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Synthesis and reactions of an (α-D-glucopyranosyl)phenylacetylene

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Abstract

Silver tetrafluoroborate promoted addition of (phenylethynyl)tributylstannane to 6-*O*-acetyl-2,3,4-tri-*O*-benzyl-α-D-glucopyranosyl chloride stereoselectively gave a crystalline (α-D-glucopyranosyl)phenylacetylene (**4**) in 73% yield. Compound **4** was epimerized to the β isomer through its hexacarbonyldicobalt complex, and was also converted into a *C*-α-glycosyl aldehyde (**8**) by sequential zinc reduction and ozonolysis. The sensitive aldehyde **8** was conveniently isolated and manipulated through its 1,3-diphenylimidazolidine derivative.

Keywords: Synthesis; Reactions; (α-D-Glucopyranosyl)phenylacetylene

1. Introduction

C-Glycopyranosylalkynes are valuable homologated carbohydrate derivatives which are potentially useful as chiral building blocks in the synthesis of natural products [1], or as precursors of biologically active *C*-glycosyl compounds [2]. In 1958 Zelinski and Meyer [3] reported the first example of a glucosylated acetylene, prepared by the addition of phenylethynylmagnesium bromide to 2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranosyl bromide; a 3:1 mixture of β- and α-D-glucopyranosyl phenylacetylenes was obtained in 49% yield. Later, Sinaÿ [4] achieved a fully stereospecific synthesis of *C*-β-D-glucopyranosylalkynes by the sequential addition of lithium acetylides to gluconolactone and reduction of the intermediate hemiacetal by triethylsilane and a Lewis acid; the axially oriented addition of hydride ions to the pyranoid oxonium species ensured an excellent stereochemical control. On the other hand, tributyltin acetylides have been added to a glucopyranosyl bromide in the presence of zinc chloride [5] with a

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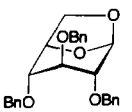
significant α-selectivity, the anomeric effect of the pyranose ring oxygen favouring an axial attack of the transient oxonium ion by the carbon nucleophile. We have recently reported [6] that the latter reaction could be efficiently promoted by *silver tetrafluoroborate* at low temperature. Various alkynes have thus been coupled with hexopyranosyl halides, even those containing electron-withdrawing substituents such as an azide function at C-2 or an acetate group at C-6. A convenient synthesis of *C*-glycosyl derivatives of D-glucosamine and D-galactosamine could then be achieved [7]. Following this new methodology we now describe the stereospecific preparation of an (α-D-glucopyranosyl)phenylacetylene. Some transformations of synthetic interest are also reported.

2. Results and discussion

6-*O*-Acetyl-2,3,4-tri-*O*-benzyl-α-D-glucopyranosyl chloride (**3**) was selected as the electrophilic partner in the coupling reaction. This stable halide [8] was obtained either by ring opening of 1,6-anhydro-2,3,4-tri-*O*-benzyl-β-D-glucopyranose (**1**) with acetyl chloride as described by Gigg et al. [9], or by treatment of 6-*O*-acetyl-2,3,4-tri-*O*-benzyl-D-glucopyranose (**2**) with a Vilsmeier-type reagent (oxalyl chloride and a catalytic amount of *N,N*-dimethylformamide) [10]. The choice of 1,6-anhydro sugars as starting materials in this study was dictated by the following considerations: the desirability of comparison with our previous results [7], where 2-azido-2-deoxyhexopyranosyl bromides have been obtained through a sequence of reactions having the 1,6-iodocyclization of glycals as a key step; the possibility of further functionalization of C-6, which could lead to biologically interesting compounds (uronic acids or 6-deoxy sugar derivatives); and easier interpretation of ^{1}H NMR spectra.



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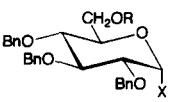
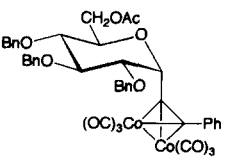


	R	X
2	Ac	OH
3	Ac	Cl
4	Ac	C≡C-Ph
5	H	C≡C-Ph
6	Ac	(Z) CH=CH-Ph
7	H	(Z) CH=CH-Ph
8	Ac	CHO
9	Bn	CHO
10	Ac	
11	H	



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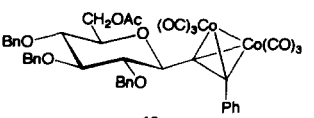

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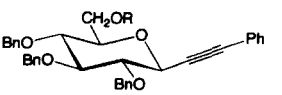

14 R = Ac
15 R = H

Commercial (phenylethynyl)tributylstannane reacted smoothly at 0°C with chloride **3** in the presence of silver tetrafluoroborate to afford the crystalline (α-D-glucopyranosyl)phenylacetylene **4** in 73% yield, no trace of the β isomer being detected in the reaction mixture. The α configuration at C-1 was assigned on the basis of the ^{1}H NMR data for H-1, which resonated as a doublet at δ 4.99 and had $J_{1,2}$ 5.5 Hz. The large values of $J_{2,3}$ (9.5 Hz), $J_{3,4}$ (9 Hz), and $J_{4,5}$ (9.5 Hz) are in accordance with the $^4C_1$ D-glucopyranose conformation. It is known [11] that steric demand of alkynyl substituents is rather low ($-\Delta G^0$ 0.34 kcal/mol for 2-ethynyltetrahydropyran compared with $-\Delta G^0$ 2.86 kcal/mol for 2-methyltetrahydropyran), and therefore the 1,3-diaxial interaction between H-5 and the alkyne appendage at C-1 of **4** does not lead to any noticeable distortion of the usual chair form in spite of a proximity effect due to shorter C–O bond lengths.

Hexacarbonyldicobalt complexes of propargyl alcohols and ethers [12] can be easily converted by acids to the corresponding carbocations where the electron-deficient propargylic carbon is stabilized by interaction with both cobalt tricarbonyl units [13]. These cations are readily captured by various nucleophiles (Nicholas reaction) in inter- or intra-molecular reactions, and Isobe [14] has recently shown that alkynyl groups attached at C-1 of a pyranose ring promote easy epimerization by acidic equilibration of their dicobalt complexes. However, none of the described compounds was a fully substituted pyranose derivative. Some were unsaturated, with a double bond between C-2 and C-3 or C-3 and C-4, others were 2,3-dideoxy sugars. Besides, the substituent at C-1 was generally a silylalkynyl group. It was therefore of interest to test whether a similar epimerization could be performed upon **4**.

Treatment of **4** with octacarbonyldicobalt in dichloromethane gave the hexacarbonyldicobalt complex **12** as a dark red oil in excellent yield. The IR spectrum showed characteristic strong ν bands of metal-coordinated carbon monoxide at 2075 and 2040–2000 cm^{-1}. The ^{1}H NMR spectrum (300 MHz) in deuterated benzene (but not in chloroform) could be completely analyzed on a first-order basis. The propargylic proton (H-1) appeared as a doublet at δ 5.44 ($J_{1,2}$ 5.5 Hz); in $CDCl_3$ a broad doublet was observed at δ 5.45. Comparison of the ^{1}H NMR data of **4** and **12** in C_6D_6 showed that only the propargylic H-1 and homopropargylic H-2 protons are significantly shifted downfield (Δδ −0.39 and −0.27 ppm, respectively) after complexation. But the most striking feature was the still quite large values of the coupling constants $J_{2,3}$ (8.8 Hz), $J_{3,4}$ (8 Hz), and $J_{4,5}$ (9 Hz), indicating a slightly distorted $^4C_1$ chair conformation or a small contribution of some $^1C_4$ form to the conformational equilibrium. By contrast, all the α-complexes reported by Isobe have their bulky complexed-alkyne substituent at C-1 in an equatorial or pseudoequatorial orientation, the pyranose ring assuming a $^1C_4$ or ^5H_O conformation. The presence of *O*-benzyl groups at C-2, C-3, and C-4 of **12** involves, when the molecule assumes a $^1C_4$ conformation, two severe 1,3-diaxial interactions which are absent in Isobe's products.

Addition of a catalytic amount of trifluoromethanesulfonic acid to a solution of **12** in dichloromethane brought about an equilibrium between the two epimers **12** (α) and **13** (β), the ratio of which was estimated at 23:77 by comparative integration of the OAc signals at δ 1.73 and 1.78, respectively, in C_6D_6. This composition reflects the higher thermodynamic stability of **13**, but is far from the values observed by Isobe (β:α 100:1

for a 3,4-unsaturated compound with a bulky *O-tert*-butyldiphenylsilyl group at C-2). A sample of pure **13** could be obtained by flash chromatography, and it was analyzed by ^{1}H NMR in $CDCl_3$; the large coupling constants $J_{1,2} \sim J_{2,3} \sim J_{3,4} \sim 9$ Hz and $J_{4,5}$ 9.5 Hz revealed a $^4C_1$ conformation for the pyranose ring, with the complexed alkynyl group at C-1 in an equatorial orientation.

The complexation and epimerization could be performed in the same flask, giving a mixture of **12** and **13** in 87% yield. Decomplexation was accomplished by oxidation with iodine in tetrahydrofuran to afford a mixture of alkyne **4** and its β isomer **14**. Deacetylation permitted an easier chromatographic separation, the (β-D-glucopyranosyl)phenylacetylene **15** being obtained in 53% overall yield along with 26% of the α isomer **5**.

Partial reduction of alkynes to *cis* olefins is commonly effected by hydrogenation in the presence of Lindlar catalyst [15], but conjugated alkynes can also be stereoselectively reduced by activated zinc. Potassium cyanide [16], 1,2-dibromoethane–cuprous bromide [17], and conversion to zinc–copper couple [18] have been used for activation. Only *Z* olefins are obtained, probably through an organozinc intermediate. We found indeed that alkyne **4** was reduced to *cis*-α-D-glucopyranosylstyrene (**7**), with concomitant deacetylation, by refluxing in methanol in the presence of a freshly prepared zinc–copper couple. However the reaction is slow (2–5 days) and sometimes not reproducible. When **4** was refluxed for 4–5 h in 10:1 methanol–acetic acid in the presence of powdered zinc [19], the *Z* olefin **6** was isolated as a syrup in 80% yield. The vinylic protons H-1′ and H-2′ have their NMR signals at δ 6.05 and 6.88, respectively, with a coupling constant, $J_{1',2'}$, of 12 Hz. It is known [20] that an electron-donating substituent such as a phenyl ring increases the J_{vinyl} value, which normally averages 10 Hz. (*E*)-1-(3,4,6-Tri-*O*-benzyl-α-D-glucopyranosyl)-2-phenylethylene, which has been prepared by a samarium iodide mediated intramolecular reaction [21], shows a much higher $J_{1',2'}$ value of 16.2 Hz [22]. No trace of the *E* isomer of **6** could be detected after the zinc reduction of **4**. The coupling constants of the pyranose ring protons in **6**, $J_{1,2}$ 6, $J_{2,3}$ 9.2, $J_{3,4}$ 8.8, and $J_{4,5}$ 10 Hz, reveal a $^4C_1$ chair conformation with an axial bond between C-1 and C-1′.

Compound **6** was deacetylated to give crystalline **7**, identical to the product obtained by treatment of **4** with zinc–copper couple in boiling methanol.

cis-α-D-Glucopyranosylstyrene (**6**) can be considered as a masked *C*-α-glycosyl aldehyde, a type of compound highly appreciated for the synthesis of complex *C*-glycosyl derivatives. Various approaches to this class of synthons have been reported in literature: periodate oxidation of *C*-α-D-glucopyranosyl ethylene glycol [23], lithium aluminum hydride reduction of a cyano group [24], ozonolysis of vinyl [5,25] or allenyl [26] groups, Swern oxidation of *C*-α-D-glucopyranosylmethanol [27,28], and use of a thiazole ring as a formyl group equivalent [29]. 2,6-Anhydro-3,4,5,7-tetra-*O*-benzyl-D-*glycero*-D-*ido*-heptose (**9**), which can be prepared from 2,3,4,6-tetra-*O*-benzyl-D-glucopyranose by one of the previous procedures, is reported [29] as a labile compound prone to decomposition on flash chromatography. Its epimerization to the more stable D-*gulo* isomer can be accomplished by mild alkaline treatment [26], but is often accompanied by partial β-elimination of the benzyloxy substituent at C-3. For these reasons it is

usually immediately transformed by borohydride reduction [5,23], addition to a Grignard reagent [28], or Wittig olefination [27]. Such labile aldehydes can be efficiently trapped by 1,2-dianilinoethane (Wanzlick reagent) to give base-stable 1,3-diphenylimidazolidines, and are regenerated by mild acidic treatment [30–32].

The olefinic compound **6** was first treated with sodium periodate and a catalytic amount of osmium tetroxide in dioxane–water at room temperature [33]. Although a brown osmic adduct was rapidly formed, analysis of the reaction products by mass spectrometry revealed only minor amounts of the desired aldehyde **8**, the major products being those resulting from *cis* hydroxylation of the double bond. When a solution of **6** in dichloromethane was saturated with ozone at −70°C, formation of an ozonide occurred rapidly as detected by TLC. The reduction of the ozonide by dimethyl sulfide was not satisfactory, being too slow even at room temperature. The best results were obtained with triphenylphosphine [34], a complete conversion to aldehyde **8** being observed after 3 h at room temperature. Although contaminated by PPh_3, $OPPh_3$, and benzaldehyde, crude **8** obtained by evaporation of the mixture was shown by ^{1}H NMR analysis to be free of any epimerization or elimination product and to be present in nonhydrated, monomeric form (C*H*O appeared as a singlet at δ 9.10); however it gave rise to severe streaking during migration on TLC plates. Coupling constants $J_{2,3}$ (6.2 Hz), $J_{3,4}$ (8.5 Hz), $J_{4,5}$ (8 Hz), and $J_{5,6}$ (9.5 Hz) again showed a chair conformation ($^5C_2$) with an axial bond between C-1 and C-2. We found that prolonged contact of **6** with ozone even at −70°C must be avoided, since traces of a monobenzoylated product could be detected by mass spectrometry in one of the first assays. The oxidation of benzyl ethers by ozone has been reported to be quite effective at 0°C [35].

Addition of 1,2-dianilinoethane (3 equiv) to the crude aldehyde in methanol afforded the 1,3-diphenylimidazolidine **10**, isolated as an oil by flash chromatography in 61% overall yield. The ^{1}H NMR spectrum of **10** showed a doublet at low field (δ 5.93, $J_{1,2'}$ 3.2 Hz), interpreted as the signal of H-2′ in the imidazolidine ring. The value of $J_{1,2'}$ reflects a mixture of rotamers around the bond between C-1 and C-2′, since an antiperiplanar arrangement of H-1 and H-2′ would give $J \sim 8$–9 Hz [36], whereas a gauche disposition would give $J \sim 0$–1 Hz [31]. Coupling constants $J_{1,2}$ (5.5 Hz), $J_{2,3}$ (8 Hz), $J_{3,4}$ (7 Hz), and $J_{4,5}$ (8.5 Hz) indicated a slightly distorted $^4C_1$ conformation of the pyranose ring.

Aldehyde **8** was regenerated by treatment of imidazolidine **10** with *p*-toluenesulfonic acid monohydrate in 6:1 dichloromethane–acetone at room temperature [31]. Compound **10** could also be deacetylated to give **11** as a syrup. For **11**, a much more distorted conformation in the C-2,3,4 region of the pyranose ring was revealed by the values $J_{1,2}$ 4.8, $J_{2,3} \sim J_{3,4} \sim 6.5$, and $J_{4,5}$ 9.2 Hz; deacetylation evidently induced a change in the rotamer population around the bond between C-1 and C-2′ ($J_{1,2'}$ 4.8 Hz), and a 1,3-diaxial interaction between H-3 and the bulky 1,3-diphenylimidazolidine ring now had to be released.

In conclusion, the stereospecific addition of stannylated phenylacetylene to the anomeric position of the D-glucopyranose ring gives a convenient access to a *C*-α-glucopyranosyl aldehyde; this methodology will be extended to other sugars and particularly to the 2-azido-2-deoxyhexopyranoses.

3. Experimental

General methods.—Melting points were recorded with a Büchi apparatus and are uncorrected. Optical rotations were measured with a Perkin–Elmer model 141 polarimeter. IR spectra were recorded on a Philips Pye-Unicam SP3-100 spectrometer. ^{1}H NMR spectra were recorded with a Bruker AM-300 WB (300.013 MHz) spectrometer. Chemical shifts (δ) are reported relative to tetramethylsilane. Mass spectra were recorded with a Ribermag R-10-10 instrument in the desorption, chemical-ionization mode. TLC was conducted on precoated Silica Gel 60 F_{254} (Merck cat. no. 5554) plates with detection by UV fluorescence and by charring with 1:10 H_2SO_4–EtOH. Flash chromatography was performed on Silica Gel 60 (E. Merck, 3–63 μm). "Ether" refers to diethyl ether. All solvents were dried and distilled using standard methods [37]. Elemental analyses were performed by the Service Central de Micro-Analyse du Centre National de la Recherche Scientifique.

6-O-Acetyl-2,3,4-tri-O-benzyl-α-D-glucopyranosyl chloride (**3**).—*Procedure A.* Dry MeOH (2.3 mL) was added under Ar to an ice-cooled solution of 1,6-anhydro-2,3,4-tri-*O*-benzyl-β-D-glucopyranose (**1**, 3 g, 6.9 mmol) [38] in acetyl chloride (180 mL). After 24 h at room temperature a further amount of MeOH (3 mL) was added and the solution was left for another 24 h. Evaporation gave crude **3**, which was purified by flash chromatography (7:3 heptane–EtOAc) to give a colorless oil (3.06 g, 86%); $[\alpha]_D$ +83° (*c* 1, $CHCl_3$); lit. [8] $[\alpha]_D$ +90° (*c* 1, $CHCl_3$); R_f 0.44 (7:3 heptane–EtOAc); ^{1}H NMR ($CDCl_3$): δ 1.94 (s, 3 H, OAc), 3.55 (dd, 1 H, $J_{3,4}$ 9.5, $J_{4,5}$ 10 Hz, H-4), 3.72 (dd, 1 H, $J_{1,2}$ 3.5, $J_{2,3}$ 9.5 Hz, H-2), 4.08 (dd, 1 H, H-3), 4.15 (m, 1 H, H-5), 4.28 (m, 2 H, H-6a,6b), 4.56–5.50 (m, 6 H, 3 CH_2Ph), 6.02 (d, 1 H, H-1), and 7.20–7.40 (m, 15 H, 3 Ph).

Procedure B. A solution of oxalyl chloride (0.52 mL, 6 mmol) in dry CH_2Cl_2 (2.5 mL) was added dropwise under Ar to an ice-cooled solution of 6-*O*-acetyl-2,3,4-tri-*O*-benzyl-D-glucopyranose (**2**, 1 g, 2 mmol) [39] and DMF (50 μL) in dry CH_2Cl_2 (5 mL). The mixture was stirred for 2 h at room temperature, then concentrated. The residue was purified by flash chromatography (7:3 heptane–EtOAc) to give **3** (0.82 g, 79%) identical to the product obtained by procedure *A*.

1-(6-O-Acetyl-2,3,4-tri-O-benzyl-α-D-glucopyranosyl)-2-phenylacetylene (**4**).—A mixture of **3** (1.53 g, 3 mmol), (phenylethynyl)tributylstannane (Aldrich, 5.26 mL, 15 mmol), and powdered 3A molecular sieves (1 g) in dry 1,2-dichloroethane (10 mL) was stirred under Ar at room temperature for 30 min, then cooled to −30°C. Dry silver tetrafluoroborate (Fluka, 1.17 g, 6 mmol) was added rapidly and the mixture was allowed to slowly attain 0°C, then stirred overnight at 0°C under Ar. Dichloromethane (100 mL) was added, and the mixture was filtered over Celite. The filtrate was washed with satd aq $NaHCO_3$ and water, and evaporated to dryness. Flash chromatography (pure heptane first, then 4:1 heptane–EtOAc) gave **4**, which crystallized from EtOH (1.26 g, 73%); mp 70°C; $[\alpha]_D$ +130° (*c* 1, $CHCl_3$); R_f 0.30 (3:2 heptane–EtOAc); ^{1}H NMR ($CDCl_3$): δ 2.03 (s, 3 H, OAc), 3.50 (dd, 1 H, $J_{3,4}$ 9, $J_{4,5}$ 9.5 Hz, H-4), 3.69 (dd, 1 H, $J_{1,2}$ 5.5, $J_{2,3}$ 9.5 Hz, H-2), 4.04 (dd, 1 H, H-3), 4.12 (m, 1 H, H-5), 4.31 (m, 2 H, H-6a,6b), 4.57 and 5.03 (2 d, 2 H, *J* 10.8 Hz, CH_2Ph), 4.74 (s, 2 H, CH_2Ph), 4.84 and

4.89 (2 d, 2 H, *J* 11 Hz, CH_2Ph), 4.99 (d, 1 H, H-1), and 7.25–7.50 (m, 20 H, 4 Ph). Anal. Calcd for $C_{37}H_{36}O_6$: C, 77.06; H, 6.29. Found: C, 76.89; H, 6.33.

Hexacarbonyldicobalt complex (**12**) *derived from (α-*D*-glucopyranosyl)phenylacetylene* (**4**).—A solution of **4** (58 mg, 0.1 mmol) in dry CH_2Cl_2 (1 mL) was added under Ar to a solution of dicobalt octacarbonyl (Merck, 62 mg, 0.18 mmol) in dry CH_2Cl_2 (1 mL) at room temperature. After 90 min the solution was concentrated and the residue was purified by flash chromatography (4:1 heptane–EtOAc) to give **12** as a dark red oil (81 mg, 93%); R_f 0.42 (3:2 heptane–EtOAc); R_f 0.20 (7:3 heptane–acetone); IR (film): ν_{max} 2075 and 2000–2040 (C ≡ O), and 1735 cm^{-1} (C = O); ^{1}H NMR (C_6D_6): δ 1.73 (s, 3 H, OAc), 3.63 (dd, 1 H, $J_{3,4}$ 8, $J_{4,5}$ 9 Hz, H-4), 3.93 (dd, 1 H, $J_{1,2}$ 5.5, $J_{2,3}$ 8.8 Hz, H-2), 4.29 (dd, 1 H, H-3), 4.32, 4.45, 4.56, 4.79, 4.80, and 4.92 (6 d, 6 H, *J* 11.5 Hz, 3 CH_2Ph), 4.38 (m, 1 H, H-5), 4.45 (dd, 1 H, $J_{5,6a}$ 5, $J_{6a,6b}$ 11.5 Hz, H-6a), 4.55 (dd, 1 H, $J_{5,6b}$ 2.2 Hz, H-6b), 5.44 (d, 1 H, H-1), and 6.90–7.60 (m, 20 H, 4 Ph).

Hexacarbonyldicobalt complex (**13**) *derived from (β-*D*-glucopyranosyl)phenylacetylene* (**14**).—Trifluoromethanesulfonic acid (2 drops) was added under Ar to a solution of **12** (86 mg, 0.1 mmol) in dry CH_2Cl_2 (2 mL) at room temperature. The solution was stirred for 150 min, then poured into satd aq $NaHCO_3$. The organic layer was dried and concentrated. The residue was purified by flash chromatography (pure heptane first, then 10:1 heptane–acetone). The first fractions gave a small amount of **13** as red crystals; R_f 0.26 (7:3 heptane–acetone); IR (film): ν_{max} 2080 and 2000–2040 (C ≡ O), and 1735 cm^{-1} (C = O); ^{1}H NMR ($CDCl_3$): δ 1.98 (s, 3 H, OAc), 3.50 (dd, 1 H, $J_{1,2} \sim J_{2,3} \sim 9$ Hz, H-2), 3.71 (dd, 1 H, $J_{3,4}$ 9, $J_{4,5}$ 9.5 Hz, H-4), 3.81 (m, 1 H, H-5), 3.98 (dd, 1 H, H-3), 4.21 (dd, 1 H, $J_{5,6a}$ 4.5, $J_{6a,6b}$ 11.5 Hz, H-6a), 4.36, 4.65, 4.84, 4.89, and 4.99 (5 d, 6 H, *J* 11 Hz, 3 CH_2Ph), 4.45 (dd, 1 H, $J_{5,6b}$ 2 Hz, H-6b), 4.74 (d, 1 H, H-1), and 6.85–7.55 (m, 20 H, 4 Ph); ^{1}H NMR (C_6D_6): δ 1.78 (s, 3 H, OAc), 4.61 (dd, 1 H, $J_{1,2}$ 9.5 Hz, H-1); MS: *m/z* 779 (M + 1 − 3 CO), 723 (M + 1 − 5 CO), and 695 (M + 1 − 6 CO).

The next fractions gave a mixture of **12** and **13** (75 mg, 87%); ^{1}H NMR (C_6D_6): δ 1.73 (s, 0.7 H, OAc of **12**) and 1.78 (s, 2.3 H, OAc of **13**).

*1-(2,3,4-Tri-*O*-benzyl-α- and -β-*D*-glucopyranosyl)-2-phenylacetylene* (**5** *and* **15**).—A solution of **4** (115 mg, 0.2 mmol) in dry CH_2Cl_2 (2 mL) was treated with dicobalt octacarbonyl (123 mg, 0.36 mmol) as described above. Trifluoromethanesulfonic acid (5 μL, 40 μmol) was then added and the resulting mixture was stirred under Ar for 150 min at room temperature. After workup the mixture of **12** and **13** (150 mg) was dissolved in dry THF (3 mL). A solution of iodine (790 mg, 3.1 mmol) in dry THF (7 mL) was added and the mixture was stirred under Ar for 2 h at room temperature, then poured into satd aq Na_2SO_3. Ether was added and the organic layer was dried, then concentrated. The residue was dissolved in MeOH (10 mL). A catalytic amount of sodium was added and the solution was left overnight at room temperature, then neutralized with Amberlite IR-120 (H^+) ion-exchange resin. The mixture was filtered and concentrated to give a mixture of **5** and **15**, which was separated by flash chromatography (4:1 heptane–EtOAc). The first-eluted fractions gave **15** as an oil (56 mg, 53%); $[\alpha]_D$ −43° (*c* 1, $CHCl_3$); R_f 0.28 (3:2 heptane–EtOAc); IR (film): ν_{max} 2240 cm^{-1} (C ≡ C); ^{1}H NMR (C_6D_6): δ 3.14 (ddd, 1 H, $J_{4,5}$ 9, $J_{5,6a}$ 2.8, $J_{5,6b}$ 4 Hz,

H-5), 3.56 (dd, 1 H, $J_{2,3} \sim J_{3,4} \sim 9$ Hz, H-3), 3.62 (dd, 1 H, H-4), 3.64 (m, 1 H, H-6a), 3.69 (dd, 1 H, $J_{1,2}$ 9.8 Hz, H-2), 3.78 (m, 1 H, H-6b), 4.25 (d, 1 H, H-1), 4.61, 4.82, 4.83, 4.89, 4.92, and 5.15 (6 d, 6 H, J 11 Hz, 3 CH_2Ph), and 6.90–7.50 (m, 20 H, 4 Ph). Anal. Calcd for $C_{35}H_{34}O_5$: C, 78.63; H, 6.41. Found: C, 78.71; H, 6.40.

The next fractions gave **5** as an oil (28 mg, 26%); $[\alpha]_D$ +147° (*c* 1, $CHCl_3$); R_f 0.24 (3:2 heptane–EtOAc); ^{1}H NMR (C_6D_6): δ 3.62 (dd, 1 H, $J_{1,2}$ 5.5, $J_{2,3}$ 9.5 Hz, H-2), 3.69 (dd, 1 H, $J_{3,4} \sim J_{4,5} \sim 9.5$ Hz, H-4), 3.79 (dd, 1 H, $J_{5,6a}$ 4, $J_{6a,6b}$ 12 Hz, H-6a), 3.86 (dd, 1 H, $J_{5,6b}$ 3 Hz, H-6b), 4.25 (m, 1 H, H-5), 4.29 (dd, 1 H, H-3), 4.48, 4.54, 4.69, 4.86, 4.95, and 5.04 (6 d, 6 H, J 11Hz, 3 CH_2Ph), 5.02 (d, 1 H, H-1), and 6.90–7.48 (m, 20 H, 4 Ph). Anal. Calcd for $C_{35}H_{34}O_5 \cdot 0.5H_2O$: C, 77.32; H, 6.49. Found: C, 77.27; H, 6.77.

*(Z)-1-(6-*O*-Acetyl-2,3,4-tri-*O*-benzyl-α-*D*-glucopyranosyl)-2-phenylethylene* (**6**).—A mixture of compound **4** (577 mg, 1 mmol) and powdered zinc (13.4 g) in 10:1 MeOH–AcOH (220 mL) was heated at reflux under vigorous stirring for 4 h. The mixture was cooled, then filtered over Celite. The filtrate was concentrated and the residue was taken up in CH_2Cl_2. The extract was washed with water. The organic layer was dried, then concentrated. The residue was purified by flash chromatography (4:1 heptane–EtOAc) to give **6** as an oil (484 mg, 84%); $[\alpha]_D$ +154° (*c* 1, $CHCl_3$); R_f 0.33 (7:3 heptane–acetone); IR (film): ν_{max} 1740 cm^{-1} (C = O); ^{1}H NMR ($CDCl_3$): δ 1.95 (s, 3 H, OAc), 3.52 (dd, 1 H, $J_{3,4}$ 8.8, $J_{4,5}$ 10 Hz, H-4), 3.77 (dd, 1 H, $J_{1,2}$ 6, $J_{2,3}$ 9.2 Hz, H-2), 3.78 (m, 1 H, H-5), 3.98 (dd, 1 H, H-3), 4.03 (dd, 1-H, $J_{5,6a}$ 2.5, $J_{6a,6b}$ 12 Hz, H-6a), 4.26 (dd, 1 H, $J_{5,6b}$ 5 Hz, H-6b), 4.47, 4.54, 4.55, 4.83, 4.88, and 5.01 (6 d, 6 H, J 11 Hz, 3 CH_2Ph), 4.81 (ddd, 1 H, $J_{1,1'}$ 8, $J_{1,2'}$ 1.8 Hz, H-1), 6.05 (dd, 1 H, $J_{1',2'}$ 12 Hz, H-1'), 6.88 (dd, 1 H, H-2'), and 7.25–7.50 (m, 20 H, 4 Ph). Anal. Calcd for $C_{37}H_{38}O_6$: C, 76.79; H, 6.62. Found: C, 77.06; H, 6.67.

*(Z)-1-(2,3,4-Tri-*O*-benzyl-α-*D*-glucopyranosyl)-2-phenylethylene* (**7**).—A solution of **6** (289 mg, 0.5 mmol) in MeOH (20 mL) was treated overnight at room temperature with a catalytic amount of sodium, then neutralized with Amberlite IR 120 (H^+) ion-exchange resin. The mixture was filtered, then concentrated, and the residue was crystallized from heptane (241 mg, 90%); mp 69°C; $[\alpha]_D$ +133° (*c* 1, $CHCl_3$); R_f 0.25 (3:2 heptane–EtOAc); ^{1}H NMR ($CDCl_3$): δ 3.52–3.66 (m, 4 H, H-4,5,6a,6b), 3.74 (dd, 1 H, $J_{1,2}$ 6, $J_{2,3}$ 9.5 Hz, H-2), 3.97 (dd, 1 H, $J_{3,4}$ 8 Hz, H-3), 4.49 and 4.57 (2 d, 2 H, J 11.5 Hz, CH_2Ph), 4.65 and 5.02 (2 d, 2 H, J 11 Hz, CH_2Ph), 4.85 (ddd, 1 H, $J_{1,1'}$ 8, $J_{1,2'}$ 1.5 Hz, H-1), 4.88 (t, 2 H, J 11 Hz, CH_2Ph), 6.08 (dd, 1 H, $J_{1',2'}$ 12 Hz, H-1'), 6.87 (dd, 1 H, H-2'), and 7.25–7.50 (m, 20 H, 4 Ph). Anal. Calcd for $C_{35}H_{36}O_5$: C, 78.33; H, 6.76. Found: C, 78.28; H, 6.72.

*7-*O*-Acetyl-2,6-anhydro-3,4,5-tri-*O*-benzyl-*D*-glycero-*D*-ido-heptose* (**8**) *and 2-(6-*O*-acetyl-2,3,4-tri-*O*-benzyl-α-*D*-glucopyranosyl)-1,3-diphenylimidazolidine* (**10**).—A solution of compound **6** (579 mg, 1 mmol) in dry CH_2Cl_2 (25 mL) was treated with ozone at −70°C until a persistent blue color appeared. The excess of ozone was then removed within 10 min by a stream of Ar at −70°C. Triphenylphosphine (787 mg, 3 mmol) was added and the solution was stirred at −70°C for 40 min, then at room temperature for 3 h. A small portion of the solution was concentrated to give crude **8**; R_f 0.23 (3:2 heptane–EtOAc); ^{1}H NMR ($CDCl_3$): δ 2.03 (s, 3 H, OAc), 3.47 (dd, 1 H, $J_{4,5}$ 8, $J_{5,6}$ 9.5 Hz, H-5), 3.68 (dd, 1 H, $J_{3,4}$ 8.5 Hz, H-4), 3.97 (dd, 1 H, $J_{2,3}$ 6.2 Hz, H-3), 4.09

(ddd, 1 H, $J_{6,7a}$ 4.8, $J_{6,7b}$ 2.5 Hz, H-6), 4.23 (dd, 1 H, $J_{7a,7b}$ 12 Hz, H-7a), 4.32 (dd, 1 H, H-7b), 4.36 (d, 1 H, H-2), 4.51–4.86 (m, 6 H, 3 CH_2Ph), 7.20–7.70 (m, Ph), and 9.10 (s, 1 H, H-1).

A solution of 1,2-dianilinoethane (637 mg, 3 mmol) in MeOH (10 mL) was added to the solution containing the bulk of the compound **8**, and the resulting mixture was stirred under Ar for 2 h at room temperature. After evaporation the residue was taken up in toluene. The extract was washed with water and the organic layer was dried, then concentrated. The residue was purified by flash chromatography (8:1 heptane–acetone) to give **10** as an oil (428 mg, 61%); $[\alpha]_D$ +33° (*c* 1.08, $CHCl_3$); R_f 0.41 (3:2 heptane–EtOAc); ^{1}H NMR ($CDCl_3$): δ 1.93 (s, 3 H, OAc), 3.33 (dd, 1 H, $J_{3,4}$ 7, $J_{4,5}$ 8.5 Hz, H-4), 3.51–3.85 (m, 4 H, CH_2 of imidazolidine), 3.83 (dd, 1 H, $J_{1,2}$ 5.5, $J_{2,3}$ 8 Hz, H-2), 3.90 (dd, 1 H, H-3), 4.06–4.28 (m, 3 H, H-5,6a,6b), 4.35 (dd, 1 H, $J_{1,2'}$ 3.2 Hz, H-1), 4.45, 4.53, 4.69, and 4.83 (4 d, 4 H, *J* 11.5 Hz, 2 CH_2Ph), 4.66 (t, 2 H, *J* 11.5 Hz, CH_2Ph), 5.93 (d, 1 H, H-2′), and 6.70–7.40 (m, 25 H, 5 Ph); MS: *m/z* 699 (M + 1) and 223 (1,3-diphenylimidazolidine). Anal. Calcd for $C_{44}H_{46}N_2O_6$: C, 75.62; H, 6.63; N, 4.01. Found: C, 75.43; H, 6.98; N, 3.93.

A solution of *p*-toluenesulfonic acid monohydrate (52 mg, 0.27 mmol) in acetone (1 mL) was added to a solution of **10** (70 mg, 0.1 mmol) in CH_2Cl_2 (6 mL). The mixture was left at room temperature for 40 min, then filtered over Celite. The filtrate was concentrated and the residue was taken up in EtOAc. The extract was washed with aq $NaHCO_3$ and water, then dried and concentrated to give a colorless oil (42 mg, 83%) identified by TLC and ^{1}H NMR analysis as compound **8**.

*2-(2,3,4-Tri-O-benzyl-α-*D*-glucopyranosyl)-1,3-diphenylimidazolidine* (**11**).—A solution of **10** (70 mg, 0.1 mmol) in 10:10:1 MeOH–H_2O–Et_3N (10 mL) was stirred for 48 h at room temperature, then concentrated. The residue was purified by flash chromatography (4:1 heptane–EtOAc) to give **11** as a colorless oil (53 mg, 81%); $[\alpha]_D$ +37° (*c* 1.13, $CHCl_3$); R_f 0.40 (3:2 heptane–EtOAc); ^{1}H NMR ($CDCl_3$): δ 3.44 (dd, 1 H, $J_{3,4}$ 6.5, $J_{4,5}$ 9.2 Hz, H-4), 3.50–3.81 (m, 7 H, H-2,6a,6b, and CH_2 of imidazolidine), 3.89 (dd, 1 H, $J_{2,3}$ 6.5 Hz, H-3), 4.06 (m, 1 H, H-5), 4.23 (dd, 1 H, $J_{1,2} \sim J_{1,2'} \sim 4.8$ Hz, H-1), 4.48–4.80 (m, 6 H, 3 CH_2Ph), 5.92 (d, 1 H, H-2′), and 6.70–7.40 (m, 25 H, 5 Ph).

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