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Application of the Wharton Rearrangement for the de novo Synthesis of Pyranosides with *ido*, *manno*, and *colito* Stereochemistry

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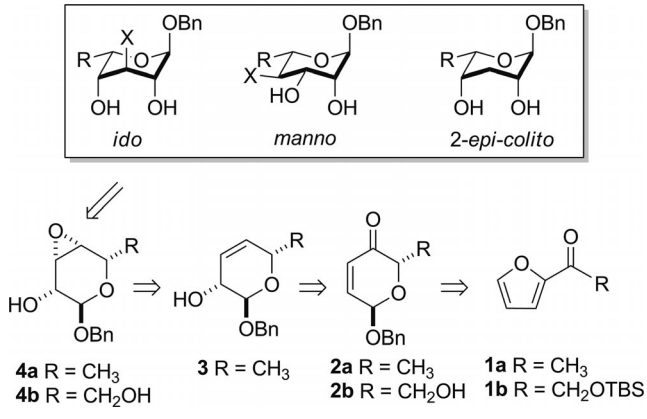
A de novo asymmetric synthesis of α-*ido*-pyranosides, as well as several deoxy and amino variants, has been achieved. The procedure involves a palladium(0)-catalyzed glycosylation in combination with a Wharton rearrangement/epoxide-opening reaction sequence to access sugars with *ido*, *manno*, and *colito* stereochemistry as well as several azido analogues.

Introduction

Although rare in nature, sugars with *ido* stereochemistry are present in many natural products, such as heparins and dermatan sulfates (L-iduronic acid),[1] the antibiotic neomycin (2,6-dideoxydiamino-idose), and labdane diterpenes (6-deoxy-idose).[2] Despite its occurrence in biologically important structural motifs, idose can be prohibitively expensive and is only available in its L configuration. As a result, there has been considerable interest in the synthesis of *ido*-pyranosides. A preponderance of these routes start with commonly found sugar diastereomers and rely on the use of inversion and epimerization reactions to install the *ido* stereochemistry. For example, L-idose has been synthesized by bis-inversion of the C-2 and C-3 positions of D-galactose[3] or by epimerization of the C-5 position of D-glucose in its pyranose[4] and furanose forms.[5] Similarly, a route starting with L-ascorbic acid has also been used to prepare idose by a late-stage Sharpless dihydroxylation strategy to install the critical hydroxy groups.[6]

As part of a larger effort aimed at the development of a generalized strategy for the synthesis of natural and unnatural oligosaccharide structural motifs, we have endeavored to find new approaches to either enantiomer of rare sugars.[7] These de novo asymmetric approaches rely on the use of asymmetric catalysis in combination with a highly diastereoselective palladium-catalyzed glycosylation and post-glycosylation strategy.[8] The assembly of the absolute α/β and D/L sugar stereochemistry involves the use of Noyori asymmetric reduction, Achmatowicz rearrangement, and diastereoselective carbonate formation to transform acylfuran **1** into *aculo* sugar **2** (Scheme 1). The enone moiety of aculose can be further functionalized through a series of post-glycosylation transformations to access different polyol stereoisomers. Most commonly, this involves ketone reduction and double-bond dihydroxylation to install mannose stereochemistry.[9] In addition, we have used epoxidation and nucleophilic ring-opening for the net *anti* installation of two hydroxy groups across the C-2/C-3 olefin.[10] We then envisioned the use of the Wharton rearrangement, which stereoselectively converts an α,β-epoxide ketone into an unsaturated alcohol via a hydrazone intermediate.[11] We have demonstrated the use of the Wharton rearrangement as a key step in the conversion of *aculo* sugar **1** into allyl alcohol **3**, which in turn provided access to sugars with *altro*, *allo*, *galacto*, and *ascarylo* stereochemistry.[12] Herein we describe our efforts to extend this strategy to the epoxidation of the pyran C-3/C-4 double bond, arriving at epoxide **4**, to access idose and its related C-3 deoxy sugar congeners (Scheme 1).



Scheme 1. Wharton rearrangement strategy.

We envisioned our synthetic strategy (Scheme 2) beginning with the achiral acylfuran **1**, which could be asymmetrically converted into epoxide ketone **5**. Wharton rearrange-

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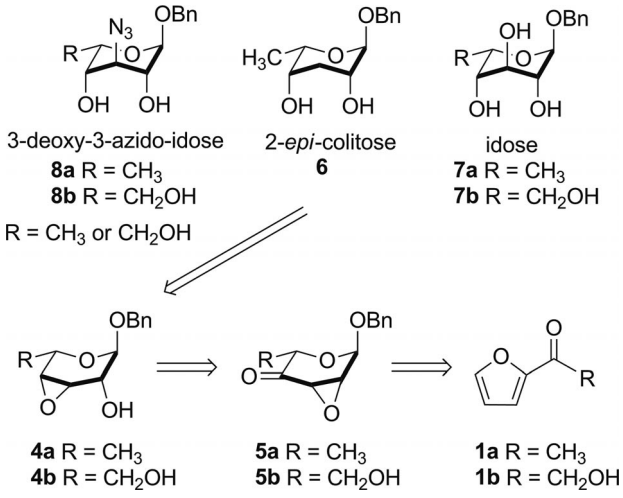
ment and epoxidation of **5** should produce epoxide alcohol **4**, which, depending on the regioselectivity, could be opened to give sugars with either *ido* or *manno* stereochemistry.

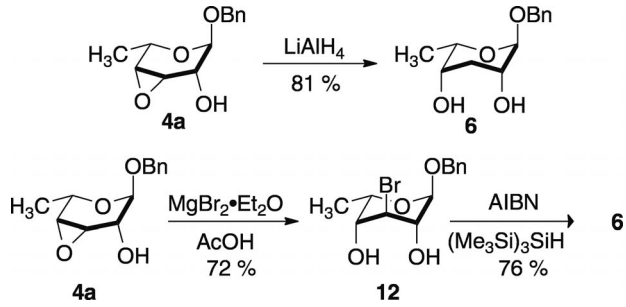


Scheme 2. Retrosynthetic approach to sugars with *ido* or *manno* stereochemistry.

Results and Discussion

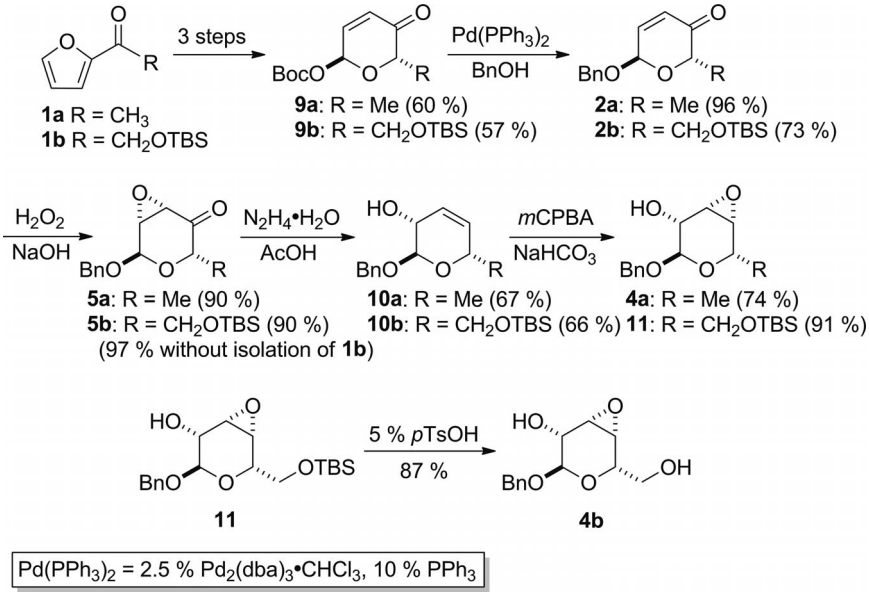
As we have previously reported, Boc-pyranones **9a** and **9b** were obtained optically pure from furans **1a** and **1b** in three steps by Noyori atom-transfer asymmetric reduction[13] [formic acid/Et_3N, (*R*)-Ru(η^6-mesitylene)-(*S*,*S*)-TsDPEN], Achmatowicz cyclization (NBS, H_2O), and *tert*-butoxycarbonylation with Boc_2O (Scheme 3).[14] Palladium-catalyzed glycosylation with benzyl alcohol resulted in benzyl pyranones **2a** and **2b**. Epoxides **5a** and **5b** were obtained by nucleophilic epoxidation with hydrogen peroxide in the presence of a catalytic amount of NaOH. These epoxide ketones **5** were treated with hydrazine to produce the corresponding epoxide hydrazone, which, upon addition of acetic acid, rearranged to allylic alcohols **10a** and **10b**. Hydroxy-directed epoxidation with *m*CPBA resulted in epoxide alcohols **4a** and **11** as single diastereomers.[15] TBS-protected epoxide alcohol **11** was deprotected by using catalytic *p*TsOH to arrive at 6-hydroxy epoxide alcohol **4b**.

We next explored the versatility of epoxide alcohol **4a** in the synthesis of the 3-deoxy sugar by using epoxidation/epoxide-opening chemistry (Scheme 4). Treatment of epoxide alcohol **4a** with $LiAlH_4$ gave the expected *trans*-diaxial ring-opened product 2-*epi*-colitose **6**.[16] Interestingly, the same regioselective opening was also observed under Lewis acid conditions. For example, treatment of epoxide alcohol **4a** with $MgBr_2 \cdot Et_2O$ promoted regioselective epoxide ring-opening to form bromide **12**. The axial bromide was cleanly removed to give **6** by AIBN-promoted $(Me_3Si)_3SiH$ radical reduction.



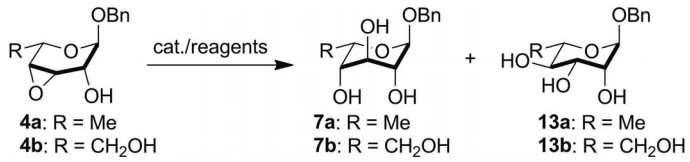
Scheme 4. Synthesis of 2-*epi*-colitose.

Presumably, the difficulty associated with the synthesis of *ido*-pyranosides is associated with the three axial hydroxy substituents at the 2-, 3-, and 4-positions. Building upon



Scheme 3. Synthesis of epoxide alcohols by the Wharton rearrangement.

Table 1. Optimization of the reaction conditions for the epoxide ring-opening **4a** and **4b**.



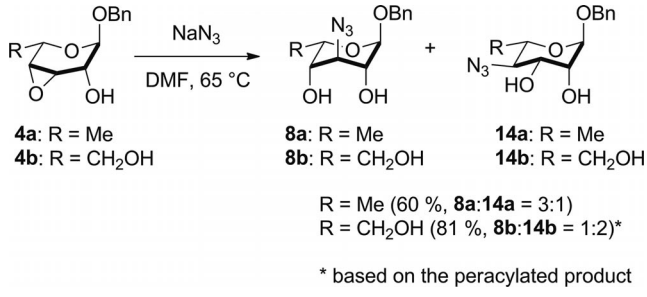
Entry[a]	R	Cat./reagents	Solvent	*t*	Temp.	Yield[b]	Ratio (**7**/**13**)[c]
1	Me	$Sc(OTf)_3$	AcOH	7 h	r.t.	72 %	1: > 99
2	CH_2OH[d]	$Sc(OTf)_3$	AcOH	3 h	55 °C	12 %	1: > 99
3	Me	BF_3	H_2O	18 h	r.t.	66 %	1: > 99
4	Me	$AlCl_3$	H_2O	18 h	r.t.	0 %	—
5	Me	$InCl_3$	H_2O	18 h	r.t.	0 %	—
6	Me	LiOAc	MeOH/H_2O[e]	3 d	90 °C	18 %	2:1
7	Me	NaOAc	MeOH/H_2O[e]	3 d	90 °C	43 %	2:1
8	Me	$Mg(OAc)_2$	MeOH/H_2O[e]	3 d	90 °C	40 %	2:1
9	Me	NaOH[f]	MeOH/H_2O[e]	48 h	90 °C	81 %	5:1
10	CH_2OH[d]	NaOH[f]	CH_3CN	72 h	90 °C	59 %	1:3

[a] Entries 2–4 were performed in 0.2 mmol of epoxide alcohol in 1 M of solvent with 10 mol-% of Lewis acid; entries 5–7 were performed in 0.1 mmol of epoxide alcohol in 0.1 M of solvent with excess reagents (>10 equiv.) and NH_4Cl (3 equiv.). [b] Isolated combined yield. [c] The ratio is based on crude NMR analysis. [d] The yields and ratios of the 6-oxy variants were determined based on the peracylated product. [e] MeOH/H_2O (v/v, 8:1). [f] 0.5 mL of a 2 M NaOH solution was used.

the success achieved in the ring opening of epoxide **4a** to give **12** with *ido* stereochemistry, we envisioned that the remaining 3,4-*trans*-diol of idose could be installed through a similar *trans* diaxial ring-opening of epoxide **4a** (i.e., Fürst–Plattner rule).[17] Our initial attempts to open the epoxide with $Sc(OTf)_3$ in AcOH failed to give the desired *ido* sugars **7a** and **7b**, instead giving exclusively the *rhamno* isomers **13a** and **13b**, the unusual product of *trans* diequatorial epoxide ring-opening (Table 1, entry 1). Other Lewis acids were also examined (i.e., BF_3, $AlCl_3$, and $InCl_3$), however, BF_3 (entry 3) resulted in only the *rhamno* sugars **13a** and **13b** and the other Lewis acids failed to react (entries 4 and 5).

In contrast, switching to less Lewis acidic conditions had a positive effect upon the regioselectivity of the epoxide ring-opening. For example, when LiOAc was used (entry 6), the regiopreference was switched to a 2:1 ratio with the major isomer having idose stereochemistry. The stereochemistry of the *ido*-pyranoside was confirmed by ^1H NMR analysis, which revealed a distinct difference in the H^4,H^5 and H^4,H^3 couplings compared with those in *rhamno*-pyranoside; $J_{4,5}$ = 3.2 Hz and $J_{4,3}$ = 5.2 Hz for the *ido*-pyranoside and $J_{4,5}$ = 9.6 Hz and $J_{4,3}$ = 9.6 Hz for the *rhamno*-pyranoside. Changing the Lewis acidity of the counterion (Na and Mg) increased the yield of the reaction without changing the selectivity towards idose **7a** (entries 6–8). Finally, switching to basic conditions seemed to have the most profound effect. Thus, treatment of **3a** with aqueous NaOH at 90 °C resulted in 6-deoxy-idose **7a** as the major isomer in 81 % yield (entry 9). Unfortunately, this effect on regioselectivity disappears when applied to hexoses with 6-hydroxy groups. Thus, when **4b** was exposed to identical aqueous NaOH conditions, the *manno* isomer **13b** was favored over the *ido* isomer **7b** in a ratio of 2:1. This loss of regioselectivity could be the result of chelation to the free 6-hydroxy group, which overrides the stereoelectronic effects that govern the opening of **4b**.

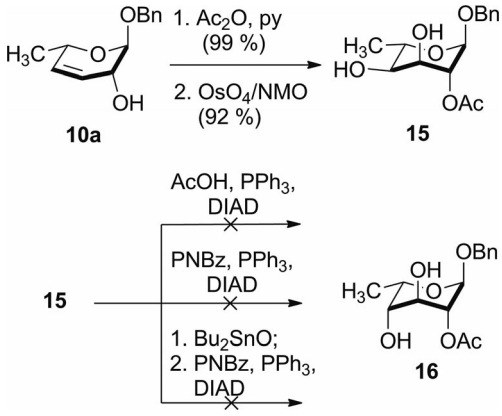
Similar regioselectivity patterns were found when the hydroxide nucleophile was changed to an azide anion (Scheme 5), and again the 6-hydroxy group displayed a profound effect on the regioselective epoxide ring-opening. Thus, when epoxy alcohol **4a** was heated at reflux with NaN_3/NH_4Cl in DMF at 65 °C, a 3:1 ratio of the regioisomers 3-azido-3,6-dideoxy-idose **8a** and 4-azido-4-deoxy-rhamnose **14a** was observed.[18] In contrast, when epoxide



Scheme 5. Synthesis of amino glycoside variants.

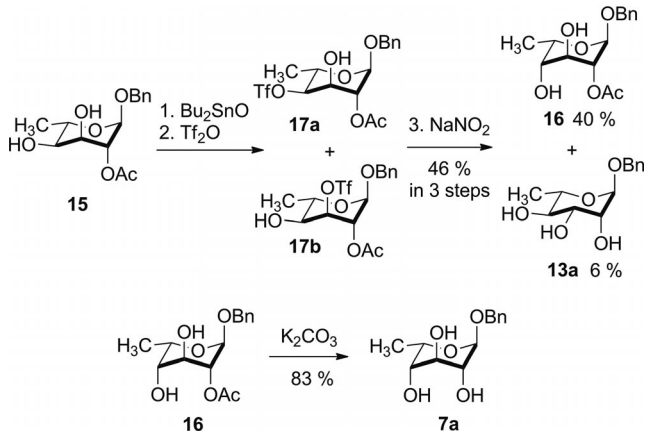
4b with a 6-hydroxy group was treated under the same conditions (NaN_3/NH_4Cl, DMF, 65 °C), a 1:3 ratio of regioisomers was obtained with the *manno* isomer **14b** being the major isomer.

In an alternative approach to the synthesis of *ido*-pyranoside, we envisioned that regioselective 4-OH epimerization of altrose could afford the desired *ido* stereochemistry. This route began with the 2-acylated *altro* sugar **15**, which was prepared from **10a** in a two-step acylation/dihydroxylation sequence (Scheme 6). Unfortunately, all attempts to regioselectively invert the 4-hydroxy group under Mitsunobu-like conditions failed to give products with *ido* stereochemistry (e.g., **16**).



Scheme 6. Attempts at regioselective Mitsunobu inversion for the synthesis of *ido*-pyranoside.

We next explored the use of regioselective acylation conditions (Scheme 7) with the aim of selectively functionalizing and epimerizing the 4-OH position of diol **15**. Unfortunately, all efforts to purify the sulfonylate products led to decomposition. Thus, we turned to a one-pot protocol. To this end, *altro*-pyranoside **15** was subjected to tin–acetal-forming conditions followed by in situ triflation (Tf_2O, CH_2Cl_2, 0 °C), which gave a mixture of triflates **17a** and **17b** (Scheme 7). The triflate groups in **17a** and **17b** were then displaced by nitrite ions to generate a 6:1 ratio of the *ido* and *rhamno* sugars **16** and **13a**, respectively. Interestingly, the 2-acetyl group in the *rhamno* sugar **13a** was also hydrolyzed concomitantly during the displacement of triflate. Finally, the desired *ido* sugar **7a** was obtained after the removal of the 2-acetyl group in **16** by K_2CO_3 hydrolysis.



Scheme 7. Triflation and S_N2 displacement for the synthesis of 6-deoxy-idose.

Conclusions

Highly enantio- and diastereoselective routes for the preparation of various 3-, 4-, and 6-deoxy-pyranosides have been developed. We found that several unusual and deoxy sugars could be obtained by incorporating the Wharton rearrangement into our post-glycosylation transformation strategy. These sugars include 2-*epi*-*colito*- and 6-deoxy-*ido*-pyranosides. Importantly, these sugars can be prepared as either the D or L enantiomeric series by selecting either enantiomeric form of the Noyori catalyst (*R*,*R*) or (*S*,*S*). The route allows for the divergent synthesis of a diverse range of sugars from an advanced-stage intermediate. We believe that this approach will be particularly useful for medicinal chemists. Further work exploring the potential of this strategy in medicinal chemistry[19] and for developing oligosaccharides is underway.

Experimental Section

General: Commercial reagents and solvents were used without further purification, unless otherwise stated. R_f values are reported for analytical TLC using the specified solvents and 0.25 mm EMD silica gel 60 F254 plates that were visualized by UV irradiation (254 nm) or by staining (465 mL of 95% EtOH, 17 mL of conc. H_2SO_4, 5 mL of acetic acid, and 13 mL of anisaldehyde). Solvents were removed by rotary evaporation, followed by further drying of the residual products under high vacuum. Column chromatography was performed on 40–63 μm silica gel using flash column chromatography. NMR spectra using a Varian Unity Inova 600 MHz, Varian 400 MHz NMR spectrometer and Joel 270 MHz NMR spectrometer. ^1H NMR spectra in $CDCl_3$ were referenced at δ = 7.26 ppm. ^{13}C NMR spectra in $CDCl_3$ were referenced at δ = 77.23 ppm. ^1H NMR spectra in CD_3OD were referenced at δ = 3.31 ppm. ^{13}C NMR spectra in CD_3OD were referenced at δ = 49.00 ppm. FT-IR spectra were recorded with a PerkinElmer 100 Series FT-IR spectrophotometer with a polarized Universal Attenuated Total Reflectance (UATR) sampling accessory. Melting points were determined with a capillary melting-point apparatus by Mel-Temp® S2 equipped with a digital thermometer by Fluke Corporation. The melting points were directly reported from the digital thermometer with no prior correction for the apparatus used in this experimental section. The specific rotation for an optically active substance, where α is the observed angle of optical rotation, T is a temperature, λ is the wavelength in nanometers, was measured with a Jasco P-2000 Polarimeter equipped with a sodium D line (λ = 589 nm) light source. Each optically active substance in solution (concentration c in g/100 mL) was measured in a cylindrical glass cell (model number CG3-50, inner diameter 3.5 mm, path length 0.5 dm). High resolution mass spectrometric analyses were performed with an FT mass spectrometer.

Synthetic Procedures

2*H*-Pyran-3-ol 4a: A solution of allylic alcohol **10a** (500 mg, 2.27 mmol) in CH_2Cl_2 (23 mL) was cooled to 0 °C and $NaHCO_3$ (858 mg, 10.2 mmol) was added in one portion. 4-Chloroperoxybenzoic acid (*m*CPBA; 1.6 g, 9.1 mmol) was dissolved in warm CH_2Cl_2 (5 mL) and added in several portions to the reaction mixture at 30 min intervals. The reaction was stirred and slowly warmed to room temperature overnight. A small portion of the reaction mixture was removed and filtered to remove the benzoic acid byproduct. The eluent was concentrated and monitored by NMR for reaction completion. Additional *m*CPBA should be added if the reaction has not yet reached completion. Upon completion, the reaction was poured into a separating funnel containing a layer of 10% aqueous Na_2CO_3 and CH_2Cl_2. The mixture was extracted with CH_2Cl_2 (2× 25 mL) and dried with Na_2SO_4. The compound was then filtered and concentrated under reduced pressure. The crude material was purified by silica gel flash chromatography eluting with 15% EtOAc in hexanes to give **4a** (395 mg, 1.67 mmol, 74%) as a colorless oil. R_f (30% EtOAc in hexanes) = 0.27. $[\alpha]_D^{23}$ = –114.2 (*c* = 1.0, CH_2Cl_2). IR (thin film): $\tilde{\nu}$ = 3452, 3030, 2983, 2933, 1071, 1043, 1009, 746, 701 cm^{-1}. ^1H NMR (600 MHz, $CDCl_3$): δ = 7.37–7.29 (m, 5 H, Ar), 4.70 (d, *J* = 12.0 Hz, 1 H, CH), 4.64 (s, 1 H, CH), 4.51 (d, *J* = 12.0 Hz, 1 H, CH), 4.11 (q, *J* = 6.6 Hz, 1 H, CH), 3.81 (d, *J* = 5.4 Hz, 1 H, CH), 3.55 (ddd, *J* = 4.2, 4.2, 1.2 Hz, 1 H, CH), 3.22 (dd, *J* = 4.2, 1.2 Hz, 1 H, CH), 2.50 (br., 1 H, OH), 1.36 (d, *J* = 6.6 Hz, 3 H, CH_3) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 137.3, 128.7 (2 C), 128.23, 128.18 (2 C), 98.6, 69.6, 63.3, 61.5, 54.9, 51.9, 17.5 ppm. HRMS (ESI): calcd. for $[C_{13}H_{16}O_4Na]^+$ 259.0941; found 259.0939.

2-*epi*-L-Colitose 6: A suspension of $LiAlH_4$ (65 mg, 1.71 mmol) in dry THF (1.0 mL) was added dropwise to a solution of epoxy alcohol **4a** (135 mg, 0.57 mmol) in dry THF (2.0 mL) at –78 °C under argon. The reaction was stirred at –78 °C and monitored by TLC for reaction completion. Upon completion the reaction mixture was warmed to 0 °C and quenched with ice-cold water, extracted with EtOAc (3× 10 mL) and a satd. NaCl solution, and dried with Na_2SO_4. The compound was then filtered and concentrated under reduced pressure. The crude product was purified by silica gel flash chromatography eluting with 25% EtOAc in hexanes to give **6** (110 mg, 0.46 mmol, 81%) as a colorless oil. R_f (30% EtOAc in hexanes) = 0.25. $[\alpha]_D^{23}$ = –74.3 (*c* = 1.0, MeOH). IR (thin film): $\tilde{\nu}$ = 3384, 2931, 1118, 1049 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 7.38–7.28 (m, 5 H, Ar), 4.81 (s, 1 H, CH), 4.74 (d, *J* = 12.0 Hz, 1 H, CH), 4.55 (d, *J* = 12.0 Hz, 1 H, CH), 3.97 (q, *J* = 6.4 Hz, 1 H, CH), 3.75 (br., 2 H, OH), 3.62 (br., 1 H, CH), 3.27 (d, *J* = 6.4 Hz, 1 H, CH), 2.06 (m, 2 H, CH_2), 1.24 (d, *J* = 6.8 Hz, 3 H, CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 137.7, 128.6 (2 C), 128.1 (2 C), 128.0, 99.4, 69.2, 68.4, 66.8, 66.6, 31.6, 17.1 ppm. HRMS (ESI): calcd. for $[C_{13}H_{18}O_4Na]^+$ 261.1097; found 261.1094.

6-Deuterio-2-*epi*-L-colitose: A suspension of $LiAlD_4$ (32 mg, 0.76 mmol) in dry THF (0.5 mL) was added dropwise to a solution of epoxy alcohol **4a** (45 mg, 0.19 mmol) in dry THF (0.6 mL) at –78 °C under argon. The reaction was stirred at –78 °C and monitored by TLC for reaction completion. Upon completion the reaction mixture was warmed to 0 °C and quenched with ice-cold water, extracted with EtOAc (3× 10 mL) and a satd. NaCl solution, and dried with Na_2SO_4. The compound was then filtered and concentrated under reduced pressure. The crude product was purified by silica gel flash chromatography eluting with 20–22% EtOAc in hexanes to give **6**-D (40 mg, 0.17 mmol, 88%) as a colorless oil. R_f (30% EtOAc in hexanes) = 0.25. $[\alpha]_D^{25}$ = –85.2 (*c* = 1.0, CH_2Cl_2). IR (thin film): $\tilde{\nu}$ = 3396, 2979, 2932, 1454, 1095, 1043, 974 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 7.38–7.28 (m, 5 H, Ar), 4.82 (s, 1 H, CH), 4.75 (d, *J* = 12.0 Hz, 1 H, CH), 4.56 (d, *J* = 12.0 Hz, 1 H, CH), 3.98 (q, *J* = 6.4 Hz, 1 H, CH), 3.74 (d, *J* = 5.6 Hz, 1 H, OH), 3.64 (s, 1 H, OH), 3.32 (d, *J* = 7.6 Hz, 1 H, CH), 2.80 (d, *J* = 6.4 Hz, 1 H, CH), 2.05 (br., 1 H, CH), 1.25 (d, *J* = 6.8 Hz, 3 H, CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 137.8, 128.7 (2 C), 128.1 (2 C), 128.0, 99.5, 69.3, 68.5, 66.75, 66.68, 31.3, 17.1 ppm. HRMS (ESI): calcd. for $[C_{13}H_{17}DO_4Na]^+$ 262.1160; found 262.1160.

3-Bromo-3,6-dideoxy-L-idose 12: $MgBr_2{\cdot}OEt_2$ (60 mg, 0.233 mmol) was added in one portion to a solution of epoxy alcohol **4a** (50 mg, 0.212 mmol) in AcOH (0.7 mL) at room temperature. The reaction was stirred at room temperature overnight. Upon completion the reaction mixture was cooled to 0 °C and diluted with EtOAc followed by quenching with a cold satd. $NaHCO_3$ solution. The mixture was extracted with EtOAc (3× 10 mL) and a satd. NaCl solution and dried with Na_2SO_4. The compound was then filtered and concentrated under reduced pressure. The crude product was purified by silica gel flash chromatography eluting with 10–13% EtOAc in hexanes to give **12** (48 mg, 0.15 mmol, 72%) as a colorless oil. R_f (30% EtOAc in hexanes) = 0.17. $[\alpha]_D^{25}$ = –58.3 (*c* = 0.97, CH_2Cl_2). IR (thin film): $\tilde{\nu}$ = 3419, 3064, 3031, 2980, 2934, 1455, 1039, 736, 698 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 7.40–7.28 (m, 5 H, Ar), 4.83 (d, *J* = 12.0 Hz, 1 H, CH), 4.82 (s, 1 H, CH), 4.58 (d, *J* = 12.0 Hz, 1 H, CH), 4.45 (dq, *J* = 6.4, 2.0 Hz, 1 H, CH), 4.17 (dd, *J* = 4.4, 3.6 Hz, 1 H, CH), 3.89 (m, 1 H, OH), 3.85 (m, 1 H, OH), 2.91 (d, *J* = 5.6 Hz, 1 H, CH), 2.66 (d, *J* = 6.8 Hz, 1 H, CH), 1.25 (d, *J* = 6.8 Hz, 3 H, CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 137.5, 128.7 (2 C), 128.0, 127.9 (2 C), 99.4, 72.4, 71.1, 70.2, 64.7, 49.5, 15.4 ppm. HRMS (ESI): calcd. for $[C_{13}H_{17}BrO_4Na]^+$ 339.0202, 341.0182; found 340.1332, 341.0183.

2-*epi*-L-Colitose 6 from Idose 12: $(Me_3Si)_3SiH$ (0.1 mL, 0.322 mmol) and solid AIBN (5 mg, 0.03 mmol) were added in one portion to a solution of 3-bromo-diol **12** (45 mg, 0.142 mmol) in anhydrous toluene (1.5 mL) at 0 °C. The inert atmosphere was secured by freeze/thaw vacuum pump followed by repurging with argon gas. This procedure was repeated three times. The mixture was then heated at reflux at 75 °C for 1 h with monitoring by TLC for completion. The reaction mixture was then cooled to room temperature and directly purified by silica gel flash chromatography, eluting with 25% EtOAc in hexanes to give **6** (25 mg, 0.10 mmol, 76%) as a colorless oil. R_f (30% EtOAc in hexanes) = 0.25. $[\alpha]_D^{23}$ = –74.3 (*c* = 1.0, MeOH). IR (thin film): $\tilde{\nu}$ = 3384, 2931, 1118, 1049 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 7.38–7.28 (m, 5 H), 4.81 (s, 1 H), 4.74 (d, *J* = 12.0 Hz, 1 H), 4.55 (d, *J* = 12.0 Hz, 1 H), 3.97 (q, *J* = 6.4 Hz, 1 H), 3.75 (br., 2 H), 3.62 (br., 1 H), 3.27 (d, *J* = 6.4 Hz, 1 H), 2.06 (m, 2 H), 1.24 (d, *J* = 6.8 Hz, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 137.7, 128.6 (2 C), 128.1 (2 C), 128.0, 99.4, 69.2, 68.4, 66.8, 66.6, 31.6, 17.1 ppm.

6-Deoxy-L-idose 7a and -L-rhamnose 13a:[18] A mixture of epoxy alcohol **4a** (25 mg, 0.106 mmol) and 2 M NaOH (0.5 mL) in MeOH/H_2O (1.0 mL, 8:1, v/v) was heated at reflux at 90 °C for 2 d. Upon completion monitoring by TLC, the reaction mixture was filtered through a pad of Celite eluting with 25% MeOH in EtOAc solution. The concentrated crude material was purified by silica gel flash chromatography eluting with 55% EtOAc in hexanes to give **7a** (18.4 mg, 0.072 mmol, 68%) and **13a** (3.5 mg, 0.013 mmol, 13%) as colorless oil.

6-Deoxy-idose 7a: R_f (80% EtOAc in petroleum ether) = 0.23. $[\alpha]_D^{23}$ = –90.5 (*c* = 0.65, CH_2Cl_2). IR (thin film): $\tilde{\nu}$ = 3452, 3030, 2983, 2933, 1071, 1043, 1009, 746, 701 cm^{-1}. ^1H NMR (400 MHz,

CD_3OD): δ = 7.40–7.26 (m, 5 H, Ar), 4.75 (d, J = 12.4 Hz, 1 H, CH), 4.72 (d, J = 4.0 Hz, 1 H, CH), 4.58 (d, J = 12.4 Hz, 1 H, CH), 4.20 (dq, J = 6.8, 3.2 Hz, 1 H, CH), 3.72 (dd, J = 5.2, 5.2 Hz, 1 H, CH), 3.50 (dd, J = 5.2, 4.0 Hz, 1 H, CH), 3.46 (dd, J = 5.2, 3.2 Hz, 1 H, CH), 1.20 (d, J = 6.8 Hz, 3 H, CH_3) ppm. ^{13}C NMR (100 MHz, CD_3OD): δ = 139.1, 129.4 (2 C), 129.2 (2 C), 128.8, 101.1, 73.2, 72.4, 71.8, 70.6, 66.6, 15.6 ppm. HRMS (ESI): calcd. for $[C_{13}H_{18}O_5Na]^+$ 277.1046; found 277.1046.

Benzyl-rhamnose 13a: R_f (EtOAc) = 0.33. $[\alpha]_D^{23}$ = –60.0 (c = 0.38, CH_2Cl_2); $[\alpha]_D^{25}$ = –84.0 (c = 1.19, MeOH). IR (thin film): $\tilde{\nu}$ = 3375, 2974, 2911, 1454, 1384, 1046, 979 cm^{-1}. ^{1}H NMR (400 MHz, CD_3OD): δ = 7.35–7.26 (m, 5 H, Ar), 4.76 (d, J = 1.6 Hz, 1 H, CH), 4.69 (d, J = 12.0 Hz, 1 H, CH), 4.51 (d, J = 12.0 Hz, 1 H, CH), 3.82 (dd, J = 3.6, 2.8 Hz, 1 H, CH), 3.68 (dd, J = 9.6, 2.8 Hz, 1 H, CH), 3.62 (dq, J = 9.6, 6.8 Hz, 1 H, CH), 3.39 (dd, J = 9.6, 9.6 Hz, 1 H, CH), 1.27 (d, J = 6.8 Hz, 3 H, CH_3) ppm. ^{13}C NMR (100 MHz, CD_3OD): δ = 139.1, 129.4 (2 C), 129.1 (2 C), 128.8, 100.8, 74.0, 72.4, 72.3, 70.0, 18.0 ppm. HRMS (ESI): calcd. for $[C_{13}H_{18}O_5Na]^+$ 277.1046; found 277.1046.

3,6-Dideoxy-3-azido-L-idose 8a and 3-Deoxy-3-azido-L-rhamnose 14a: A mixture of epoxy alcohol **4a** (82 mg, 0.347 mmol), NaN_3 (90 mg, 1.4 mmol), and NH_4Cl (20 mg, 0.372 mmol) in DMF (5.0 mL) was heated at reflux at 65 °C for 3 d. Upon completion monitoring by TLC, the reaction mixture was cooled to room temperature and poured into a mixture of EtOAc and a satd. $NaHCO_3$ solution. The mixture was extracted with EtOAc (3 × 10 mL) and a satd. NaCl solution and dried with Na_2SO_4. The compound was then filtered and concentrated under reduced pressure. The crude product was purified by silica gel flash chromatography with gradient elution from 0–20% EtOAc in hexanes to give **8a** (45 mg, 0.161 mmol, 46%) as an oil with 15% EtOAc/hexanes as eluent and 4-azido-4-deoxy-rhamnose **14a** (14 mg, 0.05 mmol, 14%) as a white amorphous solid with 18% EtOAc/hexanes as eluent with a regioisomeric ratio of **8a**/**14a** = 3:1.

8a: R_f (30% EtOAc in hexanes) = 0.27. $[\alpha]_D^{23}$ = –127.6 (c = 1.05, CH_2Cl_2). IR (thin film): $\tilde{\nu}$ = 3413, 2934, 2913, 2107, 1082, 1041, 980, 738, 698 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.37–7.28 (m, 5 H, Ar), 4.80 (d, J = 12.0 Hz, 1 H, CH), 4.79 (s, 1 H, CH), 4.57 (d, J = 12.0 Hz, 1 H, CH), 4.20 (dq, J = 6.4, 2.0 Hz, 1 H, CH), 3.83 (dd, J = 5.2, 4.4 Hz, 1 H, CH), 3.71 (m, 1 H, OH), 3.50 (m, 1 H, OH), 3.32 (d, J = 5.6 Hz, 1 H, CH), 2.94 (d, J = 6.0 Hz, 1 H, CH), 1.24 (d, J = 6.8 Hz, 3 H, CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 137.4, 128.7 (2 C), 128.08, 128.04 (2 C), 98.8, 70.3, 70.0, 68.8, 64.7, 61.5, 15.4 ppm. HRMS (ESI): calcd. for $[C_{13}H_{17}N_3O_4Na]^+$ 302.1111; found 302.1112.

14a: R_f (30% EtOAc in hexanes) = 0.17; m.p. 97–98 °C. $[\alpha]_D^{23}$ = –104.8 (c = 0.4, CH_2Cl_2). IR (thin film): $\tilde{\nu}$ = 3315, 2916, 2117, 1071, 1012, 695 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.38–7.29 (m, 5 H, Ar), 4.88 (d, J = 1.6 Hz, 1 H, CH), 4.69 (d, J = 12.0 Hz, 1 H, CH), 4.50 (d, J = 12.0 Hz, 1 H, CH), 3.95 (dd, J = 3.2, 1.6 Hz, 1 H, CH), 3.90 (dd, J = 9.6, 3.2 Hz, 1 H, CH), 3.65 (dq, J = 10.4, 6.8 Hz, 1 H, CH), 3.31 (dd, J = 10.4, 9.6 Hz, 1 H, CH), 2.31 (br., 2 H, OH), 1.35 (d, J = 6.8 Hz, 3 H, CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 137.1, 128.8 (2 C), 128.3, 128.2 (2 C), 98.69, 70.7, 70.4, 69.5, 67.1, 66.3, 18.6 ppm. HRMS (ESI): calcd. for $[C_{13}H_{17}N_3O_4Na]^+$ 302.1111; found 302.1112.

(2*R*,3*R*,6*S*)-2-(Benzyloxy)-6-methyl-3,6-dihydro-2*H*-pyran-3-yl Acetate (10a): At 0 °C, acetic anhydride (0.32 mL, 3.39 mmol) was added dropwise to a solution of allylic alcohol **10a** (370 mg, 1.68 mmol) in pyridine (3.5 mL). The reaction was stirred at 0 °C and monitored by TLC. Upon completion the reaction was quenched with a satd. NH_4Cl solution and extracted with CH_2Cl_2 (3 × 15 mL). The organic extract was then washed with satd. $NaHCO_3$ and brine, and dried with Na_2SO_4. The compound was filtered and concentrated under reduced pressure. The crude product was purified by silica gel flash chromatography eluting with 5% EtOAc in hexanes to give the allylic acetate of **10a** (440 mg, 1.68 mmol, 99%) as a colorless oil. R_f (30% EtOAc in hexanes) = 0.75. $[\alpha]_D^{23}$ = –239.0 (c = 1.63, CH_2Cl_2). IR (thin film): $\tilde{\nu}$ = 2978, 2934, 2872, 1734, 1370, 1232, 1025, 736, 700 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.38–7.28 (m, 5 H, Ar), 5.99 (d, J = 10.0 Hz, 1 H, CH), 5.84 (dd, J = 10.0, 4.8 Hz, 1 H, CH), 4.97 (d, J = 4.4 Hz, 1 H, CH), 4.95 (s, 1 H, CH), 4.79 (d, J = 12.0 Hz, 1 H, CH), 4.62 (d, J = 12.0 Hz, 1 H, CH), 4.35 (q, J = 6.8 Hz, 1 H, CH), 2.07 (s, 3 H, Ac), 1.32 (d, J = 6.8 Hz, 3 H, CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 170.4, 137.4, 136.2, 128.5 (2 C), 127.9, 127.9 (2 C), 119.6, 97.1, 70.0, 65.7, 63.7, 21.2, 20.3 ppm. HRMS (ESI): calcd. for $[C_{15}H_{18}O_4Na]^+$ 285.1097; found 285.1097.

(2*R*,3*R*,4*S*,5*R*,6*S*)-2-(Benzyloxy)-4,5-dihydroxy-6-methyltetrahydro-2*H*-pyran-3-yl Acetate (15): A solution of *N*-methylmorpholine *N*-oxide/water (50% w/v, 1.7 mL) was added to a *t*BuOH/acetone (5.5 mL, 1:1, v/v) solution of the allylic acetate derivative of **10a** (440 mg, 1.68 mmol) at 0 °C. Crystalline OsO_4 (4.3 mg, 1 mol-%) was added rapidly and the reaction mixture stirred at 0 °C until TLC showed complete conversion. The reaction mixture was then concentrated under reduced pressure and directly loaded onto silica gel flash chromatography eluting with 75% EtOAc in hexanes to obtain **15** (457 mg, 1.54 mmol, 92%) as a colorless oil. R_f (50% EtOAc in hexanes) = 0.35. $[\alpha]_D^{26}$ = –75.0 (c = 1.07, CH_2Cl_2). IR (thin film): $\tilde{\nu}$ = 3477, 2972, 2934, 1740, 1372, 1232, 1053, 740, 700 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.38–7.28 (m, 5 H), 5.04 (d, J = 3.6 Hz, 1 H), 4.85 (s, 1 H), 4.73 (d, J = 12.0 Hz, 1 H), 4.55 (d, J = 12.0 Hz, 1 H), 3.89 (br., 1 H), 3.79 (dq, J = 9.6, 6.8 Hz, 1 H), 3.42 (dd, J = 9.6, 2.8 Hz, 1 H), 3.34 (br., 1 H), 2.56 (br., 1 H), 2.08 (s, 3 H), 1.36 (d, J = 6.8 Hz, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 169.8, 136.3, 128.8 (2 C), 128.5, 128.3 (2 C), 96.6, 70.2, 70.1, 69.9, 68.6, 64.7, 21.1, 17.7 ppm. HRMS (ESI): calcd. for $[C_{15}H_{20}O_6Na]^+$ 319.1152; found 319.1152.

6-Deoxy-L-idose-3-acetate 16: A mixture of diol **15** (200 mg, 0.675 mmol) and *n*-Bu_2SnO (504 mg, 2.02 mmol) in anhydrous toluene (10 mL) was heated at reflux at 135 °C for 4 h. After cooling to room temperature, water and toluene were removed azerotropically with CH_2Cl_2 (2 × 10 mL) under reduced pressure. The crude stannyl acetal in CH_2Cl_2 (3 mL) at 0 °C was added dropwise to triflic anhydride (0.25 mL, 1.37 mmol) solution in CH_2Cl_2 (1 mL) and the mixture was stirred at 0 °C. After TLC monitoring for completion, which occurred within 1 h, the reaction mixture was quenched with ice-cold water and extracted with CH_2Cl_2 (3 × 10 mL). The organic extract was then washed with a satd. $NaHCO_3$ solution and brine, and dried with Na_2SO_4. The reaction mixture was then filtered and concentrated under reduced pressure. $NaNO_2$ (200 mg, 2.90 mmol) was added the crude material in DMF (3 mL) at room temperature and stirred overnight. It was then poured into a separating funnel containing a mixture of water and EtOAc. The organic extract was washed with water (2 × 10 mL) and dried with Na_2SO_4. The mixture was filtered, concentrated under reduced pressure, and purified by silica gel flash chromatography eluting with 55% EtOAc in hexanes to obtain **16** (80 mg, 0.27 mmol, 40%) and with 80% EtOAc in hexanes to give rhamnose **13a** (12 mg, 0.047 mmol, 6%).

2-Acteyl-idose 16: R_f (50% EtOAc in hexanes) = 0.17. $[\alpha]_D^{23}$ = –66.8 (c = 0.89, CH_2Cl_2). IR (thin film): $\tilde{\nu}$ = 3476, 2929, 1728, 1530, 1264, 1103, 1044, 700 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.41–7.31 (m, 5 H, Ar), 4.89 (s, 1 H, CH), 4.87 (d, J = 1.6 Hz, 1 H, CH),

4.76 (d, J = 12.0 Hz, 1 H, CH), 4.58 (d, J = 12.0 Hz, 1 H, CH), 4.29 (dq, J = 6.8, 1.2 Hz, 1 H, CH), 3.92 (d, J = 8.0 Hz, 1 H, CH), 3.48 (d, J = 9.6 Hz, 1 H, CH), 3.22 (d, J = 9.6 Hz, 1 H, OH), 2.31 (d, J = 11.6 Hz, 1 H, OH), 2.11 (s, 3 H, Ac), 1.30 (d, J = 6.8 Hz, 3 H, CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 169.1, 136.3, 128.9 (2 C), 128.6, 128.4 (2 C), 97.4, 71.0, 70.2, 68.6, 68.6, 68.4, 62.8, 21.2, 16.2 ppm. HRMS (ESI): calcd. for $[C_{15}H_{20}O_6Na]^+$ 319.1152; found 319.1152.

6-Deoxy-D-idose 7a: K_2CO_3 (15 mg, 0.11 mmol) was added in one portion to a solution of 2-acetyl-idose **16** (15 mg, 0.05 mmol) in MeOH (0.5 mL) at room temperature. The reaction was stirred for 3 h and filtered through a pad of Celite eluting with 25% methanol in EtOAc. The concentrated crude material was then purified by silica gel flash chromatography eluting with 55% EtOAc in hexanes to give 6-deoxy-idose **7a** (10 mg, 0.04 mmol, 83%) as a colorless oil.

(1*R*,2*R*,4*S*,6*S*)-2-(Benzyloxy)-4-(*tert*-butyldimethylsilyloxymethyl)-3,7-dioxabicyclo[4.1.0]heptan-5-one (5b): A 30% aqueous hydrogen peroxide (0.7 g, 20.5 mmol) solution was added dropwise to a solution of α-benzyl-pyranone **2b** (1.43 g, 4.10 mmol) in methanol (10.5 mL) at 0 °C followed by the addition of 0.5 M aqueous sodium hydroxide (0.45 mL). The reaction mixture was stirred at 0 °C overnight. It was then diluted with Et_2O (20 mL), quenched with satd. aqueous $NaHCO_3$ (20 mL), extracted with Et_2O (3× 20 mL), dried with Na_2SO_4, and concentrated under reduced pressure. The crude product was purified by silica gel flash chromatography eluting with 4% EtOAc in hexanes to give epoxide ketone **5b** (1.35 g, 3.70 mmol, 90%) as a yellow oil. R_f (10% EtOAc in hexanes) = 0.3. $[\alpha]_D^{25}$ = –80.5 (c = 1.0, MeOH). IR (thin film): $\tilde{\nu}$ = 3466, 2953, 2930, 2857, 1725, 1464, 1255, 1059, 837, 780, 699 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.40–7.31 (m, 5 H, Ar), 5.35 (d, J = 1.6 Hz, 1 H, CH), 4.81 (d, J = 11.6 Hz, 1 H, CH), 4.64 (d, J = 11.6 Hz, 1 H, CH), 4.14 (dd, J = 5.2, 2.8 Hz, 1 H, CH), 4.00 (dd, J = 10.8, 5.2 Hz, 1 H, CH), 3.92 (dd, J = 10.8, 2.8 Hz, 1 H, CH), 3.56 (dd, J = 4.0, 1.6 Hz, 1 H, CH), 3.42 (d, J = 4.0 Hz, 1 H, CH), 0.91 (s, 9 H, *t*Bu), 0.092 (s, 6 H, CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 201.3, 136.7, 128.7 (2 C), 128.4, 128.3 (2 C), 93.1, 77.5, 70.6, 63.2, 53.8, 53.4, 25.9 (3 C), 18.4, –5.2, –5.3 ppm. HRMS (ESI): calcd. for $[C_{19}H_{28}O_5SiNa]^+$ 387.1598; found 387.1592.

(2*R*,3*R*,6*R*)-2-(Benzyloxy)-6-(*tert*-butyldimethylsilyloxymethyl)-3,6-dihydro-2*H*-pyran-3-ol (10b): A solution of epoxide ketone **5b** (60 mg, 0.165 mmol) in methanol (0.55 mL) was cooled to 0 °C, and $N_2H_4{\cdot}H_2O$ (25 mg, 0.495 mmol) was added dropwise. After stirring the reaction mixture at 0 °C for 30 min, AcOH (30 mg, 0.50 mmol) was added dropwise and stirring was continued until TLC showed complete conversion to the allylic alcohol. The reaction mixture was then diluted with CH_2Cl_2 and quenched with satd. aqueous $NaHCO_3$ (10 mL) at 0 °C. The mixture was extracted with CH_2Cl_2 (3× 15 mL) and dried with $MgSO_4$. The mixture was then filtered and concentrated under reduced pressure. The crude product was purified by silica gel flash chromatography eluting with 10% EtOAc in hexanes to give allylic alcohol **10b** (38 mg, 0.108 mmol, 66%) as a colorless oil. R_f (30% EtOAc in hexanes) = 0.57. $[\alpha]_D^{25}$ = –47.5 (c = 1.0, MeOH). IR (thin film): $\tilde{\nu}$ = 3443, 2954, 2929, 2857, 1648 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.37–7.27 (m, 5 H, Ar), 6.11 (dd, J = 9.6, 5.2 Hz, 1 H, CH), 5.92 (dd, J = 10.4, 2.4 Hz, 1 H, CH), 4.97 (s, 1 H, CH), 4.80 (d, J = 12.8 Hz, 1 H, CH), 4.62 (d, J = 12.8 Hz, 1 H, CH), 4.25 (m, 1 H, CH), 3.84 (d, J = 5.2 Hz, 1 H, CH), 3.78–3.71 (m, 2 H, CH_2), 2.17 (br., 1 H, OH), 0.91 (s, 9 H, *t*Bu), 0.09 (s, 6 H, CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 137.8, 130.5, 128.7 (2 C), 128.2 (2 C), 128.0, 126.1, 99.3, 70.0 (2 C), 65.0, 63.8, 26.1 (3 C), 18.6, –5.2 (2 C) ppm. HRMS (ESI): calcd. for $[C_{19}H_{30}O_4SiNa]^+$ 373.1806; found 373.1799.

(1*R*,2*S*,4*R*,5*R*,6*S*)-4-(Benzyloxy)-2-(*tert*-butyldimethylsilyloxymethyl)-3,7-dioxabicyclo[4.1.0]heptan-5-ol (11): Allyl alcohol **10b** (1.63 g, 4.65 mmol) was added to a 50 mL round-bottomed flask and dissolved in dichloromethane (23 mL). $NaHCO_3$ (Na_2HPO_4 can also be used as an alternative base to provide the epoxide with similar yield) was then added and the mixture cooled to 0 °C in an ice bath. A solution of *m*CPBA (3.42 g, 27.9 mmol) in methanol (23 mL) was then added through a pipette. The reaction mixture was allowed to slowly warm to room temp. and stirred overnight. It was then extracted with ethyl acetate (3× 30 mL) and the aqueous layer was back-extracted with ethyl acetate (2× 30 mL). The combined organic solutions were washed with a satd. solution of $Na_2S_2O_3$ (2×, 10 mL), dried with Na_2SO_4, and concentrated under reduced pressure. The product was isolated without further purification to give epoxide **11** as a yellow oil (1.55 g, 4.23 mmol, 91%). R_f (30% EtOAc in hexanes) = 0.63. $[\alpha]_D^{25}$ = –43 (c = 0.17, CH_2Cl_2). IR (thin film): $\tilde{\nu}$ = 2928, 1251, 1070, 1037, 833, 776, 736, 696 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.42–7.27 (m, 5 H, Ar), 4.71 (d, J = 11.8 Hz, 1 H, CH), 4.64 (s, 1 H, CH), 4.50 (d, J = 11.7 Hz, 1 H, CH), 4.04 (dd, J = 6.8 Hz, 1 H, CH), 3.80 (d, J = 6.8 Hz, 2 H, CH_2), 3.57 (dd, J = 4.3 Hz, 1 H, CH), 3.47–3.43 (m, 1 H, CH), 2.46 (s, 1 H, OH), 0.92 (s, 9 H, *t*Bu), 0.11 (s, 6 H, CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 137.0, 128.7, 128.2, 98.2, 69.5, 66.1, 63.5, 63.2, 52.1, 51.2, 26.0, –5.2, –5.3 ppm. HRMS (ESI): calcd. for $[C_{19}H_{31}O_5Si]^+$ 367.1941, found 367.1937.

(1*R*,2*S*,4*R*,5*R*,6*S*)-4-(Benzyloxy)-2-(hydroxymethyl)-3,7-dioxabicyclo[4.1.0]heptan-5-ol (4b): Epoxide **11** (1.5 g, 4.09 mmol) was added to a 25 mL round-bottomed flask and dissolved in methanol (8 mL). *p*-Toluenesulfonic acid (35 mg, 0.205 mmol) was then added at room temp. After stirring for 2 h, the reaction was determined complete by TLC and diluted with ethyl acetate (10 mL) and quenched with satd. sodium hydrogen carbonate (3 mL). The reaction was extracted with ethyl acetate (4× 20 mL), dried with Na_2SO_4, and concentrated under reduced pressure. The crude product was purified by silica gel flash chromatography eluting with a gradient of 3 to 5% methanol in CH_2Cl_2 to give epoxide **3b** as a colorless oil (895 mg, 3.55 mmol, 87%). R_f (50% EtOAc in hexanes) = 0.25. $[\alpha]_D^{25}$ = –70 (c = 0.15, CH_2Cl_2). IR (thin film): $\tilde{\nu}$ = = 3401, 1253, 1029, 900, 852, 737, 697 ppm. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.39–7.27 (m, 5 H, Ar), 4.70 (s, 1 H, CH), 4.70 (d, J = 12.0 Hz, 1 H, CH), 4.51 (d, J = 11.7 Hz, 1 H, CH), 4.09 (dd, J = 5.5 Hz, 1 H, CH), 3.91–3.81 (m, 3 H), 3.53 (dd, J = 6.9, 2.4 Hz, 1 H, CH), 3.34 (dd, J = 4.1, 0.6 Hz, 1 H, CH), 3.04 (s, 2 H, OH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 137.0, 128.8, 128.4, 128.3, 98.7, 69.8, 66.0, 63.6, 63.4, 52.0, 50.4 ppm. HRMS (ESI): calcd. for $[C_{13}H_{16}O_5Na]^+$ 275.0895, found 275.0897.

D-Mannose 13b: Epoxide **4b** (100 mg, 0.396 mmol) was added to a 25 mL round-bottomed flask and dissolved in acetic acid (4 mL). Scandium triflate (214 mg, 0.436 mmol) was then added at room temp. The reaction mixture was heated to 55 °C and stirred for 3 h, diluted with ethyl acetate (5 mL), and quenched with satd. sodium hydrogen carbonate (5 mL). The reaction was extracted with ethyl acetate (3× 10 mL), dried with Na_2SO_4, and concentrated under reduced pressure. The crude product was purified by silica gel flash chromatography eluting with a gradient of 3 to 5% methanol in dichloromethane to give epoxide **13b** as a colorless oil (15 mg, 48 μmol, 12%). R_f (5% methanol in CH_2Cl_2) = 0.27. $[\alpha]_D^{25}$ = –48 (c = 0.15, CH_2Cl_2). IR (thin film): $\tilde{\nu}$ = 3401, 1722, 1368, 1238, 1043, 698 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.40–7.27 (m, 5 H), 4.94 (s, 1 H), 4.70 (d, J = 11.8 Hz, 1 H), 4.57 (dd, J = 12.3, 4.2 Hz,

1 H), 4.52 (d, J = 11.8 Hz, 1 H), 4.16 (d, J = 12.2 Hz, 1 H), 3.99 (s, 1 H), 3.89 (d, J = 7.2 Hz, 1 H), 3.75 (d, J = 7.9 Hz, 1 H), 3.62 (t, J = 9.5 Hz, 1 H), 2.89 (s, 3 H), 2.14 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 172.4, 137.1, 128.8, 128.3, 128.3, 99.3, 71.7, 70.8, 69.6, 67.8, 63.9, 21.2 ppm. HRMS (ESI): calcd. for $[C_{15}H_{21}O_7]^+$ 313.1287; found 313.1293.

L-Idopyranoside Pentaacetate 7b and L-Mannopyranoside Pentaacetate 13b: Epoxide **3b** (89 mg, 0.351 mmol) was added to a 25 mL round-bottomed flask and dissolved in acetonitrile (5 mL). A 2 M NaOH solution (2 mL) was added and the reaction was heated to 90 °C in an oil bath. After stirring for 48 h, the reaction was determined complete by TLC and the solvents were removed under reduced pressure. The crude product was dissolved in pyridine (50 µL, 0.63 mmol) followed by the addition of acetic anhydride (0.5 mL, 5 mmol). After stirring at room temp. for 2 h, the reaction was extracted with ethyl acetate (4× 5 mL), dried with Na_2SO_4, and concentrated under reduced pressure. The crude product was purified by silica gel flash chromatography eluting with a gradient of 20 to 50% ethyl acetate in hexanes to give peracylated idose and mannose as a mixture of isomers in a 1:3 ratio, respectively (91 mg, 0.208 mmol, 59%), as a colorless oil. The resulting triols were immediately converted to pentaacetates for characterization. Neither the triols nor the pentaacetates could be separated. R_f (50% EtOAc in hexanes) = 0.74. $[\alpha]_D^{25}$ = –41 (c = 2.0, CH_2Cl_2). IR (thin film): $\tilde{\nu}$ = 1740, 1369, 1213, 1043, 732, 699, 600 cm^{-1}.

Mannose 13b: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.39–7.30 (m, 5 H, Ar), 5.37 (dd, J = 10.0, 3.6 Hz, 1 H, CH), 5.29–5.25 (m, 1 H, CH), 4.89 (m, 2 H, CH), 4.70 (d, J = 12.0 Hz, 1 H, CH), 4.56 (d, J = 12.0 Hz, 1 H, CH), 4.27 (dd, J = 12.0, 5.0 Hz, 1 H, CH), 4.19 (d, J = 6.0 Hz, 1 H, CH), 4.01–3.95 (m, 1 H, CH), 2.13 (s, 3 H, Ac), 2.11 (s, 3 H, Ac), 2.02 (s, 3 H, Ac), 1.98 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 170.9–169.4 (4 C), 136.4, 128.8–127.8 (4 C), 97.0, 70.0, 69.8, 69.4, 68.9, 66.4, 62.6, 21.1, 21.0, 20.9, 20.9 ppm.

Idose 7b: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.39–7.30 (m, 5 H, Ar), 5.31 (s, 1 H, CH), 5.28 (m, 1 H, CH), 5.00 (dd, J = 4.8, 3.6 Hz, 1 H, CH), 4.77 (d, J = 12.0 Hz, 1 H, CH), 4.51 (s, 1 H, CH), 4.47 (ddd, J = 6.4, 2.0 Hz, 1 H, CH), 4.05 (d, J = 2.4 Hz, 2 H, CH_2), 4.02 (s, 2 H, CH), 2.12 (s, 3 H, Ac), 2.07 (s, 3 H, Ac), 2.06 (s, 3 H, Ac), 2.04 (s, 3 H, Ac) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 170.9, –169.4 (4 C), 137.15, 128.7–127.8 (4 C), 69.49, 67.39, 67.30, 67.01, 64.80, 60.62, 21.28, 21.06, 20.95, 14.42 ppm. HRMS (ESI): calcd. for $[C_{21}H_{26}O_{10}Na]^+$ 461.1424; found 461.1421.

3-Azido-D-idose-2,3,6-triacetate (8b) and 3-Azido-D-mannose-2,3,6-triacetate (14b): Epoxide **4b** (10 mg, 40 µmol) was added to a 10 g screw-cap vial and dissolved in DMF/H_2O (1:1, 0.2 mL total vol.). Solid NaN_3 (15 mg, 0.198 mmol) was then added at room temp. and the mixture was heated to 50 °C and stirred overnight. It was then extracted with ethyl acetate (3× 2 mL), dried with Na_2SO_4, and concentrated under reduced pressure. The crude product was dissolved in dichloromethane (0.2 mL) followed by the addition of acetic anhydride (0.3 mL, 3.2 mmol), triethylamine (0.2 mL, 1.4 mmol), and 4-(dimethylamino)pyridine (5 mg, 0.040 mmol), and the mixture stirred for 3 h. The reaction was extracted with ethyl acetate (3× 2 mL), dried with Na_2SO_4, and concentrated under reduced pressure. The crude product was purified by silica gel flash chromatography eluting with a gradient of 10 to 20% ethyl acetate in hexanes to give 4-azido-mannose and 3-azido-idose in a 2:1 ratio of isomers (13.6 mg, 0.0323 mmol, 81%) as colorless oils.

4-Azido-mannose 14b: R_f (50% EtOAc in hexanes) = 0.68. $[\alpha]_D^{25}$ = –28 (c = 0.05, CH_2Cl_2). IR (thin film): $\tilde{\nu}$ = 2925, 2109, 1743, 1371, 1227, 1044, 699 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.40–7.27 (m, 5 H, Ar), 5.32 (dd, J = 9.9, 3.4 Hz, 1 H, CH), 5.26 (dd, J = 3.3, 1.7 Hz, 1 H, CH), 4.86 (d, J = 1.5 Hz, 1 H, CH), 4.68 (d, J = 11.9 Hz, 1 H, CH), 4.54 (d, J = 11.9 Hz, 1 H, CH), 4.30 (d, J = 3.4 Hz, 2 H, CH_2), 3.82 (dd, J = 19.6, 9.6 Hz, 1 H, CH), 3.78–3.73 (m, 1 H, CH), 2.14 (s, 3 H, Ac), 2.13 (s, 3 H, Ac), 2.07 (s, 3 H, Ac) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 170.8, 170.0, 169.7, 136.4, 128.8, 128.5, 128.4, 97.0, 70.8, 70.0, 69.1, 69.1, 63.4, 57.3, 21.0, 20.9 ppm. HRMS (ESI): calcd. for $[C_{19}H_{23}N_3O_8Na]^+$ 444.1388; found 444.1392.

3-Azido-idose 8b: R_f (20% EtOAc in hexanes) = 0.78. $[\alpha]_D^{25}$ = –51 (c = 0.08, CH_2Cl_2). IR (thin film): $\tilde{\nu}$ = 2111, 1742, 1368, 1212, 1131, 1072, 909, 739, 699 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.42–7.29 (m, 5 H, Ar), 4.91 (dd, J = 4.2, 2.1 Hz, 1 H, CH), 4.87 (s, 1 H, CH), 4.81 (d, J = 4.1 Hz, 1 H, CH), 4.79 (d, J = 12.0 Hz, 1 H, CH), 4.57 (d, J = 12.1 Hz, 1 H, CH), 4.44–4.36 (m, 1 H, CH), 4.18 (m, 2 H), 3.92 (dd, J = 4.2 Hz, 1 H, CH), 2.13 (s, 3 H, Ac), 2.09 (s, 3 H, Ac), 2.07 (s, 3 H, Ac) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 170.7, 170.1, 169.5, 136.7, 128.8, 128.3, 128.1, 96.7, 69.6, 68.2, 67.8, 64.7, 62.4, 57.6, 21.1, 21.0 ppm. HRMS (ESI): calcd. for $[C_{19}H_{23}N_3O_8Na]^+$ 444.1383; found 444.1383.

Supporting Information (see footnote on the first page of this article): Copies of ^{1}H and ^{13}C NMR spectra for all the new compounds.

Acknowledgments

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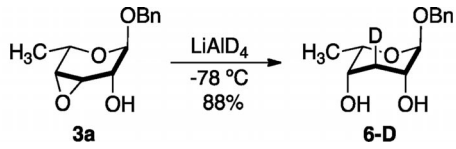
[16] The regioselective formation of 2-*epi*-colitose was confirmed by a deuterium labeling experiment. Treatment of epoxide **3a** with $LiAlD_4$ afforded the mono-deuteriated diol **6**-D.



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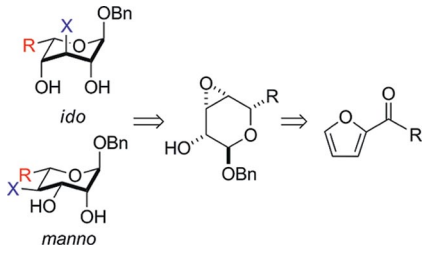
Synthesis of Sugars

A de novo asymmetric synthesis of α-*ido*-pyranosides, as well as several deoxy and amino variants, has been achieved. The procedure involves a palladium(0)-catalyzed glycosylation in combination with a Wharton rearrangement/epoxide-opening reaction sequence to access sugars with *ido*, *manno*, and *colito* stereochemistry as well as several azido analogues.



Keywords: Carbohydrates / Glycosylation / Rearrangement / Palladium / Epoxides

