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ORIGINAL ARTICLE

TMSOTf mediated stereoselective synthesis of α-*C*-glycosides from unactivated aryl acetylenes

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Abstract A metal free and highly stereoselective procedure for the synthesis of 2,3-unsaturated-*C*-glycosides has been developed between glycals and unactivated aryl acetylenes in the presence of TMSOTf through a triflated *C*-vinyl glycosides intermediate. The flexibility of the procedure was tested by a wide variety of glycals and unactivated aryl acetylenes (20 examples). The corresponding alkynyl *C*-glycosides were obtained in good yields with completely α-selectivity in a short time (<25 min). And a plausible mechanism for the synthesis of alkynyl *C*-glycosides was depicted.

Keywords Metal free · *C*-glycosides · TMSOTf · Aryl acetylenes · Glycals

Stereoselective synthesis of *C*-glycosides has become very significant in the fields of carbohydrate and biological chemistry, since *C*-glycosides widely exist in the biologically active natural products [1–3]. *C*-glycosides are versatile chiral building blocks for the synthesis of optically active compounds and many biologically natural products, since it allows for the introduction of carbon chains into sugar chirons [4–6]. Moreover, specifically *C*-alkynyl glycosides are attractive due to the presence of a triple bond that can be easily transformed into other chiral carbon analogues of synthetic carbohydrates or used to build up building blocks of natural products (*i.e.* ciguatoxin, gambiertoxin, tautomycin) [7–11]. The previous methods for the synthesis of *C*-alkynyl glycosides are using the activated alkynes, such as silylacetylenes [12–14], iodoacetylenes, [15] alkynyltrifluoroborates, [16] reacted with the glycals through a Ferrier-type rearrangement, which involves two steps namely activation of alkynes and then Ferrier-type alkynylation of gycals using activated alkynes. These methods often suffer the drawbacks such as intricacy operation and low overall yield. Recently, Yousuf's group have reported the direct access to alkynyl *C*-glycosides under coppertriflate/ascorbic acide catalysis [17] or zinc/bromoethylacetate catalysis [18]. Another method for directed *C*-alkynylation of glycals was reported by Shah, et.al., [19], which used TMSOTf as a promoter to generate *in situ* trimethylsilylacetylene for *C*-alkynylation at low -20 °C in dichloromethane. In the present paper we describe the *in situ* generation of triflated *C*-vinyl glycosides catalyzed by TMSOTf between glycals and unactivated aryl acetylenes and its subsequent usage for highly stereoselective synthesis of alkynyl *C*-glycosides in dichloroethane at 80 °C. As far as we know, this is the first report which describes the *in situ* generation of triflated *C*-vinyl glycosides and its further application to synthesis of *C*-glycosides.

In the last years we have developed efficient methods to synthesize 2,3-unsaturated-*O*-glycosides, *S*-glycosides, aryl-*C*-glycosides and 2-deoxy-*O*-aryl-glycosides using solid acid or Lewis acid as catalysts [20–25], which are often used to synthesize bioactive glycoconjugates. Since *C*-glycosides are stable analogs of *O*-glycosides and less prone to hydrolysis by acids and glycosidases, we have now developed a metal free

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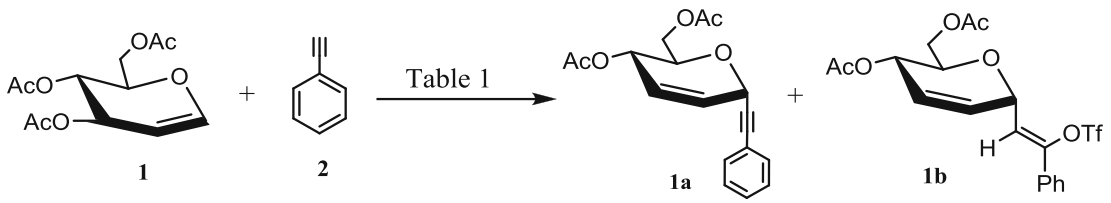
and highly stereoselective method to synthesize *C*-glycosides from unactivated aryl acetylenes.

At the outset, tri-*O*-acetyl-D-glucal **1** and phenylacetylene **2** were chosen as starting materials and dichloroethane as solvent. The reaction between **1** and **2** was first investigated with two kinds of solid acids as catalyst, but the reaction did not lead to the desired compound (Table 1, entries 1, 2). We then used $BF_3{\cdot}OEt_2$ to promote the reaction, it afforded a mixture, and after tedious separation, **1a** was isolated in a low 18 % yield (Table 1, entry 3).

As we have successfully used TMSOTf to synthesize 2-deoxy-*O*-aryl-glycosides before [24], we then tried to use it to promote the reaction at room temperature. At the beginning, the **1b** was got as the major product and little amount **1a** was observed in TLC; and some of **1b** transformed to **1a** after extending the reation time. Finally, 24 % yield **1a** and 20 % yield **1b** were obtained after 4 h (Table 1, entry 4). Increasing the amount of TMSOTf from 0.3 eq to 0.6 eq, **1a** could be obtained in 30 % yield. Further increasing the catalyst amount (up to 1.2 eq) would

Table 1 Optimization of reaction conditions for *C*-alkynylation of glycals[a]



Entry	Catalyst(equiv)	Solvent	Temperature (^oC)	Time (min)	Yield[b] (%) **1a**	Yield[b] (%) **1b**
1	H_2SO_4-SiO_2(1.2)	DCE	20	240	ND[c]	ND[c]
2	H_2SO_4/4ÅMS(1.2)	DCE	20	240	ND[c]	ND[c]
3	$BF_3{\cdot}OEt_2$(1.2)	DCE	20	240	18	ND[c]
4	TMSOTf(0.3)	DCE	20	240	24	20
5	TMSOTf(0.6)	DCE	20	240	30	40
6	TMSOTf(0.9)	DCE	20	240	30	40
7	TMSOTf(1.2)	DCE	20	240	30	40
8	TMSOTf(0.6)	DCE	40	240	51	24
9	TMSOTf(0.6)	DCE	60	120	60	12
10	TMSOTf(0.6)	DCE	80	25	67	5
11	TMSOTf(0.6)	CH_3CN	80	60	30	ND[c]
12	TMSOTf(0.6)	THF	80	60	ND[c]	ND[c]
13	TMSOTf(0.6)	Toluene	80	60	51	10
14[d]	TMSOTf(0.6)	DCE	80	25	63	5

[a] In all case 0.1 mmol of **1**, 1.2 Eq. **2**, 30 mg 4 Å molecular sieves (powder), 1.5 mL solvent

[b] Isolated yield, In all case α:β > 19:1, determined by ^{1}H NMR

[c] ND = not determined. [d] Without 4 Å molecular sieves

not improve the yields of both **1a** and **1b** (**Table 1**, entries 5–7). Interestingly, rising the reaction temperature from 20 °C to 80 °C largely favors the transformation from **1b** to **1a** and 80 °C was found to be the best temperature (Table 1, entries 7–10). Further optimization revealed that using 0.6 equivalent TMSOTf (at 80 °C) to promote the reaction could afforded the **1a** in highest yield (67 %) in a short time (Table 1, entry 10). With respect to other solvents, no improvement in the yield was observed. Using toluene as solvent, *C*-glycoside was obtained only in 51 % yield. When using THF as solvent, no product could be obtained (Table 1, entries 11–13). Without adding 4 Å molecular sieves to the reaction, the yield of **1a** was slight decreased (Table 1, entries 14), while the start materials keep intact if only used 4 Å molecular sieves as catalyst. Under these optimization conditions, **1a** was formed as a single α-isomer without any anomerization. The structure of **1a** was determined through spectroscopic analysis and the spectrum data is well agreement with the reported data [12, 15].

With the optimal condition developed, we next investigated the reaction scope using a variety of acceptors. As show in Table 2, glycosidation of tri-*O*-acetyl-D-glucal with various phenylacetylenes bearing electron-donating or electron-withdrawing groups proceeded smoothly under the specified conditions (**1a-4a**). The reaction afforded the corresponding acetylene glycosides in good yields with completely α-selectivity. Although the reaction between tri-*O*-acetyl-D-glucal and 4-methoxyphenylacetylene failed under the optimal conditions, modification of the reaction temperature (at 50 °C) successfully obtained the desired product **5a** in moderate yield in 3 min. Motivated by these results, other glycals were also subjected to the same reaction to obtain the corresponding products. Likewise, when tri-*O*-acetyl-D-galactal was treated with various phenylacetylenes under the optimal condition, corresponding acetylene galactosides **6a-9a** were obtained in good yields with excellent stereoselectivity. It has been observed that in general the galactal series reacted faster than glucal series. Meanwhile, tri-*O*-benzoyl-D-glucal and tri-*O*-benzoyl-D-galactal also undergo the same reaction smoothly under the optimal condition to afford the corresponding sugar acetylene **14a-17a** in good yields within a short time.

In a further set of experiments, we investigated the generality of the method with respect to the deoxysugars. As depicted in Table 2, the reaction of deoxysugars with phenylacetylenes proceeded cleanly in good yields with completely α-selectivity (**10a-13a, 18a**). Compared with other sugars, the reaction time is shorter in deoxysugars series, which possibly due to their higher reactivity [24]. Importantly, the procedure is also reliable to disaccharides. The exclusive α-*C*-disaccharides **19a**, **20a** were obtained in 65 % and 70 % yields, respectively, and the 1,4-glycosidic bonds remained intact. In all cases the *C*-glycosides (**1a–20a**) were obtained in 50–70 % isolated yields with completely α-selectivity at a short time (3-25 min). The structures of the products **1a–20a** were determined by ^{1}H and ^{13}C NMR and also by comparison with the reported data [12, 13, 16, 17].

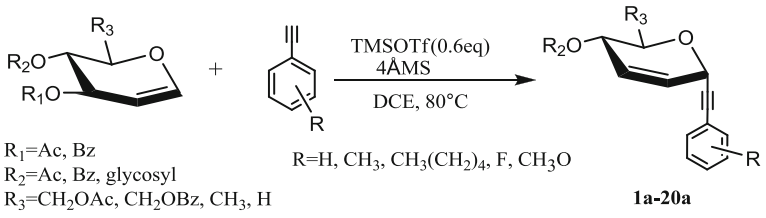
According to the experimental results and literature precedent, [7, 26, 27] a possible mechanism is outlined in Scheme 1. Firstly, tri-*O*-acetyl-D-glucal was activated by TMSOTf to generate oxocarbonium ion intermediate **21a**, with concomitant release of $[OTf]^-$ anion, then the $[OTf]^-$ anion activated the phenylacetylene and attacked the intermediate **21a** from the α-side, affording the vinyl triflate **1b**, which further eliminated at 80 °C to afford the alkynyl *C*-glycoside. The stereochemistry should largely be determined by the coordination between two π-electron orbitals of the oxocarbonium and acetylene groups, while the stereoelectronic control allows the α-pseudo-axial orbital to make the bond [7]. When the reaction proceeded at 0 °C with other conditions unchanged, the vinyl triflate **1b** was obtained as major product. The structure of the vinyl triflate **1b** was confirmed by ^{1}H NMR spectrum and high resolution mass spectrum (see supporting information). The molecular formula of **1b** was determined to be $C_{19}H_{19}F_3O_8S$ by HRMS (ESI) and ^{1}H NMR spectroscopy experiments. The ^{1}H NMR spectra confirmed the presence of 19 protons, including two acetate groups and five aromatic proton signals. Resonances at 6.01 (d, J = 9.7 Hz, 1H), 5.90 (dd, J = 10.7, 1.7 Hz, 1H), 5.86 (ddd, J = 10.5, 2.6, 1.4 Hz, 1H), apart from the aromatic proton signals in the ^{1}H NMR spectrum were assigned to the protons of vinyl triflate (H-7) and the double bond in pyranoid ring (H-2 and H-3). The coupling constant between the anomeric proton H-1 and H-7 ($J_{H1,\ H7}$ = 9.7 Hz) confirms **1b** in a α-isomer.

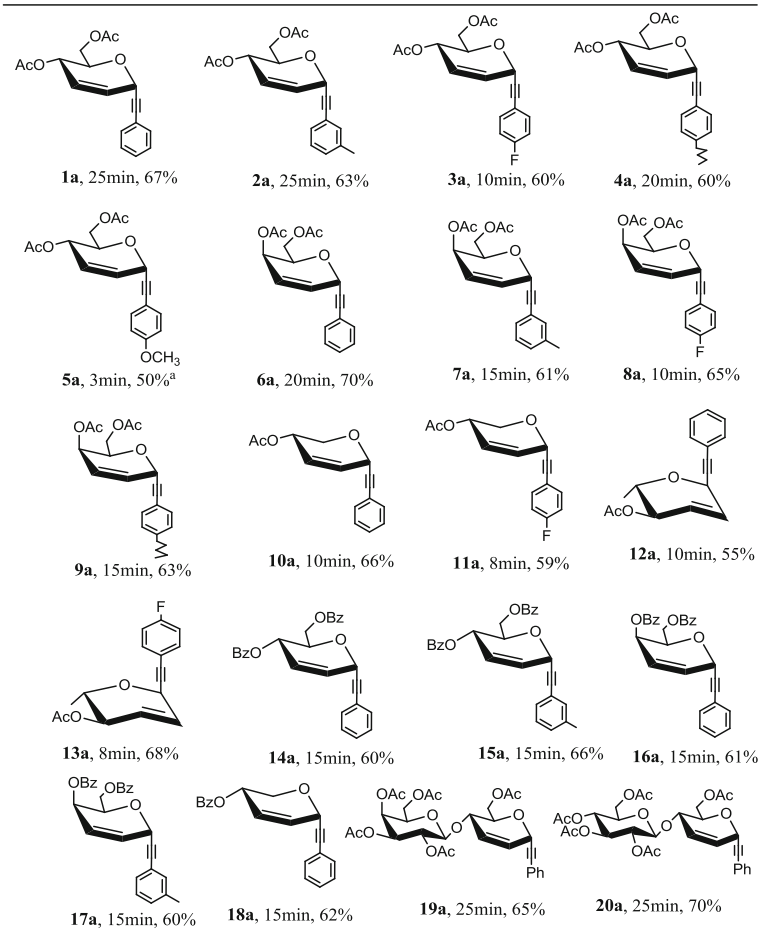
In summary, we have developed an efficient and metal free method for the direct synthesis alkynyl *C*-glycosides from glycals and unactivated aryl acetylenes. Various glycals, including acetyl glycals, benzoyl glycals, deoxysugars, disaccharides, and aryl acetylenes containning alkyl, fluoro, methoxy groups were successfully used in the reaction. This method offers several advantages, such as high stereoselectivity, short reaction time and simplicity in operation. These features make this method an attractive alternative to existing methodologies for the preparation of *C*- glycosides. Further studies on using the triflated *C*-vinyl glycosides to synthesis of other compounds are underway.

General experimental methods

All reagents were purchased with purity of AR and used as such. All the solvents for chromatography were distilled before use. Silica gel (10–40 μm, Yantai, China) was used for column chromatography. TLC plates (10–40 μm, Yantai, China) were applied to monitor reactions. ^{1}H and ^{13}C NMR

Table 2 Substrate scope of the reaction process under optimized conditions



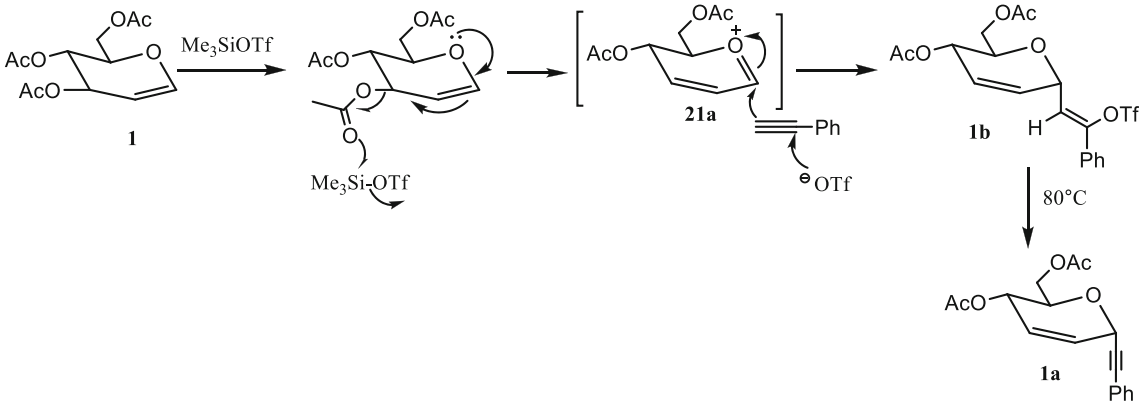


[a] The reaction temperature is 50 °C

spectra were recorded on 500 MHz and 125 MHz, respectively, with a Bruker DRX 500 spectrometer in $CDCl_3$. Chemical shifts are expressed in parts per million (ppm) with TMS as the internal standard. MS experiments were performed on LTQ-XL (Thermo Scientific, USA) with an electrospray (ESI) ion source. Glycals were prepared following the literature [25].

Typical procedure for the synthesis of *C*-alkynylglycosides

A mixture of 3, 4, 6-tri-*O*-acetyl-D-glucal (40.8 mg, 0.15 mmol), 4Å molecular sieves (60 mg) and phenylacetylene (19.8uL, 0.18 mmol, 1.2 equiv) in dry dichloroethane (2 mL) at 80 °C under nitrogen atmosphere was added the TMSOTf (16.2uL, 0.09 mmol), The reaction mixture was stirred at 80 °C for 25 min. After complete conversion, as indicated by TLC analysis, the reaction mixture was diluted with dichloromethane (8 mL) and quenched with saturated $NaHCO_3$ (8 mL). The layers were partitioned and the aqueous layer was extracted with dichloromethane (2 × 8 mL). The combined organic layers were washed with saturated $NaHCO_3$ (12 mL) and saturated brine (12 mL), then dried over anhydrous Na_2SO_4. After evaporation of the solvent under reduced pressure, the crude product was purified by column chromatography on silica gel (ethyl acetate - petroleum ether =1:12) affording **1a** (31.6 mg, 67 % yield).



Scheme 1 Plausible mechanism of TMSOTf mediated reaction of acetylene and glucal

Product characterization data

1-(4,6-di-*O*-acetyl-2,3-dideoxy-α-D-erythro-hex-2-enopyranosyl)-2-phenylacetylene(1a) ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.45 (dd, *J* = 7.4, 1.7 Hz, 2H), 7.36–7.30 (m, 3H), 5.98 (ddd, *J* = 10.0, 3.3, 1.7 Hz, 1H), 5.83 (d, *J* = 10.2 Hz, 1H), 5.34 (dd, *J* = 8.9, 1.8 Hz, 1H), 5.23–5.18 (m, 1H), 4.27 (d, *J* = 3.7 Hz, 2H), 4.23–4.17 (m, 1H), 2.11 (s, 3H), 2.10 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 171.07, 170.48, 131.97(2C), 129.36, 128.90, 128.47(2C), 125.63, 122.32, 86.82, 84.81, 70.17, 64.95, 64.60, 63.22, 21.17, 20.97. HRMS (ESI): m/z Calculated for $[M + Na]^+$ $C_{18}H_{18}O_5Na$ 337.1046, found 337.1057.

1-(4,6-di-*O*-acetyl-2,3-dideoxy-α-D-erythro-hex-2-enopyranosyl)-(*m*-tolylethynyl) (2a) ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.30–7.12 (m, 4H), 5.97 (dd, *J* = 8.4, 1.5 Hz, 1H), 5.82 (d, *J* = 10.0 Hz, 1H), 5.39–5.30 (m, 1H), 5.19 (s, 1H), 4.27 (d, *J* = 3.4 Hz, 2H), 4.23–4.15 (m, 1H), 2.33 (s, 3H), 2.11 (s, 3H), 2.10 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.89, 170.30, 138.02, 132.38, 129.62, 129.26, 128.88, 128.21, 125.41, 121.95, 86.84, 84.27, 69.96, 64.79, 64.47, 63.05, 21.16, 21.00, 20.81. HRMS (ESI): m/z Calculated for $[M + Na]^+$ $C_{19}H_{20}O_5Na$ 351.1203, found 351.1216.

1-(4,6-di-*O*-acetyl-2,3-dideoxy-α-D-erythro-hex-2-enopyranosyl)-(2-(4-fluorophenyl)ethynyl) (3a) ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.46–7.40 (m, 2H), 7.02 (t, *J* = 8.6 Hz, 2H), 5.97 (ddd, *J* = 10.2, 3.4, 1.8 Hz, 1H), 5.83 (dt, *J* = 10.2, 1.7 Hz, 1H), 5.34 (dd, *J* = 8.9, 1.9 Hz, 1H), 5.21–5.16 (m, 1H), 4.27 (d, *J* = 3.9 Hz, 2H), 4.20–4.15 (m, 1H), 2.10 (s, 6H). HRMS (ESI): m/z Calculated for $[M + Na]^+$ $C_{18}H_{17}FO_5Na$ 355.0952, found 355.0971.

1-(4,6-di-*O*-acetyl-2,3-dideoxy-α-D-erythro-hex-2-enopyranosyl)-(2-(4-pentylphenyl)ethynyl) (4a) ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.36 (d, *J* = 8.1 Hz, 2H), 7.13 (d, *J* = 8.0 Hz, 2H), 5.98 (ddd, *J* = 10.2, 3.4, 1.9 Hz, 1H), 5.81 (dt, *J* = 10.2, 1.8 Hz, 1H), 5.34 (dd, *J* = 8.9, 1.9 Hz, 1H), 5.21–5.17 (m, 1H), 4.26 (d, *J* = 3.9 Hz, 2H), 4.22–4.17 (m, 1H), 2.62–2.57 (m, 2H), 2.11 (s, 3H), 2.10 (s, 3H), 1.64–1.58 (m, 2H), 1.35–1.29 (m, 4H), 0.88 (t, *J* = 6.9 Hz, 3H). HRMS (ESI): m/z Calculated for $[M + Na]^+$ $C_{23}H_{28}O_5Na$ 407.1829, found 407.1844.

1-(4,6-di-*O*-acetyl-2,3-dideoxy-α-D-erythro-hex-2-enopyranosyl)-(2-(4-methoxyphenyl)ethynyl) (5a) ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.43–7.35 (m, 2H), 6.88–6.80 (m, 2H), 5.98 (ddd, *J* = 10.2, 3.5, 1.9 Hz, 1H), 5.81 (dt, *J* = 10.2, 1.8 Hz, 1H), 5.37–5.31 (m, 1H), 5.19 (dt, *J* = 3.5, 1.8 Hz, 1H), 4.26 (d, *J* = 3.9 Hz, 2H), 4.22–4.16 (m, 1H), 3.82 (s, 3H), 2.10 (s, 6H). HRMS (ESI): m/z Calculated for $[M + Na]^+$ $C_{19}H_{20}O_6Na$ 367.1152, found 367.1171.

1-(4,6-di-*O*-acetyl-2,3-dideoxy-α-D-threo-hex-2-enopyranosyl)-2-phenylacetylene(6a) ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.44 (dd, *J* = 7.6, 1.8 Hz, 2H), 7.37–7.29 (m, 3H), 6.15 (dd, *J* = 10.0, 3.8 Hz, 1H), 6.06 (ddd, *J* = 10.0, 5.4, 1.8 Hz, 1H), 5.27 (dd, *J* = 3.6, 1.9 Hz, 1H), 5.12 (dd, *J* = 5.4, 2.3 Hz, 1H), 4.44 (ddd, *J* = 7.4, 5.3, 2.4 Hz, 1H), 4.32 (dd, *J* = 11.5, 5.2 Hz, 1H), 4.22 (dd, *J* = 11.5, 7.3 Hz, 1H), 2.10 (s, 3H), 2.08 (s, 3H). HRMS (ESI): m/z Calculated for $[M + Na]^+$ $C_{18}H_{18}O_5Na$ 337.1046, found 337.1050.

1-(4,6-di-*O*-acetyl-2,3-dideoxy-α-D-threo-hex-2-enopyranosyl)-(*m*-tolylethynyl) (7a) ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.29–7.18 (m, 4H), 6.15 (dd, *J* = 9.9, 3.6 Hz, 1H), 6.05 (ddd, *J* = 9.8, 5.3, 1.6 Hz, 1H), 5.26 (d, *J* = 1.4 Hz, 1H), 5.12 (dd, *J* = 5.0, 2.0 Hz, 1H), 4.43 (dd, *J* = 8.4, 3.4 Hz, 1H), 4.32 (dd, *J* = 11.5, 5.3 Hz, 1H), 4.22 (dd, *J* = 11.4, 7.3 Hz, 1H), 2.33 (s, 3H), 2.10 (s, 3H), 2.08 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.69, 170.39, 138.02, 132.35, 132.05, 129.63, 128.84, 128.20, 122.35, 121.86, 87.03, 83.68, 69.64, 64.37, 63.31, 62.80, 21.14, 20.83, 20.78. HRMS (ESI): m/z Calculated for $[M + Na]^+$ $C_{19}H_{20}O_5Na$ 351.1203, found 351.1223.

1-(4,6-di-*O*-acetyl-2,3-dideoxy-α-D-threo-hex-2-enopyranosyl)-(2-(4-fluorophenyl)ethynyl) (8a) ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.42 (dd, J = 8.5, 5.4 Hz, 2H), 7.01 (t, J = 8.6 Hz, 2H), 6.13 (dd, J = 9.9, 3.6 Hz, 1H), 6.09–6.02 (m, 1H), 5.25 (d, J = 1.3 Hz, 1H), 5.11 (dd, J = 4.9, 2.0 Hz, 1H), 4.42 (t, J = 5.9 Hz, 1H), 4.31 (dd, J = 11.5, 5.3 Hz, 1H), 4.22 (dd, J = 11.4, 7.3 Hz, 1H), 2.08 (d, J = 13.4 Hz, 6H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.66, 170.36, 162.71 (d, Jc_F = 247.5 Hz), 133.77, 133.70, 131.82, 122.49, 118.12 (d, Jc_F = 3.5 Hz), 115.71, 115.53, 85.75, 83.74, 69.65, 64.27, 63.21, 62.74, 20.80, 20.75. HRMS (ESI): m/z Calculated for $[M + Na]^+$ $C_{18}H_{17}FO_5Na$ 355.0952, found 355.0966.

1-(4,6-di-*O*-acetyl-2,3-dideoxy-α-D-threo-hex-2-enopyranosyl)-(2-(4-pentylphenyl)ethynyl) (9a) ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.35 (d, J = 8.2 Hz, 2H), 7.13 (d, J = 8.2 Hz, 2H), 6.14 (dd, J = 10.1, 3.8 Hz, 1H), 6.05 (ddd, J = 10.0, 5.4, 1.9 Hz, 1H), 5.26 (dd, J = 3.7, 1.9 Hz, 1H), 5.11 (dd, J = 5.4, 2.4 Hz, 1H), 4.44 (ddd, J = 7.5, 5.3, 2.4 Hz, 1H), 4.31 (dd, J = 11.5, 5.3 Hz, 1H), 4.21 (dd, J = 11.5, 7.3 Hz, 1H), 2.63–2.55 (m, 2H), 2.08 (d, J = 11.7 Hz, 6H), 1.60 (dd, J = 14.2, 6.7 Hz, 2H), 1.31 (tdd, J = 12.9, 9.5, 3.5 Hz, 4H), 0.88 (t, J = 7.0 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.74, 170.43, 144.03, 132.17, 131.73 (2C), 128.44 (2C), 122.31, 119.19, 87.10, 83.36, 69.64, 64.45, 63.38, 62.86, 35.83, 31.38, 30.87, 22.48, 20.87, 20.82, 13.98. HRMS (ESI): m/z Calculated for $[M + Na]^+$ $C_{23}H_{28}O_5Na$ 407.1829, found 407.1839.

1-(4-*O*-acetyl-2,3-dideoxy-α-D-erythro-penta-2-enopyranosyl)-2-phenylacetylene(10a) ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.44 (dd, J = 7.5, 1.8 Hz, 2H), 7.32 (t, J = 6.2 Hz, 3H), 6.14 (dd, J = 10.1, 3.6 Hz, 1H), 6.00 (dd, J = 10.0, 4.8 Hz, 1H), 5.20–5.14 (m, 1H), 5.10–5.03 (m, 1H), 4.27 (dd, J = 13.0, 3.0 Hz, 1H), 3.93 (d, J = 13.0 Hz, 1H), 2.11 (s, 3H). HRMS (ESI): m/z Calculated for $[M + CH_3OH + Na]^+$ $C_{16}H_{18}O_4Na$ 297.1103, found 297.0629.

1-(4-*O*-acetyl-2,3-dideoxy-α-D-erythro-penta-2-enopyranosyl)-(2-(4-fluorophenyl)ethynyl) (11a) ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.42 (dd, J = 8.6, 5.4 Hz, 2H), 7.00 (t, J = 8.6 Hz, 2H), 6.12 (dd, J = 9.9, 3.1 Hz, 1H), 6.00 (dd, J = 9.3, 4.3 Hz, 1H), 5.15 (s, 1H), 5.07 (s, 1H), 4.25 (dd, J = 12.9, 2.8 Hz, 1H), 3.93 (d, J = 12.9 Hz, 1H), 2.11 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.68, 162.67 (d, Jc_F = 249 Hz), 133.79, 133.71, 131.91, 122.60, 118.18, 115.68, 115.50, 85.44, 84.22, 64.25, 63.83, 63.36, 21.07. HRMS (ESI): m/z Calculated for $[M + Na]^+$ $C_{15}H_{13}FO_3Na$ 283.0741, found 283.0729.

1-(4-*O*-acetyl-2,3,6-trideoxy-α-L-erythro-hex-2-enopyranosyl)-2-phenylacetylene (12a) ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.52–7.41 (m, 2H), 7.32 (dd, J = 6.0, 4.9 Hz, 3H), 5.96 (ddd, J = 10.2, 3.4, 1.8 Hz, 1H), 5.80 (dt, J = 10.2, 1.9 Hz, 1H), 5.17–5.11 (m, 1H), 5.07 (ddd, J = 8.2, 3.9, 1.9 Hz, 1H), 4.08 (dq, J = 12.6, 6.3 Hz, 1H), 2.10 (s, 3H), 1.29 (d, J = 6.3 Hz, 3H). HRMS (ESI): m/z Calculated for $[M + Na]^+$ $C_{16}H_{16}O_3Na$ 279.0992, found 279.0997.

1-(4-*O*-acetyl-2,3,6-trideoxy-α-L-erythro-hex-2-enopyranosyl)-(2-(4-fluorophenyl)ethynyl) (13a) ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.44 (dd, J = 8.5, 5.5 Hz, 2H), 7.04–6.97 (m, 2H), 5.94 (ddd, J = 10.1, 2.7, 1.7 Hz, 1H), 5.80 (d, J = 10.2 Hz, 1H), 5.12 (d, J = 1.3 Hz, 1H), 5.07 (dd, J = 8.1, 1.7 Hz, 1H), 4.09–4.02 (m, 1H), 2.10 (s, 3H), 1.29 (d, J = 6.3 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.51 s), 162.65(d, Jc_F = 247 Hz), 133.78 (2C), 129.17, 125.71, 118.43, 115.65, 115.47, 85.25, 84.91, 70.24, 68.22, 63.74, 21.10, 18.05. HRMS (ESI): m/z Calculated for $[M + Na]^+$ $C_{16}H_{15}FO_3Na$ 298.0897, found 298.0899.

1-(4,6-di-*O*-benzoyl-2,3-dideoxy-α-D-erythro-hex-2-enopyranosyl)-2-phenylacetylene(14a) ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.11–8.00 (m, 4H), 7.60–7.28 (m, 11H), 6.06 (ddd, J = 10.2, 3.4, 1.8 Hz, 1H), 5.99 (dt, J = 10.2, 1.7 Hz, 1H), 5.71 (dd, J = 8.7, 1.8 Hz, 1H), 5.27 (dt, J = 3.5, 1.9 Hz, 1H), 4.65 (dd, J = 11.1, 1.8 Hz, 1H), 4.56–4.46 (m, 2H). HRMS (ESI): m/z Calculated for $[M + Na]^+$ $C_{28}H_{22}O_5Na$ 461.1359, found 461.1376.

1-(4,6-di-*O*-benzoyl-2,3-dideoxy-α-D-erythro-hex-2-enopyranosyl)-(*m*-tolylethynyl) (15a) ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.05 (dd, J = 11.1, 4.1 Hz, 4H), 7.60–7.49 (m, 2H), 7.43 (t, J = 7.8 Hz, 2H), 7.36 (t, J = 7.8 Hz, 2H), 7.26–7.12 (m, 4H), 6.05 (ddd, J = 10.2, 3.4, 1.8 Hz, 1H), 5.98 (dt, J = 10.2, 1.7 Hz, 1H), 5.70 (dd, J = 8.7, 1.8 Hz, 1H), 5.26 (dt, J = 3.5, 1.8 Hz, 1H), 4.65 (dd, J = 10.9, 1.7 Hz, 1H), 4.51 (ddd, J = 17.2, 8.7, 4.1 Hz, 2H), 2.32 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.34, 165.87, 138.00, 133.34, 132.96, 132.35, 129.85, 129.79 (2C), 129.74 (2C), 129.58, 129.54, 129.40, 128.86, 128.42 (2C), 128.26 (2C), 128.19, 125.78, 121.99, 86.75, 84.48, 70.35, 65.83, 64.63, 63.87, 21.17. HRMS (ESI): m/z Calculated for $[M + Na]^+$ $C_{29}H_{24}O_5Na$ 475.1516, found 475.1527.

1-(4,6-di-*O*-benzoyl-2,3-dideoxy-α-D-threo-hex-2-enopyranosyl)-2-phenylacetylene(16a) ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.08–8.02 (m, 4H), 7.62–7.27 (m, 11H), 6.22 (p, J = 10.2 Hz, 2H), 5.45 (d, J = 1.9 Hz, 1H), 5.34 (d, J = 1.6 Hz, 1H), 4.76–4.62 (m, 2H), 4.55 (dd, J = 11.1, 4.7 Hz, 1H). HRMS (ESI): m/z Calculated for $[M + Na]^+$ $C_{28}H_{22}O_5Na$ 461.1359, found 461.1375.

1-(4,6-di-*O*-benzoyl-2,3-dideoxy-α-D-threo-hex-2-enopyranosyl)-(*m*-tolylethynyl) (17a) ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.05 (m, 4H), 7.55 (dt, J = 21.1, 7.3 Hz, 2H), 7.41

(m, 4H), 7.25–7.11 (m, 4H), 6.27–6.16 (m, 2H), 5.45 (s, 1H), 5.33 (s, 1H), 4.75–4.62 (m, 2H), 4.56 (dd, J = 11.2, 4.6 Hz, 1H), 2.30 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.21, 165.97, 137.97, 133.26, 133.00, 132.32, 132.31, 129.81, 129.77 (2C), 129.70 (2C), 129.62, 129.56, 128.80, 128.43 (2C), 128.29 (2C), 128.17, 122.59, 121.89, 86.95, 83.91, 70.24, 64.5, 64.11, 63.52, 21.14. HRMS (ESI): m/z Calculated for $[M + Na]^+$ $C_{29}H_{24}O_5Na$ 475.1516, found 475.1515.

1-(4-*O*-benzoyl-2,3-dideoxy-α-D-erythro-penta-2-enopyranosyl)-2-phenylacetylene(18a) ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.12–8.05 (m, 2H), 7.59–7.55 (m, 1H), 7.46 (dt, J = 12.6, 4.6 Hz, 4H), 7.37–7.30 (m, 3H), 6.19 (ddd, J = 10.1, 3.6, 0.7 Hz, 1H), 6.12 (dddd, J = 10.1, 4.7, 1.8, 1.1 Hz, 1H), 5.35–5.31 (m, 1H), 5.22 (dd, J = 3.1, 2.3 Hz, 1H), 4.39 (dd, J = 13.0, 3.2 Hz, 1H), 4.07 (ddd, J = 12.9, 1.9, 1.1 Hz, 1H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 166.20, 133.13, 132.21, 131.83 (2C), 129.94, 129.78 (2C), 128.69, 128.36 (2C), 128.30 (2C), 122.71, 122.18, 86.52, 84.63, 64.45, 64.42, 63.52. HRMS (ESI): m/z Calculated for $[M + Na]^+$ $C_{20}H_{16}O_3Na$ 327.0992, found 327.0989.

1-(2-phenylacetylene)-penta-*O*-acetyl-D-lactal-2-ene(19a) ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.46–7.40 (m, 2H), 7.36–7.29 (m, 3H), 6.07–6.01 (m, 1H), 5.90 (ddd, J = 10.3, 3.5, 1.8 Hz, 1H), 5.39 (d, J = 2.8 Hz, 1H), 5.24 (dd, J = 10.4, 8.0 Hz, 1H), 5.16 (dt, J = 3.3, 1.8 Hz, 1H), 5.02 (dd, J = 10.4, 3.4 Hz, 1H), 4.61 (d, J = 8.0 Hz, 1H), 4.34 (dt, J = 9.2, 4.6 Hz, 1H), 4.24–4.16 (m, 3H), 4.15–4.09 (m, 2H), 3.94 (t, J = 6.6 Hz, 1H), 2.15 (s, 3H), 2.12 (s, 3H), 2.08 (s, 3H), 2.03 (s, 3H), 1.98 (s, 3H). HRMS (ESI): m/z Calculated for $[M + Na]^+$ $C_{30}H_{34}O_{13}Na$ 625.1892, found 625.1922.

1-(2-phenylacetylene)-penta-*O*-acetyl-D-cellobial-2-ene(20a) ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.46–7.41 (m, 2H), 7.36–7.29 (m, 3H), 6.02 (d, J = 10.2 Hz, 1H), 5.93–5.88 (m, 1H), 5.21 (t, J = 9.5 Hz, 1H), 5.15 (s, 1H), 5.07 (t, J = 9.7 Hz, 1H), 5.03–4.98 (m, 1H), 4.65 (d, J = 8.0 Hz, 1H), 4.36 (d, J = 10.7 Hz, 1H), 4.24–4.15 (m, 4H), 4.10 (dd, J = 7.2, 5.4 Hz, 1H), 3.72 (ddd, J = 9.8, 4.9, 2.6 Hz, 1H), 2.12 (s, 3H), 2.07 (s, 6H), 2.03 (s, 3H), 2.00 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.78, 170.56, 170.21, 169.38, 169.36, 131.86 (2C), 128.71, 128.36, 128.29 (2C), 127.71, 122.13, 101.81, 86.61, 84.64, 73.05, 72.71, 71.86, 71.32, 70.37, 68.31, 64.53, 63.11, 61.91, 20.85, 20.66, 20.55 (2C), 20.53. HRMS (ESI): m/z Calculated for $[M + Na]^+$ $C_{30}H_{34}O_{13}Na$ 625.1892, found 625.1930.

The vinyl triflates 1b ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.54 (dd, J = 7.6, 1.5 Hz, 2H), 7.49–7.44 (m, 3H), 6.01 (d, J = 9.7 Hz, 1H), 5.90 (dd, J = 10.7, 1.7 Hz, 1H), 5.86 (ddd, J = 10.5, 2.6, 1.4 Hz, 1H), 5.20 (dd, J = 7.4, 1.7 Hz, 1H), 4.78 (dd, J = 9.6, 1.5 Hz, 1H), 4.23 (dd, J = 12.1, 6.3 Hz, 1H), 4.17 (dd, J = 12.0, 2.9 Hz, 1H), 3.99 (ddd, J = 9.1, 5.2, 1.5 Hz, 1H), 2.12 (s, 3H), 2.07 (s, 3H). Calculated for $[M + Na]^+$ $C_{19}H_{19}F_3O_8SNa$ 487.0645, found 487.0633.

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Compliance with ethical standards

Conflicts of interest The authors declare that they have no conflicts of interest.

Ethical approval This article does not contain any studies with human participants or animals performed by any of the authors.

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