Carbohydrate Research 396 (2014) 43–47

Contents lists available at ScienceDirect

Carbohydrate Research

journal homepage: www.elsevier.com/locate/carres

Note

Highly stereoselective synthesis of *C*-vinyl pyranosides via a Pd^0-mediated cycloetherification of 1-acetoxy-2, 3-dideoxy-oct-2-enitols

Ernest G. Nolen *, Vivian C. Ezeh, Matthew J. Feeney

Colgate University, 13 Oak Drive, Hamilton, NY 13347, USA

ARTICLE INFO

Article history:
Received 6 June 2014
Received in revised form 2 July 2014
Accepted 3 July 2014
Available online 16 July 2014

Keywords:
C-Glycosides
C-Vinyl pyranosides
1,2-Dideoxy-hept-1-enitols
2,3-Dideoxy-oct-2-enitols
Cycloetherification
Pd^0-mediated

ABSTRACT

Oct-2-enitols undergo a Pd^0-mediated cyclization to produce *C*-vinyl α-gluco- and α-galactopyranosides, and *C*-vinyl β-mannopyranoside in good yield and with high stereoselectivity. While substrate control demonstrates a clear stereochemical preference during cyclization, the α- and β-epimeric ratios are enhanced by double diastereoselection using the (*S*,*S*) or (*R*,*R*)-DACH ligands.

The *C*-alkyl glycosides are useful for their enhanced stability over the natural acetal-linked *O*-glycosides.[1] These glyco-mimetics are most often prepared from *C*-alkenyl pyranosides. In particular, *C*-allyl and *C*-vinyl substrates serve as starting points in many synthetic endeavors. Perhaps surprisingly, a literature search reveals there are greater than five times more citations for *C*-allyl pyranosides over *C*-vinyl pyranosides.[2] To emphasize the disparity in availability, one useful approach to a *C*-vinyl analogue is via the Pd- or Ir-catalyzed alkene isomerization from a *C*-allyl substrate.[3,4] Thus, the relative shortage of *C*-vinyl pyranosides served as the impetus for our exploration of alternative synthetic schemes for the production of these key starting materials.

The *C*-vinyl pyranosides have found utility in the formation of carbasugars[5] and various C-linkages,[6] including glycoconjugates with amino acids,[3,7–10] lipids,[4,11] nucleoside phosphonates,[12] and other saccharides,[13] for the production of compounds with immunogenic, antiproliferative, and glycosidase inhibitory properties. Strategies for *C*-vinyl pyranoside syntheses entail vinyl addition to glucono and galactono-1,5-lactones followed by reduction with Et_3SiH and $BF_3{\cdot}Et_2O$ to yield β-*C*-vinyl products;[14–16] alkyne addition followed by controlled hydrogenation to afford an α-*C*-vinyl galactoside;[17,4] or vinyl addition to α-halo glycosides to provide low yields of predominantly β-*C*-vinyl glucosides and mannosides.[18,19] As a variation of this last approach, Gervay-Hague recently reported a route to α-*C*-vinyl products by first equilibrating an α-galactosyl iodide to the beta-position.[11] While most of these routes transpire on fully protected glycosides, ring opening of glycal epoxides affords *C*-vinyl glycosides with a free C-2 OH. In these examples, the vinyl addition mediated by Al, Zn, and Zr favor alpha gluco- and galactosides[17,20–22] and Mg favors beta products at lower temperatures.[21,23]

Our approach to *C*-vinyl glycosides enlists the Pd^0-catalyzed Tsuji–Trost allylation, which has been generally used for tetrahydropyran syntheses.[24–26] Parenthetically, Cossy has recently reported similar cyclizations using the first-row metal Fe(III).[27] Herein we describe a Pd^0-catalytic method for the direct synthesis of *C*-vinyl glucosides, galactosides, and mannosides using Pd^0 itself and in the presence of C_2-asymmetric diaminocyclohexane diphenylphosphinobenzoic acid ligands (DACH).[28] The retrosynthesis of *C*-vinyl pyranosides (Scheme 1) thus requires the allylic acetates, which are available by cross-metathesis between known 1,2-dideoxy-hept-1-enitols and 1,4-diacetoxybutene.

Preparation of the precursors for the Pd^0-catalyzed cyclization required the formation of the 1,2-dideoxy-hept-1-enitols. The D-*gluco*-hept-1-enitol **1a** was readily available by a highly stereoselective divinylzinc addition to commercially available tri-*O*-benzyl D-arabinofuranose described by Nicotra.[29] The D-*galacto*- and D-*manno*-hept-1-enitols, **1b** and **1c**, were also reported by Nicotra

* Corresponding author. Tel.: +1 315 228 7234.
E-mail address: enolen@colgate.edu (E.G. Nolen).

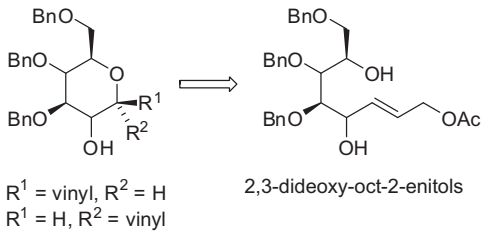
http://dx.doi.org/10.1016/j.carres.2014.07.002
0008-6215/

by similar Grignard additions to pentoses, but we found the Wittig methylenation[30] of 3,4,6-tri-*O*-benzyl galactoside **2b**[31] and mannoside **2c**,[32,33] to be more convenient (Scheme 2). Both **2b** and **2c** are readily prepared in five steps with minimal chromatographic purification from their respective pentaacetates on a 30 g scale according to the citations listed. The Wittig methylenation runs cleanly, although the lower yield for the D-*galacto*-hept-1-enitol **1b** is solely due to difficulty in the separation of the triphenylphosphine oxide byproduct. Extension to 1-acetoxy-oct-2-enitols was accomplished by cross-metathesis with 1,4-diacetoxybutene (5 equiv) in refluxing dichloromethane using the second generation Grubbs Ru-catalyst to give oct-2-enitols **3a–c** in good yield.

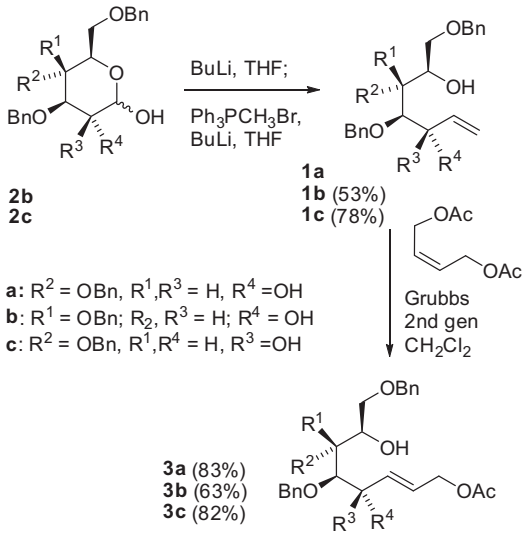
The final step in the synthesis of *C*-vinyl pyranosides involves the Pd^0-catalyzed cyclization of the oct-2-enitol compounds. Two conditions were tested: cyclization utilizing approximately 0.15 mol equiv of $Pd(PPh_3)_4$ and triethylamine (Et_3N) and an adaptation of the Tsuji–Trost allylation that required $Pd_2(dba)_3$ with a C_2 symmetric diphenylphosphinobenzoic acid (*R*,*R*-DACH or *S*,*S*-DACH, also commonly abbreviated DPPBA). An attraction of these chiral ligands is their availability in both enantiomeric forms to explore double diastereoselection. In general, the oct-2-enitols **3a–c** were mixed with the Pd^0 catalyst in either THF or toluene under anaerobic atmosphere and left to stir at rt for 24 h to furnish high yields of *C*-vinyl pyranosides. The configurational assignments at the pseudo-anomeric position correlated to the literature spectral data for α- and β-*C*-vinyl D-glucopyranoside, at least to the extent it has been revealed.[6,20–23] Our ^1H NMR data, including $J_{1,2}$ coupling constants, COSY, and NOESY, confirmed the known assignments and established the new *C*-glycosides reported herein, namely the α-*C*-vinyl D-galactopyranoside and α- and β-*C*-vinyl D-mannosides. In addition, the chemical shift of C-1 H was characteristic depending on its conformational placement equatorial or axial, so for all α-*C*-vinyl products the equatorially positioned C-1 H was 0.5–0.7 ppm further downfield than its β-*C*-vinyl isomer with an axially disposed C-1 H.

Cyclization of the oct-2-enitols using $Pd(PPh_3)_4$ showed a clear substrate preference for α or β isomers in each example (Scheme 3). The ratios of isomers were determined by integrating the peaks associated with the vinyl protons, one of which was clearly resolved in each case. This cycloetherification showed good substrate control of diastereoselectivity with greater than 10:1 preference for the α-isomer over the β-isomer for the *C*-vinyl Glc **4** and *C*-vinyl Gal **5**. In contrast, the **6β**-isomer was preferred 6:1 over the **6α**-isomer for D-*manno*-oct-2-enitol **3c** cyclization. The different C-2 configuration between Glc/Gal and Man appears to play a role in orienting the Pd^0 catalyst and subsequently determining the major product.

By introducing the chiral ligands, (*R*,*R*) and (*S*,*S*)-DACH with $Pd_2(dba)_3$, we were able to observe matched double diastereoselection leading to greater selectivity in the cyclization, while mismatched cases led to a reversal of selectivity or no cyclization. With the *S*,*S*-DACH, the selectivity for the α-isomer was amplified for the *gluco*- and *galacto*-substrates, giving solely the α-isomer **5α** (Table 1). For the *manno*-substrate, it was the *R*,*R*-DACH that



Scheme 1. Retrosynthesis for *C*-vinyl pyranosides.



Scheme 2.

amplified the selectivity for the β-isomer, giving **6β** exclusively. Turning to the mismatched ligand chirality, the *R*,*R*-DACH with $Pd_2(dba)_3$ afforded a reversal in selectivity for **4**, albeit in a modest 1.0:3.5 (α:β) diastereomeric ratio. Under the same conditions the *galacto*-octenitol **3b** failed to react. Consequently, the *S*,*S*-DACH switched the diastereomeric ratio for **6** giving 4.7:1.0 selectivity for the α-isomer.

In summary, we have demonstrated the stereoselective syntheses of *C*-vinyl α-gluco- and α-galactopyranosides, and *C*-vinyl β-mannopyranoside using a Pd^0-mediated cyclization. The α- and β-epimeric ratios have been enhanced by double diastereoselection using the (*S*,*S*) or (*R*,*R*)-DACH ligands for the key cyclization. This strategy nicely complements the glycal epoxide openings and provides a unique entry to these *C*-vinyl pyranosides with a free C-2 hydroxyl.

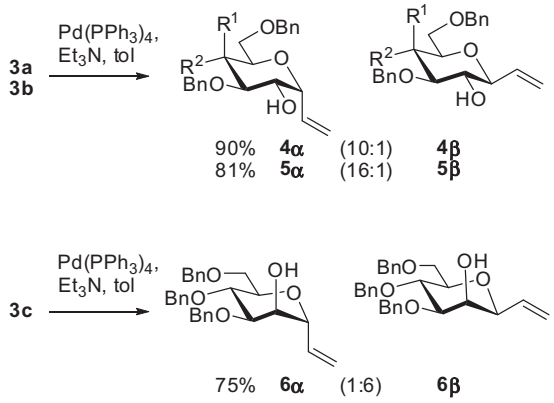
1. Experimental

1.1. General methods

Chemicals were purchased from commercial sources and used without further purification. All reactions were carried out under an argon atmosphere using oven-dried glassware. Anhydrous THF, toluene, and dichloromethane were obtained from activated commercial columns. Thin-layer chromatography was performed using commercially prepared 60-mesh silica gel plates and visualization was achieved with UV light (254 nm) or a stain made from mixing phosphomolybdic acid and cerium(IV) sulfate in sulfuric acid. Silica gel (230–400) was used for flash column chromatography. Optical rotations were recorded in $CHCl_3$ using a 1.0 dm cell at 23 °C. All NMR spectral assignments were determined by ^1H (400 MHz), ^{13}C (100 MHz) attached proton tests, COSY, HMQC and NOESY 2D techniques in $CDCl_3$. Peaks were referenced to residual chloroform signals (δ_H 7.26 ppm, or δ_C 77.0 ppm). Standard abbreviations s, d, t, dd, br, app, and m refer to singlet, doublet, triplet, doublet of doublets, broad, apparent, and multiplet, respectively. High-resolution mass spectra were obtained from a Q-TOF instrument by electron spray ionization (ESI) technique.

1.2. 1-Acetoxy-5,6,8-tri-*O*-benzyl-2,3-dideoxy-D-*gluco*-oct-2-enitol (3a)

To Grubbs second generation catalyst (130 mg, 0.152 mmol) under Ar was added a solution of **1a** (695 mg, 1.53 mmol) and



Scheme 3. Substrate control during cycloetherification.

1,4-diacetoxy-2-butene (1.2 mL, 7.6 mmol) in CH_2Cl_2 (3.0 mL). The reaction was refluxed for 3 h, cooled, and stirred with 20 μL 1:1 DMSO/ethyl vinyl ether for 30 min. The sample was concentrated onto SiO_2 gel and chromatography using 20–30% EtOAc/Hex afforded **3a** (661 mg, 83%). $[\alpha]_D$ +5.5 (*c* 1.9, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$): δ 7.46–7.25 (m, 14H), 5.94–5.75 (m, 2H), 4.75 (d, J = 11.4 Hz, 1H), 4.70–4.43 (m, 7H), 4.21–4.06 (m, 1H), 3.83–3.64 (m, 3H), 3.31 (s, 2H), 2.06 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.5, 137.8, 137.6, 137.6, 134.4, 128.2, 128.2, 128.2, 128.1, 127.8, 127.7, 127.6, 127.6, 125.0, 81.4, 78.5, 74.3, 73.5, 73.2, 70.8, 70.7, 70.5, 64.1, 20.7; HRMS: *m*/*z* calcd for $C_{31}H_{37}O_7$: 521.2534 $[M+H]^+$, found 521.2532.

1.3. 1-Acetoxy-5,6,8-tri-*O*-benzyl-2,3-dideoxy-D-*galacto*-oct-2-enitol (3b)

To **2b** (2.05 g, 4.55 mmol) in THF (34 mL) was added 2 equiv of 2.5 M BuLi (3.46 mL, 8.65 mmol) at −78 °C over 15 min. The mixture was stirred for 10 min and then allowed to warm to rt for the next 1 h. In a separate flask, to triphenylphosphonium bromide (4.88 g, 13.6 mmol) in THF (34 mL) was added BuLi (5.28 mL, 13.2 mmol) at −78 °C, stirred for 10 min, and then 1 h at rt. The ylide solution was slowly cannulated into the **2b** solution, forming a cloudy orange mixture. The reaction was then heated to 45 °C for 2 h, then it was concentrated in vacuo, and chromatography with 20% EtOAc/Hex produced **1b**[29] (1.10 g, 53%).

To Grubbs second generation catalyst (73 mg, 0.085 mmol) under Ar was added a solution of **1b** (384 mg, 0.856 mmol) and 1,4-diacetoxy-2-butene (410 μL, 2.57 mmol) in CH_2Cl_2 (1.7 mL). The reaction was refluxed for 3 h, cooled, and stirred with 20 μL 1:1 DMSO/ethyl vinyl ether for 30 min. The sample was concentrated onto SiO_2 gel and chromatography using 20–30% EtOAc/Hex afforded **3b** as a solid (281 mg, 63%), mp 65–69 °C; $[\alpha]_D$ −1.0 (*c* 2.0, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$): δ 7.46–7.27 (m, 16H), 6.00–5.83 (m, 2H), 4.79–4.70 (m, 2H), 4.68–4.48 (m, 6H), 4.45 (d, J = 4.6 Hz, 1H), 4.10 (s, 1H), 3.88–3.74 (m, 2H), 3.57 (ddd, J = 34.2, 9.4, 6.3 Hz, 2H), 2.73 (d, J = 9.0 Hz, 1H), 2.64 (d, J = 7.5 Hz, 1H), 2.06 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.6, 137.7, 137.5, 137.5, 128.2, 128.2, 127.7, 124.8, 80.0, 77.4, 74.5, 74.4, 73.3, 71.2, 70.2, 69.3, 64.2, 20.8; HRMS: *m*/*z* calcd for $C_{31}H_{37}O_7$: 521.2534 $[M+H]^+$, found 521.2534.

Table 1
Synthesis of *C*-vinyl pyranosides with and without asymmetric ligands

Oct-2-enitol	*C*-Vinyl pyranoglycosides **4**–**6**, Yield[a] (%) [α/β]		
	$Pd(PPh_3)_4$	$Pd_2(dba)_3$ + *R*,*R*-DACH	$Pd_2(dba)_3$ + *S*,*S*-DACH
gluco **3a**	**4** 90 [10:1]	99 [1:3.5]	90 [31:1]
galacto **3b**	**5** 81 [16:1]	NR	81 [α only]
manno **3c**	**6** 75 [1:6]	55 [β only]	77 [4.7:1]

[a] Isolated yield after column chromatography primarily to filter out catalysts. Controls indicate that the diastereomeric ratio was not altered during chromatography.

1.4. 1-Acetoxy-5,6,8-tri-*O*-benzyl-2,3-dideoxy-D-*manno*-oct-2-enitol (3c)

The diol **2c** (2.05 g, 4.55 mmol) was dissolved in THF (35 mL), and 1.6 M BuLi (5.3 mL, 8.6 mmol) was slowly added over 15 min at −78 °C. The reaction was stirred and allowed to warm to rt over 1 h. In a separate flask, Ph_3PCH_3Br salt (9.6 g, 27 mmol) was suspended in THF (68 mL), and 1.6 M BuLi (16.4 mL, 26.3 mmol) was added at 0 °C. The suspension was stirred for 10 min at 0 °C, and warmed to rt over 1 h. The **2c** solution was slowly cannulated over to the ylide suspension, heated to 45 °C, and stirred for 2.5 h. After cooling to rt, it was quenched with acetone (10 mL) and stirred overnight. The suspension was filtered, concentrated onto SiO_2 gel, and chromatography using 20–30% EtOAc/Hex afforded **1c**[29] (1.58 g, 78%).

To Grubbs second generation catalyst (86 mg, 0.10 mmol) under Ar was added a solution of **1c** (455 mg, 1.02 mmol) and 1,4-diacetoxy-2-butene (817 μL, 5.08 mmol) in CH_2Cl_2 (2.0 mL). The reaction was refluxed for 3 h, cooled, and stirred with 15 μL 1:1 DMSO/ethyl vinyl ether for 30 min. The sample was concentrated onto SiO_2 gel and chromatography using 30% EtOAc/Hex afforded **3c** (436 mg, 82%). $[\alpha]_D$ +4.5 (*c* 2.0, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$): δ 7.43–7.25 (m, 15H), 5.96 (ddd, J = 17.2, 10.5, 5.2 Hz, 1H), 5.44 (dt, J = 17.2, 1.7 Hz, 1H), 5.26 (dt, J = 10.5, 1.6 Hz, 1H), 4.71 (d, J = 11.3 Hz, 1H), 4.64–4.46 (m, 6H), 4.16–4.06 (m, 1H), 3.88 (dd, J = 6.7, 3.0 Hz, 1H), 3.73–3.62 (m, 3H), 2.99 (d, J = 5.9 Hz, 1H), 2.92 (d, J = 6.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.6, 137.6, 137.5, 134.1, 128.3, 128.3, 128.2, 128.2, 128.1, 127.8, 125.5, 80.2, 78.1, 73.3, 73.2, 73.0, 70.9, 70.7, 69.9, 64.2, 20.7; HRMS: *m*/*z* calcd for $C_{31}H_{37}O_7$: 521.2534 $[M+H]^+$, found 521.2533.

1.5. General cyclization procedure of oct-2-enitols with $Pd(PPh_3)_4$

To a solution of the appropriate oct-2-enitol in toluene (3 mL) under Ar was added via cannula a yellow solution of 0.15 mol equiv of $Pd(PPh_3)_4$ and Et_3N (48 μL) in toluene (3 mL) giving rise to an immediate dark brown color. The reaction was left to stir at rt for 20 h and concentrated on SiO_2. Chromatography with 15% EtOAc/hexanes afforded the *C*-vinyl compounds as oils.

1.6. (2α,3*S*,4*R*,5*R*,6*R*)-4,5-Bis(benzyloxy)-6-((benzyloxy)methyl)-2-vinyltetrahydro-2*H*-pyran-3-ol (4α)[21]

Compound **3a** (119 mg, 0.229 mmol), $Pd(PPh_3)_4$ (31.8 mg, 0.0275 mmol) yielded 103 mg, 98% of [**4α**:**4β**] = [10:1]. ^1H NMR (400 MHz, $CDCl_3$, α-isomer): δ 7.40–7.24 (m, 15H, 3× PhH), 6.09 (ddd, J = 5.4, 10.8, 16.8 Hz, 1H, H-A), 5.47 (dt, J = 1.6, 17.5 Hz, 1H, H-B′), 5.41 (dt, J = 1.6, 10.8 Hz, 1H, H-B″), 4.89–4.55 (m, 6H, 3× CH_2Ph), 4.52 (app t, J = 4.9 Hz, 1 H, H-1), 4.06 (q, J = 5.1 Hz, 1H, H-5), 3.81 (m, 1H, H-2), 3.77–3.69 (m, 4H, H-3, H-4 and H-6a,b), 2.74 (d, J = 6.4 Hz, 1H, OH); ^{13}C NMR (100 MHz, $CDCl_3$, α-isomer): δ 138.1, 138.0, 137.6, 135.1, 132.9, 128.5, 128.4, 128.3, 127.9, 127.8, 127.6, 118.9, 80.7, 79.8, 78.8, 76.2, 74.1, 73.6, 73.6, 73.3, 73.2, 70.6, 68.3; HRMS: *m*/*z* calcd for $C_{29}H_{36}NO_5$ 478.2588 $[M+NH_4]^+$; found 478.2590.

1.7. (2α,3*S*,4*R*,5*S*,6*R*)-4,5-Bis(benzyloxy)-6-((benzyloxy)methyl)-2-vinyltetrahydro-2*H*-pyran-3-ol (5α)

Compound **3b** (128 mg, 0.246 mmol), $Pd(PPh_3)_4$ (35 mg, 0.031 mmol) yielded 92 mg, 81% of [**5α**:**5β**] = [16:1]. ^1H NMR

(400 MHz, $CDCl_3$, α-isomer): δ 7.40–7.28 (m, 15H, 3× PhH), 6.03 (ddd, *J* = 5.1, 10.9, 15.3 Hz, 1H, H-A), 5.50 (dt, *J* = 3.7, 17.6 Hz, 1H, H-B′), 5.40 (dt, *J* = 3.7, 10.9 Hz, 1H, H-B″), 4.79 (dd, *J* = 11.6, 11.6 Hz, 2H, –CH_2Ph), 4.64–4.51 (m, 5H, 2× CH_2Ph and H-1), 4.24 (br m, 1H, H-2), 4.11 (m, 1H, H-5), 4.06 (t, *J* = 2.7 Hz, 1H, H-4), 3.80 (dd, *J* = 3.0, 6.7 Hz, 1H, H-6), 3.70 (dd, *J* = 4.0, 5.9 Hz,1H, H-6), 3.63 (dd, *J* = 2.5 5.9 Hz, 1H, H-3), 2.28 (d, *J* = 3.2 Hz, 1H, OH); ^{13}C NMR (100 MHz, $CDCl_3$, α-isomer): δ 138.3, 138.1, 137.9, 131.9, 128.5, 128.4, 128.3, 127.9, 127.8, 127.7, 127.7, 127.7, 118.6, 79.1, 73.7, 73.5, 73.4, 72.2, 68.4, 67.9; HRMS: *m*/*z* calcd for $C_{29}H_{36}NO_5$ 478.2588 $[M+NH_4]^+$, found 478.2584.

1.8. (2β,3*R*,4*R*,5*R*,6*R*)-4,5-Bis(benzyloxy)-6-((benzyloxy)methyl)-2-vinyltetrahydro-2*H*-pyran-3-ol (6β)

Compound **3c** (112 mg, 0.216 mmol), $Pd(PPh_3)_4$ (37.1 mg, 0.0321 mmol) yielded 74 mg, 75% of [**6α**:**6β**] = [1:6]. ^{1}H NMR (400 MHz, $CDCl_3$, β-isomer): δ 7.43–7.20 (m, 15H, 3× PhH), 6.03 (ddd, *J* = 5.3, 10.7, 15.9 Hz, 1H, H-A), 5.48 (dt, *J* = 1.5, 17.4 Hz, 1H, H-B′), 5.35 (dt, *J* = 1.4, 10.7 Hz, 1H, H-B″), 4.92–4.54 (m, 6H, 3× CH_2Ph), 4.06 (d, *J* = 2.6 Hz, 1H, H-2), 3.97 (dd, *J* = 1.2, 5.2 Hz, 1H, H-1), 3.89 (t, *J* = 9.4 Hz, 1H, H-4), 3.78 (m, 2H, H-6a,b), 3.69 (dd, *J* = 3.1, 9.1 Hz, 1H, H-3), 3.52 (ddd, 1H, H-5), 2.3 (s, 1H, OH); ^{13}C NMR (100 MHz, $CDCl_3$, β-isomer): δ 138.4, 138.3, 137.9, 134.6, 128.7, 128.5, 128.4, 128.2, 128.0, 127.9, 127.8, 127.7, 117.5, 83.3, 79.3, 78.6, 75.3, 74.5, 73.6, 71.7, 69.4, 69.2; HRMS: *m*/*z* calcd for $C_{29}H_{36}NO_5$ 478.2588 $[M+NH_4]^+$, found 478.2590.

1.9. General cyclization procedure of oct-2-enitols with $Pd_2(dba)_3$·$CHCl_3$ and (*R*,*R*)-DACH or (*S*,*S*)-DACH

A mixture of $Pd_2(dba)_3$·$CHCl_3$ and either (*R*,*R*) or (*S*,*S*) DACH ligand was dissolved in THF (3 mL) to give a deep-red solution. The solution was stirred for 30 min under a flow of Ar until the color turned yellow. The activated catalyst was transferred via a cannula to a solution of the appropriate oct-2-enitol in THF (5 mL). The reaction was left to stir at rt for 24 h and concentrated onto SiO_2. Chromatography with 15% EtOAc/hexanes afforded the *C*-vinyl compounds as oils.

1.10. (2α,3*S*,4*R*,5*R*,6*R*)-4,5-Bis(benzyloxy)-6-((benzyloxy)methyl)-2-vinyltetrahydro-2*H*-pyran-3-ol (4α)[21]

Compound **3a** (127 mg, 0.244 mmol), $Pd_2(dba)_3$·$CHCl_3$ (8.8 mg, 0.0085 mmol, 0.04 mol equiv), (*S*,*S*)-DACH (12.6 mg, 0.0182 mmol, 0.08 mol equiv) yielded 111 mg (99%) of [**4α**:**4β**] = [31:1]. $[\alpha]_D$ +15 (*c* 1, $CHCl_3$); other spectral data reported in Section 1.6.

1.11. (2β,3*S*,4*R*,5*R*,6*R*)-4,5-Bis(benzyloxy)-6-((benzyloxy)methyl)-2-vinyltetrahydro-2*H*-pyran-3-ol (4β)[21]

Compound **3a** (127 mg, 0.244 mmol), $Pd_2(dba)_3$·$CHCl_3$ (171 mg, 0.0165 mmol, 0.07 mol equiv), (*R*,*R*)-DACH (26.4 mg, 0.0382 mmol, 0.16 mol equiv) yielded 111 mg (99%) of [**4α**:**4β**] = [1:3.5]. ^{1}H NMR (400 MHz, $CDCl_3$, β-isomer reported from the mixture): δ 7.42–7.24 (m, 15H, 3× PhH), 5.97 (ddd, *J* = 6.1, 10.5, 17.2 Hz, 1H, H-A), 5.48 (d, *J* = 17.3 Hz, 1H, H-B′), 5.37 (d, *J* = 10.5 Hz, 1H, H-B″), 5.00–4.54 (m, 6H, 3× CH_2Ph), 3.86–3.40 (m, 7H, includes H-1), 2.2 (s, 1H, OH).

1.12. (2α,3*S*,4*R*,5*S*,6*R*)-4,5-Bis(benzyloxy)-6-((benzyloxy)methyl)-2-vinyltetrahydro-2*H*-pyran-3-ol (5α)

Compound **3b** (150 mg, 0.287 mmol), $Pd_2(dba)_3$·$CHCl_3$ (22.2 mg, 0.0214 mmol, 0.08 mol equiv), (*S*,*S*)-DACH (29.8 mg, 0.0431 mmol, 0.15 mol equiv) yielded 105 mg, 81% of **5α**. $[\alpha]_D$ + 20 (*c* 1, $CHCl_3$); other spectral data reported in Section 1.7.

1.13. (2β,3*R*,4*R*,5*R*,6*R*)-4,5-Bis(benzyloxy)-6-((benzyloxy)methyl)-2-vinyltetrahydro-2*H*-pyran-3-ol (6β)

Compound **3c** (98 mg, 0.189 mmol), $Pd_2(dba)_3$·$CHCl_3$ (20.2 mg, 0.0155 mmol, 0.08 mol equiv), (*R*,*R*)-DACH (19.2 mg, 0.0278 mmol, 0.15 mol equiv). Yielded 48 mg, 55% of **6β**. $[\alpha]_D$ + 1.0 (*c* 1, $CHCl_3$); other spectral data reported in Section 1.8.

1.14. (2α,3*R*,4*R*,5*R*,6*R*)-4,5-Bis(benzyloxy)-6-((benzyloxy)methyl)-2-vinyltetrahydro-2*H*-pyran-3-ol (6α)

Compound **3c** (102 mg, 0.197 mmol), $Pd_2(dba)_3$·$CHCl_3$ (16.9 mg, 0.0163 mmol, 0.08 mol equiv), (*S*,*S*)-DACH (23.5 mg, 0.0340 mmol, 0.17 mol equiv). Yielded 70 mg, 77% of [**6α**:**6β**] = [4.7:1]. ^{1}H NMR (400 MHz, $CDCl_3$, α-isomer reported from the mixture): δ 7.43–7.23 (m, 15H, 3× PhH), 5.88 (ddd, *J* = 5.3, 10.7, 15.9 Hz, 1H, H-A), 5.35 (dt, *J* = 1.5, 17.4 Hz, 1H, H-B′), 5.31 (dt, *J* = 1.4, 10.7 Hz, 1H, H-B″), 4.74–4.51 (m, 7H, 3× CH_2Ph and H-1), 4.06 (t, *J* = 3.1 Hz, 1H, H-2), 3.92–3.83 (m, 2H, H-4 and H-6a), 3.80–3.67 (m, 4H, H-3, H-5 and H-6b), 2.63 (s, 1H, OH); ^{13}C NMR (100 MHz, $CDCl_3$, α-isomer): δ 138.3, 138.2, 137.8, 134.0, 128.7, 128.5, 128.4, 128.2, 128.1, 128.0, 127.9, 127.8, 127.7, 118.6, 79.6, 76.4, 74.8, 74.6, 73.5, 73.4, 72.3, 69.4, 69.2; HRMS: *m*/*z* calcd for $C_{29}H_{36}NO_5$ 478.2588 $[M+NH_4]^+$, found 478.2590.

Acknowledgements

The authors EGN and MJF express appreciation to the Jean Dreyfus Boissevain program for their support.

Supplementary data

Supplementary data (^{1}H and ^{13}C NMR data for all new pure compounds **3a**–**c**, **5α**, and **6β** and ^{1}H NMR data illustrating the diastereomeric determinations for **4**, **5**, and **6**) associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.carres.2014.07.002.

References

1. Levy, D. E.; Tang, C. *The Chemistry of C-Glycosides*; Pergamon: Oxford, 1995.
2. SciFinder accessed May 22, 2014.
3. McGarvey, G. J.; Schmidtmann, F. W.; Benedum, T. E.; Kizer, D. E. *Tetrahedron. Lett.* **2003**, *44*, 3775–3779.
4. Chen, G.; Schmieg, J.; Tsuji, M.; Franck, R. W. *Org. Lett.* **2004**, *6*, 4077–4080.
5. Wang, W.; Zhang, Y.; Zhou, H.; Bleriot, Y.; Sinay, P. *Eur. J. Org. Chem.* **2001**, 1053–1059.
6. Sanhueza, C. A.; Mayato, C.; Garcia-Chicano, M.; Diaz-Penate, R.; Dorta, R. L.; Vazquez, J. T. *Bioorg. Med. Chem. Lett.* **2006**, *16*, 4223–4227.
7. Dondoni, A.; Giovannini, P. P.; Marra, A. *J. Chem. Soc., Perkin Trans. 1* **2001**, 2380–2388.
8. Nolen, E. G.; Kurish, A. J.; Wong, K. A.; Orlando, M. D. *Tetrahedron Lett.* **2003**, *44*, 2449–2453.
9. Durrat, F.; Xie, J.; Valery, J.-M. *Tetrahedron Lett.* **2004**, *45*, 1477–1479.
10. Westermann, B.; Walter, A.; Florke, U.; Altenbach, H.-J. *Org. Lett.* **2001**, *3*, 1375–1378.
11. Kulkarni, S. S.; Gervay-Hague, J. *Org. Lett.* **2006**, *8*, 5765–5768.
12. Chang, R.; Vo, T.-T.; Finney, N. S. *Carbohydr. Res.* **2006**, *341*, 1998–2004.
13. Postema, M. H. D.; Piper, J. L. *Tetrahedron Lett.* **2002**, *43*, 7095–7099.
14. Kraus, G. A.; Molina, M. T. *J. Org. Chem.* **1988**, *53*, 752–753.
15. Xie, J.; Durrat, F.; Valery, J.-M. *J. Org. Chem.* **2003**, *68*, 7896–7898.
16. Caputo, R.; Festa, P.; Guaragna, A.; Palumbo, G.; Pedatella, S. *Carbohydrate Res.* **2003**, *338*, 1877–1880.
17. Leeuwenburgh, M. A.; van der Marel, G. A.; Overkleeft, H. S.; van Boom, J. H. *J. Carbohydr. Chem.* **2003**, *22*, 549–564.
18. Shulman, M. L.; Shiyan, S. D.; Khorlin, A. Y. *Carbohydr. Res.* **1974**, *33*, 229–235.
19. Jurs, S.; Thiem, J. *Tetrahedron: Asymmetry* **2005**, *16*, 1631–1638.
20. Rainier, J. D.; Cox, J. M. *Org. Lett.* **2000**, *2*, 2707–2709.
21. Allwein, S. P.; Cox, J. M.; Howard, B. E.; Johnson, H. W. B.; Rainier, J. D. *Tetrahedron* **2002**, *58*, 1997–2009.
22. Wipf, P.; Pierce, J. G.; Zhuang, N. *Org. Lett.* **2005**, *7*, 483–485.
23. Doddi, V. R.; Kokatla, H. P.; Pal, A. P. J.; Basak, R. K.; Vankar, Y. D. *Eur. J. Org. Chem.* **2008**, 5731–5739.

24. Keller, V. A.; Kim, I.; Burke, S. D. *Org. Lett.* **2005**, *7*, 737–740. and references cited therein.
25. Cannon, J. S.; Olson, A. C.; Overman, L. E.; Solomon, N. S. *J. Org. Chem.* **2012**, *77*, 1961–1973.
26. Zacuto, M. J.; Leighton, J. L. *Org. Lett.* **2005**, *7*, 5525–5527.
27. Guerinot, A.; Serra-Muns, A.; Bensoussan, C.; Reymond, S.; Cossy, J. *Tetrahedron* **2011**, *67*, 5024–5033.
28. Trost, B. M.; Fandrick, D. R. *Aldrichchim. Acta* **2007**, *40*, 59–72.
29. Boschetti, A.; Nicotra, F.; Panza, L.; Russo, G. *J. Org. Chem.* **1988**, *53*, 4181–4185.
30. Vidal, T.; Haudrechy, A.; Langlois, Y. *Tetrahedron Lett.* **1999**, *40*, 5677–5680.
31. Broder, W.; Kunz, H. *Carbohydrate Res.* **1993**, *249*, 221–241.
32. Franks, N. E.; Montgomery, R. *Carbohydrate Res.* **1968**, *6*, 286–298.
33. Beignet, J.; Tiernan, J.; Woo, C. H.; Kariuki, B. M.; Cox, L. R. *J. Org. Chem.* **2004**, *69*, 6341–6356.