# An improved two-step synthetic route to primary allylic alcohols from aldehydes†

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An improved two-step synthetic route to allylic alcohols from aldehydes has been developed. A modification of the HWE reaction in $H_2O$–2-PrOH (1 : 1) and a convenient protocol to prepare $AlH_3$ in THF from $LiAlH_4$ and *n*-BuBr are the key factors in the improvement.



## Introduction

Allylic alcohols are important synthons in organic synthesis, and asymmetric epoxidation[1,2] of allylic alcohols is widely used at the chiral induction stage in many syntheses of natural products. Among the many ways to prepare allylic alcohols, an important two-step route is the Horner–Wadsworth–Emmons (HWE) olefination reaction of aldehydes with dialkyl carboalkoxymethylenephosphonates to generate α,β-unsaturated esters followed by reduction with DIBAL-H. Most generally, the HWE reaction[3] is carried out using a hydride ion or organometallic base in anhydrous aprotic solvents under an inert atmosphere. In nonpolar solvents the reaction of stabilized ylides with aldehydes proceeds very slowly.[4] Moreover, the *E*/*Z* stereoselectivity of the HWE reaction is complicated by several factors, such as the nature of the metal counterion employed,[5] the reaction temperature,[5] the size of the phosphonoester reagent used,[6] and the presence of oxygen-containing groups adjacent to the carbonyl group.[3c] In contrast to the traditional HWE reaction, the aqueous HWE reaction[7] offers several advantages, such as: (1) it can be used for large-scale preparations; (2) wet aldehydes can be used directly in the reaction as substrates; (3) water is believed to accelerate the reaction;[8] (4) it is environmentally benign; (5) base-sensitive functional groups can survive under the reaction conditions; (6) high *E*-selectivities can normally be achieved. For example, HWE reactions of triethyl phosphonoacetate with aldehydes in highly concentrated (6–10 M) aqueous solutions of $K_2CO_3$ or $KHCO_3$ have been reported.[9] However, as the introduction of water as the essential medium for performing the HWE reaction utilizing poorly water-soluble aldehydes is very limited, only isolated examples are known; therefore, phase transfer catalysts[10] and high reaction temperatures[7] (up to 100 °C) are generally required.

For the reduction of α,β-unsaturated esters, DIBAL-H[11] is the preferred reagent because other reducing reagents such as $LiAlH_4$ (LAH) and $NaBH_4$[12] generally give low yields as a result of competing 1,2- and 1,4-addition reactions. Unfortunately, DIBAL-H reduction requires more than 2 equiv., and workup is tedious because it involves the use of a large volume of aqueous potassium sodium tartrate (Rochelle salt; Seignette salt) solution. Although $AlH_3$ also reduces α,β-unsaturated esters to allylic alcohols, and in some instances may be superior to both DIBAL-H and LAH,[13] its preparation is cumbersome. Thus DIBAL-H continues to be the most commonly used reagent.

Currently, there are three methods of preparation of $AlH_3$. First, alane can be prepared by the reaction of three equivalents of LAH with $AlCl_3$.[14] $AlH_3$ prepared in this way is not always pristine since a mixed chloroaluminium hydride species can be formed, depending on the proportions of LAH and $AlCl_3$.[15] In addition, $AlCl_3$ is hygroscopic and difficult to handle. Second, $AlH_3$ can be prepared by treating LAH with the theoretical quantity of 100% $H_2SO_4$ in THF.[16] This protocol is problematical because it is difficult to prepare a standardized LAH solution in THF and to control the addition of the theoretical quantity of the very viscous 100% $H_2SO_4$ into the LAH solution. Indeed, it was reported that addition of dilute $H_2SO_4$ to a solution of LAH in THF led to an explosion.[17] In a third method, a tertiary amine–alane adduct was utilized.[18] This procedure makes the preparation simpler but still requires the extraction of the amine–alane complex from LAH under an inert atmosphere. Reports that $AlH_3$ is formed as a by-product of the reduction of an alkyl halide with LAH[19,20] and that $AlH_3$ generated in this way reduced ethyl α-(hydroxymethyl)acrylate to α-(hydroxymethyl)acrolein[21] were little noted,[22] as evident from the continued usage of 100% $H_2SO_4$ and LAH to generate $AlH_3$, *e.g.*, in the total synthesis of (±)-gelsemine.[23]

In this paper we show that the HWE reaction of a variety of aldehydes with triethyl phosphonoacetate in the presence of $K_2CO_3$ in $H_2O$–2-PrOH (1 : 1) produced (*E*)-α,β-unsaturated esters with convenience and efficiency. We used 2-PrOH as the co-solvent, and discovered that at room temperature the mixed solvent broadens the spectrum of substrates that can be used and improves the reaction yield without any detrimental effect on their high *E*-selectivities. We also report an improved and convenient procedure for the preparation of $AlH_3$ and its *in situ* reduction of (*E*)-α,β-unsaturated esters. The combination of these two provides an improved route to primary allylic alcohols from aldehydes, especially on a large scale (Scheme 1).

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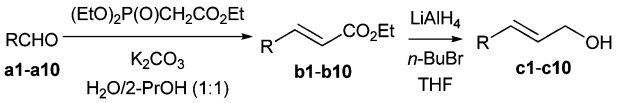
† Electronic supplementary information (ESI) available: $^1H$ and $^{13}C$ NMR spectra of all new compounds. See DOI: 10.1039/b9nj00710e




**Scheme 1** HWE reaction in $H_2O$–2-PrOH and reduction of α,β-unsaturated esters by $AlH_3$.

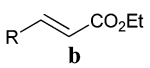
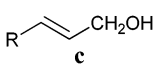
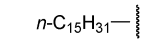
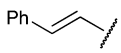
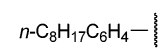
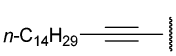
## Results and discussion

### HWE reactions in $H_2O$–2-PrOH (1 : 1)

The reactions of **a1–a4** with triethyl phosphonoacetate furnished the corresponding (*E*)-α,β-unsaturated esters **b1–b4** in high yield and *E*-selectivity (Table 1). Wet heptadec-2-ynal (**a4**), obtained by formylation of 1-hexadecyne, can be subjected to our procedure directly without column chromatography to provide the corresponding enyne ester with predominantly *E*-selectivity (entry 4). In comparison, our previous investigation[24] showed that the HWE reaction of hexadec-2-ynal with triethyl phosphonoacetate using LiBr and $Et_3N$[5b] proceeded with an *E*/*Z* ratio of 10 : 1 to 15 : 1 in the enyne ester, but the use of the sterically larger diisopropyl (ethoxycarbonylmethyl)phosphonate in the reaction, as expected,[6] provided the *E* isomer exclusively.

To expand the scope of our modified HWE reaction, we also examined the conversion of aldehydes **a6–a10**, which bear oxygen-containing groups adjacent to the carbonyl group, to α,β-unsaturated esters **b6–b10** (Table 2). It has been reported[3c] that the reaction of this type of aldehyde with stabilized phosphonium ylides ($Ph_3P{=}CHCO_2R$) often results in abnormal reaction stereochemistry, and in certain cases furnishes highly *Z*-rich acrylate mixtures. The aldehydes in entries 1–5 of Table 2 were prepared by oxidative cleavage of a vicinal diol with $NaIO_4$, followed by removal of the generated formaldehyde under reduced pressure without any further purification. Condensation of glyceraldehyde acetonide **a5** with triethyl phosphonoacetate afforded the (*E*)-conjugated ester **b5** as an 18/1 *E*–*Z* mixture (entry 1). A previous study showed that dialdehyde **a6** (entry 2) reacted with $Ph_3P{=}CHCO_2Me$ in methanol (−78 to 20 °C) to yield a mixture of diacrylates enriched in the *Z*,*Z* isomer (*Z*,*Z*/*Z*,*E*/*E*,*E* = *ca.* 12 : 10 : 1).[25] Chromatography on silica gel followed by crystallization in hexane affords the pure *Z*,*Z* isomer of the corresponding dimethyl diacrylate as colorless crystals.[26] In contrast, we found that the reaction of dialdehyde **a6** with the phosphonate in $H_2O$–2-PrOH followed by column chromatography on silica gel provided the *E*,*E* isomer **b6** in 71% yield (entry 2). The reaction with α-(*p*-methoxyphenoxy)-acetaldehyde (**a7**) provided the corresponding (*E*)-conjugated ester **b7** (entry 3), which was also prepared by a substitution reaction of alkyl 4-bromocrotonate with 4-methoxyphenol.[27] Significantly, this method is effective for the olefination of base-sensitive aldehydes, probably because the reaction of triethyl phosphonoacetate with $CO_3^{2-}$ in water produces a $CO_3^{2-}$–$HCO_3^-$ buffer (pH 10.7). The aldehydes shown in entries 4 and 5 can undergo a base-induced anomerization *via* β-elimination followed by an intramolecular hetero-Michael reaction,[28] and thus can be contaminated by the β-epimer. To our delight, in the olefination reactions shown in entries 4 and 5, no β-anomer of the conjugated esters was observed. 4-(*p*-Methoxybenzyloxy)-butanal (**a10**) was prepared by 2,2,6,6-tetramethyl-1-piperdinyloxy (TEMPO) catalyzed oxidation of the corresponding alcohol with NCS[29] because we found that partial deprotection of the *p*-methoxybenzyl group occurred during Swern oxidation of $PMBO(CH_2)_4OH$.[30] The resulting crude **a10** underwent the HWE reaction directly with moderate *E*-selectivity as well as eco-friendly character[29b] (entry 6).

**Table 1** HWE reactions of aromatic and aliphatic aldehydes (**a**) followed by $AlH_3$ reduction of the resulting α,β-unsaturated esters (**b**) to afford allylic alcohols (**c**)

| Entry | RCHO **a** |  **b** Yield[a] (%), *E* : *Z*[b] |  **c** Yield[a] (%) |
|---|---|---|---|
| 1 |  **a1** | **b1** 92, 10 : 1 | **c1** 95 |
| 2 |  **a2** | **b2** 87, *E* only | **c2** 83 |
| 3 |  **a3** | **b3** 95, *E* only | **c3** 96 |
| 4 |  **a4** | **b4** 88, *E* only | **c4** 87 |

[a] Isolated yields. [b] *E*/*Z* ratios were determined by $^{13}C$ NMR.

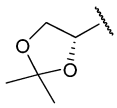
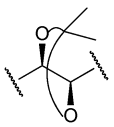
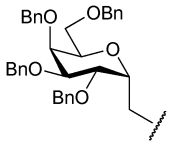
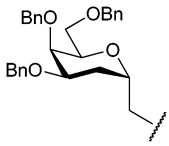
### Generation of $AlH_3$ and synthesis of allylic alcohols

The data in Tables 1 and 2 show that generation of $AlH_3$ in THF from LAH and *n*-BuBr[22] followed by *in situ* reduction of (*E*)-α,β-unsaturated esters **b1–b10** provides very high yields of allylic alcohols **c1–c10**. In comparison to the commonly used DIBAL-H-mediated reduction, this procedure has the following advantages, especially when scale-up is desired: (1) α,β-unsaturated esters can be reduced with only 1.3 equiv. of LAH;[31] and (2) the workup procedure is very simple, involving quenching the reaction by the addition of a stoichiometric quantity of 1 M NaOH solution or $Na_2SO_4{\cdot}10H_2O$ (~3 equiv. of water based on LAH), followed by filtration through a pad of Celite.

### Methoxyalane

Solvents may have a critical impact on the use of $AlH_3$. When $AlH_3$ is prepared by the reaction of LAH with $AlCl_3$ in $Et_2O$, a white precipitate is formed on standing overnight or longer, which, of course, results in a decrease in its reducing capacity.[16a] In THF at reflux, a slow cleavage reaction takes place to give *n*-BuOH.[16a] For this reason, we prepared $AlH_2(OMe)$[32,33] in toluene by the reaction of LAH with *n*-BuBr and $(CH_2O)_n$ at −78 °C. The yield of **c1** obtained by the $AlH_2(OMe)$-mediated reduction of **b1** in toluene was comparable to that found with $AlH_3$ in THF, indicating that $AlH_2(OMe)$ in toluene may be used for the 1,2-reduction of α,β-unsaturated esters to allylic alcohols when THF is not a suitable solvent.

**Table 2** HWE reaction of aldehydes (**a**) with oxygen-containing groups adjacent to the carbonyl group followed by $AlH_3$ reduction of the resulting α,β-unsaturated esters (**b**) to afford allylic alcohols (**c**)

| Entry | RCHO **a** | R–CH=CH–$CO_2Et$ **b** Yield[a] (%), $E$ : $Z$[b] | R–CH=CH–$CH_2OH$ **c** Yield[a] (%) |
|---|---|---|---|
| 1 |  | **b5** | **c5** |
| | **a5** | 85, 18 : 1 | 75 |
| 2 |  | **b6** | **c6** |
| | **a6** | 71, *E* only | 72 |
| 3 | 4-$MeOC_6H_4OCH_2$— | **b7** | **c7** |
| | **a7** | 86, 28 : 1 | 88 |
| 4 |  | **b8** | **c8** |
| | **a8** | 89, >38 : 1 | 87 |
| 5 |  | **b9** | **c9** |
| | **a9** | 87, *E* only | 85 |
| 6 | $PMBO(CH_2)_3$— | **b10** | **c10** |
| | **a10** | 85, 7 : 1 | 89 |

[a] Isolated yields. [b] $E/Z$ ratios of entries 1–4 and 6 were determined by $^{13}C$ NMR; the $E/Z$ ratio of entry 5 was determined by isolation of each compound.

## Conclusion

In summary, HWE reactions of aldehydes in $H_2O$–2-PrOH followed by *in situ* reduction of the (*E*)-α,β-unsaturated esters using alane generated from *n*-BuBr and LAH provide easy access to primary allylic alcohols.

## Experimental

### General experimental methods

All reactions were carried out under a dry nitrogen atmosphere using oven-dried glassware and magnetic stirring. The solvents were dried as follows: THF was heated at reflux over sodium benzophenone ketyl; toluene was heated at reflux over sodium. Silica gel 60 $F_{254}$ aluminium TLC plates of 0.2 mm thickness were used to monitor the reactions. The spots were visualized with short wavelength ultraviolet light or by charring after spraying with 15% $H_2SO_4$. Flash chromatography was carried out with silica gel 60 (230–400 ASTM mesh). $^1H$ NMR spectra were obtained on 400 MHz or 500 MHz spectrometers. Chemical shifts were referenced on residual solvent peaks: $CDCl_3$ ($\delta$ = 7.26 ppm for $^1H$ NMR and 77.00 ppm for $^{13}C$ NMR), $C_6D_6$ ($\delta$ = 7.16 ppm for $^1H$ NMR and 128.00 ppm for $^{13}C$ NMR).

### Typical procedure for preparation of α,β-unsaturated ester by HWE reaction in water–2-PrOH: preparation of b8

To a solution of $NaIO_4$ (4.12 g, 19.2 mmol) in 100 mL of water was added $NaHCO_3$ (160 mg, 1.91 mmol) and then a solution of 3-(2′,3′,4′,6′-tetra-*O*-benzyl-α-D-galactopyranosyl)-1,2-propanediol (8.69 g, 14.5 mmol) in 100 mL THF at 0 °C. After the oxidative cleavage was completed (about 2 h at rt), the mixture was concentrated under reduced pressure to remove THF and the formaldehyde formed. The crude aldehyde **a8** was used directly in the HWE reaction without any further purification. To a mixture of crude aldehyde **a8** and triethyl phosphonoacetate (4.68 g, 20.9 mmol) in 50 mL of 2-PrOH was added dropwise a solution of $K_2CO_3$ (26.0 g, 187 mmol) in 50 mL of water at 0 °C. The mixture was gradually warmed to rt and was stirred overnight at rt. The product was extracted with EtOAc (3 × 100 mL), and the combined organic layers were washed with brine, dried ($Na_2SO_4$), and concentrated. The product was purified by column chromatography on silica gel (elution with hexane–EtOAc 10 : 1, 8 : 1, and 6 : 1) to give 8.23 g (89%) of ethyl 4-(2′,3′,4′,6′-tetra-*O*-benzyl-α-D-galactopyranosyl)-2(*E*)-butenoate (**b8**) together with 219 mg (2.4%) of its *Z* isomer (***Z*-b8**, which was contaminated with the *E* isomer) as colorless oils. **b8**[34]: $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 1.24 (t, 3H, $J$ = 7.1 Hz), 2.36–2.46 (m, 1H), 2.49–2.59 (m, 1H), 3.66 (dd, 1H, $J$ = 4.6, 10.5 Hz), 3.69–3.75 (m, 2H), 3.79–3.87 (m, 1H), 3.97–4.01 (m, 1H), 4.01–4.09 (m, 2H), 4.14 (q, 2H, $J$ = 7.1 Hz), 4.43–4.73 (m, 8H), 5.87 (d, 1H, $J$ = 15.6 Hz), 6.91 (dt, 1H, $J$ = 7.1, 15.6 Hz), 7.20–7.36 (m, 20H); $^{13}C$ NMR (100 MHz, $CDCl_3$) $\delta$ 14.2, 30.8, 60.1, 66.9, 70.0, 72.7, 73.05, 73.09, 73.2, 74.0, 76.3, 123.2, 127.4, 127.50, 127.54, 127.61, 127.72, 127.79, 127.81, 127.9, 128.25, 128.27, 128.31, 128.34, 137.9, 138.24, 138.28, 138.33, 145.4, 166.3. HRMS (ESI) ($MNH_4^+$) $C_{40}H_{48}NO_7$ calcd for $m/z$ 654.3425, found 654.3427. ***Z*-b8**: $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 1.25 (t, $J$ = 7.1 Hz, 3H), 2.87–2.97 (m, 1H), 3.14–3.27 (m, 1H), 3.51–3.64 (m, 1H), 3.72–3.79 (m, 2H), 3.84–3.92 (m, 1H), 3.97–4.01 (m, 1H), 4.02–4.07 (m, 2H), 4.41–4.81 (m, 8H), 5.83 (d, $J$ = 11.5 Hz, 1H), 6.28 (dt, $J$ = 11.5, 7.1 Hz, 1H), 7.19–7.41 (m, 20H); $^{13}C$ NMR (100 MHz, $CDCl_3$) $\delta$ 14.2, 59.8, 67.7, 72.0, 73.0, 73.1, 73.2, 73.4, 73.5, 74.3, 120.9, 127.41, 127.49, 127.56, 127.60, 127.8, 127.9, 128.1, 128.20, 128.24, 128.28, 128.31, 128.39, 138.30, 138.32, 138.45, 138.55, 147.1, 166.4.

### Typical procedure for $AlH_3$ reduction of an α,β-unsaturated ester in THF: preparation of c8

To a mixture of LAH (700 mg, 18.4 mmol, 95% fine powder) in 100 mL of THF was added *n*-BuBr (2.0 mL, 18.5 mmol) at −78 °C. The reaction mixture was warmed to rt and stirred overnight. To the mixture was added a solution of **b8** (7.96 g, 12.5 mmol) in 50 mL of THF at −78 °C. After being stirred for 2 h, the mixture was gradually warmed to rt. After all of the starting ester was consumed (about 2 h at rt), the reaction was

quenched by addition of 2 mL of 1 M NaOH solution. The mixture was diluted with 150 mL of $CH_2Cl_2$ and passed through a pad of Celite, which was washed with 250 mL of EtOAc. The filtrate was concentrated under reduced pressure, and the residue was purified by column chromatography on silica gel (elution with hexane–EtOAc 2 : 1 and 1 : 1) to give 6.47 g (87%) of 4-(2′,3′,4′,6′-tetra-*O*-benzyl-α-D-galacto-pyranosyl)-2(*E*)-buten-1-ol (**c8**[34]) as a colorless oil: $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 1.71 (br s, 1H), 2.25–2.35 (m, 1H), 2.35–2.45 (m, 1H), 3.60 (dd, 1H, $J$ = 4.2, 10.5 Hz), 3.69–3.78 (m, 2H), 3.79–3.88 (m, 1H), 3.91–4.07 (m, 5H), 4.43–4.73 (m, 8H), 5.53–5.69 (m, 2H), 7.22–7.35 (m, 20H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 30.5, 63.4, 67.4, 70.7, 72.3, 72.90, 72.96, 73.02, 73.08, 74.2, 76.3, 76.4, 127.39, 127.46, 127.51, 127.53, 127.7, 127.81, 127.85, 128.19, 128.26, 128.8, 131.3, 138.10, 138.17, 138.29, 138.5.

### Procedure for reduction of α,β-unsaturated ester b1 with $AlH_2(OMe)$ in toluene: preparation of c1

To a suspension of LAH (2.10 g, 55.3 mmol, 95% fine powder) in 100 mL of toluene were added *n*-BuBr (6.0 mL, 55.9 mmol) and, after 2 h, paraformaldehyde (1.66 g, 55.3 mmol) at −78 °C. The mixture was gradually warmed to rt and stirred overnight. To this $AlH_2(OMe)$ mixture was added dropwise a solution of **b1** (13.2 g, 42.5 mmol) in 100 mL of toluene at 0 °C. After the mixture was gradually warmed to rt and stirred overnight, it was diluted with 50 mL of dry THF[35] and stirred for 10 min. The reaction was quenched by addition of 6 mL of 1 M NaOH solution, and the mixture was diluted with 100 mL of $CH_2Cl_2$. The mixture was passed through a pad of Celite, which was rinsed with EtOAc. The filtrate was concentrated under reduced pressure, and the residue was purified by column chromatography on silica gel (elution with hexane–EtOAc 6 : 1) to give 9.82 g (86%) of 2(*E*)-octadecen-1-ol (**c1**).

**(*E*)-Ethyl octadec-2-enoate (b1).** Matches the published data.[36]

**(*E*)-Octadec-2-en-1-ol (c1).** Matches the published data.[37] $^1$H NMR (500 MHz, $CDCl_3$) $\delta$ 0.88 (t, 3H, $J$ = 6.8 Hz), 1.26 (s, 26H), 1.34–1.39 (m, 2H), 1.56 (s, 1H), 2.04 (q, 2H, $J$ = 7.2 Hz), 4.09 (t, 2H, $J$ = 5.2 Hz), 5.61–5.72 (m, 2H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 14.1, 22.7, 29.1, 29.2, 29.4, 29.5, 29.60, 29.65, 29.68, 31.9, 32.2, 63.8, 128.7, 133.6.

**(2*E*,4*E*)-Ethyl 5-phenylpenta-2,4-dienoate (b2).** Matches the published data.[38]

**(2*E*,4*E*)-5-Phenylpenta-2,4-dien-1-ol (c2).** Matches the published data.[39]

**(*E*)-Ethyl 3-(4-octylphenyl)acrylate (b3).** $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 0.88 (t, $J$ = 7.1 Hz, 3H), 1.16–1.38 (m, 13H), 1.53–1.65 (m, 2H), 2.61 (t, $J$ = 2.6 Hz, 2H), 4.26 (q, $J$ = 7.1 Hz, 2H), 6.39 (d, $J$ = 16.0 Hz, 1H), 7.19 (d, $J$ = 8.0 Hz, 2H), 7.44 (d, $J$ = 8.0 Hz, 2H), 7.67 (d, $J$ = 16.0 Hz, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 14.1, 14.3, 22.6, 29.21, 29.26, 29.4, 31.2, 31.8, 35.8, 60.4, 117.1, 128.0, 128.9, 131.9, 144.6, 145.7, 167.2.

**(*E*)-3-(4-Octylphenyl)prop-2-en-1-ol (c3).** $^1$H NMR (500 MHz, $CDCl_3$) $\delta$ 0.88 (t, $J$ = 7.1 Hz, 3H), 1.21–1.36 (m, 10H), 1.44 (t, 4.9, 1H), 1.55–1.64 (m, 2H), 2.58 (t, $J$ = 7.8 Hz, 2H), 4.31 (t, $J$ = 4.8 Hz, 2H), 6.32 (dt, $J$ = 15.9, 5.9 Hz, 1H), 6.59 (d, $J$ = 15.9 Hz, 1H), 7.13 (d, $J$ = 8.1 Hz, 2H), 7.30 (d, $J$ = 8.1 Hz, 2H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 14.1, 22.7, 29.28, 29.33, 29.5, 31.5, 31.9, 35.7, 63.9, 126.4, 127.4, 126.7, 131.3, 134.0, 142.7.

**(*E*)-Ethyl 6-(4-methoxybenzyloxy)hex-2-enoate (b10).** Matches the published data.[29b]

**(*E*)-6-(4-Methoxybenzyloxy)hex-2-en-1-ol (c10).** Matches the published data.[40]

**(*E*)-Ethyl nonadec-2-en-4-ynoate (b4).** $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 0.88 (t, $J$ = 7.1 Hz, 3H), 1.19–1.45 (m, 25H), 1.50–1.60 (m, 2H), 2.36 (dt, $J$ = 2.2, 7.1 Hz, 2H), 4.20 (q, $J$ = 7.1 Hz, 2H), 6.13 (d, $J$ = 15.8 Hz, 1H), 6.76 (dt, $J$ = 15.8, 2.2 Hz, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 14.1, 14.2, 19.7, 22.7, 28.3, 28.8, 29.1, 29.3, 29.5, 29.58, 29.62, 29.65, 29.67, 31.9, 60.5, 77.9, 100.8, 126.1, 129.2, 166.1.

**(*E*)-Nonadec-2-en-4-yn-1-ol (c4).** $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 0.88 (t, $J$ = 7.0 Hz, 3H), 1.18–1.45 (m, 23H), 1.47–1.57 (m, 2H), 2.29 (dt, $J$ = 1.9, 7.0 Hz, 2H), 4.18 (t, $J$ = 4.7 Hz, 2H), 5.72 (dt, $J$ = 15.9, 1.9 Hz, 1H), 6.16 (dt, $J$ = 15.9, 5.5 Hz, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 14.1, 19.4, 22.7, 28.7, 28.9, 29.1, 29.4, 29.5, 29.62, 29.65, 29.67, 29.69, 31.9, 63.1, 78.2, 91.5, 111.4, 140.1.

**(*E*)-Ethyl 3-[(*S*)-2,2-dimethyl-1,3-dioxolan-4-yl]acrylate (b5)[41].** $^1$H NMR (400 MHz, $C_6D_6$) $\delta$ 0.98 (t, $J$ = 7.1 Hz, 3H), 1.24 (s, 3H), 1.28 (s, 3H), 3.25–3.30 (m, 1H), 3.66–3.71 (m, 1H), 4.00 (q, $J$ = 7.1 Hz, 2H), 4.20–4.27 (m, 1H), 6.13 (dd, $J$ = 15.6, 1.5 Hz, 1H), 6.85 (dd, $J$ = 15.6, 5.3 Hz, 1H); $^{13}$C NMR (100 MHz, $C_6D_6$) $\delta$ 14.2, 25.8, 26.5, 60.3, 68.8, 75.1, 110.0, 122.2, 145.2, 165.7.

**(*E*)-3-[(*S*)-2,2-Dimethyl-1,3-dioxolan-4-yl]prop-2-en-1-ol (c5)[41].** $^1$H NMR (500 MHz, $C_6D_6$) $\delta$ 1.36 (s, 3H), 1.42 (s, 3H), 3.41 (t, $J$ = 7.8 Hz, 1H), 3.73–3.83 (m, 3H), 4.31 (q, $J$ = 6.9 Hz, 1H), 5.55 (ddd, $J$ = 15.5, 6.7 Hz, 1H), 5.63 (dt, $J$ = 15.5, 4.7 Hz, 1H); $^{13}$C NMR (100 MHz, $C_6D_6$) $\delta$ 26.1, 26.9, 62.1, 69.5, 76.9, 109.4, 128.2, 133.7.

**(*E*)-Ethyl 4-(4-methoxyphenoxy)but-2-enoate (b7).** $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 1.28 (t, $J$ = 7.1 Hz, 3H), 1.71–1.79 (m, 2H), 2.25–2.33 (m, 2H), 3.45 (t, $J$ = 6.3 Hz, 2H), 3.79 (s, 3H), 4.17 (q, $J$ = 7.1 Hz, 2H), 4.42 (s, 2H), 5.82 (dt, $J$ = 15.7, 1.6 Hz, 1H), 6.85–6.89 (m, 2H), 6.96 (dt, $J$ = 15.7, 6.9 Hz, 1H), 7.22–7.27 (m, 2H); $^{13}$C NMR (100 MHz, $CDCl_3$) 14.2, 28.0, 28.8, 55.1, 60.2, 68.8, 72.5, 113.6, 121.5, 129.1, 130.3, 148.5, 159.1, 166.5.

**(*E*)-4-(4-Methoxyphenoxy)but-2-en-1-ol (c7).** Matches the published data.[27]

**(4*R*,5*R*)-4,5-*O*-Isopropylidene-4,5-dihydroxy-2,6-octadiene-dioate (b6)[42].** $^1$H NMR (400 MHz, $C_6D_6$) $\delta$ 0.98 (t, $J$ = 7.1 Hz, 6H), 1.25 (s, 6H), 3.95–4.04 (m, 6H), 6.12 (d, $J$ = 15.6 Hz, 2H), 6.85 (ddd, $J$ = 15.6, 1.8, 3.5 Hz, 2H);

$^{13}$C NMR (100 MHz, $C_6D_6$) $\delta$ 14.56, 27.1 60.8, 80.2, 110.9, 124.0, 142.9, 165.7.

**3-[(4*R*,5*R*)-5-(3-Hydroxy-1-(*E*)-propen-1-yl)-2,2-dimethyl-[1,3]dioxolan-4-yl]-prop-2-(*E*)-en-1-ol (c6)[43].** $^1$H NMR (400 MHz, $C_6D_6$) $\delta$ 1.47 (s, 6H), 2.83 (br s, OH, 2H), 3.94, (d, $J$ = 4.8 Hz, 4H), 4.16–4.21 (m, 2H), 5.73 (ddd, $J$ = 15.5, 4.8, 1.8 Hz, 2H), 5.897 (dt, $J$ = 15.5, 4.8 Hz, 2H); $^{13}$C NMR (100 MHz, $C_6D_6$) $\delta$ 27.3, 62.4, 82.0, 109.1, 126.8, 134.4.

**4-(2′-Deoxy-3′,4′,6′-tri-*O*-benzyl-α-D-galactopyranosyl)-2(*E*)-butenoate (b9).** $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 1.25 (t, $J$ = 7.1 Hz, 3H), 1.47–1.55 (m, 1H), 1.98–2.06 (m, 1H), 2.25–2.33 (m, 1H), 2.41–2.50 (m, 1H), 3.68–3.73 (m, 1H), 3.73–3.76 (m, 1H), 3.78–3.83 (m, 1H), 3.90–3.98 (m, 1H), 4.00–4.11 (m, 2H), 4.16 (q, $J$ = 7.1 Hz, 2H), 4.50–4.72 (m, 6H), 5.86 (d, $J$ = 15.7 Hz, 1H), 6.91 (dt, $J$ = 15.7, 7.2 Hz, 1H), 7.24–7.37 (m, 15H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 14.2, 32.6, 36.3, 60.1, 66.6, 67.3, 71.4, 72.2, 73.11, 73.14, 73.6, 74.9, 123.4, 127.2, 127.41, 127.43, 127.5, 127.6, 127.7, 128.22, 128.26, 138.28, 138.36, 138.46, 144.7, 166.2. HRMS (ESI) ($MNH_4^+$) $C_{33}H_{42}NO_6$ calcd for $m/z$ 548.3007, found 548.3002.

**4-(2′-Deoxy-3′,4′,6′-tri-*O*-benzyl-α-D-galactopyranosyl)-2(*E*)-buten-1-ol (c9).** $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 1.47–1.56 (m, 1H), 1.99–2.08 (m, 1H), 2.10–2.19 (m, 1H), 2.28–2.38 (m, 1H), 3.63–3.69 (m, 2H), 3.72–3.76 (m, 1H), 3.78–3.83 (m, 1H), 3.88–3.95 (m, 1H), 3.96–4.00 (m, 1H), 4.01–4.07 (m, 2H), 4.47–4.74 (m, 6H), 5.61–5.67 (m, 2H), 7.20–7.40 (m, 15H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 32.0, 36.1, 63.4, 67.9, 71.2, 72.4, 73.1, 73.2, 73.5, 74.9, 127.3, 127.4, 127.5, 127.8, 128.24, 128.29, 128.34, 128.6, 138.3, 138.4, 138.6. HRMS (ESI) ($MNH_4^+$) $C_{31}H_{40}NO_5$ calcd for $m/z$ 506.2901, found 506.2899.

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