# Er(OTf)<sub>3</sub> as New Efficient Catalyst for the Stereoselective Synthesis of *C*-Pseudoglycals

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**Abstract:**  $Er(OTf)_3$  is a useful catalyst for the Ferrier rearrangement furnishing high yields of products, cleaner reaction profiles, short reaction times, mild reaction conditions, high stereoselectivity and recoverability of the catalyst which is also commercially available.

Key words: C-glycosylation, Lewis catalyst, erbium (III), triflate

The discovery of naturally occurring C-glycosides having important pharmacological properties1 and the requirement of chiral building blocks for the synthesis of several biological active products (i.e. palytoxin, spongistatin, halichondrin B<sup>2</sup> and stable analogs of O- and N-glycosides potential inhibitors of carbohydrate processing enzymes,<sup>3</sup> have stimulated the development of many synthetic methodologies for the preparation of C-glycosides.<sup>1b,4</sup> C-Pseudoglycals are 2,3-unsaturated C-glycosides ( $\Delta^{2,3}$ -glycals), generally accessed via acid-mediated allylic rearrangement of glycals, otherwise known as the Ferrier rearrangement.<sup>5</sup> They possess a double bond which may be easily functionalized to produce an array of complex carbohydrates.<sup>6</sup> Moreover, specifically C-allyl and alkynyl glycosides are attractive due to the presence of a multiple bond that is easy to transform into other chiral carbon analogues of synthetic carbohydrates<sup>4c,7</sup> or used to build up building blocks of natural products (i.e. tautomycin,<sup>8</sup> ciguatoxin,<sup>9</sup> okadaic acid<sup>10</sup>). Also, C-glycoside cyanides result in versatile intermediates for the synthesis of naturally occurring C-nucleoside antibiotics and many others analogues<sup>1b,4c,11</sup> because the cyano-group can be readily transformed into a variety of other functional groups. Ferrier rearrangement furnishing C-pseudoglycals has been achieved by using many acid catalysts with carbon nucleophiles: H<sub>2</sub>SO<sub>4</sub>, HCl, EtAlCl<sub>2</sub>, SnBr<sub>4</sub>,<sup>12</sup> ZnCl<sub>2</sub>,<sup>16</sup> CH<sub>3</sub>COOH,<sup>15</sup> SbCl<sub>5</sub>,<sup>13</sup> Cl<sub>3</sub>COOH,<sup>14</sup>  $BF_{3} \cdot OEt_{2}, {}^{1c,5d,11,12,17} \text{ TiCl}_{4}, {}^{17,18} \text{ SnF}_{4}, \text{ TMSOTf}, {}^{1c,4a,18,19} \text{ montmorillonite-K}, {}^{19b} \text{ DDQ}, {}^{20} \text{ AlCl}_{3}, {}^{19a} \text{ trichloroacetim-}$ midate,  ${}^{5f}$  SnCl<sub>4</sub>,  ${}^{19}$  InCl<sub>3</sub>,  ${}^{21}$  InBr<sub>3</sub>,  ${}^{22}$  LiBF<sub>4</sub>,  ${}^{23}$  I<sub>2</sub>,  ${}^{12,24}$  and triflate derivatives of Bi(III),<sup>25</sup> In(III),<sup>26</sup> Sc(III),<sup>27</sup> and Yb(III).<sup>28</sup>

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Nevertheless, many of these reagents are corrosive, moisture-sensitive, and are required in stoichiometric amounts, having limitations in terms of yields, reaction time, temperature, selectivity, recovery of the catalyst, and availability. Moreover, in many cases the reported methods were used with only the most reactive glycals.

In the last years we developed new catalytic reagents for several strategic steps of organic synthesis with the aim to lower the environmental impact.<sup>29</sup> Now, in continuation of our work on the application of erbium(III) trifluoromethanesulfonate as Lewis acid catalyst in various transformations, we describe the utility of  $Er(OTf)_3$  as an efficient catalyst for the synthesis of 2,3-unsaturated *C*-glycosides via Ferrier rearrangement by using silylated nucleophiles.

We tested first the catalytic activity of Er(OTf)<sub>3</sub> in the allylation of 3,4,6-tri-O-acetyl-D-glucal 1 at room temperature in different solvents with 1.5 equivalents of allyltrimethylsilane (a) and different mol% of catalyst (Scheme 1). Based on our preliminary results, which are shown in Table 1, Er(OTf)<sub>3</sub> acts quite efficiently in polar aprotic solvents such as CH<sub>3</sub>CN and CH<sub>3</sub>NO<sub>2</sub> (entries 1 and 2 in Table 1), but the best result was obtained in CH<sub>2</sub>Cl<sub>2</sub> (entries 3 in Table 1) where more than 95% of allyl 2,3-unsaturated acetyl C-glycoside 1a was achieved by using only 3.0 mol% of catalyst, whilst no product was detected in Et<sub>2</sub>O, THF, CHCl<sub>3</sub> even after very prolonged reaction times (entries 4-6 in Table 1). Attempts to use lower amounts of Er(OTf)<sub>3</sub> failed because only low yields of allyl 2,3-unsaturated acetyl C-glycoside 1a were achieved by using 1.0 mol% and also 2.0 mol% of catalyst (entry 7 and 8 in Table 1).

The catalyst can be reused several times without significant loss of activity. After workup, the aqueous phase can be evaporated under reduced pressure to furnish the Er(III) salt <sup>30</sup> as a pale pink solid (85–90% recovered), which can be recycled after drying overnight over  $P_2O_5$ . The recovered catalyst was used five times in the allylation reaction of the 3,4,6-tri-*O*-acetyl-D-glucal **1** maintaining 3.0 mol% of catalyst and the yields were always higher than 90%.

Less satisfactory results were reached when the same reaction was carried out in anhydrous  $CH_3CN$  and  $CH_3NO_2$ , (entries 9 and 10 in Table 1), and even in anhydrous

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Scheme 1

 Table 1
 Allylation of 3,4,6-Tri-O-acetyl-D-glucal 1 in Various Solvents

| Entry | Solvent                                 | Er(OTf) <sub>3</sub><br>(mol%) | Time (h)  | Yield<br>(%) |
|-------|---|--------------------------------|-----------|--------------|
| 1     | CH <sub>3</sub> CN                      | 3.0                            | 8         | 75           |
| 2     | CH <sub>3</sub> NO <sub>2</sub>         | 3.0                            | 9         | 80           |
| 3     | $CH_2Cl_2$                              | 3.0                            | 7         | > 95         |
| 4     | Et <sub>2</sub> O                       | 3.0                            | overnight | _            |
| 5     | THF                                     | 3.0                            | overnight | _            |
| 6     | CHCl <sub>3</sub>                       | 3.0                            | overnight | _            |
| 7     | $CH_2Cl_2$                              | 2.0                            | 48        | 34           |
| 8     | $CH_2Cl_2$                              | 1.0                            | 24        | 13           |
| 9     | CH <sub>3</sub> CN (anhyd)              | 3.0                            | overnight | 40           |
| 10    | CH <sub>3</sub> NO <sub>2</sub> (anhyd) | 3.0                            | overnight | 35           |
| 11    | CH <sub>2</sub> Cl <sub>2</sub> (anhyd) | 3.0                            | overnight | 80           |
| 1     | CH <sub>3</sub> CN                      | 3.0                            | 8         | 75           |

 $CH_2Cl_2$  the yield of **1a** was only 80% (entry 11 in Table 1).

It is reasonable to assume that a dynamic equilibrium between the water molecules involved in the coordination sphere of the  $Er(OTf)_3$  and substrate exists. When one of the eight water molecules, which surround the metal ion<sup>31</sup> is substituted by a molecule of glycal through the coordination with one of its lone pairs on the oxygen atom, the Ferrier rearrangement can proceed via a delocalized cation formed by departure of the acyloxy moiety from starting material. As depicted in Scheme 2, the formation of cation is followed by attack of nucleophile from a side of the molecule providing maximum continuous overlap of the orbitals.

In order to explore the generality and the scope of erbium(III) triflate as Lewis acid catalyst in Ferrier rearrangement, the reaction was carried out on different substrates such as 3,4,6-tri-*O*-acetyl-D-galactal **2** and 3,4-di-*O*acetyl-6-deoxy-L-glucal **3** by using different silylnucleophiles [allyltrimethylsilane (**a**), trimethylsilyl cyanide (**b**), propargyltrimethylsilane (**c**), 1-phenyl-2-(allytrimethylsilyl)acetylene (**d**)].



#### Scheme 2

Based on results reported in Table 1, we adopted a simple experimental procedure: a solution of substrate in  $CH_2Cl_2$  was stirred at room temperature in the presence of catalytic amount of erbium(III) trifluoromethanesulfonate for about five minutes, then the silylnucleophile (1.5 equiv) was added and the course of reaction was followed by TLC (Table 2).

All products were obtained in high yields at room temperature by using low amounts of erbium(III) triflate and only a few substrates required up to 10 mol% of catalyst (entries 2, 5, 8, and 11 in Table 2) to accomplish lower reaction times. In every case, the major anomeric product was characterized by EI–MS and <sup>1</sup>H- and <sup>13</sup>C NMR spectroscopy after purification by chromatographic column.

The anomeric ratio was determined by means of <sup>1</sup>H and <sup>13</sup>C NMR spectroscopy in accordance with the earlier studies.<sup>21a,22,24,25</sup> Particularly, in the <sup>13</sup>C NMR spectra the C-5 chemical shift is always lower than 75 ppm as reported for the  $\gamma$ -gauche effect on 1,5-*trans* isomers ( $\alpha$  for D-gluco and galacto-series and  $\beta$  for L-deoxygluco series). Moreover in NOE experiments on H5 or on the methyl in C-6, the H1 signal must enhance only in  $\alpha$  for D-gluco-and galacto series and in  $\beta$  for L-deoxygluco series (Figure 1).<sup>32</sup> Experiments carried out on the major isomer confirmed the configuration proposed in Table 2.

The tri-*O*-acetyl-D-glucal **1** always gave higher yields than the galactal analog **2** during C-glycosydation as previously registered.<sup>21b,24a,27</sup> The stereoselectivity of this reaction is excellent, giving almost exclusively the  $\alpha$ -anomers for the alkyl glucal- and galactal-derivatives, while  $\alpha/\beta$  mixture for glycal cyanides is obtained according to other reports.<sup>21b,24a,27</sup>

The observed predominant formation of either  $\alpha$ -isomer or  $\beta$ -isomer in gluco- and galacto series and in the deoxygluco series respectively, may be easily explained in





 Table 2
 C-Glycosidation of Glycals Using Er(OTf)<sub>3</sub> as Catalyst

terms of the mechanism depicted in Scheme 2. The formation of the cation **A** is the key step of the reaction. In the hexopyranosides derivatives all cationic intermediates should take a conformation with C6 in pseudo-equatorial orientation, independent of the 4-AcO-group position. Then the less hindered face of the C-1–O  $\pi$ –orbital of Dgluco and galacto series orients the incoming nucleophile to form a bond always in the  $\alpha$ -axial position. On the other hand, in the L-deoxyglucal, the less hindered face of the  $\pi$ orbital allows the nucleophile to find a major orbital overlapping approaching from  $\beta$ -side of ion.

A lot of methodologies already exist to realize the synthesis of *C*-glycosides by means of Ferrier rearrangement, but many of them have limitations in terms of stringent reaction conditions, demanding workup, reaction time and amount of catalyst; some others were tested in only limited examples by using expensive or commercially unavailable reagents.

The use of  $Er(OTf)_3$  as catalyst for the Ferrier rearrangement presents several advantages which include high yields of products, cleaner reaction profiles, short reaction times, mild reaction conditions [a solution 0.1 M of  $Er(OTf)_3$  in water is only weakly acidic with pH ~ 5.9], high stereoselectivity, wide applicability and recoverability of the catalyst which is also commercially available. Moreover, the present method avoids the use of corrosive or toxic reagents and does not require any additives or stringent reaction conditions whilst no precautions need to be taken to exclude moisture from the reaction medium.

| Entry | Glycal | Nuc | Product                                  | Cat. (mol%) | Time (h) | Yield $(\%)^{a,b} \alpha$ : $\beta^c$ |
|-------|--------|-----|--|-------------|----------|---------------------------------------|
| 1     | 1      | a   | ACO                                      | 3           | 7        | 95<br>92:8                            |
| 2     | 2      | а   | 1a<br>OAc                                | 10          | 36       | 80<br>100:0                           |
| 3     | 3      | a   | 2a<br>H <sub>3</sub> C <sub>Mm</sub> , O | 5           | 16       | 95<br>10:90                           |
| 4     | 1      | b   | 3a<br>OAc                                | 3           | 6        | 95<br>60:40                           |
| 5     | 2      | b   | AcO <sup>WM</sup><br>1b<br>OAc<br>AcO    | 10          | 48       | 76<br>70:30                           |
|       |        |     | 2b                                       |             |          |                                       |

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| Entry | Glycal | Nuc | Product   | Cat. (mol%) | Time (h) | Yield (%) <sup>a,b</sup> α:β <sup>c</sup> |
|-------|--------|-----|---|-------------|----------|---|
| 6     | 3      | b   | H <sub>3</sub> C <sub>Mm</sub> O ros CN<br>AcO                            | 5           | 6        | 93<br>40:60                               |
| 7     | 1      | c   | 3b<br>OAc<br>AcO  | 3           | 20       | 82<br>100:0                               |
| 8     | 2      | c   | 1c<br>OAc<br>AcO  | 10          | 10       | 85<br>100:0                               |
| 9     | 3      | c   | 2c<br>H <sub>3</sub> C <sub><i>i</i>/<sub>1</sub>, O CH<sub>3</sub></sub> | 5           | 2        | 85<br>20:80                               |
| 10    | 1      | d   | 3c<br>OAc<br>AcO <sup>min</sup> Ph  | 3           | 21       | 75<br>100:0                               |
| 11    | 2      | d   | 1d<br>OAc<br>Aco  | 10          | 14       | 65<br>100:0                               |
| 12    | 3      | d   | 2d<br>H <sub>3</sub> C <sub>11,1</sub> , O Ph<br>AcO<br>3d                | 5           | 5        | 75<br>15:85                               |

 Table 2
 C-Glycosidation of Glycals Using Er(OTf)<sub>3</sub> as Catalyst (continued)

<sup>a</sup> All products were identified by comparison of their EI–MS and <sup>1</sup>H NMR spectral data with those of authentic compounds and literature reported data.

<sup>b</sup> Isolated yield by flash column chromatography on silica gel was reported.

<sup>c</sup> The anomeric ratio was determined by <sup>1</sup>H NMR.

<sup>1</sup>H and <sup>13</sup>C NMR spectra were recorded with a Bruker WM 300 instrument, at 300 MHz and 75 MHz respectively. Samples were dissolved in CDCl<sub>3</sub>. Chemical shifts are given in ppm from TMS as internal standard for <sup>1</sup>H NMR and for <sup>13</sup>C NMR the central line of CDCl<sub>3</sub> ( $\delta$  = 77 ppm) has been used as reference. Coupling constants (*J*) are given in Hz. MS data were recorded on a GC-MS Shimadzu QP 2010 with a direct inlet option. Microanalyses were collected on a Perkin-Elmer 2400 analyzer.

#### C-Glycosidation; Typical Procedure

In a model reaction, the 3,4,6-tri-O-acetyl-D-glucal **1** (200 mg, 0.73 mmol) was added to a CH2Cl<sub>2</sub> solution (3.0 mL) of  $Er(OTf)_3$  (13.0 mg, 0.0022 mmol, 3.0 mol%) and stirred at r.t. for **5**'. Then, allyl-trimethylsilane **a** (0.13 g, 1.10 mmol, 1.5 equiv) was added and the solution reaction was stirred at r.t. until a nearly complete conversion of substrate **1** was achieved in 7 h [TLC, Et<sub>2</sub>O–hexane (70:30)]. The organic solution was washed with sat. aq NaHCO<sub>3</sub> and then

with water. The crude product, obtained after solvent evaporation of the dried organic layers, was purified by flash chromatography [hexane–EtOAc (85:15)] affording **2a** (178 mg, > 95% yield). The structural identification of **2a** was confirmed by comparison of its EI–MS and <sup>1</sup>H NMR spectral data with those of literature data.

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#### **3**-(4',6'-Di-*O*-acetyl-2',3'-dideoxy-α-D-*erythro*-hex-2'-enopyranosyl)-1-propene (1a) Oil.<sup>25</sup>

<sup>1</sup>H NMR (CDCl<sub>3</sub>):  $\delta$  = 2.06 (s, 6 H, 2 × CH<sub>3</sub>COO), 2.22–2.34, 2.39–2.47 (m, 2 H, CH<sub>2</sub>), 3.93 (td,  $J_t$  = 6.6 Hz,  $J_d$  = 3.7 Hz, 1 H, H-5), 4.18 (dd, J = 3.9, 11.8 Hz, 1 H, H-6a), 4.27 (dd, J = 6.6, 11.8 Hz, 1 H, H-6b), 4.19–4.28 (m, 1 H, H-1), 5.05–5.13 (m, 3 H, H-4, =CH<sub>2</sub>), 5.72–5.88 (m, 2 H, H-3, CH=), 5.91 (ddd, J = 1.6, 2.3, 10.3 Hz, 1 H, H-2).

<sup>13</sup>C NMR (CDCl<sub>3</sub>): δ = 20.2 (CH<sub>3</sub>), 20.6 (CH<sub>3</sub>), 37.3 (all CH<sub>2</sub>), 62.4 (C-6), 64.6 (C-1), 69.5 (C-4), 71.1 (C-5), 117.1 (CH<sub>2</sub>=), 123.5 (CH=), 132.2 (CH=), 133.8 (CH=), 167.0 (C=O), 170.5 (C=O).

MS: m/z = 195 (9) [MH – CH<sub>3</sub>COOH]<sup>+</sup>, 135 (67) [MH – 2 × CH<sub>3</sub>COOH]<sup>+</sup>, 109 (100).

#### **3**-(4',6'-Di-*O*-acetyl-2',3'-dideoxy-α-D-*threo*-hex-2'-enopyranosyl)-1-propene (2a)

Oil.<sup>25</sup>

<sup>1</sup>H NMR (CDCl<sub>3</sub>):  $\delta$  = 2.05 (s, 3 H, CH<sub>3</sub>COO), 2.06 (s, 3 H, CH<sub>3</sub>COO), 2.21–2.32, 2.34–2.48 (m, 2 H, CH<sub>2</sub>), 4.10–4.21 (m, 3 H, H-5, H-6), 4.29–4.38 (m, 1 H, H-1), 5.04 (dd, *J* = 2.4, 4.8 Hz, 1 H, H-4), 5.09–5.18 (m, 2 H, =CH<sub>2</sub>), 5.83 (ddt, *J*<sub>t</sub> = 6.8 Hz, *J*<sub>d</sub> = 10.1, 17.2 Hz, 1 H, CH=), 5.99 (ddd, *J* = 1.7, 4.8, 10.1 Hz, 1 H, H-3), 6.04 (dd, *J* = 2.7, 10.1 Hz, 1 H, H-2).

<sup>13</sup>C NMR (CDCl<sub>3</sub>): δ = 20.5 (CH<sub>3</sub>), 20.6 (CH<sub>3</sub>), 36.5 (all CH<sub>2</sub>), 62.7 (C-6), 63.7 (C-1), 68.2 (C-4), 72.0 (C-5), 117.8 (CH<sub>2</sub>=), 122.0 (CH=), 133.6 (CH=), 134.9 (CH=), 170.9 (C=O), 170.9 (C=O).

MS: m/z = 195 (10) [MH – CH<sub>3</sub>COOH]<sup>+</sup>, 153 (21), 135 (100) [MH – 2 × CH<sub>3</sub>COOH]<sup>+</sup>.

#### **3**-(4'-O-Acetyl-2',3',6'-trideoxy-β-L-*erythro*-hex-2'-enopyranosyl)-1-propene (3a)

Oil.25

<sup>1</sup>H NMR (CDCl<sub>3</sub>):  $\delta$  = 1.23 (d, *J* = 6.5 Hz, 3 H, CH<sub>3</sub>), 2.07 (s, 3 H, CH<sub>3</sub>COO), 2.25–2.35, 2.42–2.51 (m, 2 H, CH<sub>2</sub>), 3.91–3.98 (m, 1 H, H-5), 4.14–4.28 (m, 1 H, H-1), 4.84–4.98 (m, 1 H, H-4), 5.08–5.14 (m, 2 H, =CH<sub>2</sub>), 5.73–5.89 (m, 2 H, H-3, CH=), 5.92 (ddd, *J* = 1.4, 2.2, 10.2 Hz, 1 H, H-2).

<sup>13</sup>C NMR (CDCl<sub>3</sub>): δ = 16.6 (C-6), 21.6 (*C*H<sub>3</sub>CO), 38.6 (all CH<sub>2</sub>), 68.7 (C-1), 69.7 (C-4), 69.5 (C-5), 117.5 (CH<sub>2</sub>=), 122.5 (CH=), 133.2 (CH=), 134.1 (CH=), 170.6 (C=O).

MS:  $m/z = 137 (100) [MH - CH_3COOH]^+$ , 95 (94).

# 4,6-Di-O-acetyl-2,3-dideoxy- $\alpha$ -D-erythro-hex-2-enopyranosyl Cyanide (1b)

Oil.<sup>25</sup>

<sup>1</sup>H NMR (CDCl<sub>3</sub>): δ = 2.10 (s, 3 H, CH<sub>3</sub>COO), 2.10 (s, 3 H, CH<sub>3</sub>COO), 4.01 (dt,  $J_t$  = 3.6 Hz,  $J_d$  = 9.1 Hz, 1 H, H-5), 4.26 (d, J = 3.6 Hz, 2 H, H-6), 5.10–5.13 (m, 1 H, H-1), 5.33 (dq,  $J_q$  = 9.1 Hz,  $J_d$  = 2.1 Hz, 1 H, H-4), 5.91 (ddd, J = 2.0, 3.5, 10.1 Hz, 1 H, H-2), 6.04 (dt,  $J_d$  = 10.1 Hz,  $J_t$  = 2.0 Hz, 1 H, H-3).

<sup>13</sup>C NMR (CDCl<sub>3</sub>): δ = 20.3 (CH<sub>3</sub>), 20.9 (CH<sub>3</sub>), 62.0 (C-6), 62.3 (C-1), 63.4 (C-4), 72.2 (C-5), 115.2 (CN), 123.5, 129.5 (CH=CH), 170.0 (C=O), 170.3 (C=O).

MS: m/z = 240 (1) [MH]<sup>+</sup>, 180 (100) [MH – CH<sub>3</sub>COOH]<sup>+</sup>, 153 (57) [MH – CH<sub>3</sub>COOH – HCN]<sup>+</sup>.

### 4,6-Di-*O*-acetyl-2,3-dideoxy-α-D-*threo*-hex-2-enopyranosyl Cyanide (2b)

Oil.<sup>25</sup>

<sup>1</sup>H NMR (CDCl<sub>3</sub>):  $\delta$  = 2.11 (s, 3 H, CH<sub>3</sub>COO), 2.13 (s, 3 H, CH<sub>3</sub>COO), 4.23–4.27 (m, 3 H, H-5, H-6), 5.15–5.20 (m, 2 H, H-1, H-4), 6.11 (ddd, *J* = 0.8, 3.6, 10.3 Hz, 1 H, H-2,), 6.25 (ddd, *J* = 1.9, 5.7, 10.3 Hz, 1 H, H-3).

 $^{13}\text{C}$  NMR (CDCl<sub>3</sub>):  $\delta$  = 20.4 (CH<sub>3</sub>), 20.9 (CH<sub>3</sub>), 62.3 (C-6, C-1), 62.9 (C-4), 72.0 (C-5), 115.4 (CN), 126.6, 126.7 (CH=CH), 169.0 (C=O), 170.3 (C=O).

MS: *m*/*z* = 240 (1) [MH]<sup>+</sup>, 180 (100) [MH – CH<sub>3</sub>COOH]<sup>+</sup>, 153 (57) [MH – CH<sub>3</sub>COOH – HCN]<sup>+</sup>.

## 4-*O*-Acetyl-2,3,6-trideoxy-β-L-*erythro*-hex-2-enopyranosyl Cyanide (3b)

Oil.26

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<sup>1</sup>H NMR (CDCl<sub>3</sub>):  $\delta = 1.31$  (d, J = 6.3 Hz, 3 H, CH<sub>3</sub>), 2.12 (s, 3 H, CH<sub>3</sub>COO), 3.89–3.95 (m, 1 H, H-5), 5.02–5.10 (m, 2 H, H-1, H-4), 5.88 (ddd, J = 1.9, 3.5, 10.3 Hz, 1 H, H-2), 5.98 (dd, J = 1.9, 10.3 Hz, 1 H, H-3).

<sup>13</sup>C NMR (CDCl<sub>3</sub>): δ = 17.5 (C-6), 21.2 (CH<sub>3</sub>CO), 62.3 (C-1), 69.3 (C-4), 70.3 (C-5), 116.2 (CN), 123.8, 130.1 (CH=CH), 170.2.

MS: *m*/*z* = 182 (3) [MH]<sup>+</sup>, 122 (4) [MH – CH<sub>3</sub>COOH]<sup>+</sup>, 95 (100) [MH – CH<sub>3</sub>COOH – HCN]<sup>+</sup>.

#### 1-(4',6'-Di-O-acetyl-2',3'-dideoxy-α-D-*erythro*-hex-2'-enopyranosyl)-1-propyne (1c) Liquid.<sup>24b</sup>

<sup>1</sup>H NMR (CDCl<sub>3</sub>): δ = 1.89 (d, J = 2.1 Hz, 3 H, CH<sub>3</sub>C≡), 2.11 (s, 3 H, CH<sub>3</sub>COO), 2.12 (s, 3 H, CH<sub>3</sub>COO), 4.10–4.16 (m, 1 H, H-5), 4.20 (dd, J = 3.0, 12.0 Hz, 1 H, H-6a), 4.24 (dd, J = 4.9, 12.0 Hz, 1 H, H-6b), 4.90–4.97 (m, 1 H, H-1), 5.28 (dq,  $J_d$  = 9.0 Hz,  $J_q$  = 1.8 Hz, 1 H, H-4), 5.77 (dt,  $J_d$  = 9.97 Hz,  $J_t$  = 2.1 Hz, 1 H, H-2), 5.91 (ddd, J = 1.8, 3.0, 9.97 Hz, 1 H, H-3).

<sup>13</sup>C NMR (CDCl<sub>3</sub>):  $\delta$  = 3.8 (CH<sub>3</sub>C≡), 21.0 (CH<sub>3</sub>CO), 21.2 (CH<sub>3</sub>CO), 62.8 (C-6), 64.0 (C-1), 64.6 (C-4), 69.5 (C-5), 74.9, 83.5 (C≡C), 124.4, 130.1 (CH=CH), 170.0 (C=O), 171.1 (C=O).

MS: m/z = 253 (1) [MH]<sup>+</sup>, 193 (55) [MH – CH<sub>3</sub>COOH]<sup>+</sup>, 133 (100) [MH – 2 × CH<sub>3</sub>COOH]<sup>+</sup>.

Anal. Calcd for  $C_{13}H_{16}O_5$ : C, 61.90; H, 6.35. Found: C, 61.93; H, 6.31.

# 1-(4',6'-Di-*O*-acetyl-2',3'-dideoxy-α-D-*threo*-hex-2'-enopyranosyl)-1-propyne (2c)

Liquid.

<sup>1</sup>H NMR (CDCl<sub>3</sub>):  $\delta$  = 1.87 (d, *J* = 2.2 Hz, 3 H, CH<sub>3</sub>C≡), 2.08–2.11 (m, 6 H, CH<sub>3</sub>COO), 4.14–4.38 (m, 3 H, H-5, H-6), 4.99–5.03 (m, 1 H, H-1), 5.05–5.08 (m, 1 H, H-4), 5.94–6.08 (m, 2 H, H-2, H-3).

<sup>13</sup>C NMR (CDCl<sub>3</sub>):  $\delta$  = 3.6 (CH<sub>3</sub>C≡), 20.75 (CH<sub>3</sub>CO), 20.81 (CH<sub>3</sub>CO), 62.7 (C-6), 63.3 (C-1), 64 (C-4), 69.1 (C-5), 75.3, 77 (C≡C), 121.6, 132.6 (CH=CH), 170.5 (C=O), 170.8 (C=O).

MS: m/z = 193 (16) [MH – CH<sub>3</sub>COOH]<sup>+</sup>, 133 (100) [MH – 2 × CH<sub>3</sub>COOH]<sup>+</sup>.

Anal. Calcd for  $C_{13}H_{16}O_5$ : C, 61.90; H, 6.35. Found: C, 61.96; H, 6.37.

# 1-(4'-O-Acetyl-2',3',6'-trideoxy- $\beta$ -L-erythro-hex-2'-enopyranosyl)-1-propyne (3c)

Liquid.

<sup>1</sup>H NMR (CDCl<sub>3</sub>): δ = 1.25 (d, J = 6.3 Hz, 3 H, CH<sub>3</sub>), 1.84 (d, J = 2.2 Hz, 3 H, CH<sub>3</sub>C=,), 2.09 (s, 3 H, CH<sub>3</sub>COO), 3.70–4.01 (m, 1 H, H-5), 4.90–5.15 (m, 2 H, H-1, H-4), 5.73 (dt,  $J_d$  = 10.0 Hz,  $J_t$  = 5.2 Hz, 1 H, H-3), 5.85 (ddd, J = 1.9, 3.4, 10.0 Hz, 1 H, H-2).

<sup>13</sup>C NMR (CDCl<sub>3</sub>):  $\delta$  = 3.5 (CH<sub>3</sub>C=), 17.5 (C-6), 20.9 (CH<sub>3</sub>), 62.2 (C-1), 68.4 (C-4), 72.7 (C-5), 75.0, 83.6 (C=C), 124.5, 128.7 (CH=CH), 170.2 (C=O).

MS: m/z = 195 (4) [MH]<sup>+</sup>, 135 (100) [MH – CH<sub>3</sub>COOH]<sup>+</sup>.

Anal. Calcd for  $C_{11}H_{14}O_3$ : C, 68.04; H, 7.22. Found: C, 68.09; H, 7.27.

#### 1-(4',6'-Di-O-acetyl-2',3'-dideoxy-α-D-*erythro*-hex-2'-enopyranosyl)-2-phenylethyne (1d) Liquid.<sup>22b</sup>

<sup>1</sup>H NMR (CDCl<sub>3</sub>):  $\delta$  = 2.08 (s, 3 H, CH<sub>3</sub>COO), 2.12 (s, 3 H, CH<sub>3</sub>COO), 4.15–4.31 (m, 3 H, H-5, H-6), 5.21–5.24 (m, 1 H, H-1), 5.32 (dq,  $J_d$  = 8.7 Hz,  $J_q$  = 2.0 Hz, 1 H, H-4), 5.85 (dt,  $J_d$  = 9.8 Hz,  $J_t$  = 1.8 Hz, 1 H, H-2), 6.01 (ddd, J = 1.8, 9.8, 3.5 Hz, 1 H, H-3), 7.31–7.34, 7.45–7.49 (m, 5 H, ArH).

<sup>13</sup>C NMR (CDCl<sub>3</sub>):  $\delta$  = 21.0 (CH<sub>3</sub>), 21.2 (CH<sub>3</sub>), 63.2 (C-6), 64.2 (C-1), 64.4 (C-4), 69.8 (C-5), 84.3, 86.7 (C=C), 121.9 (C), 125.3 (CH), 128.3 (CH), 128.4 (CH), 129.0 (CH), 132.0 (CH), 170.1 (C=O), 171.0 (C=O).

MS: *m*/*z* = 315 (1) [MH]<sup>+</sup>, 255 (7) [MH – CH<sub>3</sub>COOH]<sup>+</sup>, 195 (100) [MH – 2 × CH<sub>3</sub>COOH]<sup>+</sup>.

## 1-(4',6'-Di-*O*-acetyl-2',3'-dideoxy-α-D-*threo*-hex-2'-enopyranosyl)-2-phenylethyne (2d)

Liquid.

<sup>1</sup>H NMR (CDCl<sub>3</sub>):  $\delta = 2.07$  (s, 3 H, CH<sub>3</sub>COO), 2.09 (s, 3 H, CH<sub>3</sub>COO), 4.21 (dd, J = 7.4, 11.5 Hz, 1 H, H-6a), 4.31 (dd, J = 5.2, 11.5 Hz, 1 H, H-6b), 4.44 (ddd, J = 2.4, 5.2, 7.4 Hz, 1 H, H-5), 5.11 (dd, J = 2.4, 5.2 Hz, 1 H, H-4), 5.26 (dd, J = 1.8, 3.7 Hz, 1 H, H-1), 6.05 (ddd, J = 1.8, 5.2, 10.0 Hz, 1 H, H-3), 6.15 (dd, J = 3.7, 10.0 Hz, 1 H, H-3), 6.15 (dd, J = 3.7, 10.0 Hz, 1 H, H-2), 7.27–7.35, 7.41–7.46 (m, 5 H, ArH).

<sup>13</sup>C NMR (CDCl<sub>3</sub>):  $\delta = 20.8$  (CH<sub>3</sub>), 20.9 (CH<sub>3</sub>), 62.9 (C-6), 63.3 (C-1), 64.4 (C-4), 69.8 (C-5), 84.1, 86.8 (C=C), 122.1 (C), 122.4 (CH), 128.3 (CH), 128.8 (CH), 131.8 (CH), 132.0 (CH), 170.4 (C=O), 170.7 (C=O).

MS: m/z = 315 (1) [MH]<sup>+</sup>, 255 (7) [MH – CH<sub>3</sub>COOH]<sup>+</sup>, 195 (100) [MH – 2 × CH<sub>3</sub>COOH]<sup>+</sup>.

Anal. Calcd for  $C_{18}H_{18}O_5$ : C, 68.79; H, 5.73. Found: C, 68.89; H, 5.78.

# 1-(4'-O-Acetyl-2',3',6'-trideoxy-α-L-*erythro*-hex-2'-enopyranosyl)-2-phenylethyne (3d)

Liquid.

<sup>1</sup>H NMR (CDCl<sub>3</sub>):  $\delta = 1.32$  (d, J = 6.2 Hz, 3 H, CH<sub>3</sub>), 2.14 (s, 3 H, CH<sub>3</sub>COO), 4.11 (dquint,  $J_q = 6.2$  Hz,  $J_d = 1.9$  Hz, 1 H, H-5), 5.08–5.18 (m, 2 H, H-1, H-4), 5.83 (dt,  $J_d = 10.1$  Hz,  $J_t = 1.9$  Hz, 1 H, H-3), 5.99 (ddd, J = 1.8, 3.4, 10.1 Hz, 1 H, H-2).

<sup>13</sup>C NMR (CDCl<sub>3</sub>):  $\delta$  = 18.0 (C-6), 21.1 (CH<sub>3</sub>CO), 63.8 (C-1), 68.1 (C-4), 70.3 (C-5), 85.4, 86.0 (C=C), 122.3 (C), 125.6 (CH), 128.2 (CH), 128.6 (CH), 129.3 (CH), 131.8 (CH), 170.6 (C=O).

MS: m/z = 257 (3) [MH]<sup>+</sup>, 197 (100) [MH – CH<sub>3</sub>COOH]<sup>+</sup>.

Anal. Calcd for  $C_{16}H_{16}O_3$ : C, 75.00; H, 6.25. Found: C, 64.93; H, 6.31.

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