JOC The Journal of Organic Chemistry

Article

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Synthesis of 2-Deoxy-2-*C*-alkyl Glycal and Glycopyranosides from 2-Hydroxy Glycal Ester

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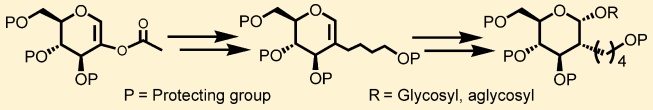
Supporting Information

ABSTRACT: A method to convert 2-hydroxy glycal ester to the corresponding 2-deoxy-2-*C*-alkyl glycal in a facile manner, through key reactions including (i) *C*-allylation at *C*-1, (ii) Wittig reaction, and (iii) Cope rearrangement of a 1,5-diene derivative, is reported. The α-anomer of the 1,5-diene derivative underwent Cope rearrangement to afford 2-deoxy-2-*C*-glycal derivative, whereas the β-anomer was found to be unreactive. Employing this sequence, 3,4,6-tri-*O*-benzyl-2-*O*-acetyl-1,5-anhydro-D-*arabino*-hex-1-enitol was transformed to 3,4,6-tri-*O*-benzyl-2-deoxy-2-*C*-alkyl-1,5-anhydro-D-*arabino*-hex-1-enitol. 2-Deoxy-2-*C*-alkyl glycal derivative is a suitable glycosyl donor to prepare 2-deoxy-2-*C*-alkyl glycosides, mediated through haloglycosylation and a subsequent dehalogenation. A number of 2-deoxy-2-*C*-alkyl glycosides, with both glycosyl and nonglycosyl moieties at the reducing end, are thus prepared from the glycal.



INTRODUCTION

Unsaturated sugars are excellent synthetic equivalents for synthetic transformations in general.[1−3] The particular class of unsaturated sugars, namely, 2-hydroxy glycals or oxyglycals, which differ from 1,2-unsaturated sugars or glycals by the presence of an oxygen functionality at *C*-2, undergo reactions to provide synthetic intermediates that offer diverse reaction possibilities. The synthetic value of oxyglycals is illustrated elegantly, for example, (i) to synthesize reactive 1-halo-2-uloses,[4] (ii) to implement allylic rearrangements so as to prepare 2,3-unsaturated glycosides,[5−8] (iii) to conduct addition across the vinyl ether functionality,[9] and (iv) to synthesize unnatural seven-membered septanosides through an insertion-ring-opening reaction sequence.[10−12] By far the greatest utilization of oxyglycals can be traced to the synthesis of 1-halo-2-ulose sugars by Lichtenthaler and co-workers and the diversified reaction possibilities arising from such uloses.[13] The presence of oxygen functionality at *C*-2 leads to altered reactivities of intermediates derived from oxyglycals, as opposed to those derived from glycals. An example is the reactivity differences and, thus, altered product formation profiles of cyclopropane adducts derived from glycals and oxyglycals. A cyclopropane adduct in the case of glycals leads to the formation of 2-*C*-branched sugars;[14] on the other hand, a similar adduct derived from oxyglycal affords seven-membered oxepine systems,[10] both under base-promoted conditions.

In further efforts to expand the scope of reactions, we undertook an effort to transform oxyglycals to the corresponding 2-deoxy-2-*C*-alkyl glycals. As a consequence of the presence of *C*-1−*C*-2 unsaturation, such 2-*C*-alkylated glycals would be subjected to activation of the double bond and subsequent reactions, as is well-known for glycals so far.[15,16] Thus, developing a synthetic methodology to transform oxyglycals to 2-deoxy-2-*C*-alkyl glycals would, in principle, offer an alternative route to prepare 2-deoxy-2-*C*-branched sugars. 2-Deoxy-2-*C*-branched sugars are prominent moieties in natural products, antibiotics, and several carbohydrate mimetics.[17,18] From a synthetic perspective, development of methods to prepare 2-deoxy-2-*C*-branched sugars relied primarily on either glycals[19−21] or cyclopropanated adducts of glycals[22−26] as the precursors or Wittig homologation of 2-ketoglycosides.[27] In contrast, the presence of an oxygen functionality at *C*-2 in oxyglycals provides an advantage for subsequent synthetic manipulations. With this perspective, we undertook an effort to transform oxyglycals to 2-deoxy-2-*C*-alkyl glycals that upon activation form precursors for the synthesis of 2-deoxy-2-*C*-alkyl glycopyranosides. Syntheses of 2-deoxy-2-*C*-alkyl glycals and the corresponding glycopyranosides are described herein.

RESULTS AND DISCUSSION

The conversion of oxyglycal to 2-deoxy-2-*C*-alkyl glycal was initiated as shown in Figure 1, for which implementation of a Cope rearrangement was planned as a key step.

In Figure 1, utilization of 2-hydroxy glycal ester relies on the possibility of facile in situ generation of vinyl oxide anion under a base-promoted condition. The vinyl oxide anion, in turn, is susceptible to an *O*- or *C*-alkylation in the presence of an acceptor alkyl moiety. This anticipation was realized readily when oxyglycal **1**, prepared through an orthoester method,[28] was reacted with allyl bromide in the presence of NaH/aq DMF (Scheme 1). The reaction led to the formation of *C*-allylated (**2**) and *O*-allylated (**3**) products. The presence of NMR signals corresponding to ketone functionality and *C*-1 of the glycal moiety indicated the formation of **2** and **3**, respectively. The presence of **3**, along with **2**, was inferred from the ^{1}H NMR spectrum, wherein anomeric proton of **3** was observed at 6.26 ppm as a singlet and $CH_2CH{=}CH_2$ of **2** at 2.34−2.66 ppm as a multiplet; the ratio of these two nuclei of

Received: October 31, 2011
Published: January 25, 2012

   dx.doi.org/10.1021/jo202240f | *J. Org. Chem.* 2012, 77, 2185−2191

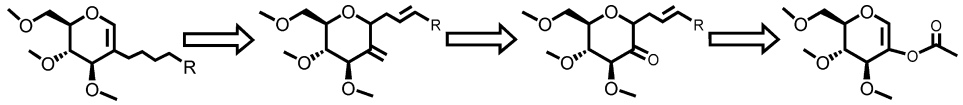
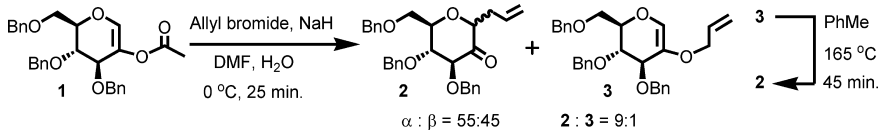


Figure 1. Synthetic plan to prepare 2-deoxy-2-*C*-glycal from 2-hydroxy glycal ester.

Scheme 1

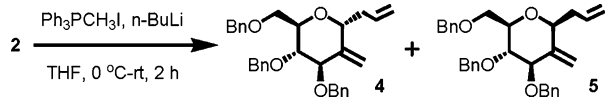


2:**3** was found to be 9:1. The *C*- (**2**) and *O*-allylated (**3**) products were an inseparable mixture, which was mitigated through heating the mixture at 165 °C in a sealed tube. The thermal rearrangement led to the disappearance of **3** and exclusive formation of **2** in an overall moderate yield of 63% from oxyglycal **1**.

The *C*-glycoside **2** was an anomeric mixture, and the anomers could not be separated in a facile manner. Whereas a *C*-alkylation at *C*-1 retained with keto-functionality at *C*-2 is achieved from an oxyglycal precursor in the present work, preparation of either anomer of **2** was reported previously by Zou and co-workers through oxidation of the *C*-2 hydroxyl group on stereochemically pure α- and β-*C*-glycosides.[29] The ratio of anomeric mixture of alkyl *C*-2-ulosides **2** in our protocol was determined on the basis of the observed distinct resonances of anomeric proton for each anomer and in conjecture with the above report. The presence of triplet at 4.25 ppm corresponding to H-1 of α-anomer and a multiplet at 4.02−4.07 ppm, corresponding to H-1of the β-anomer, facilitated determination of the ratio to be 55:45%.

With the inability to separate the anomeric mixture of **2**, the synthesis was proceeded to install the methylene moiety at *C*-2 in **2**. A Wittig methylenation of **2** afforded *C*-2-methylene *C*-glycosides **4** and **5** (Scheme 2). The anomers were separated

Scheme 2



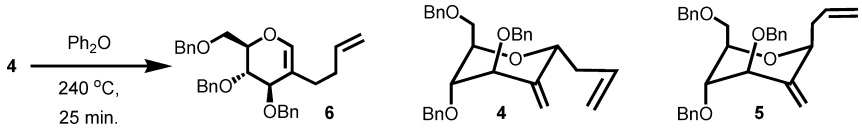
and identified by the observation of a set of multiplets at 2.34−2.44 ppm and 2.53−2.60 ppm for $CH_2CH{=}CH_2$ nuclei of the α-anomer **4** and an triplet at 2.55 ppm of the corresponding nuclei of β-anomer **5**. The newly introduced methylene moiety at *C*-2 in **4** resonated at 5.24, 5.02 ppm and that for **5** resonated at 5.31, 5.10 ppm. Further, evidence for the assignments of **4** comes through the presence of strong cross peaks of H-3 and H-5 with allylic CH_2 protons and a weak cross peak between *C*-2 methylene and allylic CH_2 protons in the NOESY spectrum. The spectrum did not exhibit a cross peak between H-1 and H-3. On the other hand, the NOESY spectrum of **5**, assigned with β-anomeric configuration, showed a strong cross peak between H-1 and H-3 and a weak cross peak between H-2 and allylic CH_2 protons. Additional cross peaks within the ring, as well as with benzylic groups, were also observed.

The installation of a methylene moiety at *C*-2 generated 1,5-diene functionalities in **4** and **5** that are amenable for a thermal rearrangement. Thus, when α-*C*-alkyl glycoside **4** in diphenyl ether was heated at 240 °C for ∼25 min, in a sealed tube, a Cope rearrangement occurred to afford 2-deoxy-2-(but-3-enyl) glycal **6**, in 72% yield (Scheme 3). Formation of **6** was confirmed by the appearance of *C*-1 resonance at 140.6 ppm and *C*-2 resonance at 111.5 ppm in ^{13}C NMR spectrum, and in place of a resonance at 78.2 ppm for the same nucleus in **4**. Whereas the reaction was facile with α-anomer **4**, attempts to subject β-anomer **5** for a similar thermal rearrangement were not successful, and only the starting material was recovered. Possible conformations of **4** and **5**, agreeing with NOESY analyses (vide supra), are shown also in Scheme 3. Further, the observation that none of the β-anomer **5** underwent rearrangement indicated that the transition state of this anomer did not encounter ring-flipping or interconversion which would initiate the rearrangement.

Implementation of Cope rearrangement completed the formal transformation of oxyglycal to 2-deoxy-2-*C*-alkyl glycal. The utility of Claisen rearrangement of 1,5-dienes originating from varied carbons of a sugar is known previously. For example, Fraser-Reid and co-workers demonstrated[30] an "out-of-ring" oxy-Cope rearrangement to produce *C*-2 and *C*-3 *gem*-disubstituted pyranosides, with exclusive stereoselectivities. Curran and Suh[31] demonstrated stepwise mono- and bis-Claisen rearrangements of glycals, equipped with appropriate bis(ketene silyl)acetal moieties to afford functionalized *C*-glycosyl compounds. On the other hand, elegant examples of Claisen rearrangements are the conversion of carbohydrates to functionalized cyclohexanes, as demonstrated by Nagarajan and Sudha,[32] and cyclooctanes, by Thiem and co-workers.[33]

In efforts to utilize 2-*C*-glycal **6** for subsequent elaboration as a donor in glycosylations, reaction at the terminal double bond was undertaken first. A hydration across the double bond through a hydroboration-oxidation was exercised. Thus, diene **6** was reacted with 9-BBN in THF, followed by treatment with H_2O_2 (30%)−aq NaOH (3 N) solution (Scheme 4).

Scheme 3



dx.doi.org/10.1021/jo202240f | J. Org. Chem. 2012, 77, 2185−2191

Scheme 4

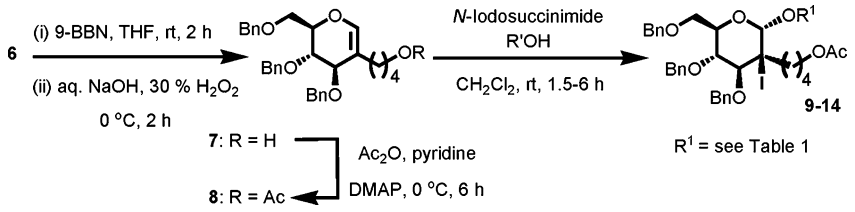


Table 1. List of 2-Iodo-2-C-alkyl Glycosides 9−14 and 15, Formed through Iodoglycosylation of 8 and 7, Respectively, and 2-Deoxy-2-C-glycosides 16 and 17, Formed from 13 and 15, Respectively[a]

Glycosyl acceptor (R'-OH)	2-Iodo-2-*C*-alkyl glycosides	Glycosyl acceptor (R'-OH)	2-Iodo-2-*C*-alkyl glycosides
MeOH	**9** (86%)		**13** : R_1 = I ; R_2 = Ac (80%) **16** : R_1, R_2 = H (81%)
OH	**10** (85%)	OMe	**14** (82%)
HO OH	**11** (78%)	HO	**15** : R = I (79%) **17** : R = H (88%)
Ph OH	**12** (77%)		

[a]Isolated yields are given in parentheses.

The reaction led to a hydration at the terminal double bond and afforded alcohol **7**.

Reactivities of 2-deoxy-2-*C*-alkyl glucal **7** were explored further by subjecting it to a haloglycosylation.[15,16] Toward this, alcohol **7** was protected as an acetate **8** (Ac_2O/pyridine) and subjected to haloglycosylation using *N*-iodosuccinimide (NIS) in the presence of acceptor alcohols, including sugars. The reaction in CH_2Cl_2 at room temperature led to the formation of haloglycosylation products **9**−**14** (Table 1) in good yields. We infer from previous reports that haloglycosylation generally has a very high propensity for 1,2-*trans* diaxial addition pattern of substituents.[34,35] Observing that anomeric carbon resonates at around 101 ppm for compounds **9**−**14**, we assign these compounds an α-anomeric configuration. *Trans*-addition being predominant in haloglycosylation, we are tempted to assign an axial configuration to the iodo-group at C-2. Whereas the intermolecular haloglycosylation led to α-anomeric glycosides in **9**−**14**, wherein *C*-1 appeared at ∼101 ppm, an intramolecular reaction with glycal **7** afforded the oxepine derivative **15**, for which the anomeric carbon appeared at 107.1 ppm in the ^{13}C NMR spectrum, which we assign to a β-anomeric configuration. The conformational constraints appeared to be dominating in the formation of **15** with β-anomeric linkage, as opposed to α-anomeric linkage with **9**−**14** predominated by the kinetic anomeric effect. On the basis of of *anti*-addition, an axial configuration in **9**−**14** and an equatorial configuration in **15** of iodide at *C*-2 were inferred.

Subsequent to iodoglycosylation, a deiodination reaction was undertaken with few glycosides. Reaction of glycosides **13** and **15** with Bu_3SnH/AIBN, followed by treatment with NaOMe/MeOH, in the case of **13**, led to a facile deiodination and *O*-deacetylation to afford 2-deoxy-2-(*n*-butyl) glycosides **16** and **17** in 81 and 88% yields, respectively. In order to assess the anomeric configuration, a NOESY experiment was performed on **17**, from which cross peaks of H-1 with H-3 and H-5 protons were observed, in addition to the C1 resonance at 102.04 ppm in the corresponding ^{13}C NMR spectrum. In the case of **16**, having two α-anomeric carbons, both C1 resonances were seen at 96.3 and 97.8 ppm. These comparisons led to assign a β-anomeric configuration to **17**. The examples studied herein showed not only a facile iodoglycosylation but also subsequent deiodination in order to realize 2-*C*-branched 2-deoxy-2-*C*-alkyl glycosides.

■ CONCLUSION

A synthetic method to transform 2-hydroxy glycal ester, namely, oxyglycal to the corresponding 2-deoxy-2-C-alkyl glycal was developed by involving (i) *C*-alkylation at anomeric carbon of an oxyglycal to afford C-alkyl-2-uloside, (ii) Wittig methylenation to 1,5-diene, namely, 2-*C*-methylenyl-*C*-alkyl glycal,

dx.doi.org/10.1021/jo202240f | J. Org. Chem. 2012, 77, 2185−2191

and (iii) a Cope rearrangement on 2-*C*-methylenyl-*C*-alkyl glycal. The presence of glycal functionality and a terminal olefin functionality in the *exo*-cyclic alkyl substituent provided feasibility to conduct reactions separately. Thus, whereas the terminal olefin was subjected to a hydration, the glycal functionality was utilized to an iodoglycosylation and deiodination reactions, leading to the formation of a series of 2-deoxy-2-*C*-alkyl glycosides, with nonglycosyl and glycosyl substituents. A bicyclic sugar−oxepine fused ring derivative was also obtained through an intramolecular glycosylation on 2-deoxy-2-*C*-alkyl glycal.

EXPERIMENTAL SECTION

3-*C*-(3′,4′,6′-Tri-*O*-benzyl-α/β-D-*arabino*-hex-2-ulopyranosyl)propene (2). Allyl bromide (0.33 mL, 3.79 mmol) was added to a solution of **1**[28] (0.9 g, 1.89 mmol) in DMF (10 mL) at 0 °C. NaH (0.095 g, 2.37 mmol, 60% in mineral oil) and H_2O (100 μL) in DMF (1 mL) were added slowly to the reaction mixture for over 5−10 min. The reaction mixture was diluted with water (50 mL), extracted with Et_2O (3 × 50 mL), washed with aq NH_4Cl (2 × 50 mL), dried (Na_2SO_4), and filtered, solvents were removed in vacuo, and the crude product was purified (SiO_2) (EtOAc/pet ether = 1:19), to afford a mixture of **2** and **3**. ^{1}H NMR (400 MHz, $CDCl_3$): 2.34−2.66 ppm (m, CH_2CH=CH_2 of **2**); 6.26 ppm (s, *H*-1 of **3**), ratio of **2**:**3** = 9:1. The *O*-allyl product **3** in toluene (4 mL) was heated at 165 °C in a sealed tube for over 45 min, and solvents were removed in vacuo to afford **2** (0.56 g, 63%) (α/β = 1.2:1) as an oil: IR 1738 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39−7.21 (band, 33.3 H), 5.90−5.72 (m, 2.22 H), 5.15−5.01 (m, 4.44 H), 4.96 (d, *J* = 11.6 Hz, 1.22 H), 4.87−4.76 (m, 2.44 H), 4.62−4.58 (m, 3.22 H), 4.51 (d, *J* = 11.6 Hz, 2.44 H), 4.43−4.38 (m, 4 H), 4.27 (t, *J* = 6.8 Hz, 1.22 H), 4.05−4.02 (m, 1 H), 3.93−3.89 (m, 2 H), 3.83−3.58 (m, 8.88 H), 3.50−3.47 (m, 1 H), 2.66−2.58 (m, 2 H), 2.47 (t, *J* = 6.4 Hz, 2.44 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 207.8, 201.9, 138.7−137.5, 133.6, 132.3, 128.6−127.6, 118.4, 117.2, 86.7, 84.4, 79.9, 78.3, 76.2, 75.5, 75.3, 74.4, 74.2, 73.9, 73.7, 73.4, 72.8, 72.2, 69.8, 68.2, 34.8, 32.9; ES-MS *m*/*z* $C_{30}H_{32}O_5Na$ cslcd 495.2147, found 495.2154.

3-*C*-(3′,4′,6′-Tri-*O*-benzyl-2-deoxy-2-*C*-methylene-α/β-D-*arabino*-hexopyranosyl)propene (4 and 5). ^{n}BuLi (1.6 M hexane) (1.47 mL, 2.36 mmol) was added dropwise to a solution of Ph_3PMeI (1.2 g, 2.96 mmol) in THF (10 mL) at 0 °C. After ∼20 min, a solution of **2** (0.56 g, 1.18 mmol) in THF (20 mL) was added dropwise and stirring continued for 2 h. The reaction mixture was diluted with H_2O (150 mL), extracted with $CHCl_3$ (3 × 50 mL), dried (Na_2SO_4), filtered, concentrated in vacuo, and purified (SiO_2) (hexane/EtOAc = 7:1) to afford **4** and **5**. **4**: 0.19 g (55%); gum; R_f = 0.24 (hexane/EtOAc = 9:1); $[\alpha]_D$ +9.7 (*c* 0.7, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz) 7.36−7.15 (band, 15 H, aromatic), 5.79−5.69 (m, 1 H, −C*H*=CH_2), 5.24 (br. s, 1 H, methylene H), 5.08−5.04 (m, 2 H, −CH=C*H*$_2$), 5.02 (br. s, 1 H, methylene H), 4.83 (d, *J* = 10.8 Hz, 1 H, PhC*H*$_2$), 4.74−4.58 (band, 3 H, PhC*H*$_2$), 4.51−4.48 (band, 2 H, PhC*H*$_2$), 4.38 (t, *J* = 7.2 Hz, 1 H, H-1), 4.22 (d, *J* = 8.4 Hz, 1 H, H-3), 3.85−3.81 (m, 1 H, H-5), 3.70 (dd, *J* = 3.6, 10.8 Hz, 1 H, H_a-6), 3.63 (dd, *J* = 2.4, 10.8 Hz, 1 H, H_b-6), 3.55 (t, *J* = 8.4 Hz, 1 H, H-4), 2.60−2.53 (m, 1 H, −C*H*$_2$CH=CH_2), 2.44−2.34 (m, 1 H, −C*H*$_2$CH=CH_2); ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.4 (C-2), 138.2−138.1 (aromatic), 134.0 (−CH=CH_2), 128.4−127.5 (aromatic), 117.1 (−CH=CH_2), 110.2 (methylene C), 81.0 (C-3), 80.3 (C-4), 78.2 (C-1), 74.1 (PhCH_2), 73.4 (PhCH_2), 73.3 (PhCH_2), 73.1 (C-5), 69.3 (C-6), 35.6 (−CH_2CH=CH_2); ES-MS *m*/*z* $C_{31}H_{34}O_4Na$ calcd 493.2355, found 493.2353.

5: 0.15 g (45%); gum; R_f = 0.28 (hexane/EtOAc = 9:1); $[\alpha]_D$ +28.0 (*c* 1, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz) 7.38−7.15 (band, 15 H, aromatic), 5.93−5.86 (m, 1 H, −C*H*=CH_2), 5.31 (br s, 1 H, methylene H), 5.14−5.05 (m, 2 H, −CH=C*H*$_2$), 5.10 (br s, 1 H, methylene H), 4.84 (d, *J* = 10.8 Hz, 1 H, PhC*H*$_2$), 4.74 (d, *J* = 11.6 Hz, 1 H, PhC*H*$_2$), 4.65−4.47 (m, 4 H, PhC*H*$_2$), 4.02 (d, *J* = 8.0 Hz, 1 H, H-3), 3.76−3.69 (m, 2 H, H-1, H-5), 3.63 (dd, *J* = 4.8, 10.8 Hz, 1 H, H_a-6), 3.54 (dd, *J* = 3.6, 10.8 Hz, 1 H, H_b-6), 3.48 (dd, *J* = 4.8, 8.0 Hz, 1 H, H-4), 2.55 (t, *J* = 6.9 Hz, 2 H, C*H*$_2$CH=CH_2); ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.9 (C-2), 138.3−138.1 (aromatic), 135.0 (−CH=CH_2), 128.3−127.4 (aromatic), 116.6 (−CH=CH_2), 107.7 (methylene C), 84.5 (C-3), 80.3 (C-4), 79.1 (C-5), 76.9 (C-1), 74.6 (PhCH_2), 73.3 (PhCH_2), 72.9 (PhCH_2), 69.3 (C-6), 35.9 (CH_2CH=CH_2); ES-MS *m*/*z* $C_{31}H_{34}O_4Na$ calcd 493.2355, found 493.2353.

1,5-Anhydro-3,4,6-tri-*O*-benzyl-2-deoxy-2-*C*-(but-3-enyl)-D-*arabino*-hex-1-enitol (6). The reaction tube was deacidified by soaking in 1,1,1,3,3,3-hexamethyldisilazane overnight. A solution of **4** (0.37 g, 0.78 mmol) in diphenyl ether (3 mL) was sealed and heated at 240 °C for ∼25 min and purified (SiO_2) (hexane/EtOAc = 10:1) to afford **6** (0.27 g, 72%) as a colorless oil: R_f = 0.25 (hexane/EtOAc = 9:1); $[\alpha]_D$ +49.0 (*c* 2, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz) 7.35−7.26 (band, 15 H, aromatic), 6.28 (s, 1 H, H-1), 5.80−5.71 (m, 1 H, −C*H*=CH_2), 5.0−4.94 (m, 2 H, −CH=C*H*$_2$), 4.75−4.48 (m, 6 H, PhC*H*$_2$), 4.16−4.12 (m, 1 H, H-5), 4.06 (d, *J* = 4.8 Hz, 1 H, H-3), 3.96 (dd, *J* = 4.8, 6.8 Hz, 1 H, H-4), 3.80 (dd, *J* = 5.6, 10.4 Hz, 1 H, H_a-6), 3.72 (dd, *J* = 3.6, 10.4 Hz, 1 H, H_b-6), 2.20−1.94 (m, 4 H, −C*H*$_2$C*H*$_2$CH=CH_2); ^{13}C NMR (100 MHz, $CDCl_3$) δ 140.6 (C-1), 138.4 (−CH=CH_2) 138.3−138.0 (aromatic), 128.4−127.7 (aromatic), 114.7 (−CH=CH_2), 111.5 (C-2), 76.1 (C-5), 75.6 (C-3), 73.8 (C-4), 73.4 (PhCH_2), 72.8 (PhCH_2), 71.3 (PhCH_2), 68.2 (C-6), 32.5 (−CH_2CH_2CH=CH_2), 28.2 (−CH_2CH$_2$CH=CH_2); ES-MS *m*/*z* $C_{31}H_{34}O_4Na$ calcd 493.2352, found 493.2357.

1,5-Anhydro-3,4,6-tri-*O*-benzyl-2-deoxy-2-*C*-(4-hydroxybutyl)-D-*arabino*-hex-1-enitol (7). 9-BBN (2 M in THF) (0.34 mL, 0.69 mmol) was added dropwise to a solution of **6** (0.26 g, 0.55 mmol) in THF (10 mL) under argon atmosphere and at room temperature and stirred for 2 h. The reaction mixture was cooled to 0 °C, and aq NaOH (3 N) (0.4 mL) and aq H_2O_2 (30%) (0.5 mL) were added dropwise. The reaction mixture was stirred for 2 h, diluted with H_2O (100 mL), extracted with Et_2O (3 × 70 mL), dried (Na_2SO_4), filtered, concentrated in vacuo, and purified (SiO_2) (hexane/EtOAc = 4:1) to afford **7** (0.22 g, 82%): gum; R_f = 0.37 (hexane/EtOAc = 2:1); $[\alpha]_D$ +47.1 (*c* 1, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.33−7.25 (band, 15 H, aromatic), 6.26 (s, 1 H, H-1), 4.72−4.44 (m, 6 H, PhC*H*$_2$), 4.13 (dd, *J* = 5.6, 10.8 Hz, 1 H, H-5), 4.02 (d, *J* = 4.8 Hz, 1 H, H-3), 3.93 (app. t, *J* = 5.6 Hz, 1 H, H-4), 3.78 (dd, *J* = 6.0, 10.8 Hz, 1 H, H_a-6), 3.70 (dd, *J* = 3.6, 10.8 Hz, 1 H, H_b-6), 3.57 (t, *J* = 6.4 Hz, 2 H, −C*H*$_2$OH), 2.14−2.07 (m, 1 H, −C*H*$_2$CH$_2$OH), 1.91−1.84 (m, 1 H, −C*H*$_2$CH$_2$OH), 1.54−1.30 (m, 4 H, −C*H*$_2$C*H*$_2$CH$_2$CH$_2$OH); ^{13}C NMR (100 MHz, $CDCl_3$): δ 140.4 (C-1), 138.3−137.9 (aromatic), 128.4−127.6 (aromatic), 111.7 (C-2), 75.9 (C-5), 75.2 (C-3), 73.6 (C-4), 73.3 (PhCH_2), 72.7 (PhCH_2), 71.2 (PhCH_2), 68.2 (C-6), 62.7 (−CH_2OH), 32.2 (−CH_2CH$_2$OH), 28.5 (−CH_2CH$_2$CH$_2$CH$_2$OH), 24.0 (−CH_2CH$_2$CH$_2$OH);ES-MS *m*/*z* $C_{31}H_{36}O_5Na$ calcd 511.2460, found 511.2458.

1,5-Anhydro-3,4,6-tri-*O*-benzyl-2-deoxy-2-*C*-(4-acetoxybutyl)-D-*arabino*-hex-1-enitol (8). Acetic anhydride (0.09 mL, 0.9 mmol) was added to a solution of **7** (0.22 g, 0.04 mmol) in pyridine (4 mL) at 0 °C and stirred for 6 h at room temperature. The reaction mixture was diluted with water (50 mL), extracted with $CHCl_3$ (3 × 50 mL), washed with aq HCl (2 N) and aq $NaHCO_3$ (2 × 50 mL), dried (Na_2SO_4), filtered, concentrated in vacuo, and purified (SiO_2) (hexane/EtOAc = 9:1) to afford **8** (0.22 g, 92%): gum; R_f = 0.33 (hexane/EtOAc = 9:1); $[\alpha]_D$ +26.0 (*c* 1, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.33−7.25 (band, 15 H, aromatic), 6.26 (s, 1 H, H-1), 4.72−4.44 (m, 6 H, PhC*H*$_2$), 4.15−4.12 (m, 1 H, H-5), 4.01−3.98 (band, 3 H, H-3, −C*H*$_2$OAc), 3.94 (dd, *J* = 5.6, 12.8 Hz, 1 H, H-4), 3.78 (dd, *J* = 5.6, 10.4 Hz, 1 H, H_a-6), 3.70 (dd, *J* = 3.6, 10.4 Hz, 1 H, H_b-6), 2.12−2.06 (m, 1 H, −C*H*$_2$CH$_2$OAc), 2.01 (s, 3 H, Me), 1.91−1.81 (m, 1 H, −C*H*$_2$CH$_2$OAc), 1.63−1.50 (band, 4 H, −C*H*$_2$C*H*$_2$CH$_2$OAc + H_2O), 1.40−1.23 (m, 2 H, −C*H*$_2$CH$_2$CH$_2$CH$_2$OAc); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.1 (−$COCH_3$), 140.5 (C-1), 138.2−137.9 (aromatic), 128.4−127.6 (aromatic), 111.5 (C-2), 75.9 (C-5), 75.2 (C-3), 73.6 (C-4), 73.4 (PhCH_2), 72.8 (PhCH_2), 71.2 (PhCH_2), 68.2 (C-6), 64.3 (−CH_2−OAc), 28.4 (−CH_2CH$_2$OAc), 28.0 (−CH_2CH$_2$CH$_2$CH$_2$OAc), 24.3 (−CH_2CH$_2$CH$_2$OAc), 20.9 (−$COCH_3$); ES-MS *m*/*z* $C_{33}H_{38}O_6Na$ calcd 553.2566, found 553.2561.

dx.doi.org/10.1021/jo202240f | J. Org. Chem. 2012, 77, 2185−2191

Methyl 3,4,6-Tri-*O*-benzyl-2-deoxy-2-iodo-(2-*C*-(4-acetoxybutyl))-α-D-*arabino*-hexopyranoside (9). *N*-Iodosuccinimide (0.06 g, 0.25 mmol) and methanol (10 μL, 0.34 mmol) were added to a solution of **8** (0.09 g, 0.17 mmol) in CH_2Cl_2 (10 mL) under argon atmosphere and at room temperature, stirred for 2 h, diluted with water (50 mL), extracted with CH_2Cl_2 (3 × 50 mL), washed with aq $Na_2S_2O_3$ solution (5%) (2 × 20 mL) and brine (2 × 20 mL), dried (Na_2SO_4), filtered, and concentrated in vacuo. The crude product was purified (SiO_2) (hexane/EtOAc = 6:1) to afford **9** (0.1 g, 86%): colorless oil; R_f = 0.31 (hexane/EtOAc = 5.5:1); $[\alpha]_D$ +23.7 (*c* 1, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.37−7.25 (band, 14 H, aromatic), 7.15−7.13 (m, 1 H, aromatic), 5.02 (d, *J* = 11.6 Hz, 1 H, PhC*H*$_2$) 4.90 (s, 1 H, H-1), 4.79−4.71 (m, 3 H, PhC*H*$_2$), 4.63−4.49 (m, 2 H, PhC*H*$_2$), 4.15−4.09 (m, 1 H, H-5), 4.04−3.99 (m, 2 H, CH_2−OAc), 3.83−3.69 (m, 3 H, H-4, -H-6$_{a,b}$), 3.33 (s, 3 H, OMe), 2.86 (d, *J* = 8.4 Hz, 1 H, H-3), 2.02 (s, 3 H, −COC*H*$_3$), 1.74−1.70 (m, 2 H, −C*H*$_2$CH$_2$OAc), 1.60−1.46 (m, 2 H, −C*H*$_2$CH$_2$CH$_2$OAc), 1.35−1.27 (m, 2 H, −C*H*$_2$-CH$_2$CH$_2$CH$_2$OAc); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.0 (−*C*OCH$_3$), 138.5−137.9 (aromatic), 128.3−127.3 (aromatic), 102.9 (C-1), 83.2 (C-3), 79.5 (C-4), 75.2 (C-5), 75.0 (PhCH$_2$), 73.3 (PhCH$_2$), 72.0 (PhCH$_2$), 68.8 (C-6), 62.9 (−CH$_2$OAc), 55.0 (OMe), 39.8 (C-2), 28.3 (−*C*H$_2$CH$_2$OAc), 22.1 (−*C*H$_2$CH$_2$CH$_2$OAc), 20.9 (−*C*H$_2$CH$_2$CH$_2$-CH$_2$OAc), 20.8 (−COC*H*$_3$); ES-MS *m*/*z* $C_{34}H_{41}O_7INa$ calcd 711.1795, found 711.1794.

Butyl 3,4,6-Tri-*O*-benzyl-2-deoxy-(2-iodo)-(2-*C*-(4-acetoxybutyl))-α-D-*arabino*-hexopyranoside (10). *N*-Iodosuccinimide (0.04 g, 0.17 mmol) and *n*-butanol (17 μL, 0.22 mmol) were added to a solution of **8** (0.06 g, 0.11 mmol) in CH_2Cl_2 (10 mL) under argon atmosphere and stirred for 2 h at room temperature, and the reaction was followed further as described for **9**. The crude product was purified (SiO_2) (hexane/EtOAc = 5.6:1) to afford **10** (0.07 g, 85%): gum; R_f = 0.39 (hexane/EtOAc = 9:1); $[\alpha]_D$ +26.0 (*c* 1, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.37−7.28 (band, 14 H, aromatic), 7.26−7.13 (m, 1 H, aromatic), 5.03 (d, *J* = 11.6 Hz, 1 H, PhC*H*$_2$), 4.99 (s, 1 H, H-1), 4.8−4.72 (m, 3 H, PhC*H*$_2$), 4.55−4.51 (m, 2 H, PhC*H*$_2$), 4.14 (app t, *J* = 9.2 Hz, 1 H, H-4), 4.03−4.0 (m, 2 H, −C*H*$_2$OAc), 3.86−3.78 (m, 2 H, H-5, H$_a$-6), 3.69−3.65 (m, 2 H, H$_b$-6, −OC*H*$_2$-CH$_2$CH$_2$CH$_3$), 3.35−3.29 (m, 1 H, −OC*H*$_2$CH$_2$CH$_2$CH$_3$), 2.89 (d, *J* = 8.8 Hz, 1 H, H-3), 2.02 (s, 3 H, −COCH$_3$), 1.88−1.82 (m, 1 H, −C*H*$_2$CH$_2$CH$_3$), 1.74−1.68 (m, 2 H, CH$_2$C*H*$_2$CH$_3$), 1.55−1.51 (m, 5 H, −C*H*$_2$C*H*$_2$CH$_2$OAc, −OCH$_2$CH$_2$C*H*$_2$CH$_3$), 1.37−1.32 (m, 2 H, −C*H*$_2$CH$_2$CH$_2$CH$_2$OAc), 0.91 (t, *J* = 7.6 Hz, 3 H, −CH$_3$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.0 (-*C*OCH$_3$), 138.3−137.9 (aromatic), 128.4−127.4 (aromatic), 101.9 (C-1), 83.3 (C-5), 79.5 (C-4), 75.2 (C-3), 75.1 (PhCH$_2$), 73.3 (PhCH$_2$), 72.1 (PhCH$_2$), 68.8 (C-6), 64.2 (−*C*H$_2$OAc), 63.3 (−OCH$_2$CH$_2$CH$_2$CH$_3$), 39.8 (C-2), 32.3 (−*C*H$_2$-CH$_2$OAc), 31.4 (−CH$_2$CH$_2$CH$_2$OAc), 28.4 (−CH$_2$CH$_2$CH$_2$CH$_2$-OAc), 22.3 (CH$_2$CH$_2$CH$_3$), 20.9 (−COCH$_3$), 19.3 (−*C*H$_2$CH$_3$), 13.7 (−CH$_3$); ES-MS *m*/*z* $C_{37}H_{47}O_7INa$ calcd 753.2264, found 753.2259.

4-Hydroxybutyl 3,4,6-Tri-*O*-benzyl-2-deoxy-(2-iodo)-(2-*C*-(4-acetoxybutyl))-α-D-*arabino*-hexopyranoside (11). *N*-Iodosuccinimide (0.05 g, 0.22 mmol) and 1,4-butanediol (7 μL, 0.07 mmol) were added to a solution of **8** (0.08 g, 0.15 mmol) in CH_2Cl_2 (15 mL) under argon atmosphere and stirred for 6 h at room temperature, and the reaction was followed further as described for **9**. The crude product was purified (SiO_2) (hexane/EtOAc = 5.6:1) to afford **11** (0.090 g, 80%): gum; R_f = 0.37 (hexane/EtOAc = 4:1); $[\alpha]_D$ +28.4 (*c* 1, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.38−7.29 (band, 14 H, aromatic), 7.26−7.13 (m, 1 H, aromatic), 5.03 (d, *J* = 12.2 Hz, 1 H, PhC*H*$_2$), 5.01 (s, 1 H, H-1), 4.79−4.70 (m, 3 H, PhC*H*$_2$), 4.58−4.50 (m, 2 H, PhC*H*$_2$), 4.13 (app t, *J* = 9.2 Hz, 1 H, H-4), 4.05−3.98 (m, 2 H, −C*H*$_2$OAc), 3.84 (dd, *J* = 3.6, 10.8 Hz, 1 H, H-5), 3.78 (dd, *J* = 4.8, 10.8 Hz, 1 H, H$_a$-6), 3.74−3.68 (m, 1 H, H$_b$-6), 3.62 (app t, *J* = 7.2 Hz, 2 H, −C*H*$_2$OH), 3.53 (app t, *J* = 6.0 Hz, 2 H, −OC*H*$_2$CH$_2$CH$_2$-CH$_2$OH), 2.88 (d, *J* = 8.8 Hz, 1 H, H-3), 2.0 (s, 3 H, −COC*H*$_3$), 1.73−1.69 (m, 2 H, −OCH$_2$C*H*$_2$C*H*$_2$CH$_2$OH), 1.63−1.51 (m, 6 H, C*H*$_2$C*H*$_2$CH$_2$OAc, C*H*$_2$C*H*$_2$CH$_2$OH), 1.37−1.30 (m, 2 H, −C*H*$_2$CH$_2$-CH$_2$CH$_2$OAc); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.1 (−*C*OCH$_3$), 138.3−137.8 (aromatic), 128.4−127.5, (aromatic) 102.0 (C-1), 83.3 (C-3), 79.6 (C-4), 75.2 (PhCH$_2$), 73.4 (PhCH$_2$), 72.2 (PhCH$_2$), 68.8 (C-5), 67.7 (C-6), 64.3 (−CH$_2$OAc), 63.0 (−CH$_2$OH), 62.4 (−OCH$_2$CH$_2$CH$_2$CH$_2$OH), 39.8 (C-2), 30.0 (−CH$_2$CH$_2$OAc), 29.5 (−*C*H$_2$CH$_2$CH$_2$OH), 28.3 (−CH$_2$CH$_2$CH$_2$CH$_2$OAc), 25.8 (−CH$_2$-CH$_2$OH), 22.3 (−CH$_2$CH$_2$CH$_2$OAc), 20.9 (CH$_3$); ES-MS *m*/*z* $C_{37}H_{47}O_8INa$ calc 769.2213, found 769.2217.

2-(Phenylethyl)-3,4,6-tri-*O*-benzyl-2-deoxy-2-iodo-(2-*C*-(4-acetoxybutyl))-α-D-*arabino*-hexopyranoside (12). *N*-Iodosuccinimide (0.038 g, 0.17 mmol) and 2-phenylethanol (28 μL, 0.23 mmol) were added to a solution of **8** (0.06 g, 0.11 mmol) in CH_2Cl_2 (10 mL) under argon atmosphere and at room temperature and stirred for 2 h, and the reaction was followed further as described for **9**. The crude product was purified (SiO_2) (hexane/EtOAc = 6:1) to afford **12** (0.068 g, 77%): gum; R_f = 0.36 (hexane/EtOAc = 9:1); $[\alpha]_D$ +3.0 (*c* 1, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.38−7.24 (band, 15 H, aromatic), 7.20 (d, *J* = 11.6 Hz, 1 H, aromatic), 7.16−7.14 (band, 4 H, aromatic), 5.02 (d, *J* = 11.8 Hz, 1 H, PhC*H*$_2$), 4.94 (s, 1 H, H-1), 4.87 (m, 2 H, PhC*H*$_2$), 4.77 (d, *J* = 11.2 Hz, 1 H, PhC*H*$_2$), 4.71 (d, *J* = 11.8 Hz, 1 H, PhC*H*$_2$), 4.51 (d, *J* = 11.2 Hz, 1 H, PhC*H*$_2$), 4.12 (app t, *J* = 9.2 Hz, 1 H, H-4), 3.92−3.83 (m, 2 H, −C*H*$_2$OAc), 3.75−3.73 (m, 1 H, H-5), 3.65 (d, *J* = 9.6 Hz, 1 H, H$_a$-6), 3.51 (dd, *J* = 9.6, 16.4 Hz, 1 H, H$_b$-6), 2.87−2.80 (m, 3 H, H-3, −OC*H*$_2$CH$_2$Ph), 2.01 (s, 3 H, −COC*H*$_3$), 1.90−1.80 (m, 2 H, −OCH$_2$C*H*$_2$Ph), 1.74−1.66 (m, 2 H, −C*H*$_2$CH$_2$OAc), 1.59−1.52 (m, 1 H, −C*H*$_2$CH$_2$CH$_2$OAc), 1.42−1.25 (m, 2 H, −C*H*$_2$CH$_2$CH$_2$CH$_2$OAc), 1.0−0.9 (m, 1 H, −C*H*$_2$CH$_2$-CH$_2$CH$_2$OAc); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.3 (-COCH$_3$), 138.3−138.0 (aromatic), 128.8−127.4 (aromatic), 101.8 (C-1), 82.9 (C-5), 79.5 (C-4), 75.0 (C-3), 74.2 (PhCH$_2$), 73.3 (PhCH$_2$), 72.1 (PhCH$_2$), 68.7 (C-6), 64.1 (−*C*H$_2$OAc), 63.0 (-OCH$_2$−CH$_2$Ph), 35.9 (C-2), 32.3 (−OCH$_2$CH$_2$Ph), 28.2 (−CH$_2$CH$_2$OAc), 21.4 (−*C*H$_2$CH$_2$CH$_2$OAc), 20.9 (−CH$_3$), 19.9 (−*C*H$_2$CH$_2$CH$_2$CH$_2$OAc); ES-MS *m*/*z* $C_{41}H_{47}O_7INa$ calcd 801.2264, found 801.2263.

3,4,6-Tri-*O*-benzyl-2-deoxy-2-iodo-(2-*C*-(4-acetoxybutyl))-α-D-*arabino*-hexopyranosyl-(1→6)-α-D-1,2:3,4-di-*O*-isopropylidene-α-D-glucopyranose (13). *N*-Iodosuccinimide (0.05 g, 0.22 mmol) and 1,2:3,4-diisopropylidene-α-D-galactopyranoside (0.1 g, 0.37 mmol) were added to a solution of **8** (0.08 g, 0.15 mmol) in CH_2Cl_2 (15 mL) under argon atmosphere and at room temperature. The reaction mixture was stirred for 6 h, and the reaction was followed further as described for **9**. The crude product was purified (SiO_2) (hexane/EtOAc = 4:1) to afford **13** (0.115 g, 83%): gum; R_f = 0.39 (hexane/EtOAc = 4:1); $[\alpha]_D$ −5.0 (*c* 1, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.39−7.25 (band, 14 H, aromatic), 7.14−7.13 (m, 1 H, aromatic), 5.50 (d, *J* = 5.2 Hz, 1 H, H$_R$-1), 5.08 (s, 1 H, H$_{NR}$-1), 5.03 (d, *J* = 12.0 Hz, 1 H, PhC*H*$_2$), 4.76 (m, 3 H, PhC*H*$_2$), 4.61 (dd, *J* = 2.6, 8.0 Hz, 1 H, H$_R$-3), 4.55−4.51 (m, 2 H, PhC*H*$_2$), 4.32 (dd, *J* = 2.4, 5.2 Hz, 1 H, H$_R$-2), 4.20 (app t, *J* = 9.2 Hz, 1 H, H$_{NR}$-4), 4.12 (dd, *J* = 2.4, 8.0 Hz, 1 H, H$_R$-4), 4.06−3.92 (band, 2 H, −C*H*$_2$OAc), 3.93 (m, 1 H, H$_R$-5), 3.86−3.82 (m, 1 H, H$_{NR}$-5), 3.80 (app d, *J* = 4.4 Hz, 1 H, H$_{NR}$-6a), 3.78−3.69 (band, 2 H, H$_{NR}$-6$_b$, H$_R$-6$_a$), 3.61 (dd, *J* = 6.4, 10.4 Hz, 1 H, H$_R$-6$_b$), 2.89 (d, *J* = 8.8 Hz, 1 H, H$_{NR}$-3), 2.07−2.04 (m, 1 H, −C*H*$_2$CH$_2$OAc), 2.02 (s, 3 H, −COCH$_3$), 1.60−1.57 (m, 1 H, −C*H*$_2$CH$_2$OAc), 1.55−1.48 (m, 4 H, −C*H*$_2$CH$_2$CH$_2$OAc + H$_2$O), 1.53 (s, 3 H, Me), 1.42 (s, 3 H, Me), 1.33 (s, 3 H, Me), 1.31 (app s, 4 H, Me, −C*H*$_2$CH$_2$CH$_2$CH$_2$OAc), 1.26−1.23 (m, 1 H, −C*H*$_2$CH$_2$CH$_2$CH$_2$OAc); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.0 (−COCH$_3$), 138.3−137.9 (aromatic), 128.3−127.3 (aromatic), 109.3, 108.6, 101.3 (C$_{NR}$-1), 96.2 (C$_R$-1), 83.1 (C$_{NR}$-3), 79.4 (C$_{NR}$-4), 75.2 (PhCH$_2$), 75.1 (PhCH$_2$), 73.3 (PhCH$_2$), 72.3 (C$_{NR}$-5), 70.9 (C$_R$-4), 70.6 (C$_R$-3), 70.4 (C$_R$-2), 68.5 (C$_{NR}$-6), 65.0 (C$_R$-6), 64.2 (C$_R$-5), 63.3 (−CH$_2$OAc), 39.7 (C$_{NR}$-2), 28.4 (−CH$_2$CH$_2$OAc), 26.1 (Me), 25.9 (Me), 24.8 (Me), 24.5 (−CH$_2$CH$_2$CH$_2$OAc), 22.1 (−CH$_2$CH$_2$CH$_2$CH$_2$OAc), 20.9 (−CH$_3$); ES-MS *m*/*z* $C_{45}H_{57}O_{12}INa$ calcd 939.2792, found 939.2793.

Methyl 3,4,6-Tri-*O*-benzyl-2-deoxy-2-iodo-(2-*C*-(4-acetoxybutyl))-α-D-*arabino*-hexopyranosyl-(1→6)-α-D-2,3,4-tri-*O*-benzyl-α-D-glucopyranoside (14). *N*-Iodosuccinimide (0.063 g, 0.28 mmol) and methyl 1,2,3-tri-*O*-benzyl-α-D-glucopyranoside (0.18 g, 0.38 mmol) were added to a solution of **8** (0.10 g, 0.19 mmol) in CH_2Cl_2 (15 mL) under argon atmosphere and at room temperature.

dx.doi.org/10.1021/jo202240f | *J. Org. Chem.* 2012, 77, 2185−2191

The reaction mixture was stirred for 6 h, and the reaction was followed further as described for **9**. The crude product was purified (SiO_2) (hexane/EtOAc = 4:1) to afford **14** (0.174 g, 82%): gum; R_f = 0.36 (hexane/EtOAc = 4:1.5); $[\alpha]_D$ +29.0 (*c* 1, $CHCl_3$); ^1H NMR ($CDCl_3$, 400 MHz) δ 7.37−7.24 (band, 28 H, aromatic), 7.13−7.11 (m, 2 H, aromatic), 5.02 (s, 1 H, H_{NR}-1), 5.01−4.98 (band, 2 H, PhCH_2), 4.93 (d, *J* = 11.2 Hz, 1 H, PhCH_2), 4.82−4.74 (m, 4 H, PhCH_2), 4.68−4.64 (m, 2 H, PhCH_2), 4.59−4.50 (band, 3 H, H_R-1, PhCH_2), 4.44 (d, *J* = 12.0 Hz, 1 H, PhCH_2), 4.14 (app. t, *J* = 9.2 Hz, 1 H, H_{NR}-4), 4.02−3.93 (band, 3 H, H_R-5, −CH_2OAc), 3.86 (dd, *J* = 4.4, 11.2 Hz, 1 H, H_R-6_a), 3.77 (dd, *J* = 2.8, 11.2 Hz, 1 H, H_{NR}-5), 3.67 (dd, *J* = 4.4, 11.2 Hz, 2 H, H_R-3, H_{NR}-6_a), 3.57 (dd, *J* = 1.6, 11.2 Hz, 1 H, H_{NR}-6_b), 3.50 (dd, *J* = 1.6, 11.2 Hz, 1 H, H_R-6_b), 3.44−3.39 (m, 2 H, H_R-2, H_R-4), 3.34 (s, 3 H, OMe), 2.83 (d, *J* = 8.8 Hz, 1 H, H_{NR}-3), 2.04−1.99 (band, 4 H, −CH_2CH_2OAc, −COCH_3), 1.67−1.62 (m, 1 H, −CH_2CH_2OAc), 1.50−1.39 (m, 2 H, −CH_2CH_2CH_2OAc), 1.35−1.25 (m, 2 H, −CH_2CH_2CH_2CH_2OAc); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.9 (-COCH_3), 138.6−138.0 (aromatic), 128.5−127.4 (aromatic), 102.7 (C_{NR}-1), 97.8 (C_R-1), 82.5 (C_{NR}-3), 81.9 (C_R-5), 80.1 (C_R-2), 79.5 (C_{NR}-4), 77.7 (C_R-4), 75.7 (PhCH_2), 75.1 (PhCH_2),75.0 (PhCH_2), 74.9 (PhCH_2), 73.3 (PhCH_2), 73.1 (PhCH_2), 72.4 (C_{NR}-5), 69.6 (C_R-3), 68.6 (C_{NR}-6), 66.6 (C_R-4), 64.1 (−CH_2OAc), 62.5 (C_R-6), 55.1 (OMe), 39.9 (C_{NR}-2), 28.4 (−CH_2CH_2CH_2CH_2OAc), 23.5 (−CH_2CH_2CH_2OAc), 22.2 (−CH_2CH_2CH_2CH_2OAc), 20.9 (−COCH_3); ES-MS *m*/*z* $C_{61}H_{69}O_{12}INa$ calcd 1143.3731, found 1143.3734.

(4*R*,5*S*,5a*S*,6*R*,9a*R*)-6-Benzyloxymethyl-4,5-dibenzyloxy-5a-iodooctahydrooxepino[2,3-*b*]pyran (15). *N*-Iodosuccinimide (0.07 g, 0.3 mmol) was added to a solution of **7** (0.1 g, 0.2 mmol) in CH_2Cl_2 (10 mL) under argon atmosphere and at room temperature, stirred for 1.5 h, diluted with water (30 mL), extracted with CH_2Cl_2 (3 × 25 mL), washed with aq $Na_2S_2O_3$ (5%) (2 × 15 mL), dried (Na_2SO_4), filtered, and concentrated in vacuo. The crude product was purified (SiO_2) (hexane/EtOAc = 20:1) to afford **15** (0.10 g, 79%): colorless oil; R_f = 0.47 (hexane/EtOAc = 49:1); $[\alpha]_D$ +41.5 (*c* 1, $CHCl_3$); ^1H NMR ($CDCl_3$, 400 MHz) δ 7.39−7.25 (band, 14 H, aromatic), 7.25−7.13 (m, 1 H, aromatic), 5.19 (s, 1 H, H-1), 5.04 (d, *J* = 11.6 Hz, 1 H, PhCH_2), 4.83−4.71 (m, 3 H, PhCH_2), 4.57−4.52 (m, 2 H, PhCH_2), 4.09−4.03 (band, 3 H, H-4, −CH_2O), 3.77 (dd, *J* = 3.2, 10.8 Hz, 1 H, H_a-6), 3.69 (app d, *J* = 10.8 Hz, 1 H, H_b-6), 3.64−3.58 (m, 1 H, H-5), 2.83 (d, *J* = 8.0 Hz, 1 H, H-3), 2.66 (dd, *J* = 8.8, 15.2 Hz, 1 H, −CH_2CH_2CH_2CH_2O), 2.16 (dd, *J* = 8.8, 16.0 Hz, 1 H, −CH_2CH_2CH_2CH_2O), 1.75−1.68 (b, 2 H, −CH_2CH_2O), 1.62−1.53 (b, 2 H, −CH_2CH_2CH_2O); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.4−138.1 (aromatic), 128.3−127.4 (aromatic), 107.1 (C-1), 83.3 (C-3), 79.6 (C-4), 75.1 (PhCH_2), 74.8 (PhCH_2), 73.7 (−CH_2O), 73.4 (PhCH_2), 70.9 (C-5), 68.8 (C-6), 62.1 (C-2), 44.3 (−CH_2CH_2CH_2CH_2O), 31.0 (−CH_2CH_2O), 20.8 (−CH_2CH_2CH_2O); ES-MS *m*/*z* $C_{31}H_{35}O_5INa$ calcd 637.1427, found 637.1431.

3,4,6-Tri-*O*-benzyl-2-deoxy-2-*C*-(4-hydroxybutyl)-α-D-*arabino*-hexopyranosyl-(1→6)-α-D-1,2:3,4-di-*O*-isopropylidene-α-D-glucopyranose (16). Bu_3SnH (57 μL, 0.19 mmol) and AIBN (1 mg) was added to a solution of **13** (0.12 g, 0.13 mmol) in benzene (3 mL) under argon atmosphere and refluxed at 75 °C for 2 h. The solution was concentrated in vacuo, dissolved in MeOH (10 mL), admixed with NaOMe in MeOH (0.3 mL, 0.5 M), stirred for 4 h, and neutralized with Amberlite IR-120 resin (H^+), and solvents were evaporated in vacuo. The crude product was purified (SiO_2) (hexane/EtOAc = 2.5:1) to afford **16** (0.08 g, 81%): colorless oil; R_f = 0.34 (hexane/EtOAc = 2:1); $[\alpha]_D$ +32.7 (*c* 1, $CHCl_3$); ^1H NMR ($CDCl_3$, 500 MHz) δ 7.35−7.26 (band, 14 H, aromatic), 7.15−7.13 (m, 1 H, aromatic), 5.53 (d, *J* = 5.0 Hz, 1 H, H_R-1), 4.90−4.87 (m, 2 H, H_{NR}-1, H_R-4), 4.78 (d, *J* = 12.0 Hz, 1 H, PhCH_2), 4.67−4.60 (m, 3 H, PhCH_2), 4.52−4.49 (m, 2 H, PhCH_2), 4.32 (app. d, *J* = 2.4, 5.0 Hz, 1 H, H_R-2), 4.21 (d, *J* = 8 Hz, 1 H, H_R-3), 3.97 (app t, *J* = 7.5 Hz, 1 H, H_{NR}-4), 3.79−3.75 (m, 3 H, H_{NR}-5, −CH_2OH), 3.70−3.59 (m, 6 H, H_{NR}-3, H_{NR}-$6_{a,b}$, H_R-$6_{a,b}$, H_R-5), 2.35−2.28 (m, 1 H, −CH_2CH$_2$OH), 2.06−1.98 (m, 1 H, −CH_2CH$_2$OH), 1.87−1.83 (m, 1 H, H_{NR}-2), 1.68−1.58 (m, 2 H, −CH_2CH_2CH_2OH), 1.53 (s, 3 H, Me), 1.43 (s, 3 H, Me), 1.33 (s, 3 H, Me), 1.25 (s, 3 H, Me), 0.89 (app t, *J* = 7.5 Hz, 2 H, −CH_2−); ^{13}C NMR (125 MHz, $CDCl_3$) δ 138.6−138.0 (aromatic), 128.3−127.6 (aromatic), 109.3, 108.6, 97.8 (C_{NR}-1), 96.3 (C_R-1), 81.8 (C_{NR}-3), 79.5 (C_{NR}-5), 75.4 (PhCH_2), 74.8 (PhCH_2), 73.5 (PhCH_2), 71.0 (C_R-4), 70.9 (C_R-3), 70.6 (C_R-2), 70.5 (C_R-5), 68.6 (C_{NR}-6), 64.9 (C_{NR}-4), 64.8 (C_R-6), 62.5 (−CH_2OH), 46.0 (C_{NR}-2), 33.1 (−CH_2CH$_2$OH), 26.8 (−CH_2CH_2CH_2OH), 26.1 (Me), 25.9 (Me), 24.8 (Me), 24.4 (Me), 22.6 (−CH_2−); ES-MS *m*/*z* $C_{43}H_{56}O_{11}Na$ calcd 771.3720, found 771.3721.

(4*R*,5*S*,5a*S*,6*R*,9a*R*)-6-Benzyloxymethyl-4,5-dibenzyloxyocta-hydrooxepino[2,3-*b*]pyran (17). Bu_3SnH (72 μL, 0.24 mmol) and AIBN (0.5 mg) were added to a stirring solution of **15** (0.1 g, 0.16 mmol) in benzene (3 mL). The reaction mixture was refluxed at 75 °C for 2 h under argon atmosphere. The solution was concentrated in vacuo. Purified with hexane/EtOAc = 9:1 to afford **17** (0.07 g, 88%): gum; R_f = 0.39 (hexane/EtOAc = 9:1); $[\alpha]_D$ +61.8 (*c* 1, $CHCl_3$); ^1H NMR ($CDCl_3$, 400 MHz) δ 7.35−7.25 (band, 14 H, aromatic), 7.17 (d, *J* = 6.4 Hz, 1 H, aromatic), 4.91 (d, *J* = 3.6 Hz, 1 H, H-1), 4.90 (d, *J* = 11.2 Hz, 1 H, PhCH_2), 4.79 (d, *J* = 11.2 Hz, 1 H, PhCH_2), 4.64 (d, *J* = 14.0 Hz, 2 H, PhCH_2), 4.53 (t, *J* = 12.4 Hz, 2 H, PhCH_2), 3.99−3.95 (m, 2 H, H-4, H_a-6), 3.75 (ddd, *J* = 2.4, 6.0, 16.8 Hz, 2 H, H-3, H_b-6), 3.68 (dd, *J* = 4.8, 9.2 Hz, 1 H, H-5), 3.65−3.59 (m, 2 H, −CH_2O), 2.13−2.09 (m, 1 H, H-2), 1.87−1.80 (m, 1 H, −CH_2CH$_2$O), 1.67−1.61 (m, 2 H, −CH_2CH$_2$O, −CH_2CH$_2$CH$_2$O), 1.49−1.41 (m, 1 H, −CH_2CH$_2$CH$_2$O), 1.36−1.25 (m, 2 H, −CH_2CH$_2$CH$_2$CH$_2$O); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.6−138.0 (aromatic), 128.3−127.5 (aromatic), 102.0 (C-1), 81.7 (C-3), 79.5 (C-5), 75.2 (PhCH_2), 74.5 (PhCH_2), 73.4 (PhCH_2), 72.4 (C-4), 69.2 (C-6), 68.7 (−CH_2O), 45.3 (C-2), 32.0 (−CH_2−CH_2−O), 27.8 (−CH_2CH$_2$CH$_2$O), 21.5 (−CH_2CH$_2$CH$_2$CH$_2$O); ES-MS *m*/*z* $C_{31}H_{36}O_5Na$ calcd 511.2460, found 511.2459.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Experimental method and ^1H and ^{13}C NMR spectra of all new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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■ ACKNOWLEDGMENTS

We thank the Department of Biotechnology, New Delhi, for financial support of the work. G.C.D. thanks the Council of Scientific and Industrial Research, New Delhi, for a research fellowship.

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