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SHORT COMMUNICATION

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Transformation of Glycals into α,β,γ,δ-Conjugated Chirons under Metal-Free Conditions

Tatina Madhubabu,[a,b] Syed Khalid Yousuf,[a,c] Anil Kumar Kusunuru,[a,b] and Debaraj Mukherjee*[a,b]

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A diastereoselective, metal-free, one-pot domino synthetic strategy was developed for the transformation of glycals into new chiral scaffolds. Optimization of the reaction conditions to exclude normal Ferrier products, characterization of the new entities, and a plausible mechanism were investigated.

Introduction

Carbohydrates serve as a valuable source of diverse building blocks for natural product synthesis owing to their high functional density and stereochemical variations.[1] They are unique, especially because of their high density of stereochemical information, and their relative rigidity provides an excellent platform upon which a number of substituents can be displayed in a sterically defined way. Hence, they offer the opportunity to harness their matchless features for creating new molecular architecture. The innovative ways to manipulate these cheap chiral pools into new building blocks, for which segments of a target molecule can be related in shape, structure, and stereochemistry to native chiral synthons derived from small natural monosaccharides, are the hallmark of elegant carbohydrate-based synthesis.[2] Among the carbohydrate derivatives, unsaturated open-chain sugars such as enantiomerically pure δ-hydroxy α,β-unsaturated sugar aldehydes (generally called Perlin aldehydes) derived from D-glycal[3a] play a prominent role in the synthesis of innumerable natural products. The advantages of using Perlin aldehydes include their known defined stereochemistry, the presence of a conjugated double bond as Michael acceptor, the presence of a carbonyl moiety as a chain elongation site through C–C bond formation, and stereodiversity of two predefined chiral centers. In particular, optically pure triacetoxydiene[3b] derivatives obtained from olefination of Perlin aldehydes have been utilized extensively as a chiral pool in natural product synthesis and for biological activities.[4] Therefore, the one-pot generation of new optically pure triacetoxydiene derivatives containing all the other above attributes of Perlin aldehydes directly from D-glucal under metal-free conditions is highly desirable. In synthetic chemistry, stereoselective generation of C=C bonds has always remained a ubiquitous source of two-carbon units.[5] However, the synthesis of an α,β,γ,δ-conjugated diene system maintaining that diastereoselectivity poses a challenge to synthetic chemists owing to the use of specialized reagents.[6] Whereas the chiron approach has predictive power and general utility in total synthesis, sometimes the generation of predefined chiral centers occurs at the cost of one or more centers, which leads to loss of atom economy.[7] In recent years, domino strategies for which new chiral centers with high functional diversity were generated, maintaining atom economy, have assumed great importance in synthetic chemistry. With our incessant curiosity in the development of new domino processes in carbohydrate chemistry,[8,9b] herein we report a domino, atom-economic synthetic strategy for the generation of novel α,β,γ,δ-conjugated diastereoselectively pure (*E*,*E*)-chalcone derivatives from glycals.

Results and Discussion

Our reaction strategy was conceptualized on the basis of two of our reported works: one was the copper-mediated synthesis of C-alkynyl glycosides from unactivated acetylenes[9a] and the other was the preparation of halogenated vinyl *C*-glycosides from aryl acetylenes[9b] (Scheme 1). In the former, we observed that there was in situ generation of triflic acid (TfOH), which expedited the reaction course unexpectedly. In the latter, domino nucleophilic attack of a halide ion at the vinylic position afforded the halogenated product. Also, there are reports in which Lewis acids such as trimethylsilyl trifluoromethanesulfonate (TMSOTf) can open pyran rings in the presence of different nucleophiles

[a] Academy of Scientific and Innovative Research, CSIR-IIIM, Jammu, 180001, India
E-mail: dmukherjee@iiim.ac.in;
www.iiim.res.in
[b] Indian Institute of Integrative Medicine (IIIM/1691/2014), Jammu, 180001, India
[c] Indian Institute of Integrative Medicine, Srinagar, 190005, India

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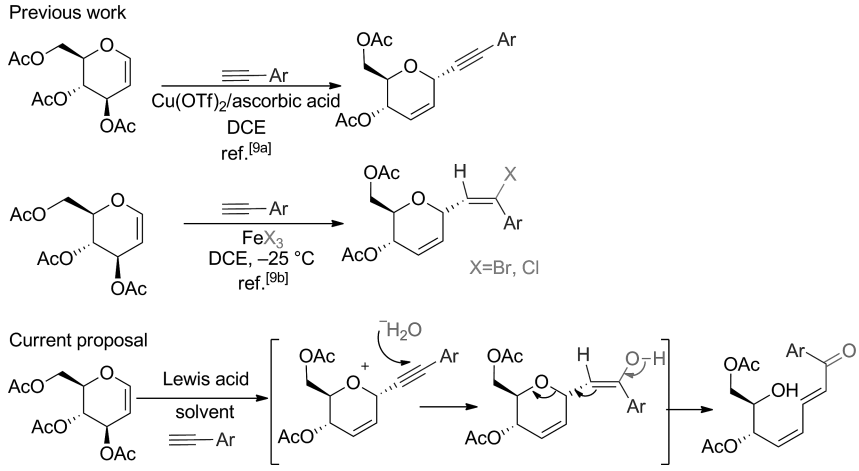
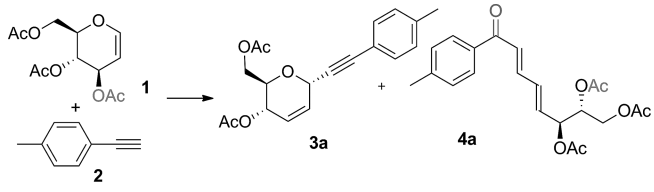


Scheme 1. Our previous reports and new proposal.

such as silyl enol ethers[9c] and thiols.[9d] Keeping all of the above facts in mind, we conceptualized that HO^- (from water) instead of halogens might attack the benzylic position as a nucleophile, which would lead to the formation of vinyl glycosides containing an enol unit; this unit may tautomerize to the keto form along with ring opening through 5-β-O-elimination to lead to the formation of alcohols (Scheme 1). This prompted us to revisit the reaction of glycals and acetylenes with nonhalogenated Lewis acids and to screen the reaction conditions for the in situ transformation of alkynyl glycosides into open-chain systems. To examine our proposed hypothesis, we investigated the reaction of tri-*O*-acetyl-D-glucal (**1**) with phenyl acetylene (**2**) in the presence of TMSOTf in 1,2-dichloroethane (DCE; Table 1, entry 1) to form phenyl acetylene glycoside (**3a**) as the sole product in excellent yield and comparable with our earlier reported $Cu(OTf)_2$/ascorbic acid conditions.[9a]

We failed to observe considerable degradation after adding a drop of water to the reaction mixture (Table 1, entry 2). Thereafter, we opted for more polar solvents. Indeed, the reaction of **1** with **2** in the presence of TMSOTf (20 mol-%) in laboratory-grade acetonitrile for a prolonged reaction time (4–6 h) led to some amount of degradation (Table 1, entry 3). We felt that the presence of moisture in acetonitrile was responsible for this degradation. Gratifyingly, adding a drop of water and increasing the amount of TMSOTf (from 20 mol-% to 1.2 equiv.) expedited the ring-opening process, and we were able to obtain **4a** (Table 1, entry 4) as the sole product. Other metal triflates (Table 1, entries 6–8) and acids (Table 1, entries 11 and 12; TFA = trifluoroacetic acid) except triflic acid (Table 1, entries 9 and 10) failed to produce desired product **4a**. The formation of **4a** was confirmed through extensive spectroscopy analysis (Figure 1). Initially, we examined the mass spectrum of **4a** and there was a clear indication of the presence of an extra acetic acid molecule in comparison to **3a**. The molecular formula of **4a** was determined to be $C_{20}H_{22}O_7$ by HRMS (ESI) and NMR spectroscopy experiments. The ^1H NMR and ^{13}C NMR spectra confirmed the presence of

Table 1. Optimization of the reaction conditions for the transformation of tri-*O*-acetyl-D-glucal into chalcone derivative **4a**.



Entry	Catalyst[a]	Solvent[b]	Temp. [°C]	Time [h]	Yield [%] **3a**/**4a**[c]
1	TMSOTf	CH_2Cl_2	–20	0.2	91:0[d]
2	TMSOTf	CH_2Cl_2/H_2O	–20	6	70:10
3	TMSOTf	MeCN	–20 to r.t.	6	70:20
4	TMSOTf[e]	$MeCN/H_2O$	–20 to r.t.	4	0:72
5	TMSOTf	THF	–20	2	0:0
6	$Fe(OTf)_3$	MeCN	r.t.	10	0:0
7	$In(OTf)_3$	MeCN	r.t.	8	0:0
8	$Sc(OTf)_3$	MeCN	r.t.	8	0:0
9	TfOH	MeCN	0	0.2	84:0
10	TfOH[e]	$MeCN/H_2O$	–20 to r.t.	6	0:65
11	TFA	MeCN	r.t.	1	0:0
12	$BF_3{\cdot}OEt_2$	CH_2Cl_2	0	2	0:0

[a] In all cases, 20 mol-% of catalyst was used. [b] For 1 mmol of **1**, solvent (3 mL) and H_2O (10–20 μL) were used. [c] Yield of product obtained after column chromatography. [d] See the Supporting Information (Table S1, entries **3a**–**k**) for a detailed study. [e] Lewis/protic acid (1.2 equiv.).

20 carbons and 22 protons, including 3 acetate groups with a double bond equivalence (DBE) of 10. The IR (neat) spectrum showed an absorption at $\tilde{\nu}$ = 1682 cm^{-1}, which indicated the presence of an α,β-unsaturated ketone group; this was further confirmed by a signal at δ = 190 ppm in the ^{13}C NMR spectrum. Resonances at δ = 7.36 (dd), 7.05 (d), 6.57 (dd), 6.10 ppm (dd) apart from the aromatic proton signals in the ^1H NMR spectrum and the corresponding ^{13}C NMR signals at δ = 141.8, 134.9, 132.8, 127.5 ppm were assigned to a conjugated dienenone system. The stereochemistry at the two conjugated double bonds was determined through examination of the H–H coupling constants ($J_{H2,H3}$ = $J_{H4,H5}$ = 15.3 Hz and $J_{H3,H4}$ = 11.3 Hz),

which are characteristic of an *anti trans,trans* (*E*,*E*) double bond.[4a] The DBE value of 10 was accounted for by the presence of one aromatic ring, one keto group, two double bonds, and three acetates. Finally, complete structural elucidation of **4a** as well as assignment of all ^{1}H NMR and ^{13}C NMR signals was achieved (Figure 1) by 2D NMR spectroscopy experiments (HMBC, HSQC, and COSY).

Other metal triflates such as Fe, Sc, and In failed to give the alkynyl glycoside in satisfactory yield. Use of triflic acid yielded glycoside **3** in 84% yield, but desired product **4a** was not generated, even upon the addition of water to the reaction flask. Thus, we concluded that the use of TMSOTf (1.2 equiv.) and H_2O (1.2 equiv.) in acetonitrile (3 mL) at –20 °C constituted the optimal conditions to generate **4a** (Table 1, entry 4). Encouraged by these results, we next checked the feasibility and generality of the reaction conditions in other acetylenes (Scheme 2).

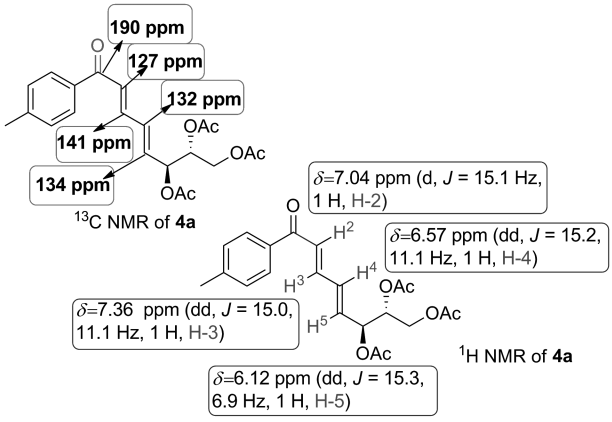
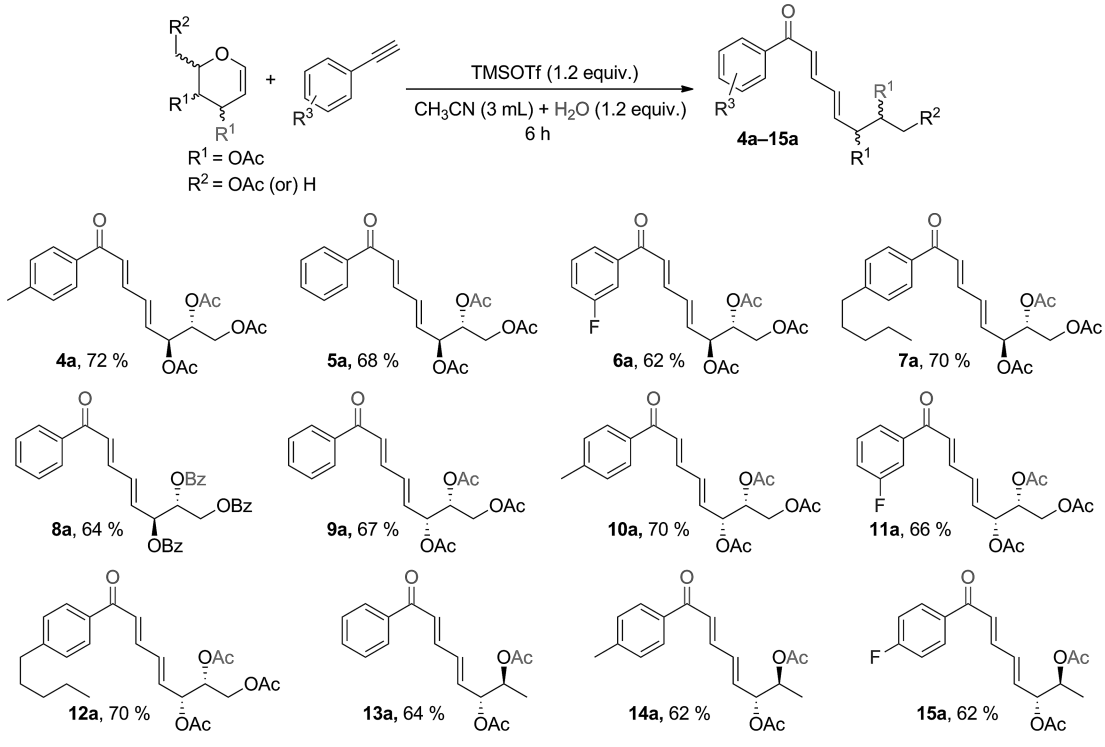


Figure 1. Spectroscopic analysis of **4a**.

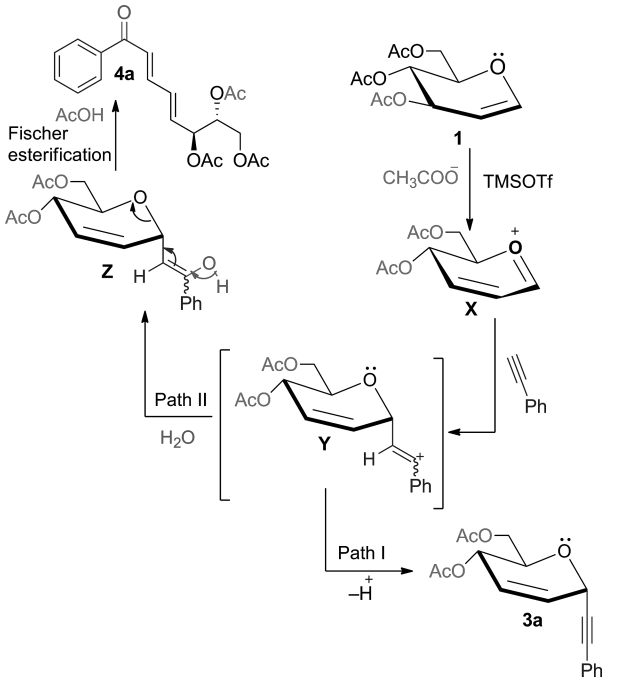
In this endeavor, a series of aromatic acetylenes were treated with **1** under the standardized reaction conditions (Scheme 2, compounds **4a**–**8a**). All of the reactions proceeded smoothly and led to the formation of the desired products in good to high yields. The nature of the substituent was found to play no role in deciding the course and yield of the reaction, as acetylenes with both electron-donating and electron-withdrawing groups afforded similar products. Further, other glycals such as tri-*O*-acetyl-D-galactal (Scheme 2, compounds **9a**–**12a**) and di-*O*-acetyl-L-rhamnal (Scheme 2, compounds **13a**–**15a**) also underwent the reaction to give the corresponding products in good yields. The utility and scope of the reaction lies in the fact that we can generate stereochemistry of choice by using various substrates. Another advantage of this reaction is that conjugated double bonds are created with complete stereocontrol and without loss of any chiral center. Aliphatic alkynes under similar conditions did not undergo glycal ring opening and yielded Ferrier products, albeit in low yields (see the Supporting Information for details).

To explain the formation of the open-chain product, the mechanism outlined in Scheme 3 was proposed on the basis of our experimental observations and literature precedent. The key step is the formation of oxocarbonium ion **X** from glycal (**1**) by TMSOTf-mediated elimination of the allylic



Scheme 2. Substrate scope of the one-pot domino reaction. Bz = benzoyl.

acetoxy group, which is followed by nucleophilic attack of phenylacetylene.[10] This generates reactive carbocation intermediate **Y**, which is trapped by a water molecule to generate hydroxy vinyl glycoside **Z**.



Scheme 3. Plausible mechanism for the domino reaction of glycals with arylacetylenes in the presence of TMSOTf.

Feasibility of keto–enol tautomerism in **Z** favors ring opening to yield the alcohol, which undergoes transesterification[11] with CH_3COOH present in the reaction medium to generate **4a**. The formation of **3a** can also be explained by the loss of H^+ from **Y** to stabilize the carbocation.

Conclusions

In conclusion, we developed a highly stereoselective metal-free, one-pot domino synthetic strategy for the transformation of glycals into fully functionalized chiral scaffolds. Generation of a conjugated (*E*,*E*)-diene that is in conjugation with a carbonyl group and possible stereodiversity of two predefined chiral centers make this protocol a potential candidate for target-oriented synthesis, and presently we are working in this direction.

Experimental Section

General Information: ^{1}H NMR and ^{13}C NMR spectra were recorded with 400 and 500 MHz spectrometers with tetramethylsilane as the internal standard. Silica gel coated aluminum plates were used for TLC. The products were purified by column chromatography on silica gel (60–120/100–200 mesh) by using petroleum ether/ethyl acetate as the eluent to obtain the pure products. Exact molecular masses of all products were analyzed by using HRMS with a QTOF analyzer. Reagents used were mostly purchased from Sigma–Aldrich.

General Procedure 1

***C*-Glycosylation Followed by Ring Opening with TMSOTf:** TMSOTf (1.2 equiv.) was added to a solution of glycal (0.5 mmol) and aromatic acetylene (1.1 equiv.) in acetonitrile (3 mL) at –20 °C, and the resulting solution was stirred at the same temperature for 10–20 min. After the addition of water (10–20 μL), the mixture was stirred at room temperature for 4–6 h. Progress of the reaction was monitored by TLC. The reaction was quenched with $NaHCO_3$ after dilution with CH_2Cl_2 (10 mL), and the product was extracted with CH_2Cl_2 (10 mL). The organic phase was dried with anhydrous sodium sulfate and concentrated in vacuo. The crude product was purified by column chromatography (silica gel, ethyl acetate).

(6*S*,7*R*,2*E*,4*E*)-6,7,8-Tri-*O*-acetyl-1-(*p*-tolyl)octa-2,4-diene-1-one (4a): Prepared by general procedure 1 by using tri-*O*-acetyl-D-glucal (0.5 mmol, 136 mg) and 4-methylphenylacetylene (0.55 mmol, 69 μL). Yield: 139 mg (72%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.86 (d, *J* = 7.9 Hz, 2 H), 7.36 (dd, *J* = 14.8, 11.3 Hz, 1 H), 7.28 (d, *J* = 7.6 Hz, 2 H), 7.05 (d, *J* = 15.1 Hz, 1 H), 6.57 (dd, *J* = 15.0, 11.4 Hz, 1 H), 6.10 (dd, *J* = 15.3, 6.9 Hz, 1 H), 5.62 (t, *J* = 5.5 Hz, 1 H), 5.26 (dd, *J* = 6.3, 4.0 Hz, 1 H), 4.23 (qd, *J* = 12.1, 5.0 Hz, 2 H), 2.42 (s, 3 H), 2.12 (s, 3 H), 2.09 (s, 3 H), 2.06 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 189.7, 170.54, 170.0, 169.6, 143.8, 141.8, 135.1, 134.9, 132.8, 129.3 (2 C), 128.5 (2 C), 127.5, 71.8, 71.4, 61.7, 21.6, 20.89, 20.83, 20.6 ppm. IR (neat): $\tilde{\nu}$ = 3453, 2926, 1738, 1732, 1682, 1408, 1369, 1225, 1204, 1182, 1094, 1047, 812, 758 cm^{-1}. HRMS (ESI+): calcd. for $C_{21}H_{25}O_7$ [M + H]$^+$ 389.1600; found 389.1623.

(6*S*,7*R*,2*E*,4*E*)-6,7,8-Tri-*O*-acetyl-1-phenylocta-2,4-diene-1-one (5a): Prepared by general procedure 1 by using tri-*O*-acetyl-D-glucal (0.5 mmol, 136 mg) and phenylacetylene (0.55 mmol, 56 μL). Yield: 127 mg (68%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.94 (d, *J* = 8.0 Hz, 2 H), 7.58 (t, *J* = 7.3 Hz, 1 H), 7.48 (t, *J* = 7.6 Hz, 2 H), 7.41–7.24 (m, 1 H), 7.04 (d, *J* = 15.1 Hz, 1 H), 6.57 (dd, *J* = 15.2, 11.1 Hz, 1 H), 6.12 (dd, *J* = 15.3, 6.9 Hz, 1 H), 5.67–5.57 (m, 1 H), 5.34–5.21 (m, 1 H), 4.23 (qd, *J* = 12.1, 5.2 Hz, 2 H), 2.12 (s, 3 H), 2.09 (s, 3 H), 2.06 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 190.3, 170.5, 170.0, 169.6, 142.3, 137.7, 135.3, 132.9, 132.7, 128.6 (2 C), 128.4 (2 C), 127.4, 71.6, 71.4, 61.7, 20.9, 20.8, 20.7 ppm. IR (neat): $\tilde{\nu}$ = 3471, 2926, 1745, 1665, 1599, 1371, 1224, 1047, 1016, 773, 698 cm^{-1}. HRMS (ESI+): calcd. for $C_{20}H_{23}O_7$ [M + H]$^+$ 375.1444; found 375.1458.

(6*S*,7*R*,2*E*,4*E*)-6,7,8-Tri-*O*-acetyl-1-(3-fluorophenyl)octa-2,4-diene-1-one (6a): Prepared by general procedure 1 by using tri-*O*-acetyl-D-glucal (0.5 mmol, 136 mg) and 3-fluorophenylacetylene (0.55 mmol, 63 μL). Yield: 121 mg (62%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.72 (d, *J* = 7.7 Hz, 1 H), 7.67–7.58 (m, 1 H), 7.47 (td, *J* = 8.0, 5.6 Hz, 1 H), 7.38 (dd, *J* = 15.0, 11.1 Hz, 1 H), 7.29 (br. s, 1 H) 6.99 (d, *J* = 15.1 Hz, 1 H), 6.57 (dd, *J* = 15.3, 11.1 Hz, 1 H), 6.15 (dd, *J* = 15.3, 6.8 Hz, 1 H), 5.70–5.56 (m, 1 H), 5.27 (dt, *J* = 6.6, 4.2 Hz, 1 H), 4.27 (dd, *J* = 12.1, 3.7 Hz, 1 H), 4.20 (dd, *J* = 12.1, 6.6 Hz, 1 H), 2.13 (s, 3 H), 2.10 (s, 3 H), 2.07 (s, 3 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 188.6, 170.7, 170.2, 169.4, 162.8, 142.3, 139.7, 135.7, 132.3, 129.8, 126.3, 124.1, 120.0, 114.9, 71.8, 71.1, 61.5, 20.88, 20.83, 20.6 ppm. IR (neat): $\tilde{\nu}$ = 3471, 3074, 2961, 2933, 1747, 1667, 1586, 1372, 1223, 1047, 1021, 789, 724 cm^{-1}. HRMS (ESI+): calcd. for $C_{20}H_{22}FO_7$ [M + H]$^+$ 393.1350; found 393.1374.

(6*S*,7*R*,2*E*,4*E*)-6,7,8-Tri-*O*-acetyl-1-(4-pentylphenyl)octa-2,4-diene-1-one (7a): Prepared by general procedure 1 by using tri-*O*-acetyl-D-glucal (0.5 mmol, 136 mg) and 4-pentylphenylacetylene (0.55 mmol, 106 μL). Yield: 155 mg (70%) ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.80 (d, *J* = 7.6 Hz, 2 H), 7.28 (dd, *J* = 14.9, 11.2 Hz,

1 H), 7.21 (d, *J* = 7.4 Hz, 2 H), 6.98 (d, *J* = 15.1 Hz, 1 H), 6.49 (dd, *J* = 15.1, 11.2 Hz, 1 H), 6.03 (dd, *J* = 15.3, 6.9 Hz, 1 H), 5.60–5.47 (m, 1 H), 5.26–5.11 (m, 1 H), 4.19 (dd, *J* = 12.0, 3.4 Hz, 1 H), 4.12 (dd, *J* = 12.1, 6.6 Hz, 1 H), 2.59 (t, *J* = 7.7 Hz, 2 H), 2.05 (s, 3 H), 2.02 (s, 3 H), 1.99 (s, 3 H), 1.62–1.51 (m, 2 H), 1.25 (d, *J* = 3.0 Hz, 4 H), 0.82 (t, *J* = 6.4 Hz, 3 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 189.7, 170.5, 170.0, 169.6, 148.8, 141.8, 135.3, 134.9, 132.8, 128.7 (2 C), 128.6 (2 C), 127.5, 71.8, 71.4, 61.7, 35.9, 31.4, 30.7, 22.4, 20.9, 20.8, 20.7, 14.0 ppm. IR (neat): ṽ = 3471, 2957, 2930, 1747, 1664, 1607, 1371, 1222, 1048, 1025, 1013, 816, 795, 683 cm^{-1}. HRMS (ESI+): calcd. for $C_{25}H_{32}NaO_7$ [M + Na]$^+$ 467.2046; found 467.2022.

(6*S*,7*R*,2*E*,4*E*)-6,7,8-Tri-*O*-benzoyl-1-phenylocta-2,4-diene-1-one (8a): Prepared by general procedure 1 by using tri-*O*-benzoyl-D-glucal (0.5 mmol, 229 mg) and phenylacetylene (0.55 mmol, 58 μL). Yield: 179 mg (64%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.94 (m, 6 H), 7.83 (d, *J* = 7.3 Hz, 2 H), 7.47 (m, 4 H), 7.42–7.26 (m, 9 H), 6.92 (d, *J* = 15.1 Hz, 1 H), 6.63 (dd, *J* = 15.2, 11.1 Hz, 1 H), 6.31 (dd, *J* = 15.3, 6.6 Hz, 1 H), 6.07–6.00 (m, 1 H), 5.78 (m, 1 H), 4.70 (dd, *J* = 12.0, 4.1 Hz, 1 H), 4.59 (dd, *J* = 12.0, 6.6 Hz, 1 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 190.2, 166.1, 165.5, 165.1, 142.2, 137.7, 133.6, 133.5, 133.3, 132.9, 132.8, 129.8, 129.7, 129.37, 129.34, 128.65, 128.64, 128.57, 128.50, 128.46, 127.5, 72.8, 72.1, 62.4 ppm. IR (neat): ṽ = 3438, 3062, 2925, 1723, 1664, 1634, 1600, 1450, 1262, 1106, 1095, 710 cm^{-1}. HRMS (ESI+): calcd. for $C_{35}H_{28}NaO_7$ [M + Na]$^+$ 583.1733; found 583.1746.

(6*R*,7*R*,2*E*,4*E*)-6,7,8-Tri-*O*-acetyl-1-phenylocta-2,4-diene-1-one (9a): Prepared by general procedure 1 by using tri-*O*-acetyl-D-galactal (0.5 mmol, 136 mg) and phenylacetylene (0.55 mmol, 56 μL). Yield: 125 mg (67%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.87 (d, *J* = 7.3 Hz, 2 H), 7.51 (t, *J* = 7.3 Hz, 1 H), 7.41 (t, *J* = 7.5 Hz, 2 H), 7.28 (dd, *J* = 15.0, 11.1 Hz, 1 H), 6.96 (d, *J* = 15.1 Hz, 1 H), 6.48 (dd, *J* = 15.2, 11.2 Hz, 1 H), 6.01 (dd, *J* = 15.3, 6.6 Hz, 1 H), 5.55 (t, *J* = 5.9 Hz, 1 H), 5.21 (dd, *J* = 10.1, 5.8 Hz, 1 H), 4.29 (dd, *J* = 12.0, 4.1 Hz, 1 H), 3.98 (dd, *J* = 12.0, 6.3 Hz, 1 H), 2.07 (s, 3 H), 2.03 (s, 3 H), 2.00 (s, 3 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 190.3, 170.5, 169.9, 142.3, 137.7, 135.3, 133.0, 132.5, 128.6 (2 C), 128.4 (2 C), 127.4, 71.5, 70.9, 61.9, 20.9, 20.8, 20.74 ppm. IR (neat): ṽ = 3476, 3462, 2925, 1746, 1588, 1374, 1224, 1048, 1016, 773, 698 cm^{-1}. HRMS (ESI+): calcd. for $C_{20}H_{23}O_7$ [M + H]$^+$ 375.1444; found 375.1458.

(6*R*,7*R*,2*E*,4*E*)-6,7,8-Tri-*O*-acetyl-1-(*p*-tolyl)octa-2,4-diene-1-one (10a): Prepared by general procedure 1 by using tri-*O*-acetyl-D-glucal (0.5 mmol, 136 mg) and 4-methylphenylacetylene (0.55 mmol, 69 μL). Yield: 135 mg (70%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.86 (d, *J* = 8.1 Hz, 2 H), 7.34 (dd, *J* = 15.0, 11.1 Hz, 1 H), 7.29 (br. s, 1 H), 7.27 (br. s, 1 H), 7.03 (d, *J* = 15.1 Hz, 1 H), 6.55 (dd, *J* = 15.3, 11.1 Hz, 1 H), 6.06 (dd, *J* = 15.3, 6.6 Hz, 1 H), 5.62 (t, *J* = 5.9 Hz, 1 H), 5.28 (dd, *J* = 10.1, 5.9 Hz, 1 H), 4.36 (dd, *J* = 12.0, 4.2 Hz, 1 H), 4.05 (dd, *J* = 12.0, 6.4 Hz, 1 H), 2.42 (s, 3 H), 2.14 (s, 3 H), 2.10 (s, 3 H), 2.07 (s, 3 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 189.7,170.5, 169.9, 169.7, 143.9, 141.9, 135.1, 135.0, 132.6, 129.3 (2 C), 128.6 (2 C), 127.4, 71.5, 70.9, 61.9, 21.7, 20.9, 20.79, 20.74 ppm. IR (neat): ṽ = 3471, 2926, 1745, 1665, 1599, 1371, 1224, 1047, 1016, 773, 698 cm^{-1}. HRMS (ESI+): calcd. for $C_{21}H_{24}NaO_7$ [M + Na]$^+$ 411.1420; found 411.1438.

(6*R*,7*R*,2*E*,4*E*)-6,7,8-Tri-*O*-acetyl-1-(3-fluorophenyl)octa-2,4-diene-1-one (11a); Prepared by general procedure 1 by using tri-*O*-acetyl-D-galactal (0.5 mmol, 136 mg) and 3-fluorophenylacetylene (0.55 mmol, 63 μL). Yield: 129 mg (66%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.65 (d, *J* = 7.7 Hz, 1 H), 7.56 (d, *J* = 9.3 Hz, 1 H), 7.40 (dd, *J* = 13.5, 7.9 Hz, 1 H), 7.34–7.25 (m, 1 H), 7.22 (dd, *J* = 8.4, 2.4 Hz, 1 H), 6.91 (d, *J* = 15.1 Hz, 1 H), 6.48 (dd, *J* = 15.3, 11.1 Hz, 1 H), 6.04 (dd, *J* = 15.3, 6.5 Hz, 1 H), 5.55 (t, *J* = 5.9 Hz, 1 H), 5.22 (dd, *J* = 10.1, 5.8 Hz, 1 H), 4.28 (dd, *J* = 12.0, 4.2 Hz, 1 H), 3.98 (dd, *J* = 12.0, 6.4 Hz, 1 H), 2.08 (s, 3 H), 2.03 (s, 3 H), 2.00 (s, 3 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 188.9, 170.51, 169.9, 169.6, 162.8, 139.8, 136.0, 132.2, 130.3, 126.8, 124.1, 120.0, 115.24, 71.4, 70.9, 61.9, 20.8, 20.79, 20.74 ppm. IR (neat): ṽ = 3453, 3075, 2925, 17446, 1586, 1372, 1221, 1046, 1020, 789, 723 cm^{-1}. HRMS (ESI+): calcd. for $C_{20}H_{22}FO_7$ [M + H]$^+$ 393.1350; found 393.1362.

(6*R*,7*R*,2*E*,4*E*)-6,7,8-Tri-*O*-acetyl-1-(4-pentylphenyl)octa-2,4-diene-1-one (12a): Prepared by general procedure 1 by using tri-*O*-acetyl-D-galactal (0.5 mmol, 136 mg) and 4-pentylphenylacetylene (0.55 mmol, 106 μL). Yield: 155 mg (70%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.80 (d, *J* = 8.1 Hz, 2 H), 7.28 (dd, *J* = 15.1, 11.2 Hz, 1 H), 7.21 (d, *J* = 8.1 Hz, 2 H), 6.96 (d, *J* = 15.1 Hz, 1 H), 6.48 (dd, *J* = 15.3, 11.2 Hz, 1 H), 5.99 (dd, *J* = 15.3, 6.6 Hz, 1 H), 5.55 (t, *J* = 6.0 Hz, 1 H), 5.21 (dd, *J* = 10.0, 5.8 Hz, 1 H), 4.29 (dd, *J* = 12.0, 4.2 Hz, 1 H), 3.97 (dd, *J* = 12.0, 6.3 Hz, 1 H), 2.60 (t, *J* = 7.57 Hz, 2 H), 2.07 (s, 3 H), 2.03 (s, 3 H), 2.00 (s, 3 H), 1.61–1.54 (m, 2 H), 1.27–1.22 (m, 4 H), 0.82 (t, *J* = 6.6 Hz, 3 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 189.8, 170.5, 169.9, 169.7, 148.8, 141.8, 135.3, 134.9, 132.6, 128.7 (2 C), 128.6 (2 C), 127.5, 71.5, 70.9, 61.9, 36.0, 31.4, 30.8, 22.5, 20.9, 20.8, 20.7, 14.0 ppm. IR (neat): ṽ = 3453, 3075, 2925, 1746, 1586, 1372, 1221, 1046, 1020, 789, 723 cm^{-1}. HRMS (ESI+): calcd. for $C_{25}H_{32}NaO_7$ [M + Na]$^+$ 467.2046; found 467.2034.

(6*R*,7*S*,2*E*,4*E*)-6,7-Di-*O*-acetyl-1-phenylocta-2,4-diene-1-one (13a): Prepared by general procedure 1 by using 3,4-di-*O*-acetyl-L-rhamnal (0.5 mmol, 107 mg) and phenylacetylene (0.55 mmol, 56 μL). Yield: 101 mg (64%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.95 (d, *J* = 7.5 Hz, 2 H), 7.58 (t, *J* = 7.2 Hz, 1 H), 7.49 (t, *J* = 7.4 Hz, 2 H), 7.39 (dd, *J* = 14.8, 11.4 Hz, 1 H), 7.04 (d, *J* = 15.1 Hz, 1 H), 6.55 (dd, *J* = 14.7, 11.7 Hz, 1 H), 6.13 (dd, *J* = 15.3, 6.8 Hz, 1 H), 5.50 (br. s, 1 H), 5.12 (m, 1 H), 2.13 (s, 3 H), 2.06 (s, 3 H), 1.24 (d, *J* = 6.5 Hz, 3 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 190.3, 170.3, 169.9, 142.7, 137.7, 136.0, 132.9, 132.4, 128.6 (2 C), 128.4 (2 C), 126.9, 74.6, 70.4, 21.1, 21.0, 15.1 ppm. IR (neat): ṽ = 3462, 2932, 1745, 1664, 1598, 1404, 1367, 1236, 1016, 1023, 772, 848, 601 cm^{-1}. HRMS (ESI+): calcd. for $C_{18}H_{21}O_5$ [M + H]$^+$ 317.1389; found 317.1396.

(6*R*,7*S*,2*E*,4*E*)-6,7-Di-*O*-acetyl-1-(*p*-tolyl)octa-2,4-diene-1-one (14a): Prepared by general procedure 1 by using 3,4-di-*O*-acetyl-L-rahmnal (0.5 mmol, 107 mg) and 4-methylphenylacetylene (0.55 mmol, 69 μL). Yield: 102 mg (62%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.79 (d, *J* = 7.4 Hz, 2 H), 7.30 (dd, *J* = 14.5, 11.6 Hz, 1 H), 7.21 (d, *J* = 7.2 Hz, 2 H), 6.97 (d, *J* = 15.1 Hz, 1 H), 6.51–6.42 (m, 1 H), 6.04 (dd, *J* = 15.3, 6.8 Hz, 1 H), 5.42 (br. s, 1 H), 5.08–4.99 (m, 1 H), 2.35 (s, 3 H), 2.04 (s, 3 H), 1.98 (s, 3 H), 1.15 (d, *J* = 6.4 Hz, 3 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 189.8, 170.3, 169.9, 143.8, 142.3, 135.7, 135.2, 132.5, 129.3 (2 C), 128.5 (2 C), 127.0, 74.6, 70.4, 21.6, 21.1, 21.0, 15.1 ppm. IR (neat): ṽ = 3455, 3074, 2935, 1741, 1666, 1682, 1600, 1408, 1369, 1238, 1180, 1023, 850, 604 cm^{-1}. HRMS (ESI+): calcd. for $C_{19}H_{23}O_5$ [M + H]$^+$ 331.1545; found 331.1523.

(6*R*,7*S*,2*E*,4*E*)-6,7-Di-*O*-acetyl-1-(4-fluorophenyl)octa-2,4-diene-1-one (15a): Prepared by general procedure 1 by using 3,4-di-*O*-acetyl-L-rahmnal (0.5 mmol, 107 mg) and 4-fluorophenylacetylene (0.55 mmol, 63 μL). Yield: 103 mg (62%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.97–7.85 (m, 2 H), 7.31 (dd, *J* = 14.6, 11.5 Hz, 1 H), 7.08 (t, *J* = 7.9 Hz, 2 H), 6.94 (d, *J* = 15.0 Hz, 1 H), 6.53–6.40 (m, 1 H), 6.06 (dd, *J* = 15.3, 6.8 Hz, 1 H), 5.42 (br. s, 1 H), 5.05 (br. s,

1 H), 2.05 (s, 3 H), 1.98 (s, 3 H), 1.16 (d, J = 6.4 Hz, 3 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 188.6, 170.3, 169.9, 165.6, 142.9, 136.3, 134.1, 132.2, 131.09, 131.02, 126.4, 115.8, 115.7, 74.5, 70.3, 21.1, 21.0, 15.1 ppm. IR (neat): $\tilde{\nu}$ = 3455, 2987, 2935, 1741, 1600, 1372, 1238, 1022, 848, 602 cm^{-1}. HRMS (ESI+): calcd. for $C_{18}H_{20}FO_5$ $[M + H]^+$ 335.1295; found 335.1274.

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

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