), 4.66 (broad s, 2 H), 4.57, 4.48 (ABq, 2 H, *J* = 12.4 Hz), 3.97 (broad dt, 1 H), 3.89 (dd, 1 H, *J* = 7.0, 3.7 Hz), 3.87−3.66 (m, 4 H), 3.63 (t, 1 H, *J* = 3.7 Hz), 2.48−2.26 (m, 2 H); ^{13}C NMR (75.43 MHz, $CDCl_3$) *δ* 133.4 (d), 117.9 (t), 78.26 (d), 74.1 (t), 74.1 (d), 73.5 (d), 73.4 (t), 72.9 (d), 72.7 (t), 68.8 (t), 60.5 (d), 35.0 (t). Anal. Calcd for $C_{30}H_{33}N_3O_4$: C, 72.12%; H, 6.66%; N, 8.41%. Found: C, 71.97%; H, 6.50%; N, 8.55%.

1-(2′-Amino-3′,4′,6′-tri-*O*-benzyl-2′-deoxy-α-D-mannopyranosyl)-2-propene (8). Product **7** (25 mg, 0.05 mmol) was dissolved in dry THF (2 mL) under N_2 atmosphere, and a 1 M solution of $LiAlH_4$ in THF (125 *μ*L) was added; the reaction mixture was stirred for 20 min and then quenched with EtOAc. Usual workup and chromatography (9.5:0.5, CH_2Cl_2−MeOH) afforded **8** (23 mg, quantitative yield) as a colorless oil. $[\alpha]_D$ +25.6° (*c* 0.9, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) *δ* 7.35−7.24 (m, 15 H), 5.88−5.72 (m, 1 H), 5.08 (d, 1 H, *J* = 16.2 Hz), 5.05 (d, 1 H, *J* = 11.0 Hz), 4.76, 4.53 (ABq, 2 H, *J* = 11.3 Hz), 4.59 (broad s, 2 H), 4.57, 4.50 (ABq, 2 H, *J* = 12.2 Hz), 3.88 (dt, 1H, *J* = 7.2, 3.3 Hz), 3.83−3.69 (m, 4H), 3.65 (dd, 1H, *J* = 9.5, 3.2 Hz), 3.10 (t, 1 H, *J* = 3.2 Hz), 2.47 (dt, 1 H, *J* = 14.5, 7.2 Hz), 2.33 (dt, 1 H, *J* = 14.5, 7.2 Hz), 1.71 (broad s, 2 H); ^{13}C NMR (75.43 MHz, $CDCl_3$) *δ* 134.42 (d), 117.2 (t), 79.8 (d), 76.1 (d), 74.3 (t), 74.0 (d), 73.4 (t), 73.0 (d), 71.9 (t), 69.2 (t), 50.8 (d), 29.7 (t). Anal. Calcd for $C_{30}H_{35}NO_4$: C, 76.08%; H, 7.45%; N, 2.96%. Found: C, 75.97%; H, 7.53%; N, 3.04%.

1-(3′,4′,6′-Tri-*O*-benzyl-α-D-*arabino*-hexulopyranosyl)-2-propene (9). In a double-necked flask, under N_2 atmosphere, containing 1 g of 4 Å activated powdered molecular sieves and PCC (457 mg, 2.12 mmol), was added a solution of **3** (503 mg, 1.06 mmol) in dry CH_2Cl_2 (20 mL) by a double ended needle. After 2 h, the reaction was complete; the reaction mixture was filtered over a Celite pad and the filtrate concentrated. The residue was purified on a short chromatographic column of 70−230 mesh silica gel (9:1, hexane−EtOAc), affording **9** (372 mg,

74%) as a colorless oil. $[\alpha]_D$ +50.0° (*c* 1, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 7.50−7.15 (m, 15 H), 5.80−5.71 (m, 1 H), 5.10 (d, 1 H, *J* = 17.8 Hz), 5.08 (d, 1 H, *J* = 11.7 Hz), 4.95, 4.51 (Abq, 2 H, *J* = 11.6 Hz), 4.80, 4.60 (Abq, 2 H, *J* = 11.5 Hz), 4.50, 4.42 (Abq, 2 H, *J* = 12.0 Hz), 4.39 (d, 1 H, *J* = 8.0 Hz), 4.26 (t, 1 H, *J* = 8.0 Hz), 4.04 (dt, 1 H, *J* = 8.0, 3.5 Hz), 3.89 (dd, 1 H, *J* = 8.8, 7.5 Hz), 3.65−3.56 (m, 2 H), 2.50 (broad t, 2 H, J = 8.0 Hz); ^{13}C NMR (75.43 MHz, $CDCl_3$) δ 208.4 (s), 133.0 (d), 119.0 (t), 85.1 (d), 80.5 (d), 79.0 (d), 76.1 (d), 75.0 (t), 74.5 (t), 74.1 (t), 70.3 (t), 35.5 (t). Anal. Calcd for $C_{30}H_{32}O_5$: C, 76.25%; H, 6.83%. Found: C, 76.03%; H, 6.74%.

1-(3′,4′,6′-Tri-*O*-benzyl-α-D-*arabino*-hexulopyranosyl)-2-propene methyloxime (10). The ketone **9** (97 mg, 0.20 mmol) dissolved in a 1/1 mixture of THF−MeOH (1 mL) was stirred overnight with a buffer solution (1.7 mL) prepared dissolving NH_2OH·HCl (500 mg) and AcONa·3HCl (1.00 g) in water (the pH was adjusted to 4.5 with AcOH). Usual workup and chromatography (9:1, hexane−EtOAc) afforded **10** (96 mg, 96%) as a colorless oil. $[\alpha]_D$ +17.2° (*c* 1.2, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 7.45−7.20 (m, 15 H), 5.92−5.74 (m, 1 H), 5.18−5.08 (m, 3H), 4.95, 4.53 (ABq, 2H, *J* = 12.2 Hz), 4.82, 4.61 (ABq, 2 H, *J* = 12.2 Hz), 4.66, 4.51 (ABq, 2 H, *J* = 12.9 Hz), 4.36 (d, 1 H, *J* = 7.9 Hz), 3.95−3.88 (m, 4 H), 3.77 (t, 1 H, *J* = 7.9 Hz), 3.67 (dd, 1 H, *J* = 10.5, 8.0 Hz), 3.58 (dd, 1 H, *J* = 10.5, 3.8 Hz), 2.60 (dt, 1 H, *J* = 14.7, 8.7 Hz), 2.47 (dd, 1 H, *J* = 14.7, 7.0 Hz); ^{13}C NMR (75.43 MHz, $CDCl_3$) δ 156.1 (s), 134.2 (d), 118.2 (t), 79.6 (d), 78.9 (d), 74.7 (d), 74.7 (t), 74.4 (d), 74.1 (t), 73.7 (t), 70.4 (t), 62.9 (q), 34.5 (t). Anal. Calcd for $C_{31}H_{35}NO_5$: C, 74.23%; H, 7.03%; N, 2.79%. Found: C, 74.07%; H, 7.10%; N, 2.85%.

1-(2′-Amino-3′,4′,6′-tri-*O*-benzyl-2′-deoxy-α-D-glucopyranosyl)-2-propene (11). To a solution of the methyloxime **10** (350 mg, 0.70 mmol) in dry THF (7 mL) was added a 1 M solution of $LiAlH_4$ in THF (4.2 mL, 4.2 mmol) under N_2 atmosphere. After 4 days the reaction was quenched with EtOAc. Usual workup and chromatography (9:1, hexane−EtOAc) afforded the *gluco* isomer **11** (169 mg, 51%) as a colorless oil (and 34 mg of the *manno* isomer, 10%). $[\alpha]_D$ +59.7° (*c* 1, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 7.40−7.25 (m, 15 H), 5.90−5.76 (m, 1 H), 5.11 (d, 1 H, *J* = 17.0 Hz), 5.06 (d, 1 H, *J* = 10.0 Hz), 4.82, 4.50 (ABq, 2 H, *J* = 12.4 Hz), 4.70, 4.64 (ABq, 2 H, *J* = 11.2 Hz), 4.61, 4.54 (ABq, 2 H, *J* = 11.3), 4.00 (dt, 1 H, *J* = 9.9, 4.7 Hz), 3.84−3.75 (m, 2 H), 3.66 (dd, 1 H, *J* = 9.7, 3.1 Hz), 3.63 (t, 1 H, *J* = 7.6 Hz), 3.57 (t, 1 H, *J* = 7.6 Hz), 3.03 (dd, 1 H, *J* = 7.6, 4.7 Hz), 2.47−2.28 (m, 2 H), 1.50 (broad s, 2 H); ^{13}C NMR (50.29 MHz, $CDCl_3$) δ 135.70 (d), 117.4 (t), 82.5 (d), 78.4 (d), 78.0 (d), 77.7 (d), 74.8 (t), 74.3 (t), 74.1 (t), 69.9 (t), 54.2 (d), 32.8 (t). Anal. Calcd for $C_{30}H_{35}NO_4$: C, 76.08%; H, 7.45%; N, 2.96%. Found: C, 76.13%; H, 7.37%; N, 2.89%.

(3′,4′,6′-Tri-*O*-benzyl-β-D-*arabino*-hexulopyranosyl)-2-propene (12). A mixture of **6** (2.00 g, 4.2 mmol) and 2:1 DMSO−Ac_2O (100 mL) was stirred for 5 h under N_2 atmosphere. The reaction was quenched with ice-cold water. Usual workup and chromatography (9:1, hexane−EtOAc) afforded **12** (1.76 g, 88% yield), a white solid which crystallizes from EtOAc by addition of hexane: mp 64−66 °C, $[\alpha]_D$ −42.7° (*c* 1.1, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 7.48−7.20 (m, 15H), 5.93−5.82 (m, 1H), 5.14 (broad dd, 1H, *J* = 17.9, 1.4 Hz), 5.09 (broad d, 1H, *J* = 10.5 Hz), 4.99, 4.61 (Abq, 2H, *J* = 11.3 Hz), 4.84, 4.55 (Abq, 2H, *J* = 10.8 Hz), 4.62−4.57 (m, 2H), 4.18 (d, 1H, *J* = 8.9 Hz), 3.87 (t, 1H, *J* = 8.9 Hz) 3.83−3.68 (m, 4H), 2.63 (dt, 1H, *J* = 14.8, 5.8 Hz), 2.41 (dt, 1H, *J* = 14.8, 7.2 Hz); ^{13}C NMR (75.43 MHz, $CDCl_3$) δ 201.9 (s), 133.7 (d), 117.5 (t), 86.6 (d), 80.5 (d), 80.3 (d), 79.4 (d), 75.0 (t), 73.8 (t), 73.5 (t), 68.9 (t), 32.9 (t). Anal. Calcd for $C_{30}H_{32}O_5$: C, 76.25%; H, 6.83%. Found: C, 75.97%; H, 6.68%.

1-(3′,4′,6′-Tri-*O*-benzyl-β-D-mannopyranosyl)-2-propene (13). To a solution of the ketone **12** (200 mg, 0.42 mmol) in dry THF (2 mL), cooled to −40 °C and under N_2 atmosphere, was added a 1 M solution of $LiAlH_4$ in THF (200 μL). After 10 min, the reaction was quenched with EtOAc. Usual workup and chromatography (8:2, hexane−EtOAc) afforded **13** (130 mg, 65%), colorless oil. $[\alpha]_D$ −10.9° (*c* 0.75, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 7.45−7.25 (m, 15 H), 5.91−5.80 (m, 1 H), 5.18 (dd, 1 H, *J* = 17.1, 1.3 Hz), 5.10 (broad d, 1 H, *J* = 10.0 Hz), 4.87, 4.56 (Abq, 2 H, *J* = 10.9 Hz), 4.76, 4.67 (Abq, 2 H, *J* = 11.4 Hz), 4.64, 4.58 (Abq, 2 H, *J* = 12.5 Hz), 3.96 (d, 1 H, *J* = 3.4 Hz), 3.79 (t, 1 H, *J* = 9.2 Hz), 3.78 (dd, 1 H, *J* = 10.9, 3.2 Hz), 3.70 (dd, 1 H, *J* = 10.9, 5.1 Hz), 3.60 (dd, 1 H, *J* = 9.2, 3.4 Hz), 3.46−3.42 (m, 1 H), 3.38 (t, 1 H, *J* = 7.2 Hz), 2.58 (dt, 1 H, *J* = 14.1, 7.2 Hz), 2.47 (dt, 1 H, *J* = 14.1, 7.2 Hz), 2.25 (broad s, 1 H); ^{13}C NMR (75.43 MHz, $CDCl_3$) δ 134.5 (d), 117.5 (t), 83.6 (d), 79.4 (d), 77.7 (d), 75.2 (t), 74.8 (d), 73.5 (t), 71.6 (t), 69.5 (t), 67.6 (d), 35.4 (t). Anal. Calcd for $C_{30}H_{34}O_5$: C, 75.92%; H, 7.22%. Found: C, 75.78%; H, 7.11%.

1-(2′-Azido-3′,4′,6′-tri-*O*-benzyl-2′-deoxy-β-D-glucopyranosyl)-2-propene (15). Reaction of **13** (100 mg, 0.21 mmol) as described for the preparation of **7**, afforded the crude azide **15** which was directly submitted to the next reaction. An analytical sample of **15** was purified by flash chromatography, eluting with a gradient of 95:5 → 9:1 of hexane−EtOAc. IR (film) 2100 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 7.40−7.20 (m, 15 H), 6.00−5.83 (m, 1 H), 5.18 (dd, 1 H, *J* = 19.0, 1.5 Hz), 5.15 (d, 1 H, *J* = 9.9 Hz), 4.89 (broad s, 2H), 4.82, 4.60 (ABq, 2H, *J* = 10.7 Hz), 4.64, 4.55 (ABq, 2H, *J* = 12.7 Hz), 3.72−3.68 (m, 2 H), 3.64 (t, 1 H, *J* = 9.4 Hz), 3.60 (t, 1 H, *J* = 9.4 Hz), 3.40 (dt, 1 H, *J* = 9.4, 3.0 Hz), 3.32 (t, 1 H, *J* = 9.4 Hz), 3.19 (ddd, 1 H, *J* = 9.8, 6.3, 3.7 Hz), 2.66−2.54 (m, 1 H), 2.38 (dt, 1 H, *J* = 13.6, 6.3 Hz); ^{13}C NMR (75.43 MHz, $CDCl_3$) δ 133.6 (d), 117.8 (t), 85.4 (d), 81.0 (d), 79.2 (d), 77.9(d), 75.5 (t), 73.5 (t), 73.1 (t), 69.2 (t), 55.2 (d), 36.7 (t). Anal. Calcd for $C_{30}H_{33}N_3O_4$: C, 72.12%; H, 6.66%; N, 8.41%. Found: C, 71.88%; H, 6.45%; N, 8.62%.

1-(2′-Amino-3′,4′,6′-tri-*O*-benzyl-2′-deoxy-β-D-glucopyranosyl)-2-propene (17). The crude azide **15** obtained in the previous preparation was reduced following the same procedure described for the preparation of **8**. Chromatographic purification (6:4, hexane−EtOAc + 0.1% Et_3N) afforded **17** (57 mg, 57% yield from **13**), as a pale yellow oil. $[\alpha]_D$ +49.0° (*c* 1.1, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 7.49−7.10 (m, 15 H), 5.96−5.90 (m, 1 H), 5.11 (d, 1 H, *J* = 18.0 Hz), 5.07 (d, 1 H, *J* = 10.1 Hz), 4.98, 4.57 (ABq, 2 H, *J* = 12.0 Hz), 4.79−4.50 (m, 4 H), 3.72−3.70 (m, 2 H), 3.62 (t, 1H, *J* = 9.5 Hz), 3.45 (dt, 1H, *J* = 9.5, 2.9 Hz), 3.35 (t, 1H, *J* = 9.5 Hz) 3.21−3.15 (m, 1H), 2.69 (t, 1 H, *J* = 9.5 Hz) 2.55−2.50 (m, 1 H), 2.29 (dt, 1 H, *J* = 14.5, 7.0 Hz), 2.16 (broad s, 2H); ^{13}C NMR (75.43 MHz, $CDCl_3$) δ 134.6 (d), 116.9 (t), 86.8 (d), 80.0 (d), 79.4 (d), 79.2 (d), 75.3 (t), 74.7 (t), 73.5 (t), 69.1 (t), 56.3 (d), 36.6 (t). Anal. Calcd for $C_{30}H_{35}NO_4$: C, 76.08%; H, 7.45%; N, 2.96%. Found: C, 76.11%; H, 7.30%; N, 2.72%.

1-(3′,4′,6′-Tri-*O*-benzyl-β-D-*arabino*-hexulopyranosyl)-2-propene Methyloxime (14). Following the same procedure described for the preparation of **10**, **12** (200 mg, 0.42 mmol) was converted into **14** (199 mg, 94%). Oil; ^{13}C NMR (50.29 MHz, $CDCl_3$) δ 155.9 (s), 134.8 (d), 116.4 (t), 79.4 (d), 77.6 (d), 76.8 (d), 74.7 (d), 73.2 (t), 71.1 (t), 70.3 (t), 69.9 (t), 62.2 (q), 36.8 (t). Anal. Calcd for $C_{31}H_{35}NO_5$: C, 74.23%; H, 7.03%; N, 2.79%. Found: C, 74.27%; H, 6.98%; N, 2.73%.

1-(2′-Amino-3′,4′,6′-tri-*O*-benzyl-2′-deoxy-β-D-mannopyranosyl)-2-propene (16). The methyloxime **14** (86 mg, 0.17 mmol) in dry THF (4 mL) was treated overnight with $LiAlH_4$ (1.6 mL of a 1 M solution in THF) at 40 °C under N_2 atmosphere. Usual workup and chromatographic purification (6:4, hexane−EtOAc) afforded **16** (41 mg, 54%) (and 4 mg, 5%, of its C-2 epimer **17**). $[\alpha]_D$ −15.5° (*c* 1.65, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 7.43−7.10 (m, 15 H), 5.88−5.79 (m, 1 H), 5.15 (broad d, 1 H, *J* = 17.5 Hz), 5.07 (broad d, 1 H, *J* = 10.7 Hz), 4.86, 4.51 (ABq, 2 H, *J* = 10.9 Hz), 4.72, 4.60 (ABq, 2 H, *J* = 11.5 Hz), 4.60, 4.53 (ABq, 2 H, 11.7 Hz), 3.80−3.69 (m, 3 H), 3.56 (dd, 1 H, *J* = 8.9, 3.8 Hz), 3.43−3.37 (m, 2 H), 3.21 (d, 1 H, *J* = 3.8 Hz), 2.52 (dt, 1 H, *J* = 13.9, 6.9 Hz), 2.39 (dt, 1 H, *J* = 13.9, 6.9 Hz), 2.26 (broad s, 2 H); ^{13}C NMR (75.43 MHz, $CDCl_3$) δ 134.53 (d), 117.3 (t), 84.2 (d), 79.4 (d), 77.9 (d), 75.1 (t), 74.3 (d), 73.5 (t), 71.2 (t), 69.3 (t), 50.4 (d), 35.9 (t). Anal. Calcd for $C_{30}H_{35}NO_4$: C, 76.08%; H, 7.45%; N, 2.96%. Found: C, 75.90%; H, 7.51%; N, 3.07%.

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