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Palladium-Catalyzed Improved Regio- and Stereoselective O-Glycosylation of D-Glucal-Derived β- and α-Vinyl Oxiranes

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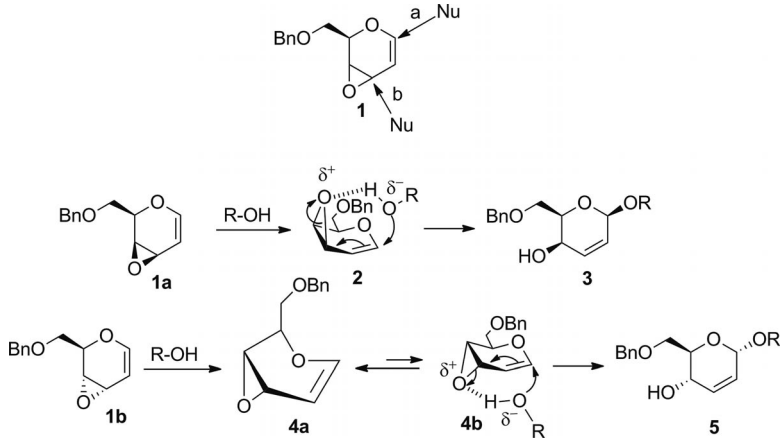
Keywords: Allylic compounds / Glycosylation / Epoxides / Palladium / Glycosides

A Pd^0-catalyzed glycosylation of D-glucal-derived vinyl oxiranes as excellent glycosyl donors has been accomplished in a regio- and stereoselective manner. Various glycosyl acceptors upon reaction with vinyl oxiranes **1a** and **1b** produced the corresponding 2,3-unsaturated *O*-glycosides in good to excellent yields within five minutes. The above reaction has also been utilized in the synthesis of 2,3-unsaturated trisaccharides, which are potential precursors of fully oxygenated, deoxy and dideoxy sugars.

Introduction

Oligosaccharides, which are fully oxygenated structural entities that are present in many natural and unnatural compounds,[1] have been used as antibacterial,[1b,1g,1h] antiviral,[1c] antifungal,[1d] and antitumor agents.[1e] Furthermore, oligosaccharides are structural components of several glycoproteins and glycolipids and are involved in a wide range of biological processes.[2] Oligosaccharides are produced[3] by glycosylations involving variously functionalized monosaccharides including pseudoglycals.[3b,3c] Furthermore, 2,3-unsaturated sugars, which are readily obtained from pseudoglycals through the well-known Ferrier reaction,[4] are also important intermediates in the synthesis of unnatural glycopeptide building blocks.[5] These compounds allow further useful functionalizations that can lead to structurally diverse 2,3-dideoxy sugars,[1h,6] which are found as structural units in uronic acid derived polysaccharides,[7] as well as in many significant molecules such as vineomycin B2,[8a,8b] lactonamycin,[8c–8e] PI-080,[8f] and some other antibiotics.[8g] Thus, due to their remarkable structural scaffold and their broad range of applications, the synthesis of glycosides derived from 2,3-unsaturated sugars has become important.[1h,6a,6b,9]

As mentioned above, one of the most convenient ways of producing 2,3-unsaturated glycosides is through the Ferrier reaction[4] from glycals. However, this reaction sometimes proceeds with incomplete stereoselectivity. An alternative and highly stereocontrolled strategy introduced by O'Doherty[6a,10] et al. involves palladium-catalyzed synthesis of 2,3-unsaturated glycosides that readily leads to many natural and unnatural sugars. Likewise, Toshima and coworkers have reported Lewis acid catalyzed chemoselective glycosylation by using 2,3-unsaturated-4-keto glycosyl acetates as disarmed glycosyl donors.[9a–9d]



Scheme 1. Stereoselective addition of O-nucleophiles to allyl epoxides **1a** and **1b**.[11,12]

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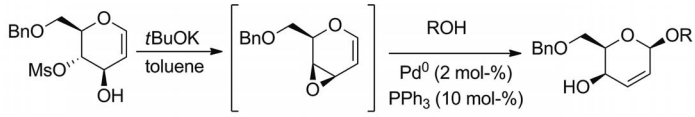
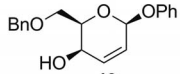
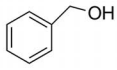
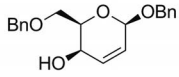
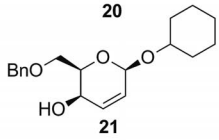
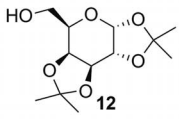
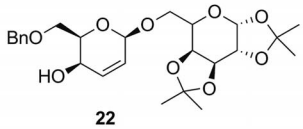
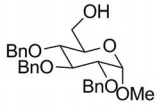
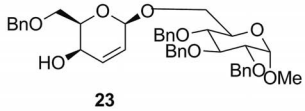
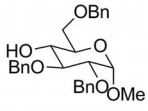
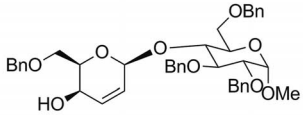
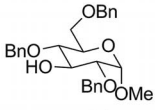
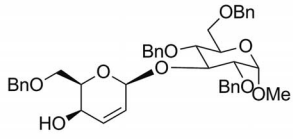
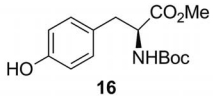
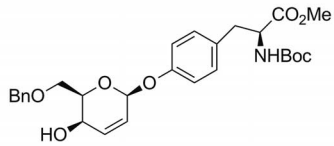
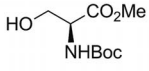
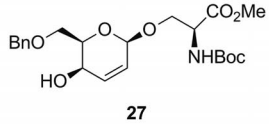
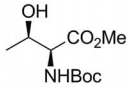
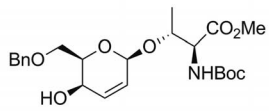
Table 1. Glycosylation of epoxide **1a** formed in situ.

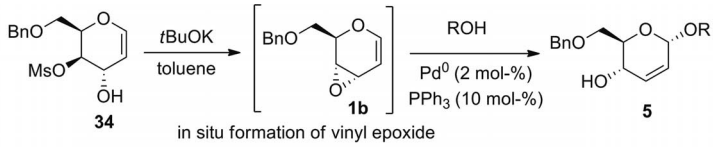


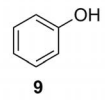
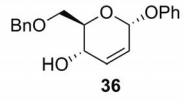
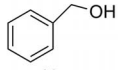
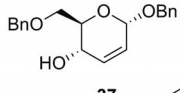
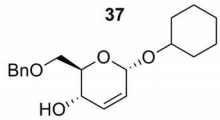
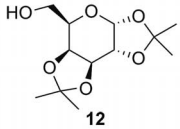
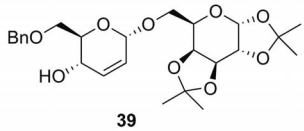
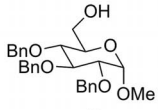
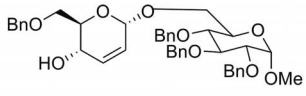
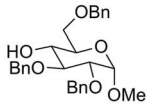
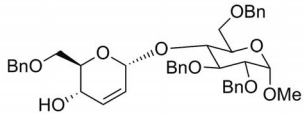
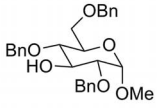
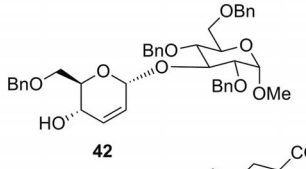
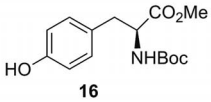
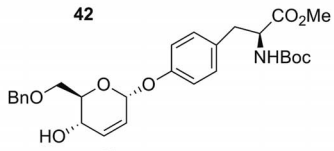
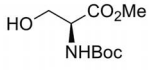
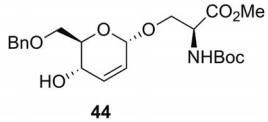
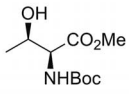
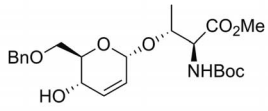
in situ formation of vinyl epoxide

Entry	Glycal acceptor	Product	% Yield/ non-catalyzed reaction time	% Yield with Pd^0
a	 **9**	 **19**	88 (3h)	83
b	 **10**	 **20**	84 (3h)	86[a]
c	 **11**	 **21**	15 (24h)	79
d	 **12**	 **22**	68 (18h)	65[a]
e	 **13**	 **23**	0 (48h)	62[a]
f	 **14**	 **24**	0 (48h)	58[a]
g	 **15**	 **25**	0 (48h)	52[a]
i	 **16**	 **26**	62 (24h)	65[a]
j	 **17**	 **27**	67 (18h)	62[a]
k	 **18**	 **28**	69 (18h)	61[a]

[a] The β-configuration of the product was attributed by analogy with molecules **8**, **19**, and **21**.

Table 2. Glycosylation of epoxide **1b** formed in situ.



Entry	Glycal acceptor	Product	% Yield/ non-catalyzed reaction time	% Yield with Pd^0
a	 **9**	 **36**	84 (1 h)	80
b	 **10**	 **37**	89 (1 h)	84
c	 **11**	 **38**	25 (24 h)	71
e	 **12**	 **39**	58 (1 h)	77[a]
f	 **13**	 **40**	0 (48 h)	64[a]
g	 **14**	 **41**	0 (48 h)	57[a]
h	 **15**	 **42**	0 (48 h)	56[a]
i	 **16**	 **43**	63 (24 h)	67[a]
j	 **17**	 **44**	65 (12 h)	68[a]
k	 **18**	 **45**	60 (18 h)	64[a]

[a] The α-configuration of the product was attributed by analogy to molecules **36**–**38**.

With the aim of developing new approaches to the synthesis of 2,3-unsaturated-*O*-glycosides, the efficacy of epoxide **1** (Scheme 1), a glycal-derived vinyl oxirane, as a new glycosyl donor has been extensively investigated by Crotti et al.[11,12] using various O- and C-glycosyl acceptors without the use of any catalyst. Epoxide **1** (Scheme 1), having two reactive sites (i.e., vinyl and allyl termini), allowed either 1,2-addition (S_N2 process, route b) or 1,4-addition (S_N2' process, route a) to be carried out. During their studies, the authors found that the reaction of diastereoisomeric D-glucal-derived allyl epoxides **1a**[11b,11c] and **1b**[11a] with various O-nucleophiles gave 2,3-unsaturated-β-*O*-glycosides from **1a** and 2,3-unsaturated-α-*O*-glycosides from **1b** in a regio- and stereospecific manner. The regio- and stereochemical outcome of the 2,3-unsaturated-*O*-glycosides depends on the glycosyl donor, i.e., glycal derived vinyl oxirane **1a** or **1b** employed, and is guided by coordination of the alcohol followed by nucleophilic attack, as shown in Scheme 1.

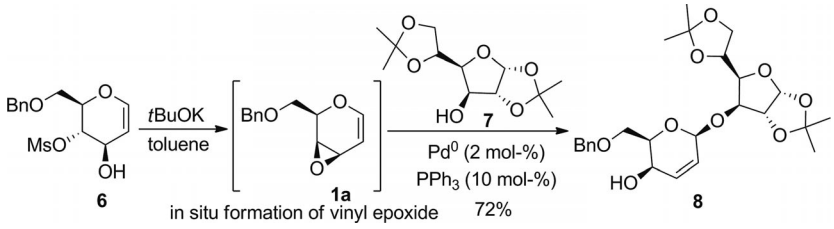
Result and Discussion

Palladium-catalyzed nucleophilic opening of vinyl epoxides is well-studied[13] and permits ready access to a large number of allylic (or homoallylic) alcohols. Hence, in a continuation of our efforts[4c,14] to functionalize glycals to access a diverse range of carbohydrate structures, we anticipated that palladium-catalyzed nucleophilic ring opening of sugar-derived vinyl epoxides may be more facile. Indeed, this was found to be the case and, herein, we report our results on palladium-catalyzed glycosylation reactions of glucal-derived vinyl oxiranes to form 2,3-unsaturated *O*-glycosides in a highly regio- and stereoselective manner within a very short time (ca. 5 min).

We present the results of our studies on the reactions of various alcohols both in the absence (for comparison purposes) and in the presence of [$Pd(PPh_3)_4$] as a catalyst. It was found that palladium catalysis not only hastens the completion of the reaction, but also allows the reaction to work well with sterically hindered alcohols in a completely regioselective manner. However, the stereoselectivity of the noncatalyzed and catalyzed glycosylations were observed to be same (cf. Tables 1 and 2). It is likely that the palladium catalyst acts more like a Lewis acid because the stereoselectivity seems to depend on the geometry of the glycal and not on the presumed π-allyl palladium complex. Epoxide **1a** was prepared by using a known procedure developed by Crotti[11c] et al. from hydroxy mesylate **6** (Scheme 2), which has the desired stereochemical requirement around C(3) and C(4). The glucal-derived hydroxy mesylate **6** was treated with 1 equiv. of *t*BuOK in toluene at ambient temperature and, after completion of the reaction (i.e., formation of the corresponding epoxide was observed by TLC monitoring), the glycosyl acceptor diacetone-D-glucose **7**, Pd^0, and PPh_3 were added. The reaction was optimized by using Pd^0 (2 mol-%), PPh_3 (10 mol-%) and glycosyl acceptor (3 equiv.) in toluene at ambient temperature to afford O-glycosylated 2,3-unsaturated sugar **8** in 72% yield within only five minutes. The same reaction performed in the absence of Pd^0 catalyst required[11c] 18 h to form the glycosylated product **8** in 75% yield, the spectroscopic data of which was in complete agreement with those in the literature.[11c] The anomeric proton appeared as a broad singlet at δ = 5.31 ppm, indicating a β-configuration for molecule **8**. Thus, this reaction proceeded through a regio- and stereoselective oxirane ring opening through an S_N2' mechanism. The scope of this methodology could be extended with glycosyl donor **1a** by using acceptors such as PhOH (**9**), BnOH (**10**), and CyOH (**11**) to afford the corresponding β-glycosides in good yields (Table 1).

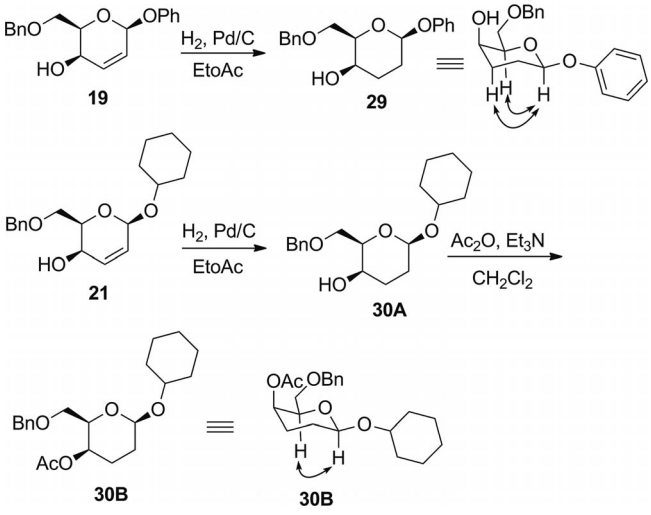
Interestingly, although the sugar derived alcohols **13**–**15** (Table 1) reacted readily, within 5 min, with glycosyl donor **1a** to give the coupled products in good yields in a highly stereocontrolled manner, the same reactions did not work in the absence of Pd^0. This clearly suggests that palladium catalysis plays a crucial role in the success of the glycosylation reactions leading to disaccharides having a 2,3-unsaturated sugar unit. Furthermore, the palladium-catalyzed reactions worked reasonably well with three amino acids **16**–**18** (Table 1) as glycosyl acceptors and gave the desired glycosylated products in good yields.

The regio- and stereoselectivity of the reactions of O-nucleophiles (alcohols) with epoxide **1a** was confirmed by transforming two of the glycosylated products **19** and **21** into **29** and **30B**, respectively, as shown in Scheme 3. Thus, saturated compound **29** was obtained by hydrogenation (Pd/C, EtOAc) of the glycosylated adduct **19** in 80% yield. The chemical shifts of the protons in the ^1H NMR spectra of **29** were assigned on the basis of COSY spectroscopic data. The ^1H NMR spectrum of **29** showed the anomeric H-1 proton (δ = 5.14 ppm) as a doublet of doublets (J = 9.2, 2.4 Hz). Furthermore, the absolute configuration at the anomeric center (C-1) was confirmed by NOE spectroscopic analysis. Thus, in an NOE experiment, irradiation of the signal for H-1 at δ = 5.14 ppm in the saturated derivative **29** led to an enhancement of the signals for H-5 and



Scheme 2. Glycosylation of vinyl oxirane **1a** with diacetone-D-glucose by using Pd^0 catalyst.

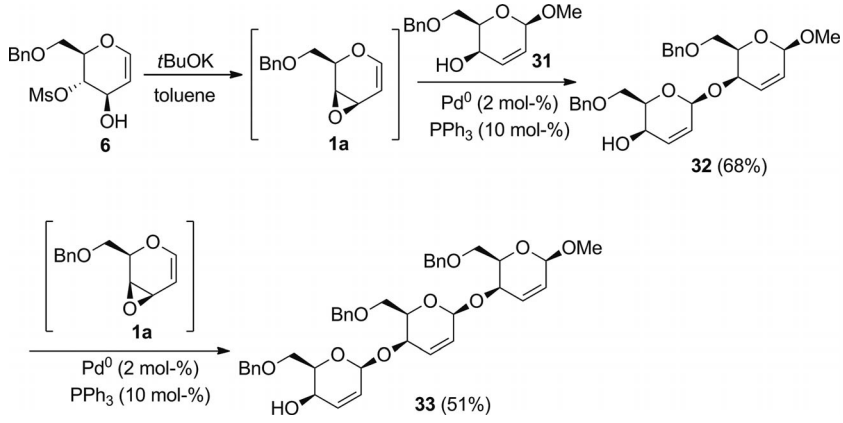
H-3′ at δ = 3.77 and 1.76 ppm, respectively, indicating that H-1 is *cis* to H-5 and H-3′, thus concluding *S* configuration (β-glycoside) of the anomeric center (C-6). Likewise, the sugar derivative **21** was also subjected to hydrogenation to give the corresponding saturated derivative **30A** in good yield. Acetylation of **30A** led to the formation of **30B**, which presented the anomeric proton as a well-resolved broad singlet at δ = 4.89 ppm in the ^{1}H NMR spectrum. Furthermore, the absolute stereochemistry at the anomeric center was proved by NOE spectral analysis as shown in Scheme 3. The structures of glycosides **20**, **22**, and **33** were established by comparison of their ^{1}H and ^{13}C NMR spectra with previously reported data for closely related compounds.[6a,10,11,15]



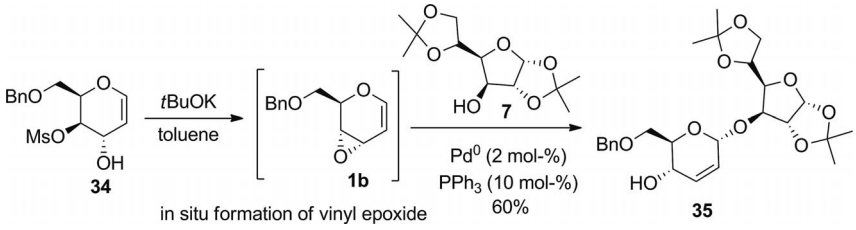
Scheme 3. Synthesis of compounds **29**, **30A**, and **30B**.

With this methodology in hand, we turned our attention to the synthesis of D-glucal-derived 2,3-unsaturated di- and trisaccharide analogues **32** and **33** (Scheme 4). For this purpose, we treated vinyl oxirane **1a** with glycosyl acceptor **31**[11c] in the presence of Pd^0 and PPh_3 to give the coupled product **32** in 68% yield. The disaccharide analogue **32** was then utilized as a glycosyl acceptor for the construction of trisaccharide **33**. Thus, treatment of vinyl oxirane **1a** with glycosyl acceptor **32** gave the desired 2,3-unsaturated disaccharide **33** in 51% yield. The structures of the di- and trisaccharides were fully established[16] on the basis of their spectroscopic data.

After examining the reactivity pattern of vinyl oxirane **1a** and the stereochemical outcome of the coupling, we turned our attention to the use of vinyl oxirane **1b** in the presence, or absence, of Pd^0 catalyst. For this purpose, the precursor hydroxy mesylate **34** (Scheme 5) was prepared by using the procedure reported by Crotti et al.[11b] Thus, after treatment of hydroxy mesylate **34** with 1 equiv. of *t*BuOK in toluene at ambient temperature to form the epoxide (reaction monitored by TLC analysis), the glycal acceptor (diacetone-D-glucose **7**), Pd^0, and PPh_3 were added. This reaction also gave the best results by using Pd^0 (2 mol-%), PPh_3 (10 mol-%) and glycosyl donor (3 equiv.) in toluene at ambient temperature within five minutes, affording O-glycosylated 2,3-unsaturated sugar **35** in 65% yield. However, in the absence of Pd^0 catalyst, the same reaction required one hour and gave the glycosylated product **35** in 60% yield. The spectroscopic data of **35** was in complete agreement with the literature data.[11b] The exclusive formation of the α-*O*-glycoside with the anomeric proton appearing as a broad singlet at δ = 5.19 ppm indicated that this reaction proceeded through



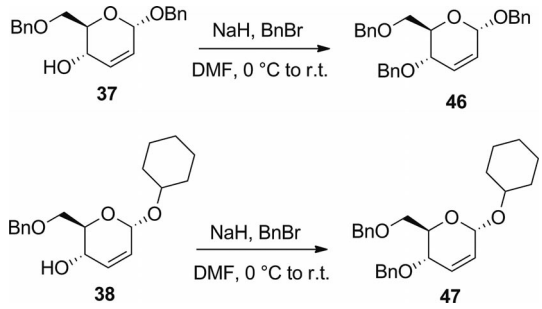
Scheme 4. Stereoselective synthesis of trisaccharide **33** by using Pd^0 catalyst.



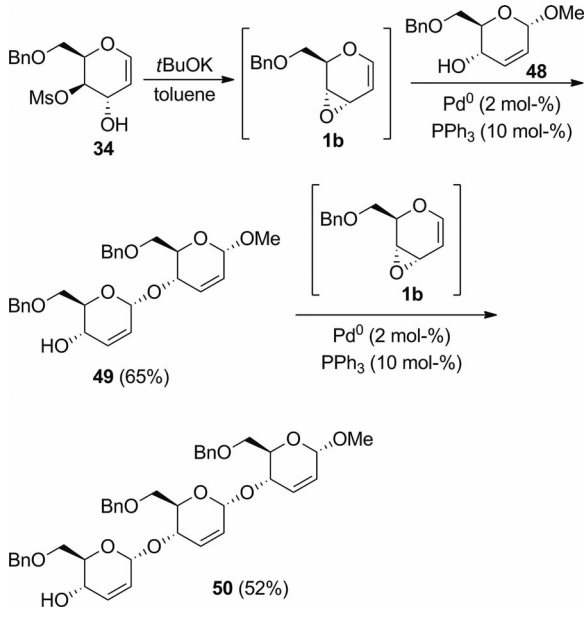
Scheme 5. Glycosylation of vinyl oxirane **1b** with diacetone-D-glucose by using Pd^0 catalyst.

a highly regio- and stereoselective oxirane ring opening via an S_N2' mechanism. Likewise, we could extend the scope of the palladium catalysis to compare the reactivity of glycosyl donor **1b** in the absence of any catalyst with phenol, benzyl alcohol, cyclohexanol and other chiral alcohols viz. **13**–**15** and three amino acids **16**–**18** as glycosyl acceptors, which afforded a good yield of the corresponding α-glycosides (Table 2).

The regio- and stereoselectivity of these reactions with O-nucleophiles (alcohols) and epoxide **1b** was confirmed by transforming two of the glycosylated products, **37** and **38**, into known[15c] compounds **46** and **47**, respectively (Scheme 6). Thus, the glycosylated adducts **37** and **38** were subjected to benzylation by treatment with NaH and benzyl bromide to give the corresponding benzylated derivatives **46** and **47** in excellent yields. The data of these compounds are in complete agreement with the reported compounds.[15c] The remaining structures of glycosides **36** and **40**–**50** were established by comparison of their ^1H and ^{13}C NMR spectra with previously reported data for closely related compounds.[6a,10,11,15]



Scheme 6. Synthesis of benzylated derivatives **46** and **47**.



Scheme 7. Stereoselective synthesis of trisaccharide **50** by using a Pd^0 catalyst.

The corresponding di- and trisaccharide analogues **49** and **50** (Scheme 7) were also synthesized from glycosyl donor **1b**. Thus, treatment of the vinyl oxirane **1b** with glycosyl acceptor **48**[11b] in the presence of Pd^0 and PPh_3 gave the coupled product **49** in 65% yield. Finally, treatment of the vinyl oxirane **1b** with glycosyl acceptor **49** gave the desired 2,3-unsaturated trisaccharide **50** in 52% yield.

Conclusions

We have developed a rapid (ca. 5 min) palladium-catalyzed glycosylation reaction by using vinyl epoxides. This protocol allows easy construction of di- and trisaccharide analogues with excellent stereocontrol. It is expected that such palladium-catalyzed reactions of vinyl oxiranes to form 2,3-unsaturated sugars will find use in organic synthesis.

Experimental Section

General Considerations: FTIR spectra were recorded as a thin film or as KBr pellets and are expressed in cm^{-1}. ^1H (400 or 500 MHz) and ^{13}C (100 or 125 MHz) NMR spectra were recorded with JEOL JNM-LA 400 and 500 spectrometers as solutions in $CDCl_3$; chemical shifts are reported in ppm downfield of tetramethylsilane and coupling constants are expressed in Hz; splitting patterns are designated as br (broad), s (singlet), d (doublet), dd (double doublet), q (quartet), m (multiplet). Optical rotations were measured with an Autopol II automatic polarimeter at 28 °C. All reactions were carried out using freshly distilled and anhydrous solvents. The visualization of spots on TLC plates was effected by exposure to iodine or by spraying with 10% H_2SO_4 and charring. Column chromatography was performed over silica gel (100–200 Mesh) using hexane and ethyl acetate as eluent. HRMS were obtained with a Waters Q-TOF premier ESI mass spectrometer.

General Procedure for the Glycosylation of Vinyl Oxirane by Using Pd^0 Catalyst: To a stirred solution of the requisite hydroxy mesylate (40 mg, 0.23 mmol) in anhydrous toluene (2 mL), was added *t*BuOK (0.020 g, 0.18 mmol) and the reaction mixture was stirred at room temp. for 15 min. After consumption of the starting material (TLC monitoring), alcohol (3 equiv.), $[Pd(PPh_3)_4]$ (2 mg, 0.001 mmol), and PPh_3 (10 mg, 0.03 mmol) were added and the mixture was stirred at ambient temperature. Upon completion of the reaction (TLC monitoring; ca. 5 min), the reaction mixture was filtered through a pad of Celite and the filtrate was concentrated under vacuum to give the crude coupled product along with unreacted alcohol. The crude product was purified by chromatography over SiO_2, which was previously deactivated with a 30% solution of $NaHCO_3$.

Phenyl 6-*O*-Benzyl-2,3-dideoxy-β-D-*threo*-hex-2-enopyranoside (19): Yield: 83% (33 mg); R_f = 0.45 (hexane/ethyl acetate, 7:3); colorless liquid; $[\alpha]_D^{28}$ = –76.0 (*c* = 0.5, CH_2Cl_2). IR (neat): $\tilde{\nu}_{max}$ = 3400, 3030, 2919, 2864, 1594, 1492, 1453, 1393, 1326, 1289, 1226, 1174, 1152, 1050, 1004, 974, 877, 852, 754, 694 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 7.34–7.25 (m, 7 H, Ar*H*), 7.17 (d, *J* = 7.75 Hz, 2 H, Ar*H*), 7.12–7.02 (m, 1 H, Ar*H*), 6.25–6.22 (m, 1 H), 5.99 (d, *J* = 10.0 Hz, 1 H), 5.70 (br. s, 1 H), 4.58 (br. s, 2 H), 4.02 (t, *J* = 5.15 Hz, 2 H), 3.86 (dd, *J* = 10.30, 10.30 Hz, 1 H), 3.75 (dd, *J* = 10.00, 10.35 Hz, 1 H), 2.09–2.04 (m, 1 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 156.9, 137.9, 129.6–127.6 (m, Ar-C), 122.4,

116.5, 95.6, 74.7, 73.6, 69.7, 62.7 ppm. HRMS (ESI): calcd. for $C_{19}H_{20}NaO_4$ [M + Na]$^+$ 335.1254; found 335.1250.

Benzyl 6-*O*-Benzyl-2,3-dideoxy-β-D-*threo*-hex-2-enopyranoside (20): Yield: 86% (36 mg); R_f = 0.4 (hexane/ethyl acetate, 4:1); yellow liquid; $[\alpha]_D^{28}$ = +12.0 (*c* = 1.0, CH_2Cl_2). IR (neat): $\tilde{\nu}_{max}$ = 3417, 3030, 2920, 2859, 1725, 1598, 1496, 1453, 1378, 1321, 1255, 1208, 1157, 1116, 1051, 1020, 849, 788, 736, 697 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.37–7.25 (m, 10 H, Ar*H*), 6.15–6.12 (m, 1 H), 5.87 (d, *J* = 10.10 Hz, 1 H), 5.16 (d, *J* = 1.40 Hz, 1 H), 4.90 (d, *J* = 11.95 Hz, 1 H), 4.66 (d, *J* = 11.95 Hz, 1 H), 4.61 (br. s, 2 H), 3.98–3.95 (m, 1 H), 3.87–3.81 (m, 2 H), 3.76–3.73 (m, 1 H), 2.04 (br. s, 1 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 138.1, 137.4, 130.9, 130.8, 128.5–127.8 (m, Ar-C), 96.8, 74.5, 73.7, 70.1, 69.9, 63.0 ppm. HRMS (ESI): calcd. for $C_{20}H_{22}NaO_4$ [M + Na]$^+$ 349.1410; found 349.1419.

Cyclohexyl 6-*O*-Benzyl-2,3-dideoxy-β-D-*threo*-hex-2-enopyranoside (21): Yield: 79% (32 mg); R_f = 0.45 (hexane/ethyl acetate, 3:2); $[\alpha]_D^{28}$ = –90.34 (*c* = 1.45, CH_2Cl_2). IR (neat): $\tilde{\nu}_{max}$ = 3041, 3032, 2931, 2855, 1650, 1495, 1452, 1373, 1316, 1259, 1177, 1163, 1119, 1044, 1024, 963, 890, 869, 848, 785, 736, 697 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.34–7.25 (m, 5 H, Ar*H*), 6.11–6.08 (m, 1 H), 5.80 (d, *J* = 9.65 Hz, 1 H), 5.16 (d, *J* = 1.40 Hz, 1 H), 4.59 (s, 2 H), 3.90 (br. s, 1 H), 3.83–3.77 (m, 2 H), 3.74–3.67 (m, 2 H), 2.03–1.90 (m, 3 H), 1.74–1.70 (m, 2 H), 1.58–1.52 (m, 1 H), 1.41–1.19 (m, 5 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 138.1, 131.7, 130.4, 128.3–127.6 (m, Ar-C), 96.0, 74.5, 73.5, 69.9, 62.8, 33.7, 32.1, 25.5–24.1 (m) ppm. HRMS (ESI): calcd. for $C_{19}H_{26}NaO_4$ [M + Na]$^+$ 341.1723; found 341.1727.

6-*O*-(6′-*O*-Benzyl-2′,3′-dideoxy-β-D-*threo*-hex-2′-enopyranosyl)-1,2,3,4-di-*O*-isopropylidene-α-D-galactopyranose (22): Yield: 65% (40 mg); R_f = 0.4 (hexane/ethyl acetate, 7:3); colorless liquid; $[\alpha]_D^{28}$ = –86.66 (*c* = 0.9, CH_2Cl_2). IR (neat): $\tilde{\nu}_{max}$ = 3459, 2987, 2924, 1725, 1647, 1445, 1382, 1308, 1256, 1212, 1168, 1070, 1002, 918, 899, 863 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.34–7.25 (m, 5 H, Ar*H*), 6.13–6.10 (m, 1 H), 5.89 (d, *J* = 10.00 Hz, 1 H), 5.53 (d, *J* = 4.90 Hz, 1 H), 5.15 (d, *J* = 1.45 Hz, 1 H), 4.59–4.57 (m, 3 H), 4.31–4.29 (m, 1 H), 4.21 (dd, *J* = 1.40, 1.75 Hz, 1 H), 4.02–3.98 (m, 2 H), 3.92 (br. s, 1 H), 3.82–3.76 (m, 3 H), 3.70–3.68 (m, 1 H), 2.22 (br. s, 1 H), 1.52 (br. s, 3 H), 1.43 (br. s, 3 H), 1.31 (br. s, 6 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 138.1, 130.8, 130.7, 128.5, 127.8 (m, Ar-C), 109.4, 108.7, 98.5, 96.4, 74.5, 73.6, 71.3, 70.7, 70.4, 69.7, 68.3, 67.8, 62.8, 26.1, 26.0, 25.0, 24.5 ppm. HRMS (ESI): calcd. for $C_{25}H_{34}NaO_9$ [M + Na]$^+$ 501.2095; found 501.2108.

Methyl 6-*O*-(6′-*O*-Benzyl-2′,3′-dideoxy-β-D-*threo*-hex-2′-enopyranosyl)-2,3,4-tri-*O*-benzyl-α-D-glucopyranoside (23): Yield: 62% (54 mg); R_f = 0.4 (hexane/ethyl acetate, 3:2); $[\alpha]_D^{28}$ = +25.41 (*c* = 1.2, CH_2Cl_2). IR (neat): $\tilde{\nu}_{max}$ = 3428, 3030, 2918, 1597, 1496, 1453, 1385, 1257, 1159, 1048, 912, 871, 737, 697 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.35–7.25 (m, 20 H, Ar*H*), 6.11–6.09 (m, 1 H), 5.76 (d, *J* = 9.75 Hz, 1 H), 4.99 (d, *J* = 8.00 Hz, 1 H), 4.97 (d, *J* = 2.30 Hz, 1 H), 4.87 (d, *J* = 12.60 Hz, 1 H), 4.81 (d, *J* = 11.45 Hz, 1 H), 4.78 (d, *J* = 12.60 Hz, 1 H), 4.65–4.53 (m, 5 H), 4.04 (d, *J* = 8.60 Hz, 1 H), 3.98 (t, *J* = 9.15 Hz, 1 H), 3.89 (br. s, 1 H), 3.78–3.71 (m, 4 H), 3.64–3.52 (m, 3 H), 3.35 (s, 3 H), 1.83 (d, *J* = 10.0 Hz, 1 H) ppm. ^{13}C NMR (125 MHz): δ = 138.7, 138.3, 138.2, 138.1, 130.8, 130.6, 128.3–127.5 (m, Ar-C), 98.1, 98.1, 82.1, 79.7, 75.7, 74.8, 74.5, 74.5, 73.5, 73.3, 69.6, 69.6, 66.5, 62.6, 55.1 ppm. HRMS (ESI): calcd. for $C_{41}H_{46}NaO_9$ [M + Na]$^+$ 705.3034; found 705.3047.

Methyl 4-*O*-(6′-*O*-Benzyl-2′,3′-dideoxy-β-D-*threo*-hex-2′-enopyranosyl)-2,3,6-tri-*O*-benzyl-α-D-glucopyranoside (24): Yield: 58% (50 mg); R_f = 0.5 (hexane/ethyl acetate, 3:2); colorless liquid; $[\alpha]_D^{28}$ = +40.17 (*c* = 1.4, CH_2Cl_2). IR (neat): $\tilde{\nu}_{max}$ = 3434, 3062, 3030, 2916, 2865, 1495, 1453, 1367, 1158, 1098, 1045, 738, 697 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.37–7.25 (m, 20 H, Ar*H*), 6.08–6.05 (m 1 H), 5.72 (d, *J* = 10.24 Hz, 1 H, -OC*H*Ph), 5.25 (br. s, 1 H), 4.88 (br. s, 2 H), 4.78 (d, *J* = 12.20 Hz, 1 H, -OC*H*Ph), 4.63 (d, *J* = 12.20 Hz, 1 H, -OC*H*Ph), 4.62 (d, *J* = 12.20 Hz, 1 H, -OC*H*Ph), 4.59 (d, *J* = 3.64 Hz, 1 H), 4.53–4.47 (m, 3 H), 3.98–3.86 (m, 3 H), 3.83–3.78 (m, 1 H), 3.72–3.67 (m, 2 H), 3.64–3.46 (m, 4 H), 3.36 (br. s, 3 H), 2.48 (d, *J* = 10.52 Hz, 1 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 139.0, 138.2, 138.1, 137.7, 131.3, 130.4, 128.3–127.3 (m, Ar-C), 98.1, 98.0, 80.7, 79.5, 77.2, 75.6, 74.9, 74.7, 73.8, 73.4, 70.5, 69.3, 68.1, 62.0, 55.1 ppm. HRMS (ESI): calcd. for $C_{41}H_{46}NaO_9$ [M + Na]$^+$ 705.3034; found 705.3039.

Methyl 3-*O*-(6′-*O*-Benzyl-2′,3′-dideoxy-β-D-*threo*-hex-2′-enopyranosyl)-2,4,6-tri-*O*-benzyl-α-D-glucopyranoside (25): Yield: 60% (52 mg); colorless liquid; R_f = 0.45 (hexane/ethyl acetate, 3:2); $[\alpha]_D^{28}$ = +15.0 (*c* = 0.6, CH_2Cl_2). IR (neat): $\tilde{\nu}_{max}$ = 3466, 3030, 2864, 1496, 1453, 1369, 1161, 1090, 1048, 906, 849, 737, 698 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.39–7.24 (m, 20 H, Ar*H*), 6.17–6.13 (m, 1 H), 5.90 (d, *J* = 10.04 Hz, 1 H), 5.54 (br. s, 1 H), 5.06 (d, *J* = 10.48 Hz, 1 H, -OC*H*Ph), 4.73 (d, *J* = 11.96 Hz, 1 H, -OC*H*Ph), 4.67–4.62 (m, 3 H), 4.58–4.48 (m, 3 H), 4.44 (d, *J* = 10.72 Hz, 1 H, -OC*H*Ph), 4.33 (t, *J* = 9.28 Hz, 1 H), 3.99–3.94 (m, 1 H), 3.82–3.72 (m, 3 H), 3.69–3.63 (m, 3 H), 3.60–3.53 (m, 2 H), 3.39 (s, 3 H), 1.75 (d, *J* = 10.00 Hz, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 138.6, 138.1, 137.9, 137.8, 131.5, 130.3, 128.5–127.4 (m, Ar-C), 99.3, 97.7, 80.0, 79.6, 77.2, 76.8, 76.1, 74.5, 74.0, 73.4, 73.1, 69.9, 68.9, 68.5, 62.3 ppm. HRMS (ESI): calcd. for $C_{41}H_{46}NaO_9$ [M + Na]$^+$ 705.3034; found 705.3044.

L-Tyrosine *N*-[(1,1-Dimethylethoxy)carbonyl]-*O*-(6-*O*-benzyl-2,3-dideoxy-β-D-*threo*-hex-2-enopyranosyl) Methyl Ester (26): Yield: 65% (43 mg); yellow liquid; R_f = 0.5 (hexane/ethyl acetate, 1:1); $[\alpha]_D^{28}$ = +92.85 (*c* = 0.7, CH_2Cl_2). IR (neat): $\tilde{\nu}_{max}$ = 3424, 3063, 3027, 2977, 2927, 2867, 1743, 1712, 1610, 1556, 1509, 1452, 1393, 1367, 1229, 1165, 1108, 1051, 1017, 854, 738, 698 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.35–7.25 (m, 5 H, Ar*H*), 7.04–7.00 (m, 4 H, Ar*H*), 6.24–6.21 (m, 1 H), 5.97 (d, *J* = 10.10 Hz, 1 H), 5.65 (s, 1 H), 4.94 (d, *J* = 7.95 Hz, 1 H), 4.61–4.53 (m, 3 H), 4.02–3.99 (m, 2 H), 3.86–3.69 (m, 5 H), 3.04–3.01 (m, 2 H), 2.07 (d, *J* = 9.80 Hz, 1 H), 1.40 (br. s, 9 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 172.4, 156.1, 155.2, 138.0, 131.5, 130.4–127.8 (m, Ar-C), 116.6, 95.8, 80.0, 74.7, 73.7, 69.8, 62.7, 54.5, 52.3, 37.5, 28.3 ppm. HRMS (ESI): calcd. for $C_{28}H_{39}N_2O_8$ [M + NH_4]$^+$ 531.2701; found 531.2709.

L-Serine *N*-[(1,1-Dimethylethoxy)carbonyl]-*O*-(6-*O*-benzyl-2,3-dideoxy-β-D-*threo*-hex-2-enopyranosyl) Methyl Ester (27): Yield: 62% (35 mg); R_f = 0.6 (hexane/ethyl acetate, 1:1); colorless liquid; $[\alpha]_D^{28}$ = –38.46 (*c* = 1.3, CH_2Cl_2). IR (neat): $\tilde{\nu}_{max}$ = 3386, 2976, 2931, 2875, 1748, 1713, 1509, 1454, 1438, 1391, 1367, 1296, 1249, 1212, 1164, 1119, 1053, 867, 850, 812, 781 cm^{-1}. ^{1}H NMR (500 MHz): δ = 7.34–7.25 (m, 5 H, Ar*H*), 6.16–6.13 (m, 1 H), 5.77 (d, *J* = 10.35 Hz, 1 H), 5.50 (d, *J* = 8.55 Hz, 1 H), 5.09 (br. s, 1 H), 4.58 (d, *J* = 2.75 Hz, 2 H), 4.45–4.41 (m, 1 H), 4.19–4.15 (m, 1 H), 3.95 (br. s, 1 H), 3.85–3.81 (m, 2 H), 3.78–3.75 (m, 1 H), 3.73 (s, 3 H), 3.69–3.66 (m, 1 H), 2.08 (d, *J* = 9.45 Hz, 1 H), 1.44 (br. s, 9 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 171.0, 155.5, 138.0, 131.4, 130.0, 128.5–127.8 (m, Ar-C), 97.4, 80.1, 74.4, 73.7, 69.6, 67.7, 62.6, 53.9, 52.6, 28.4 ppm. HRMS (ESI): calcd. for $C_{22}H_{31}NNaO_8$ [M + Na]$^+$ 460.1942; found 460.1942.

L-Threonine *N*-[(1,1-Dimethylethoxy)carbonyl]-*O*-(6-*O*-benzyl-2,3-dideoxy-β-D-*threo*-hex-2-enopyranosyl) Methyl Ester (28): Yield: 61% (35 mg); colorless liquid; R_f = 0.5 (hexane/ethyl acetate, 1:1); $[\alpha]_D^{28}$ = –51.11 (*c* = 0.45, CH_2Cl_2). IR (neat): $\tilde{\nu}_{max}$ = 3430, 3063,

3030, 2977, 2930, 1750, 1715, 1505, 1453, 1392, 1367, 1253, 1208, 1165, 1118, 1053, 1000, 964, 908, 864, 788, 741, 699 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.34–7.25 (m, 5 H, Ar*H*), 6.14–6.11 (m, 1 H), 5.82 (d, *J* = 10.05 Hz, 1 H), 5.30 (br. s, 1 H), 4.99 (br. s, 1 H), 4.59 (d, *J* = 3.70 Hz, 2 H), 4.30–4.23 (m, 1 H), 3.84–3.69 (m, 5 H), 3.51 (s, 3 H), 2.09 (d, *J* = 4.85 Hz, 1 H), 1.44 (br. s, 9 H), 1.23 (d, *J* = 6.60 Hz, 3 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 172.0, 156.1, 138.1, 130.9, 130.7, 128.5, 127.8, 98.7, 74.4, 73.7, 69.8, 68.2, 62.9, 58.7, 55.9, 52.5, 28.3, 19.9 ppm. HRMS (ESI): calcd. for $C_{23}H_{33}NNaO_8$ [M + Na]$^+$ 474.2098; found 474.2101.

Phenyl 6-*O*-Benzyl-2,3-dideoxy-β-D-*threo*-hexopyranoside (29): To a stirred solution of olefin **19** (50 mg, 0.16 mmol) in ethyl acetate (3 mL) was added 10% Pd/C (5 mg) in one portion. The resulting mixture was stirred under 1 atm of hydrogen for 10 min. After completion of the reaction, the catalyst was removed by filtration through Celite and washed with ethyl acetate (5 mL). The combined organic layer was concentrated in vacuo and the residue was purified by column chromatography to give **29** as an oil. Yield: 80% (40 mg); R_f = 0.5 (hexane/ethyl acetate, 3:1); $[\alpha]_D^{28}$ = –22.85 (*c* = 0.4, CH_2Cl_2). IR (neat): $\tilde{\nu}_{max}$ = 3463, 3063, 3030, 2924, 2857, 1600, 1588, 1494, 1453, 1387, 1329, 1289, 1233, 1200, 1174, 1102, 1056, 1025, 970, 911, 848, 812, 754, 694 cm^{-1}. ^{1}H NMR (500 MHz): δ = 7.34–7.25 (m, 7 H, Ar*H*), 7.06–6.99 (m, 3 H, Ar*H*), 5.14 (dd, *J* = 9.20, 2.40 Hz, 1 H, 1-H), 4.55 (dd, *J* = 11.60, 11.90 Hz, 2 H, -OC*H*Ph), 3.87–3.85 (m, 1 H, 4-H), 3.81–3.79 (m, 1 H, 6-H), 3.79–3.76 (m, 1 H, 5-H), 3.73–3.69 (m, 1 H, 6′-H), 2.68 (d, *J* = 7.05 Hz, 1 H, -O*H*), 2.12–2.04 (m, 2 H, 3-H, 2-H), 1.87–1.81 (m, 1 H, 2′-H), 1.78–1.73 (m, 1 H, 3′-H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 157.1, 137.9, 129.4, 128.5, 127.8, 122.2, 116.6, 99.9, 73.8, 70.5, 64.7, 29.3, 25.5 ppm. HRMS (ESI): calcd. for $C_{19}H_{22}NaO_4$ [M + Na]$^+$ 337.1411; found 337.1411.

Cyclohexyl 6-*O*-Benzyl-2,3-dideoxy-β-D-*threo*-hexopyranoside (30A): Compound **30A** was obtained as a colorless liquid from **21** using the same procedure that was used to obtain **29**. Yield: 76% (38 mg); R_f = 0.4 (hexane/ethyl acetate, 3:1); $[\alpha]_D^{28}$ = –22.22 (*c* = 1.8, CH_2Cl_2). IR (neat): $\tilde{\nu}_{max}$ = 3436, 3063, 3030, 2931, 2855, 1604, 1496, 1452, 1365, 1319, 1248, 1206, 1163, 1124, 1100, 1068, 1019, 960, 913, 890, 845, 735, 697 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.34–7.25 (m, 5 H, Ar*H*), 4.61–4.54 (m, 3 H), 3.77–3.61 (m, 5 H), 2.51 (d, *J* = 7.95 Hz, 1 H), 1.98–1.16 (m, 14 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 138.1, 128.5–127.8 (m, Ar-C), 100.2, 76.9, 76.3, 73.7, 70.5, 64.7, 33.8, 32.0, 29.5, 26.2, 25.7, 24.4, 24.2 ppm. HRMS (ESI): calcd. for $C_{19}H_{28}NaO_4$ [M + Na]$^+$ 343.1880; found 343.1885.

Cyclohexyl 4-Acetoxy-6-*O*-benzyl-2,3-dideoxy-β-D-*threo*-hexopyranoside (30B): To a solution of alcohol **30A** (20 mg, 0.06 mmol) in anhydrous CH_2Cl_2 (4 mL) was added Et_3N (13 mg, 0.12 mmol) and Ac_2O (12 mg, 0.11 mmol) at room temperature. The reaction mixture was stirred for 2 h at the same temperature. After completion of the reaction, the reaction mixture was washed with water (5 mL) and brine (5 mL), then the organic layer was dried with Na_2SO_4 and evaporated to obtain the crude acetylated derivative, which was subjected to column chromatography to give pure acetylated product **30B**. Yield: 93% (21 mg); colorless liquid; R_f = 0.4 (hexane/ethyl acetate, 9:1); $[\alpha]_D^{28}$ = –60.0 (*c* = 0.55, CH_2Cl_2). IR (neat): $\tilde{\nu}_{max}$ = 3063, 3030, 2932, 2856, 1737, 1496, 1452, 1370, 1242, 1207, 1165, 1127, 1073, 1017, 956, 927, 908, 890, 862, 738, 698 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.34–7.25 (m, 5 H, Ar*H*), 4.89 (br. s, 1 H, 1-H), 4.62–4.60 (m, 1 H, 4-H), 4.57 (d, *J* = 12.05 Hz, 1 H, -OC*H*Ph), 4.45 (d, *J* = 11.75 Hz, 1 H, -OC*H*Ph), 3.79–3.76 (m, 1 H, 5-H), 3.69–3.65 (m, 1 H, 1′-H), 3.58–3.53 (m, 2 H, 6-H, 6′-H), 2.07–2.04 (m, 1 H, 2-H), 2.02–1.99 (m, 4 H, 3-H, -OAc), 1.91–1.22 (m, 12 H, 3′-H, 2′-H, Cy-C*H*) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 170.7, 138.1, 128.4–127.7 (m, Ar-C), 99.9, 76.4, 75.8, 73.5, 69.2, 66.0, 33.8, 31.9, 27.1, 26.8, 25.7, 24.4, 24.2, 21.2 ppm. HRMS (ESI): calcd. for $C_{21}H_{34}NO_5$ [M + NH_4]$^+$ 380.2431; found 380.2433.

Methyl 4-*O*-(6′-*O*-Benzyl-2′,3′-dideoxy-β-D-*threo*-hex-2′-enopyranosyl)-6-*O*-benzyl-2,3-dideoxy-β-D-*threo*-hex-2-enopyranoside (32): Yield: 68% (41 mg); colorless liquid; R_f = 0.5 (hexane/ethyl acetate, 1:1); $[\alpha]_D^{28}$ = –30.0 (*c* = 0.55, CH_2Cl_2). IR (neat): $\tilde{\nu}_{max}$ = 3411, 3063, 3031, 2923, 2857, 1641, 1602, 1496, 1453, 1368, 1315, 1272, 1096, 1027, 913, 825, 740, 699 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.34–7.25 (m, 10 H, Ar*H*), 6.16–6.13 (m,1 H), 6.12–6.07 (m, 1 H), 5.89 (d, *J* = 10.40 Hz, 1 H), 5.80 (d, *J* = 10.10 Hz, 1 H), 5.23 (br. s, 1 H), 5.01 (br. s, 1 H), 4.65–4.52 (m, 4 H), 4.24 (br. s, 1 H), 3.99–3.90 (m, 2 H), 3.79–3.70 (m, 4 H), 3.62 (dd, *J* = 9.80, 10.05 Hz, 1 H), 3.52 (br. s, 3 H), 1.87 (br. s, 1 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 138.5, 138.1, 131.6, 131.2, 130.6, 128.5–127.6 (m, Ar-C), 98.0, 95.5, 74.5, 74.3, 73.6, 73.5, 69.9, 69.8, 66.8, 62.7, 55.9 ppm. HRMS (ESI): calcd. for $C_{27}H_{32}NaO_7$ [M + Na]$^+$ 491.2040; found 491.2042.

Methyl 4-*O*-[4′-*O*-(6′′-*O*-Benzyl-2′′,3′′-dideoxy-β-D-*threo*-hex-2′′-enopyranosyl)-6′-*O*-benzyl-2′,3′-dideoxy-β-D-*threo*-hex-2′-enopyranosyl]-2,3-dideoxy-β-D-*threo*-hex-2-enopyranoside (33): Yield: 51% (44 mg); colorless liquid; R_f = 0.45 (hexane/ethyl acetate, 1:1); $[\alpha]_D^{28}$ = –90.0 (*c* = 0.60, CH_2Cl_2). IR (neat): $\tilde{\nu}_{max}$ = 3429, 3061, 3030, 2922, 2859, 1646, 1496, 1453, 1395, 1315, 1248, 1206, 1179, 1158, 1118, 1046, 962, 907, 874, 848, 795, 737, 698 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.35–7.25 (m, 15 H, Ar*H*), 6.21–6.17 (m, 1 H), 6.14–6.05 (m, 2 H), 5.87 (dd, *J* = 3.70, 3.75 Hz, 1 H), 5.74 (d, *J* = 10.00 Hz, 1 H), 5.26 (s, 1 H), 5.22 (s, 1 H), 5.01 (s, 1 H), 4.62–4.48 (m, 7 H), 4.26 (br. s, 1 H), 4.18 (br. s, 1 H), 3.97–3.93 (m, 1 H), 3.91–3.87 (m, 2 H), 3.79–3.70 (m, 5 H), 3.68–3.60 (m, 2 H), 3.52 (s, 3 H), 1.85 (d, *J* = 8.30 Hz, 1 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 138.5, 138.4, 138.1, 132.3, 132.1, 131.5, 131.1, 130.7, 128.7–127.6 (m, Ar-C), 98.1, 95.4, 94.8, 74.5, 74.4, 73.6, 73.5, 73.4, 73.4, 70.1, 70.0, 69.7, 66.6, 66.2, 62.7, 55.8 ppm. HRMS (ESI): calcd. for $C_{40}H_{50}NO_{10}$ [M + NH_4]$^+$ 704.3429; found 704.3431.

Phenyl 6-*O*-Benzyl-2,3-dideoxy-α-D-*erythro*-hex-2-enopyranoside (36): Yield: 80% (32 mg); colorless liquid; R_f = 0.6 (hexane/ethyl acetate, 3:1); $[\alpha]_D^{28}$ = +63.52 (*c* = 0.85, CH_2Cl_2). IR (neat): $\tilde{\nu}_{max}$ = 3401, 3031, 2918, 2866, 1593, 1492, 1453, 1389, 1331, 1288, 1223, 1186, 1115, 1076, 1048, 1027, 1003, 981, 814, 754, 735, 694 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.35–7.25 (m, 7 H, Ar*H*), 7.09–6.99 (m, 3 H, Ar*H*), 6.08 (d, *J* = 10.30 Hz, 1 H), 5.91–5.88 (m, 1 H), 5.65 (br. s, 1 H), 4.56 (dd, *J* = 12.00, 12.05 Hz, 2 H), 4.32 (d, *J* = 7.15 Hz, 1 H), 3.98–3.95 (m, 1 H), 3.76 (dd, *J* = 10.05, 9.75 Hz, 1 H), 3.66 (dd, *J* = 10.05, 9.70 Hz, 1 H), 2.48 (d, *J* = 4.60 Hz, 1 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 157.2, 137.5, 133.7, 129.4, 128.4, 127.8, 127.7, 125.1, 122.1, 116.8, 92.7, 73.6, 70.6, 70.2, 65.8 ppm. HRMS (ESI): calcd. for $C_{19}H_{20}NaO_4$ [M + Na]$^+$ 335.1254; found 335.1259.

Benzyl 6-*O*-Benzyl-2,3-dideoxy-α-D-*erythro*-hex-2-enopyranoside (37): Yield: 84% (35 mg); colorless liquid; R_f = 0.5 (hexane/ethyl acetate, 3:2); $[\alpha]_D^{28}$ = +34.28 (*c* = 0.35, CH_2Cl_2). IR (neat): $\tilde{\nu}_{max}$ (=/cm^1: 3347, 3087, 3063, 3030, 2926, 2873, 1605, 1495, 1453, 1207, 1079, 1037, 1021, 912, 816, 735, 697 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.37–7.25 (m, 10 H, Ar*H*), 5.94 (d, *J* = 10.30 Hz, 1 H), 5.77–5.74 (m, 1 H), 5.07 (br. s, 1 H), 4.77 (d, *J* = 11.70 Hz, 1 H), 4.63–4.56 (m, 3 H), 4.24 (d, *J* = 8.60 Hz, 1 H), 3.88–3.84 (m, 1 H), 3.69 (dd, *J* = 9.75, 10.00 Hz, 1 H), 3.63 (dd, *J* = 9.75, 9.75 Hz, 1 H), 2.33 (br. s, 1 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ =

137.8, 137.6, 133.0, 128.4–127.6 (m, Ar-C), 126.0, 93.5, 73.6, 70.6, 70.1, 69.7, 65.9 ppm. HRMS (ESI): calcd. for $C_{20}H_{22}NaO_4$ [M + Na]$^+$ 349.1410; found 349.1418.

Cyclohexyl 6-*O*-Benzyl-2,3-dideoxy-α-D-*erythro*-hex-2-enopyranoside (38): Yield: **71**% (29 mg); colorless liquid; R_f = 0.5 (hexane/ethyl acetate, 3:1); $[\alpha]_D^{28}$ = +25.45 (*c* = 0.55, CH_2Cl_2). IR (neat): $\tilde{\nu}_{max}$ = 3426, 3063, 3031, 2930, 2856, 1723, 1698, 1496, 1452, 1367, 1274, 1182, 1095, 1027, 737, 698 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.34–7.25 (m, 5 H, Ar*H*), 5.92 (d, *J* = 10.40 Hz, 1 H), 5.73–5.70 (m, 1 H), 5.11 (br. s, 1 H), 4.60 (dd, *J* = 11.90, 11.95 Hz, 2 H), 4.21 (d, *J* = 6.75 Hz, 1 H), 3.90–3.86 (m, 1 H), 3.75 (dd, *J* = 9.80, 9.75 Hz, 1 H), 3.68 (dd, *J* = 10.10, 9.80 Hz, 1 H), 3.63–3.58 (m, 1 H), 2.23 (d, *J* = 5.15 Hz, 1 H), 1.93–1.86 (m, 2 H), 1.74–1.68 (m, 2 H), 1.54–1.51 (m, 1 H), 1.40–1.14 (m, 5 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 137.8, 132.7, 128.5–126.9 (m, Ar-C), 92.6, 76.4, 73.7, 70.9, 69.6, 66.0, 34.0, 32.2, 25.6, 24.5, 24.3 ppm. HRMS (ESI): calcd. for $C_{19}H_{26}NaO_4$ [M + Na]$^+$ 341.1723; found 341.1729.

Methyl 6-*O*-(6′-*O*-Benzyl-2′,3′-dideoxy-α-D-*erythro*-hex-2′-enopyranosyl)-2,3,4-tri-*O*-benzyl-α-D-glucopyranoside (40): Yield: 64% (56 mg); colorless liquid; R_f = 0.5 (hexane/ethyl acetate, 1:1); $[\alpha]_D^{28}$ = +39.20 (*c* = 1.25, CH_2Cl_2). IR (neat): $\tilde{\nu}_{max}$ = 3436, 3088, 3063, 3030, 2919, 1644, 1496, 1453, 1362, 1328, 1261, 1192, 1158, 1093, 1072, 1051, 1028, 912, 737, 697 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.34–7.24 (m, 20 H, Ar*H*), 5.91 (d, *J* = 10.10 Hz, 1 H), 5.76–5.73 (m, 1 H), 5.02 (br. s, 1 H), 4.96 (d, *J* = 11.00 Hz, 1 H, -OC*H*Ph), 4.88 (d, *J* = 11.00 Hz, 1 H, -OC*H*Ph), 4.79 (d, *J* = 10.40 Hz, 1 H, -OC*H*Ph), 4.77 (d, *J* = 11.90 Hz, 1 H, -OC*H*Ph), 4.66–4.59 (m, 3 H), 4.45–4.42 (m, 2 H), 4.21 (d, *J* = 8.55 Hz, 1 H), 4.04–3.96 (m, 2 H), 3.75–3.50 (m, 6 H), 3.37–3.32 (m, 4 H), 2.44 (br. s, 1 H) ppm. ^{13}C NMR (125 MHz): δ = 138.9, 138.5, 137.6, 132.8, 128.5–127.4 (m, Ar-C), 125.9, 98.2, 94.7, 82.1, 79.9, 77.8, 75.7, 74.9, 73.7, 73.4, 70.9, 70.0, 69.6, 67.0, 66.2, 55.2 ppm. HRMS (ESI): calcd. for $C_{41}H_{46}NaO_9$ [M + Na]$^+$ 705.3034; found 705.3045.

Methyl 4-*O*-(6′-*O*-Benzyl-2′,3′-dideoxy-α-D-*erythro*-hex-2′-enopyranosyl)-2,3,6-tri-*O*-benzyl-α-D-glucopyranoside (41): Yield: 57% (50 mg); colorless liquid; R_f = 0.5 (hexane/ethyl acetate, 1:1); $[\alpha]_D^{28}$ = +40.0 (*c* = 0.5, CH_2Cl_2). IR (neat): $\tilde{\nu}_{max}$ = 3445, 3087, 3062, 3030, 2916, 2866, 1604, 1496, 1453, 1370, 1319, 1243, 1158, 1098, 1046, 912, 869, 851, 790, 738, 698 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.36–7.22 (m, 20 H, Ar*H*), 5.84 (d, *J* = 10.10 Hz, 1 H, -OC*H*Ph), 5.49–5.43 (m, 1 H), 5.42 (br. s, 1 H), 5.01 (d, *J* = 11.30 Hz, 1 H, -OC*H*Ph), 4.71 (dd, *J* = 11.90, 11.30 Hz, 2 H, 2× -OC*H*Ph), 4.63–4.60 (m, 2 H), 4.53 (d, *J* = 12.20 Hz, 1 H, -OC*H*Ph), 4.48 (d, *J* = 12.20 Hz, 1 H, -OC*H*Ph), 4.43 (d, *J* = 12.25 Hz, 1 H, -OC*H*Ph), 4.42 (d, *J* = 11.95 Hz, 1 H, -OC*H*Ph), 4.16–4.12 (m, 1 H), 3.94 (t, *J* = 9.20 Hz, 1 H), 3.82–3.78 (m, 1 H), 3.72–3.50 (m, 6 H), 3.43–3.37 (m, 4 H), 2.30 (d, *J* = 4.60 Hz, 1 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 138.6, 138.4, 138.0, 137.6, 132.8, 128.6–127.4 (m, Ar-C), 125.7, 97.7, 95.4, 82.1, 80.1, 75.9, 75.7, 73.7, 73.3, 73.1, 70.6, 69.9, 69.7, 69.5, 65.8, 55.2 ppm. HRMS (ESI): calcd. for $C_{41}H_{46}NaO_9$ [M + Na]$^+$ 705.3034; found 705.3044.

Methyl 3-*O*-(6′-*O*-Benzyl-2′,3′-dideoxy-α-D-*erythro*-hex-2′-enopyranosyl)-2,4,6-tri-*O*-benzyl-α-D-glucopyranoside (42): Yield: 56% (49 mg); colorless liquid; R_f = 0.6 (hexane/ethyl acetate, 3:1); $[\alpha]_D^{28}$ = +52.5 (*c* = 0.4, CH_2Cl_2). IR (neat): $\tilde{\nu}_{max}$ = 3443, 3088, 3063, 3031, 2922, 2865, 1725, 1649, 1496, 1453, 1365, 1326, 1267, 1193, 1095, 1046, 909, 737, 698 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.35–7.23 (m, 20 H, Ar*H*), 5.91 (d, *J* = 10.10 Hz, 1 H), 5.66–5.62 (m, 1 H), 5.35 (br. s, 1 H), 4.69–4.60 (m, 4 H), 4.56–4.42 (m, 5 H), 4.34 (d, *J* = 11.90 Hz, 1 H, -OC*H*Ph), 4.12 (t, *J* = 9.15 Hz, 1 H), 3.75–3.68 (m, 2 H), 3.64–3.58 (m, 3 H), 3.45–3.39 (m, 3 H), 3.31 (br. s, 3 H), 2.67 (br. s, 1 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 138.5, 138.9, 138.8, 133.1, 128.6–127.5 (m, Ar-C), 125.9, 98.2, 95.0, 79.0, 78.5, 78.0, 76.9, 74.8, 73.6, 71.2, 69.8, 68.8, 68.4, 66.7, 55.1 ppm. HRMS (ESI): calcd. for $C_{41}H_{46}NaO_9$ [M + Na]$^+$ 705.3034; found 705.3041.

L-Tyrosine *N*-[(1,1-Dimethylethoxy)carbonyl]-*O*-(6-*O*-benzyl-2,3-dideoxy-α-D-*erythro*-hex-2-enopyranosyl) Methyl Ester (43): Yield: 67% (44 mg); colorless liquid; R_f = 0.5 (hexane/ethyl acetate, 1:1); $[\alpha]_D^{28}$ = +15.0 (*c* = 1.0, CH_2Cl_2). IR (neat): $\tilde{\nu}_{max}$ = 3418, 3063, 3031, 2976, 2924, 2868, 1743, 1713, 1611, 1509, 1452, 1391, 1366, 1226, 1166, 1111, 1094, 1052, 1026, 986, 836, 779, 737, 699 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.35–7.25 (m, 5 H, Ar*H*), 7.02–7.00 (m, 4 H, Ar*H*), 6.08 (d, *J* = 10.10 Hz, 1 H), 5.88–5.86 (m, 1 H), 5.60 (br. s, 1 H), 4.96 (d, *J* = 7.95 Hz, 1 H), 4.60–4.53 (m, 3 H), 4.32 (d, *J* = 8.85 Hz, 1 H), 3.95–3.92 (m, 1 H), 3.76 (dd, *J* = 4.30, 4.60 Hz, 1 H), 3.70 (br. s, 3 H), 3.65 (dd, *J* = 6.10, 6.10 Hz, 1 H), 3.08–2.97 (m, 2 H), 2.54 (br. s, 1 H), 1.41 (br. s, 9 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 172.4, 156.5, 155.2, 137.6, 133.9, 130.3, 128.6–127.8 (m, Ar-C), 125.2, 117.0, 93.0, 80.0, 73.8, 70.7, 70.3, 65.9, 54.5, 52.3, 37.5, 28.4 ppm. HRMS (ESI): calcd. for $C_{28}H_{39}N_2O_8$ [M + NH_4]$^+$ 531.2701; found 531.2715.

L-Serine *N*-[(1,1-Dimethylethoxy)carbonyl]-*O*-(6-*O*-benzyl-2,3-dideoxy-α-D-*erythro*-hex-2-enopyranosyl) Methyl Ester (44): Yield: 68% (38 mg); colorless liquid; R_f = 0.6 (hexane/ethyl acetate, 1:1); $[\alpha]_D^{28}$ = –7.14 (*c* = 0.7, CH_2Cl_2). IR (neat): $\tilde{\nu}_{max}$ = 3372, 3066, 2977, 2929, 2851, 1748, 1714, 1511, 1453, 1392, 1367, 1297, 1249, 1213, 1164, 1058, 853, 781, 738, 699 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.36–7.25 (m, 5 H, Ar*H*), 5.92 (d, *J* = 10.30 Hz, 1 H), 5.66–5.61 (m, 2 H), 4.91 (br. s, 1 H), 4.60 (dd, *J* = 12.05, 12.05 Hz, 2 H), 4.46–4.42 (m, 1 H), 4.25–4.21 (m, 1 H), 4.01 (dd, *J* = 10.60, 10.60 Hz, 1 H), 3.91 (dd, *J* = 10.60, 10.60 Hz, 1 H), 3.82–3.67 (m, 6 H), 2.45 (br. s, 1 H), 1.43 [br. s, 9 H, -C(C*H*$_3$)$_3$] ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 171.1, 155.6, 137.6, 133.2, 128.6–127.8 (m, Ar-C), 125.4, 95.2, 80.0, 73.8, 70.6, 69.9, 69.5, 65.7, 54.2, 52.5, 28.3 ppm. HRMS (ESI): calcd. for $C_{22}H_{32}NO_8$ [M + H]$^+$ 438.2122; found 438.2123.

L-Threonine *N*-[(1,1-Dimethylethoxy)carbonyl]-*O*-(6-*O*-benzyl-2,3-dideoxy-α-D-*erythro*-hex-2-enopyranosyl) Methyl Ester (45): Yield: 64% (37 mg); colorless liquid; R_f = 0.6 (hexane/ethyl acetate, 1:1); $[\alpha]_D^{28}$ = +8.0 (*c* = 0.75, CH_2Cl_2). IR (neat): $\tilde{\nu}_{max}$ = 3426, 3063, 3030, 2978, 2932, 1746, 1716, 1509, 1453, 1392, 1367, 1254, 1212, 1166, 1093, 1063, 965, 907, 879, 777, 738 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.34–7.25 (m, 5 H, Ar*H*), 5.93 (d, *J* = 10.30 Hz, 1 H), 5.75–5.71 (m, 1 H), 5.32 (d, *J* = 7.75 Hz, 1 H), 4.85 (br. s, 1 H), 4.60 (dd, *J* = 12.00, 12.00 Hz, 2 H), 4.30–4.23 (m, 1 H), 3.80–3.67 (m, 5 H), 3.41 (s, 3 H), 2.45 (d, *J* = 5.15 Hz, 1 H), 1.44 (br. s, 9 H), 1.23 (d, *J* = 6.3 Hz, 3 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 172.0, 156.2, 137.8, 133.1, 128.5–127.8 (m, Ar-C), 125.9, 95.4, 80.2, 73.7, 70.8, 69.7, 68.2, 65.9, 58.7, 55.9, 28.3, 19.9 ppm. HRMS (ESI): calcd. for $C_{23}H_{33}NNaO_8$ [M + Na]$^+$ 474.2098; found 474.2106.

Benzyl 4,6-*O*-Dibenzyl-2,3-dideoxy-α-D-*erythro*-hex-2-enopyranoside (46): To a stirred solution of NaH (60% suspension in paraffin oil, 6 mg, 0.25 mmol) in DMF (2 mL) was added allylic alcohol **37** (50 mg, 0.15 mmol) in DMF (2 mL) dropwise at 0 °C. The reaction mixture was treated with benzyl bromide (38 mg, 0.22 mmol) at the same temperature and stirring was continued for 1 h at room temperature. Excess NaH was quenched by pouring the reaction mixture onto ice and the mixture was extracted with diethyl ether (3× 10 mL) followed by washing with water (10 mL) and brine (10 mL). The organic layer was dried with Na_2SO_4 and concentrated in vacuo and the crude product purified by column

chromatography to give benzylated product **46**. Yield: 94% (60 mg); colorless liquid; R_f = 0.6 (hexane/ethyl acetate, 3:1); $[\alpha]_D^{28}$ = +79.39 (c = 1.65, CH_2Cl_2). IR (neat): $\tilde{\nu}_{max}$ = 3062, 3030, 2864, 1604, 1496, 1454, 1400, 1304, 1206, 1095, 1040, 1025, 734, 697 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 7.35–7.23 (m, 15 H, Ar*H*), 6.08 (d, J = 10.10 Hz, 1 H), 5.80–5.77 (m, 1 H), 5.12 (br. s, 1 H), 4.81 (d, J = 11.60 Hz, 1 H), 4.66–4.43 (m, 5 H), 4.20–4.18 (m, 1 H), 4.02–3.99 (m, 1 H), 3.74–3.62 (m, 2 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 138.3, 138.2, 138.1, 130.9, 128.4–127.6 (m, Ar-C), 126.6, 94.0, 73.4, 71.1, 70.4, 70.1, 69.4, 68.8 ppm. HRMS (ESI): calcd. for $C_{27}H_{28}NaO_4$ $[M + Na]^+$ 439.1880; found 439.1881.

Cyclohexyl 4,6-*O*-Dibenzyl-2,3-dideoxy-α-D-*erythro*-hex-2-enopyranoside (47): Compound **47** was obtained as a colorless liquid from **38** using the same procedure that was used to obtain **46**. Yield: 84% (54 mg); colorless liquid; R_f = 0.6 (hexane/ethyl acetate, 3:1); $[\alpha]_D^{28}$ = +85.71 (c = 0.7, CH_2Cl_2). IR (neat): $\tilde{\nu}_{max}$ = 3064, 3032, 2928, 2855, 1740, 1605, 1496, 1454, 1365, 1303, 1265, 1206, 1186, 1097, 1071, 1027, 909, 736, 698 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 7.35–7.23 (m, 10 H, Ar*H*), 6.05 (d, J = 10.10 Hz, 1 H), 5.76–5.73 (m, 1 H), 5.16 (br. s, 1 H), 4.66–4.41 (m, 4 H), 4.15 (d, J = 9.45 Hz, 1 H), 4.03–4.01 (m, 1 H), 3.75–3.63 (m, 3 H), 1.93–1.22 (m, 10 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 138.3, 138.2, 130.3, 128.4–127.6 (m, Ar-C), 127.4, 92.8, 76.1, 73.4, 71.0, 70.5, 69.1, 69.0, 33.9, 32.2, 25.7, 24.5, 24.3 ppm. HRMS (ESI): calcd. for $C_{26}H_{32}NaO_4$ $[M + Na]^+$ 431.2193; found 431.2198.

Methyl 4-*O*-(6′-*O*-Benzyl-2′,3′-dideoxy-α-D-*erythro*-hex-2′-enopyranosyl)-6-*O*-benzyl-2,3-dideoxy-α-D-*erythro*-hex-2-enopyranoside (49): Yield: 65% (39 mg); colorless liquid; R_f = 0.5 (hexane/ethyl acetate, 1:1); $[\alpha]_D^{28}$ = +54.0 (c = 0.5, CH_2Cl_2). IR (neat): $\tilde{\nu}_{max}$ = 3445), 3087, 3031, 2910, 1648, 1602, 1496, 1452, 1396, 1365, 1295, 1252, 1187, 1099, 1050, 998, 964, 822, 738, 698 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 7.36–7.23 (m, 10 H, Ar*H*), 6.02 (d, J = 10.30 Hz, 1 H), 5.93 (d, J = 10.30 Hz, 1 H), 5.81–5.78 (m, 1 H), 5.66–5.63 (m, 1 H), 5.17 (br. s, 1 H), 4.90 (br. s, 1 H), 4.56 (d, J = 4.85 Hz, 2 H), 4.49 (d, J = 12.00 Hz, 1 H), 4.42–4.38 (m, 2 H), 4.26–4.21 (m, 1 H), 3.95–3.92 (m, 1 H), 3.73–3.71 (m, 1 H), 3.70–3.61 (m, 2 H), 3.50 (dd, J = 9.45, 9.45 Hz, 1 H), 3.46–3.42 (m, 4 H), 2.34 (br. s, 1 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 138.5, 137.6, 133.2, 129.6, 128.6–127.5 (m, Ar-C), 127.0, 125.8, 95.4, 91.1, 73.7, 73.3, 70.6, 69.9, 69.6, 69.1, 67.3, 65.9, 55.8 ppm. HRMS (ESI): calcd. for $C_{27}H_{32}NaO_7$ $[M + Na]^+$ 491.2040; found 491.2048.

Methyl 4-*O*-[4′-*O*-(6′′-*O*-Benzyl-2′′,3′′-dideoxy-α-D-*erythro*-hex-2′′-enopyranosyl)-6′-*O*-benzyl-2′,3′-dideoxy-α-D-*erythro*-hex-2′-enopyranosyl]-2,3-dideoxy-α-D-*erythro*-hex-2-enopyranoside (50): Yield: 52% (45 mg); colorless liquid; R_f = 0.45 (hexane/ethyl acetate, 1:1); $[\alpha]_D^{28}$ = +58.88 (c = 0.45, CH_2Cl_2). IR (neat): $\tilde{\nu}_{max}$ = 3433, 3063, 3031, 2920, 1647, 1598, 1496, 1453, 1396, 1365, 1294, 1254, 1188, 1097, 1038, 997, 965, 820, 738, 698 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 7.33–7.22 (m, 15 H, Ar*H*), 6.04–5.93 (m, 3 H), 5.85–5.79 (m, 1 H), 5.71–5.65 (m, 2 H), 5.21 (br. s, 1 H), 5.17 (br. s, 1 H), 4.89 (br. s, 1 H), 4.56–4.36 (m, 8 H), 4.28–4.20 (m, 1 H), 3.98–3.92 (m, 1 H), 3.81–3.54 (m, 7 H), 3.49–3.46 (m, 1 H), 3.43 (br. s, 3 H), 2.43 (br. s, 1 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 138.5, 138.3, 137.5, 133.3, 129.9, 129.9, 128.6–127.5 (m, Ar-C), 127.0, 126.7, 125.7, 95.3, 91.4, 91.0, 73.7, 73.4, 73.2, 70.6, 69.8, 69.8, 69.1, 67.4, 67.3, 66.7, 66.0, 65.8, 55.8 ppm. HRMS (ESI): calcd. for $C_{40}H_{46}NaO_{10}$ $[M + Na]^+$ 709.2983; found 709.2982.

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

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[16] See the Experimental Section and the Supporting Information.

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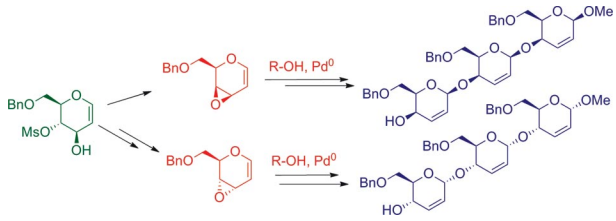
Selective O-Glycosylation



A regio- and stereoselective O-glycosylation of D-glucal-derived vinyl oxiranes as excellent glycosyl donors has been accomplished by using Pd^0 as catalyst. The reaction is completed in a short time (ca. 5 min) to give the corresponding *O*-glycosides in good to excellent yields.

Y. S. Reddy, R. Lahiri, Y. D. Vankar* 1–12

Palladium-Catalyzed Improved Regio- and Stereoselective O-Glycosylation of D-Glucal-Derived β- and α-Vinyl Oxiranes

Keywords: Allylic compounds / Glycosylation / Epoxides / Palladium / Glycosides

