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$ZnCl_2$/alumina impregnation catalyzed Ferrier rearrangement: an expedient synthesis of pseudoglycosides

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ABSTRACT

An improved method for the synthesis of 2,3-unsaturated-*O*-glycosides has been developed. $ZnCl_2$ impregnated on activated alumina acts as an excellent reagent system for the conversion of 2,4,6-tri-*O*-acetyl-D-glucal to 2,3-unsaturated-*O*-glycosides with high α-selectivity.

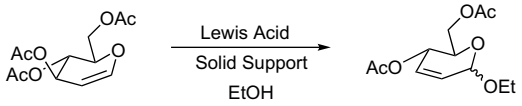
1. Introduction

2,3-Unsaturated-*O*-glycosides or pseudoglucals are known as versatile chiral intermediates in the synthesis of antibiotics, nucleosides, complex carbohydrates, and various natural products.[1] Moreover, the unsaturated part of the sugar ring allows many straightforward modifications such as hydrogenation, hydroxylation, epoxidation, and aminohydroxylation, which contribute to their diversities and complexities. To date, many continuous efforts to develop expedient syntheses of 2,3-unsaturated-*O*-glycosides have been extensively made. One of the most common procedures to achieve pseudoglucals is the acid-catalyzed allyl rearrangement of glucals, which was discovered by Ferrier et al.[2] The Ferrier rearrangement is a reliable procedure for the formation of unsaturated glycoside derivatives, which has seen expensive development over decades. This rearrangement typically occurs by treatment of glucals and alcohols with Lewis acids or oxidants such as $ZnCl_2$,[3] H_3PO_4,[4] $InCl_3$,[5] $SnCl_4$,[6] $Yb(OTf)_3$,[7] $FeCl_3$,[8] montmorillionite K-10,[9] $LiBF_4$,[10] $Dy(OTf)_3$,[11] DDQ,[12] I_2,[13] $I(Coll)_2ClO_4$,[14] CAN,[15] $CeCl_3\cdot 7H_2O$,[16] $HClO_4/SiO_2$,[17] and *N*-iodosuccinamide.[18] These methods could generate rearrangement products in one-step from glycoside derivatives, but they often suffer from incomplete stereoselectivity and the limited uses of acid-labile glucal donors and acceptors. The oxidants are usually required in stoichiometric amounts, and stringent conditions, long reaction times, and high temperatures are unavoidable. Thus, any further improvement must be judged against the vast background of current knowledge. Here, we wish to report a new synthetic component of Ferrier reaction, which delivers the desired products with exclusive α-stereoselectivity in high yield and in a short reaction time.

2. Results and discussion

A facile and highly stereoselective preparation of 2,3-unsaturated-*O*-glycoside derivatives from 3,4,6-tri-*O*-acetyl-D-glucal was initially investigated by examining the incorporation of Lewis acid on different solid supports. Pursuing the environmental impact, all reactions were carried out with minimal solvent and at ambient temperature. We surveyed the catalytic activity of various Lewis acids in the glycosylation of glucal by employing ethanol as a glucal acceptor and Al_2O_3 as a solid media (Table 1). Among them, $ZnCl_2$ was found to be superior to other catalysts in terms of yield, reaction profile and selectivity. However, strong Lewis acids [$FeCl_3$, $SnCl_2$, $AlCl_3$ and $BF_3\cdot OEt_2$] also provided pseudoglucal products, albeit with moderate yields and selectivities (Table 1, entries 1–4).

Table 1
Optimized conditions for Ferrier rearrangement with Lewis acids/solid supports[a]



Entry	Lewis Acid/solid support[b]	Time	% Yield (α/β)[c]
1	$FeCl_3\cdot 6H_2O/Al_2O_3$	30 min	86 (1:1)
2	$SnCl_2/Al_2O_3$	45 min	32 (6:1)
3	$AlCl_3/Al_2O_3$	80 min	60 (8:1)
4	$BF_3\cdot OEt_2/Al_2O_3$	30 min	56 (8:1)
5	$ZnCl_2/Al_2O_3$	10 min	92 (20:1)
6	$ZnCl_2/SiO_2$	2 h	48 (6:1)
7	$ZnCl_2$/MgO	6 h	72 (2:1)
8	$ZnCl_2$/4 Å molecular sieve	4 h	Trace
9	$ZnCl_2$/MnO	6 h	75(1:1)

[a] Ethanol (10 equiv) was used.
[b] Lewis acid (1 equiv) on 5.3 equiv of solid support was used per 1 equiv of tri-*O*-acetyl-D-glucal.
[c] α/β ratio was confirmed by the anomeric proton ratio on 500 MHz NMR.

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To study the effect of the solid media, a wide range of solid supports such as silical gel, MgO, 4 Å molecular sieves, MnO, and Al_2O_3 were examined by mixing with 1 equiv of $ZnCl_2$. The results showed that silica gel and molecular sieves had no impact on the rearrangement, whereas MgO and MnO found to be less efficient in both conversion and anomeric selectivity (Table 1, entries 6–9). $ZnCl_2$ impregnated on activated alumina was conclusively the best combination in this synthetic transformation giving rise to a good anomeric ratio (α/β=20:1) and short reaction time (10 min) as shown in Table 1, entry 5.

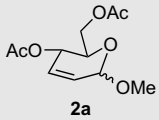
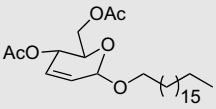
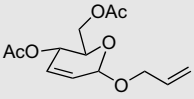
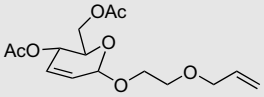
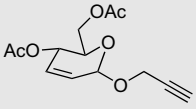
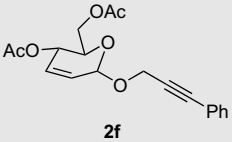
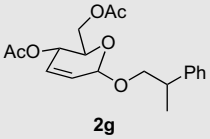
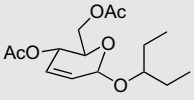
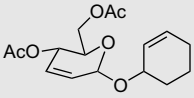
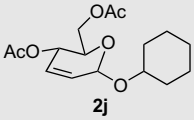
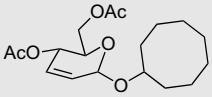
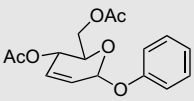
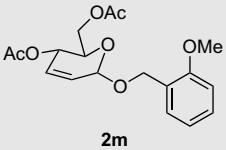
According to the published results, most of the Ferrier reactions of 3,4,6-tri-*O*-acetyl-D-glycal conducted in the solution phase[3] and the miscellaneous system[17] were sluggish (12 h) and showed the low level of the anomeric selectivity. Moreover, some reactions required considerable care when using toxic and moisture sensitive catalysts. These cause problems, the tedious procedures and work-up and require special equipments. On the other hand, the solvent free $ZnCl_2/Al_2O_3$ system[19] acts as a potential tool for synthesis of 2,3-unsaturated glycosides. The purification could be easily done after the completion of the reaction (10–30 min) by silica gel column chromatography.

Having the optimized conditions for the glycosylation of glucal over $ZnCl_2$/alumina impregnation in hand we proceeded to screen a wide range of alcohols and thiols (Table 2). In a typical reaction, a mixture of glucal and alcohol was added to the $ZnCl_2$/alumina impregnation and stirred. In order to maintain the proper stirring of the reaction mixture excess of alcohol was used (3 equiv). When the reaction was completed, the solid mass was simply filtered off, rinsed with dichloromethane (or ethyl acetate). Evaporation of the solvent and subsequent elution of the crude product on the short column chromatography afforded the desired 2,3-unsaturated glycosides (**2a**–**p**) in excellent yields. All reactions gave best yields when 1 equiv of $ZnCl_2$ used with 5.3 equiv of activated alumina. Using methanol and ethanol as nucleophiles gave a mixture of anomeric diastereomers (up to α/β 20:1), while others irrespective of size and nature furnished desired α-glycosides. Moreover, this compliment could be cooperated with a glucose derivative to give the corresponding disaccharide **2p** in 94% yield and 20:1 of α/β ratio (entry 16).

Most of the glycosylated products were obtained in exclusively pure diastereomers as resulted in Table 2. The significance of the highly stereoselective glycosylation has been highlighted in this report. We then explored the scope of this concise route for the synthesis of pseudoglucals connected to various biologically important natural products. For example, citronellol,[23] L-menthol,[24] borneol,[24] *endo*-fenchol, and pregnenolone[25] glycosides, these all have served as challenging targets to study and transform because of their diversity of the biological activities and their structural complexity.

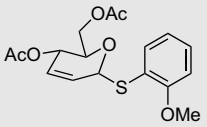
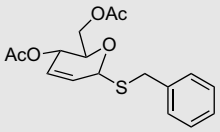
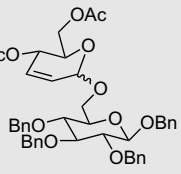
Some of them were generally synthesized by enzymatic[26] as well as Koenigs–Knorr–Zemplen[24] methods, which are expensive, lengthy, and tedious procedures. We envisioned that our solid support system would offer an easy access to natural products containing α-selective sugar moiety. As expected, transformation of glucal to the corresponding 2,3-unsaturated glycosides was rapid and the desired compounds were formed exclusively with α-anomeric selectivity within 10–15 min of reaction time (Table 3, entries 1–4). Pregnenolone glycoside, which was first isolated from *Nerium Odorum*,[25] operates as a powerful neurosteroid in the brain, modulating the transmission of messages from neuron to neuron and strongly influencing learning and memory. The synthesis of pregnenolone 2,3-unsaturated glycoside was also success with excellent α-selectivity (88% yield and 20:1 α/β selectivity) as described in Table 3, entry 5. Furthermore, its structure was elucidated by NMR spectroscopic data and confirmed by X-ray crystallography (Fig. 1).

Table 2
Ferrier reaction of 2,3-tri-*O*-acetyl-D-glucal with alcohols in the presence of the $ZnCl_2/Al_2O_3$ reagent system[a]

Entry	Product	Time (min)	Yield (%)	α/β[d]
1[b]	 **2a**	10	92[2c]	20:3
2[c]	 **2b**	20	94	α
3	 **2c**	20	83[11]	α
4	 **2d**	30	78	α
5	 **2e**	10	88[11]	α
6	 **2f**	20	82	α
7	 **2g**	45	70	α
8	 **2h**	10	85	α
9	 **2i**	10	85	α
10	 **2j**	10	85[20]	α
11	 **2k**	20	82	α
12	 **2l**	15	90[11]	α
13	 **2m**	10	75[21]	α

(*continued on next page*)

Table 2 (*continued*)

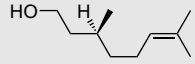
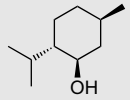
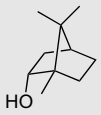
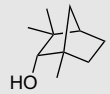
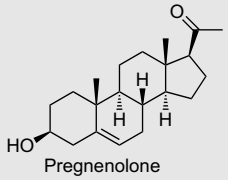
Entry	Product	Time (min)	Yield (%)	α/β[d]
14	 **2n**	10	62	α
15	 **2o**	10	65[22]	α
16[c]	 **2p**	20	94	20:1

[a] Unless otherwise noted, 3 equiv of nucleophiles were used.
[b] 10 Equiv of methanol was used.
[c] As nucleophile is solid, glucal, 1 equiv of alcohol and $ZnCl_2/Al_2O_3$ impregnation were mixed and grinded by using a mortar.
[d] α/β ratio was confirmed by the anomeric proton ratio on ^1H NMR spectra.

3. Conclusion

We have demonstrated a new protocol for forming a glycosidic linkage in high diastereoselective fashion. Many complex alcohols and thiols could be incorporated with glucal donor in a single process. Eleven new compounds, which include five natural product-like compounds, were successfully prepared. The main advantages of this method concern high anomeric selectivity, rapid reaction time, and friendly environmental conditions. Low cost reagents and no aqueous work-up are required and the alumina could be recycled (up to three times).

Table 3
Ferrier reaction of 2,3-tri-*O*-acetyl-D-glucal with various natural products alcohols in the presence of the $ZnCl_2/Al_2O_3$ reagent system

Entry	Natural product alcohols	Product	Time (min)	Yield (%)	α/β
1	 S-(-)-β-Citronellol	**3a**	15	85[26]	α
2[a]	 L-Menthol	**3b**	10	92	α
3[a]	 (+)-Borneol	**3c**	10	80	α
4[a]	 (+)-endo-Fenchol	**3d**	15	84	α
5[a]	 Pregnenolone	**3e**	20	88	20:1

[a] As these nucleophiles are solids, 1 equiv of them and glucal, $ZnCl_2/Al_2O_3$ impregnation were mixed and grinded by using a mortar.

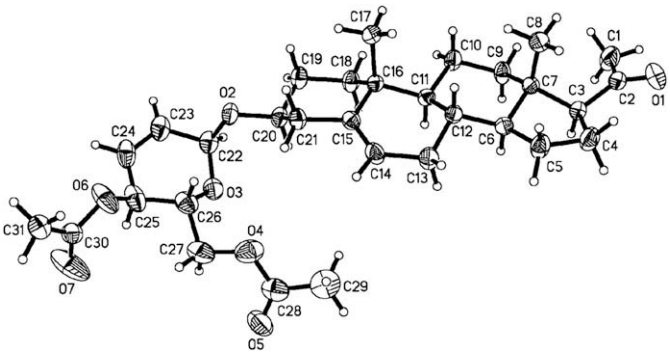


Figure 1. X-ray structure of pregnenolone 2,3-unsaturated glycoside **3e**.

4. Experimental

4.1. General

Product purification by flash column chromatography was accomplished using silica gel 60 (0.010–0.063 nm). The ^1H and ^{13}C NMR data was obtained on a 300 MHz Bruker ACF 300 and 500 MHz Bruker AMX 500 NMR spectrometers. For ^1H NMR, chemical shifts are reported in parts per million (ppm) downfield from tetramethylsilane and are, in all cases, referenced to the residual proton resonance peaks: δ 7.26 for $CHCl_3$. The ^{13}C NMR chemical shifts were reported in parts per million relative to the center peak of the multiplet for deuterated solvents: δ 77.0 (t) for $CDCl_3$. Coupling constants (J) for all spectra are reported in hertz. Following abbreviations classify the multiplicity: s=singlet, d=doublet, t=triplet, q=quartet, m=multiplet or unresolved, br=broad signal. Infrared spectra were measured on a Bio-RAD FTS 165 FT-IR Spectrometer as thin films on sodium bromide plates and are recorded in units of cm^{-1}. HRMS (ESI) spectra were recorded on a Finnigan/MAT LCQ quadrupole ion trap mass spectrometer, coupled with the TSP4000 HPLC system and the Crystal 310 CE system. X-ray crystallographic data were collected by using a Bruker X8Apex diffractometer with Mo Kα radiation (graphite monochromator).

4.2. General procedure for preparation 2,3-unsaturated glycosides

To a stirred mixture of tri-*O*-acetyl-D-glucal (100 mg, 0.37 mmol) and an alcohol (1 equiv) was added 250 mg of $ZnCl_2/Al_2O_3$ at ambient temperature. The mixture was stirred for appropriate time (Tables 2 and 3), and completion of the reaction was monitored by TLC analysis. The reaction mixture was then filtered and washed with dichloromethane, and the combined organic extract was concentrated under vacuum. All the products were purified by silica gel column chromatography (30% EtOAc/hexane).

*4.2.1. Nonadecanyl 4,6-di-O-acetyl-2,3-dideoxy-α-D-erythro-hex-2-enopyranoside (**2b**)*

R_f (30% EtOAc/hexane) 0.67; $[\alpha]_D^{24}$ +83.3 (*c* 0.7, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 5.84 (d, J=10 Hz, 1H), 5.80 (d, J=10 Hz, 1H), 5.29 (d, J=10 Hz, 1H), 5.0 (s, 1H), 4.23 (dd, J=12.1, 5.4 Hz, 1H), 4.15 (dd, J=12.1, 2.2 Hz, 1H), 4.10–4.08 (m, 1H), 3.75 (dt, J=9.4, 6.9 Hz, 1H), 3.48 (dt, J=9.5, 6.6 Hz, 1H), 2.07 (s, 3H), 2.06 (s, 3H), 1.61–1.52 (m, 2H), 1.29–1.23 (m, 30H), 0.86 (t, J=6.9 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.7, 170.2, 128.9, 127.9, 94.3, 69.0, 66.8, 65.3, 63.0, 32.8,

31.9, 29.7, 29.6, 29.6, 29.4, 29.3, 26.2, 26.0, 25.7, 22.6, 20.9, 20.7, 14.1; IR (NaCl neat) ν_{max}/cm^{-1} 1747, 1226, 1039; HRMS (ESI) m/z $[M+Na]^+$ calcd for $C_{28}H_{50}O_7Na$ 505.3505, found 505.3509.

4.2.2. 2-(Allyloxy)ethanyl 4,6-di-O-acetyl-2,3-dideoxy-α-D-erythro-hex-2-enopyranoside (**2d**)

R_f (30% EtOAc/hexane) 0.35; $[\alpha]_D^{24}$ +272.2 (*c* 0.4, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 5.90 (ABX system, J_{AX}=17.2 Hz, J_{BX}=9.6 Hz, J_{AB}=5.4 Hz, 1H), 5.85 (br s, 2H), 5.30 (d, *J*=9.7 Hz, 1H) 5.26 (dd, *J*=17.2, 1.6 Hz, 1H), 5.16 (d, *J*=9.5 Hz, 1H), 5.06 (s, 1H), 4.23 (dd, *J*=12.1, 5.2 Hz, 1H), 4.15 (dd, *J*=12.1, 2.3 Hz, 1H), 4.12–4.10 (m, 1H), 4.0 (d, *J*=5.0 Hz, 2H), 3.89 (dt, *J*=11.0, 4.5 Hz, 1H), 3.72–3.68 (m, 1H), 3.61 (t, *J*=4.8 Hz, 2H), 2.07 (s, 3H), 2.05 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.7, 170.2, 134.6, 129.1, 127.7, 117.1, 94.6, 72.1, 69.2, 67.8, 66.8, 65.2, 62.9, 20.9, 20.7; IR (NaCl neat) ν_{max}/cm^{-1} 1743, 1317, 1234, 1047; HRMS (ESI) m/z $[M+Na]^+$ calcd for $C_{15}H_{22}O_7Na$ 337.1263, found 337.1252.

4.2.3. 3-Phenylprop-2-ynyl 4,6-di-O-acetyl-2,3-dideoxy-α-D-erythro-hex-2-enopyranoside (**2f**)

R_f (50% EtOAc/hexane) 0.52; $[\alpha]_D^{24}$ +196.0 (*c* 0.5, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 7.46–7.42 (m, 2H), 7.32–7.29 (m, 3H), 5.93 (d, *J*=17.5 Hz, 1H), 5.42–5.33 (m, 2H), 4.53 (s, 1H), 4.28 (dd, *J*=12.1, 5.1 Hz, 1H), 4.20 (dd, *J*=12.1, 2.4 Hz, 1H), 4.19–4.11 (m, 1H), 2.09 (s, 3H), 2.07 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.7, 170.2, 131.8, 129.6, 128.6, 128.4, 128.3, 127.4, 122.3, 92.7, 86.5, 67.2, 65.2, 62.8, 55.8, 20.9, 20.7; IR (NaCl neat) ν_{max}/cm^{-1} 1743, 1371, 1234, 1037; HRMS (ESI) m/z $[M+Na]^+$ calcd for $C_{19}H_{21}O_6Na$ 345.1338, found 345.1339.

4.2.4. 3-Pentanyl 4,6-di-O-acetyl-2,3-dideoxy-α-D-erythro-hex-2-enopyranoside (**2h**)

R_f (50% EtOAc/hexane) 0.66; $[\alpha]_D^{24}$ +313.9 (*c* 0.2, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 5.85 (d, *J*=10.5 Hz, 1H), 5.82 (d, *J*=10.5 Hz, 1H), 5.29 (dt, *J*=9.3, 1.4 Hz, 1H), 5.11 (s, 1H), 4.24 (dd, *J*=12.1, 5.7 Hz, 1H), 4.11–4.12 (m, 3H), 3.56 (p, *J*=5.9 Hz, 1H), 2.08 (s, 3H), 2.07 (m, 3H), 1.60–1.55 (m, 3H), 0.94 (t, *J*=7.4 Hz, 3H), 0.91 (t, *J*=7.4 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.8, 170.3, 128.7, 128.2, 93.4, 81.2, 66.9, 65.3, 63.1, 27.1, 26.2, 20.9, 20.7, 10.0, 9.3; IR (NaCl neat) ν_{max}/cm^{-1} 1743, 1369, 1230, 1033; HRMS (ESI) m/z $[M+Na]^+$ calcd for $C_{15}H_{24}O_7Na$ 323.1471, found 323.1462.

4.2.5. Cyclohex-2-enyl 4,6-di-O-acetyl-2,3-dideoxy-α-D-erythro-hex-2-enopyranoside (**2i**)

R_f (30% EtOAc/hexane) 0.50; $[\alpha]_D^{24}$ +38.7 (*c* 0.5, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 5.83–5.82 (m, 3H), 5.77–5.76 (m, 1H), 5.29 (d, *J*=8.8 Hz, 1H), 5.19 (d, *J*=17.4 Hz, 1H), 4.25–4.20 (m, 2H), 4.19–4.17 (m, 2H), 2.09 (d, *J*=2.7 Hz, 3H), 2.08 (d, *J*=1.3 Hz, 2H), 2.07–2.03 (m, 2H), 1.97–1.88 (m, 2H), 1.83–1.66 (m, 2H), 1.91–1.53 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.8, 170.3, 131.5, 128.9, 128.7, 128.4, 128.3, 94.0, 72.7, 66.8, 65.3, 63.1, 30.1, 25.0, 21.0, 19.2; IR (NaCl neat) ν_{max}/cm^{-1} 1743, 1371, 1230, 1033; HRMS (ESI) m/z $[M+Na]^+$ calcd for $C_{16}H_{22}O_6Na$ 333.1314, found 323.1310.

4.2.6. Cyclooctanyl 4,6-di-O-acetyl-2,3-dideoxy-α-D-erythro-hex-2-enopyranoside (**2k**)

R_f (50% EtOAc/hexane) 0.54; $[\alpha]_D^{24}$ +156.7 (*c* 1.0, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 5.83 (d, *J*=10.2 Hz, 1H), 5.76 (dt, *J*=10.2, 2.3 Hz, 1H), 5.26 (dd, *J*=9.6, 1.4 Hz, 1H), 5.09 (s, 1H), 4.20 (d, *J*=12.1 Hz, 1H), 4.12 (dd, *J*=12.1, 5.9 Hz, 1H), 4.16–4.11 (m, 1H), 3.83 (h, *J*=4.2 Hz, 1H), 2.07 (s, 3H), 2.05 (s, 3H), 1.86–1.83 (m, 1H), 1.78–1.63 (m, 4H), 1.59–1.40 (m, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.7, 170.2, 128.6, 128.4, 92.8, 78.6, 72.6, 66.8, 66.4, 64.5, 63.5, 63.2, 33.0, 31.2, 27.3, 25.3, 23.0, 20.7; IR (NaCl neat) ν_{max}/cm^{-1} 1743, 1373, 1234, 1036; HRMS (ESI) m/z $[M+Na]^+$ calcd for $C_{18}H_{28}O_7Na$ 363.1784, found 345.1771.

4.2.7. 2-Methoxybenzenethainyl 4,6-di-O-acetyl-2,3-dideoxy-α-D-erythro-hex-2-enopyranoside (**2n**)

R_f (30% EtOAc/hexane) 0.45; $[\alpha]_D^{24}$ +262.6 (*c* 0.5, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 7.42 (dd, *J*=7.5, 1.6 Hz, 1H), 7.24 (m, 1H), 6.8 (m, 2H), 6.40 (d, *J*=5.8 Hz, 1H), 5.13 (dd, *J*=10.1, 4.5 Hz, 1H), 4.94 (t, *J*=5.8 Hz, 1H), 4.54 (m, 1H), 4.38 (dd, *J*=12.2, 4.4 Hz, 1H), 4.32 (dd, *J*=12.2, 2.1 Hz, 1H), 3.88 (s, 1H), 2.06 (s, 6H), 1.47 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.7, 169.8, 158.7, 144.7, 133.6, 129.1, 122.9, 120.8, 111.0, 98.7, 70.8, 69.8, 62.3, 55.8, 40.4, 20.7, 19.8; IR (NaCl neat) ν_{max}/cm^{-1} 1743, 1370, 1232, 1037; HRMS (ESI) m/z $[M+Na]^+$ calcd for $C_{17}H_{20}O_6SNa$ 375.0878, found 375.0871.

4.2.8. Benzyl-O-(4′,6′-di-O-acetyl-2′-3′-dideoxy-α-D-erythro-hex-2′-enopyranosyl)-(1→6)-2,3,4-tri-O-benzyl-α-D-glucopyranoside (**2p**)

R_f (30% EtOAc/hexane) 0.45; $[\alpha]_D^{24}$ +20.8 (*c* 1.0, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 7.34–7.21 (m, 20H), 5.85 (s, 2H), 5.30 (d, *J*=9.6 Hz, 1H), 5.14 (s, 1H), 4.96–4.90 (m, 4H), 4.81–4.76 (m, 2H), 4.67–4.62 (m, 3H), 4.51 (d, *J*=7.8 Hz, 1H), 4.13–4.07 (m, 2H), 3.84–3.71 (m, 1H), 3.68–3.64 (m, 2H), 3.60–3.55 (m, 1H), 3.51–3.45 (m, 2H), 2.07 (s, 3H), 2.06 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.8, 170.3, 135.5, 138.4, 137.4, 129.0, 128.5, 128.5, 128.4, 128.4, 128.2, 128.1, 128.1, 127.9, 127.9, 127.8, 127.8, 127.7, 127.7, 127.7, 102.8, 102.5, 94.8, 84.7, 84.5, 82.4, 78.0, 77.6, 75.7, 75.1, 75.1, 75.0, 74.9, 74.6, 71.6, 71.2, 67.2, 67.0, 65.2, 62.8, 62.0, 60.4, 21.0, 20.8; IR (NaCl neat) ν_{max}/cm^{-1} 1733, 1455, 1259, 1061; HRMS (ESI) m/z $[M+Na]^+$ calcd for $C_{44}H_{48}O_{11}Na$ 775.3094, found 775.3085.

4.2.9. S-(−)-β-Citronellyl 4,6-di-O-acetyl-2,3-dideoxy-α-D-erythro-hex-2-enopyranoside (**3a**)

R_f (30% EtOAc/hexane) 0.64; $[\alpha]_D^{24}$ +41.5 (*c* 0.5, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 5.86 (d, *J*=10.4 Hz, 1H), 5.87 (d, *J*=10.4 Hz, 1H), 5.29 (dd, *J*=9.6, 1.1 Hz, 1H), 5.08 (t, *J*=7.0 Hz, 1H), 5.01 (s, 1H), 4.23 (dd, *J*=12.1, 5.4 Hz, 1H), 4.16 (dd, *J*=12.1, 2.2 Hz, 1H), 4.10–4.07 (m, 1H), 3.82 (dd, *J*=7.4, 2.2 Hz, 1H), 3.55–3.50 (m, 1H), 2.08 (s, 3H), 2.07 (s, 3H), 1.99–1.93 (m, 2H), 1.67–1.65 (m, 4H), 1.59–1.55 (m, 4H), 1.41–1.30 (m, 2H), 1.17–1.12 (m, 1H), 0.88 (d, *J*=6.6 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.8, 170.2, 131.2, 128.9, 127.9, 124.6, 94.3, 67.0, 66.9, 65.3, 63.0, 37.2, 36.5, 29.5, 25.7, 25.4, 20.9, 20.7, 19.3, 17.6; IR (NaCl neat) ν_{max}/cm^{-1} 1743, 1371, 1232, 1035; HRMS (ESI) m/z $[M+Na]^+$ calcd for $C_{20}H_{32}O_6Na$ 391.2097, found 391.2086.

4.2.10. L-Menthyl 4,6-di-O-acetyl-2,3-dideoxy-α-D-erythro-hex-2-enopyranoside (**3b**)

R_f (30% EtOAc/hexane) 0.61; $[\alpha]_D^{24}$ +142.5 (*c* 0.5, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 5.85 (s, 2H), 5.26 (d, *J*=10 Hz, 1H), 5.08 (s, 1H), 4.18 (dd, *J*=12.3, 6.7 Hz, 1H), 4.17–4.14 (m, 2H), 3.39 (dt, *J*=10.6, 4.4 Hz, 1H), 2.17 (d, *J*=4.0 Hz, 1H), 2.09 (s, 3H), 2.08 (s, 3H), 1.67–1.59 (m, 2H), 1.44–1.37 (m, 1H), 1.25–1.20 (m, 1H), 1.03 (dd, *J*=23.2, 12.2 Hz, 1H), 0.95 (dd, *J*=12.1, 3.0 Hz, 1H), 0.92–0.87 (m, 7H), 0.85–0.79 (m, 1H), 0.75 (d, *J*=7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.8, 170.3, 128.5, 128.0, 96.1, 81.0, 66.6, 65.3, 63.3, 48.8, 43.3, 34.2, 31.7, 25.6, 23.1, 22.3, 21.1, 20.9, 20.8, 16.2; IR (NaCl neat) ν_{max}/cm^{-1} 1743, 1369, 1234, 1035; HRMS (ESI) m/z $[M+Na]^+$ calcd for $C_{20}H_{32}O_6Na$ 391.2097, found 391.2089.

4.2.11. (+)-Bornyl 4,6-di-O-acetyl-2,3-dideoxy-α-D-erythro-hex-2-enopyranoside (3c)

R_f (30% EtOAc/hexane) 0.61; $[\alpha]_D^{24}$ +72.6 (*c* 0.8, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 5.84–5.79 (m, 2H), 5.27 (d, *J*=9.8 Hz, 1H), 4.99 (s, 1H), 4.21 (dd, *J*=12.2, 5.6 Hz, 1H), 4.12 (dd, *J*=12.2, 2.2 Hz, 1H), 4.10–4.09 (m, 1H), 3.82 (dt, *J*=6.6, 2.1 Hz, 1H), 2.24–2.22 (m, 1H), 2.07 (s, 3H), 2.06 (s, 3H), 1.96–1.90 (m, 1H), 1.70–1.64 (m, 2H), 1.59 (t, *J*=4.5 Hz, 1H), 1.23–1.17 (m, 2H), 1.11 (dd, *J*=13.4, 3.4 Hz, 1H), 0.94–0.82 (s, 3H), 0.81(s, 3H), 0.80 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.7, 170.2, 128.4, 128.2, 96.1, 85.8, 66.8, 66.7, 64.1, 48.8,

47.7, 46.6, 38.9, 28.2, 28.2, 26.6, 20.9, 20.7, 19.7, 13.6; IR (NaCl neat) ν_{max}/cm^{-1} 1747, 1369, 1230, 1041; HRMS (ESI) *m/z* $[M+Na]^+$ calcd for $C_{20}H_{30}O_6Na$ 389.1940, found 389.1938.

4.2.12. (+)-endo-Fenacholyl 4,6-di-O-acetyl-2,3-dideoxy-α-D-erythro-hex-2-enopyranoside (**3d**)

R_f (30% EtOAc/hexane) 0.61; $[\alpha]_D^{24}$ +48.7 (*c* 0.5, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 5.83 (s, 2H), 5.25 (d, *J*=10 Hz, 1H), 4.95 (s, 1H), 4.20 (dd, *J*=12.2, 5.2 Hz, 1H), 4.13–4.09 (m, 2H), 3.42 (d, *J*=1.5 Hz, 1H), 2.06 (s, 3H), 2.05 (2, 3H), 1.65–1.61 (m, 3H), 1.45 (dd, *J*=10.1, 1.5 Hz, 1H), 1.08 (s, 3H), 1.07–1.06 (m, 1H), 1.01 (s, 3H), 0.96–0.94 (m, 1H), 0.85 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ_C 170.8, 170.2, 128.5, 127.9, 94.1, 90.1, 66.8, 65.2, 63.1, 48.8, 48.7, 41.3, 39.4, 31.8, 25.9, 21.1, 20.9, 20.8, 19.7; IR (NaCl neat) ν_{max}/cm^{-1} 1732, 1456, 1259, 1064; HRMS (ESI) *m/z* $[M+Na]^+$ calcd for $C_{20}H_{30}O_6Na$ 389.1940, found 389.1935.

4.2.13. Pregnenolonyl 4,6-di-O-acetyl-2,3-dideoxy-α-D-erythro-hex-2-enopyranoside (**3e**)

R_f (30% EtOAc/hexane) 0.40; $[\alpha]_D^{20}$ +162.4 (*c* 0.5, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 5.85 (d, *J*=10.4 Hz, 1H), 5.78 (d, *J*=10.4 Hz, 1H), 5.32 (s, 1H), 5.26 (d, *J*=10.0 Hz, 1H), 5.14 (s, 1H), 4.20 (dd, *J*=12.2, 5.9 Hz, 1H), 4.17–413 (m, 2H), 3.57–3.51 (m, 1H), 2.50 (t, *J*=8.0 Hz, 1H), 2.38–2.34 (m, 1H), 2.32 (d, *J*=11.0 Hz, 1H), 2.19–2.14 (m, 1H), 2.09 (s, 3H), 2.06 (s, 3H), 2.05 (s, 3H), 2.02 (d, *J*=9.5 Hz, 1H), 1.99–1.95 (m, 1H), 1.88–1.83 (m, 2H), 1.60–1.42 (m, 8H), 1.24–1.18 (m, 1H), 1.17–1.12 (m, 1H), 1.06–1.03 (m, 1H), 0.98–0.95 (m, 4H), 0.60 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 209.5, 170.8, 170.3, 140.7, 128.9, 128.3, 121.5, 92.8, 78.0, 66.8, 65.3, 63.6, 63.1, 56.8, 49.9, 43.9, 40.3, 38.8, 37.1, 36.6, 31.8, 31.7, 31.5, 28.1, 24.4, 22.8, 21.0, 20.9, 20.8, 19.3, 13.2; IR (NaCl neat) ν_{max}/cm^{-1} 1745, 1699, 1371, 1228, 1035; HRMS (ESI) *m/z*: calcd for $C_{31}H_{44}O_7Na$: 551.2985 $[M+Na]^+$; found: 551.2994.

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Supplementary data

Crystallographic data of compound **3e** and NMR spectra of new compounds are available. Supplementary data associated with this article can be found in the online version, at doi:10.1016/j.tet.2009.04.099.

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