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Indium-Mediated 2-Oxonia Cope Rearrangement of 1,4-Dienols to 1,3-Dienols

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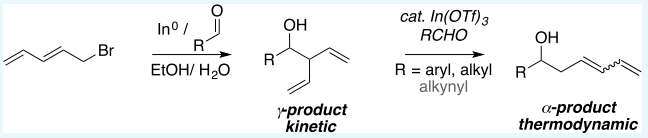
Supporting Information

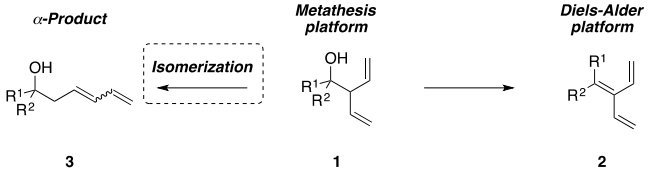
ABSTRACT: An indium-mediated isomerization of 1,4-dienols to 1,3-dienols is described. This procedure consists of the addition of pentadienylindium, in a protic solvent, to aldehydes giving the kinetic γ-allylation product in high yields. The subsequent conversion of this γ-allylation product to its thermodynamic 1,3-dienol α-isomer can be achieved by its exposure to indium triflate in the presence of a substoichiometric amount of aldehyde at room temperature. This transformation exhibited moderate to good substrate scope and has been shown to proceed by a 2-oxonia Cope rearrangement.



INTRODUCTION

1,4-Dienol motifs (**1**) are a valuable and sought after precursors in organic synthesis because of their unique functional connectivity. 1,4-Dienols **1** can undergo elimination reactions to give trienes such as **2** that have been shown to be excellent Diels−Alder platforms (Scheme 1), therefore

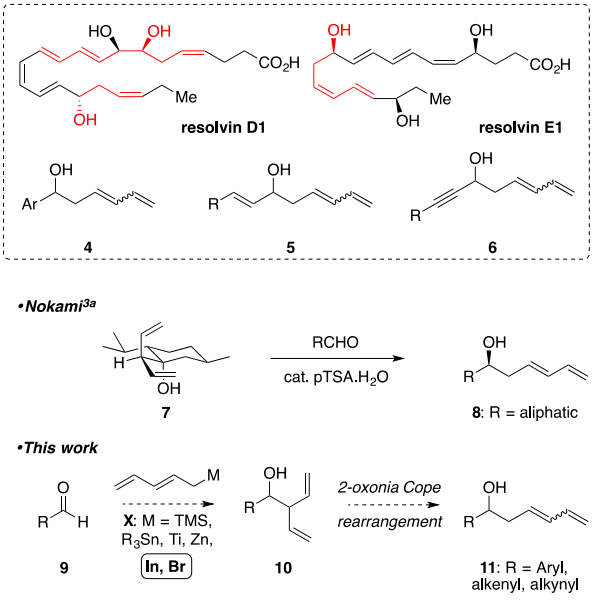
Scheme 1. Synthetic Utility of 1,4-Dienols and Their Conversion to 1,3-Dienols



enabling significant molecular complexity to be built up quickly in very few synthetic transformations.[1] The connectivity of 1,4-dienols (**1**) has been harnessed in ruthenium-catalyzed RCM transformation delivering unique cyclic and polycyclic structures.[2] Furthermore, 1,4-dienol **1** can undergo facile isomerization to the thermodynamically favored α-allylic alcohol product **3** (1,3-dienol) that is central to numerous natural products of biological importance as well as useful synthetic intermediates (Scheme 1).[3]

The resolvin D- and E-series (Scheme 2, e.g., resolving D1 and resolving E1) are a class of metabolites derived from ω-3 fatty acids, docosahexaenoic acid, and eicosapentaenoic acid. They have been implicated in the regulation of human diseases linked to chronic inflammation such as cardiovascular diseases, asthma, and rheumatoid arthritis.[4a−c] In a project looking at the biological importance of these fatty acids metabolites,[4d] we required access to a range of racemic 1,3-dienols with aryl, alkenyl, and alkynyl substitution that mirrored that within the resolvin D1 and E1 structures (Scheme 2, **4**−**6**). We envisaged that 1,3-dienols of this type could be accessed via a 2-oxonia

Scheme 2. Targeted 1,3-Dienols Using a 2-Oxonia Cope Rearrangement



Cope rearrangement of a 1,4-dienol, which in turn could be accessed from an appropriate aldehyde (**9**) and a pentadienyl equivalent (Scheme 2). This approach was based on two benchmarks (a) the ability to easily synthesize the 1,4-dienol precursors and (b) literature precedent for the thermodynamic rearrangement to the required 1,3-dienols.

First, in the literature, there are several robust synthetic methods for the synthesis of 1,4-dienol precursors (**10**), all of

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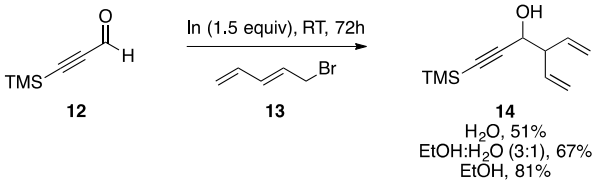
which are based on the addition of a pentadienyl equivalent to carbonyl substrate **9** (Scheme 2). These include the Lewis acid-mediated addition of 2,4-pentadienyltrimethylsilane[5−7] and pentadienyltrimethylstannane[8] to an aldehyde. Pentadienylzincates[9] and penta-2,4-dienyltitanium complexes[10] have also been successfully added to carbonyls, and the direct addition of a 1,4-pentadienyl equivalent via treatment with a strong base[11] has also been successfully employed. An alternate and more environmentally applicable approach has been the addition of pentadienylindium, generated from an indium metal and pentadienylbromide, to the requisite carbonyl. Indium has become an important metal in Barbier-type additions to carbonyls because of its functional group tolerance and low toxicity.[12,13] Second, the 2-oxonia Cope rearrangements are not unprecedented when performed on 1,4-dienols (Scheme 2); Nokami[3a] and co-workers demonstrated that 1,4-dienol **7** undergoes a diastereoselective, acid catalyzed, 2-oxonia Cope rearrangement to give its α-product **8**, in high enantiomeric excess; however, this report was limited to only three aliphatic examples. Therefore, we would like to disclose our results on using this 2-oxonia Cope rearrangement to synthesize 1,3-dienols with aryl, alkenyl, and alkynyl substitutions.

RESULTS AND DISCUSSION

The target compounds for our study necessitated the selection of aldehyde **12** as the starting point. Previous reports had already indicated that DMF, THF, and DMSO would be ideal solvents for the addition of bromide **13**, as they all gave the required γ-addition product. However, in a desire to use more environmentally benign solvents, H_2O was selected as the starting point, previously used only by Fallis within the context of bromide **13** and a small subset of aldehydes and ketones.[1f,3b] Consequently, when aldehyde **12** was exposed to **13**, indium (1.5 equiv), and H_2O, it was gratifying to isolate the desired γ-addition product **14** in 51% isolated yield (Scheme 3). This

Scheme 3. Indium-Mediated Addition of Bromide 13 to Aldehyde 12 in H_2O, Ethanol, and Mixtures Thereof

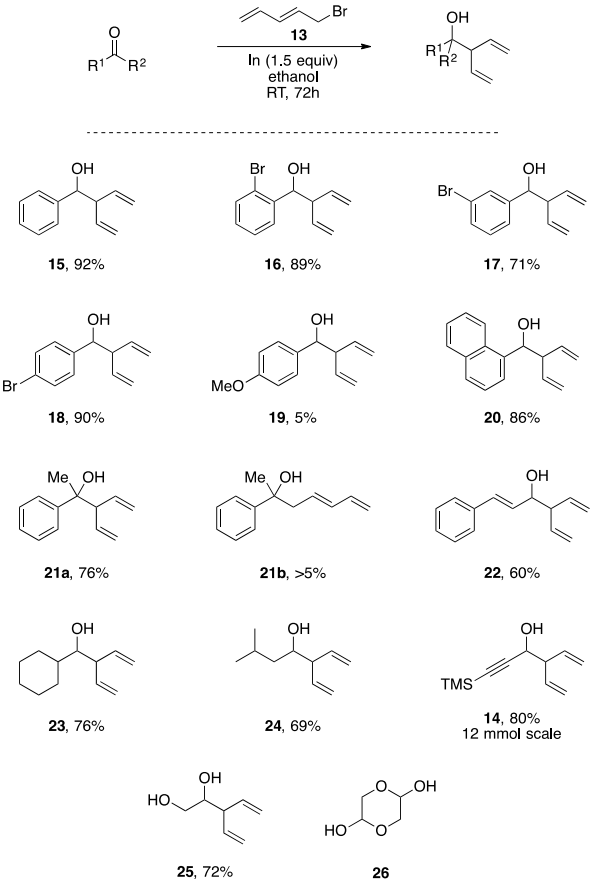


modest yield and significant amount of the unreacted starting material in the crude ^{1}H NMR led us to question the solubility of starting material **12** in H_2O as the solvent. To address this a 3:1 mixture of ethanol[14] and water was trialed, leading to a welcome increased isolated yield of 67%, confirming our speculation. Finally, a further increase in isolated yield to 81% was obtained when absolute ethanol was used.

With optimized conditions in hand, we then examined these conditions on aryl, alkenyl, and alkynyl aldehydes that were appropriate for our study (Scheme 4).

Benzaldehyde and 2-, 3-, and 4-bromobenzaldehyde gave the expected 1,4-dieneol products (**15**−**18**) in good to excellent yields of 71−92%; however, *p*-anisaldehyde yielded its addition product **19** in a very poor isolated yield of only 5%, due likely to the deactivation of the electrophile by the methoxy group. An increase in steric bulk was accommodated as indicated by

Scheme 4. Synthesis of 1,4-Dienols



the successful conversion of α-naphthaldehyde giving its addition product **20** in 86% isolated yield. Acetophenone also underwent smooth addition to give the γ-addition product **21a** in 76%; however, within the crude ^{1}H NMR, a small trace amount of the α-addition product **22b** could be identified, possibly due to the increase in steric bulk of the electrophile. Cinnamaldehyde gave its addition product **22** in 60% isolated yield, and both linear and branched aliphatic aldehydes gave the desired 1,4-dienols in good to high yields giving **23** and **24** in 76 and 69% yields, respectively. The alkynyl aldehyde **12**, crucial to our own work,[4d] could also be scaled up to 12 mmol, giving the addition product **14** in an isolated yield of 80%. We also found that glycoaldehyde dimer **26** could be utilized in this process giving access to the diol **25** in 72% isolated yield.

The isomerization of 1,4-dienols to the desired 1,3-dienols was optimized using substrate **15** (Scheme 5 and Table 1).

Initially, we found that simple heating of **15** did not yield the desired 1,3-dienol but simply returned the starting material (entries 1 and 2). We then investigated the use of a Lewis acid catalyst to effect the rearrangement of **15** to **27** and found that $In(OTf)_3$,[15a] $Sn(OTf)_2$, and $AlCl_3$, all at room temperature,

Scheme 5. Optimization Experiments for the Conversion of 1,4-Dienol 15 to Its Respective Conjugated Species 27

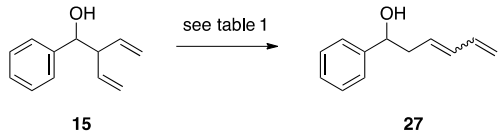


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Table 1. Optimization Experiments for the Conversion of 1,4-Dienol 15 to Its Respective Conjugated Species 27[a]

entry	Lewis acid[b]	benzaldehyde (mol %)	temp. (°C)	yield **27** [%][c]
1	–	–	rt	–
2	–	–	40	–
3	$In(OTf)_3$	–	rt	23
4	$AlCl_3$	–	rt	22
5	$Sn(OTf)_2$	–	rt	23
6	$In(OTf)_3$	10	rt	67
7	$In(OTf)_3$	20	rt	65
8	$In(OTf)_3$	50	rt	67
9	$In(OTf)_3$	100	rt	67
10	–	10	rt	–
11	$In(OTf)_3$	10	40	63
12	$In(OTf)_3$	–	40	19
13[d]	$In(OTf)_3$	10	rt	66

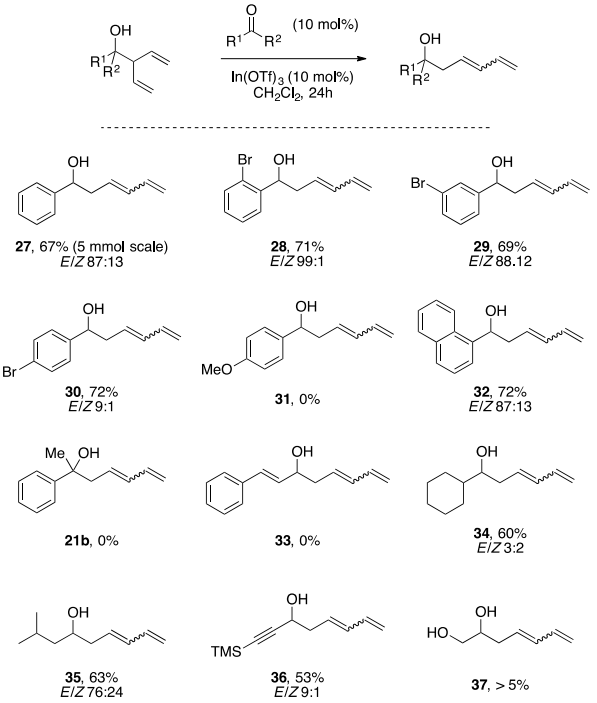
[a]Reactions were performed in CH_2Cl_2 under N_2 atmosphere at 0.5 M for 24 h unless otherwise stated. [b]10 mol % of Lewis acid. [c]Isolated yields in all cases. [d]48 h reaction time.

achieved the rearrangement, but in poor isolated yields (entries 3−5).[16] It must be noted that **27** was isolated in a *E*/*Z* ratio of approx. 9:1, in favor of the *E*-stereoisomer, in each case. With these promising results in hand, we next examined the addition of benzaldehyde in an effort to promote the 2-oxonia Cope rearrangement.[3a,15b,c] Accordingly, upon the addition of 10 mol % of benzaldehyde, in the presence of $In(OTf)_3$, we isolated the desired 1,3-diene-ol **27** in a dramatically improved yield of 67% (entry 6). A screen in the amount of benzaldehyde was then examined, but no discernible increase in isolated yields was observed (entries 7−9). A control experiment in the absence of Lewis acid, but in the presence of 10 mol % of benzaldehyde, confirmed the crucial role of the Lewis acid in this rearrangement (entry 10). An increase in the reaction temperature had no significant effect on the isolated product yield of **27** (entry 11), and when this elevated temperature attempt was performed in the absence of benzaldehyde (entry 12), the result mirrored that in entry 3. Finally, extending the reaction time had no noticeable effect in the isolated yield of **27** (entry 13).

With conditions for the 2-oxonia Cope rearrangement of 1,4-dienol **15** to **27** now identified, the scope of this reaction process was examined using 1,4-dienols from Scheme 4 (Scheme 6).

This process was met with moderate success. The 2-, 3-, and 4-bromoaryl analogues were all rearranged to the target 1,3-diene-ol in good isolated yields giving **28**, **29**, and **30**, respectively. The α-naphthyl analogue participated in the rearrangement giving the thermodynamic product **32** in good yield, and the rearrangement was tolerant of alkyl substitution as exemplified by the cyclohexyl **34** and isovaleryl **35** examples. The aryl 1,4-diene **15** could be rearranged at an increased scale of 5 mmol giving the 1,3-diene **27** in comparable chemical yield. Finally, the TMS protected alkynyl-1,4-diene **14** was converted to its 1,3-diene isomer **36** in a good yield, and pleasingly, this gave a valuable building block that could be potentially used in further work toward the synthesis of the resolvins and other marine-derived fatty acids. Unfortunately, the 4-methoxyaryl (**19**), pent-4-en-2-ol (**21a**), cinnammyl (**22**), and 1,2-diol **25** precursors gave little or none of the desired products (**31**, **33**, **21b**, and **37**, respectively), as well as yielding complex mixtures of products as identified by NMR in

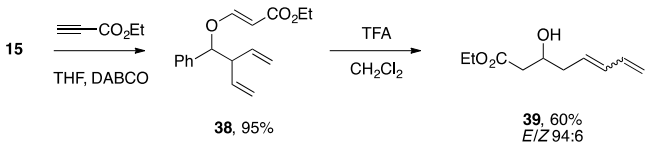
Scheme 6. Synthesis of 1,3-Dienols



each case. With regard to the *E*/*Z* stereoisomer ratio, the majority of the aryl derivatives were obtained in a ratio in-line with the parent phenyl analogue, that is, *E*/*Z* ratio of approx. 9:1. However, the 2-bromophenyl derivative, **28**, was obtained as the *E*-isomer exclusively, with none of its *Z*-isomer observed in the ^1H NMR spectra. In contrast, the cyclohexyl (**34**) and isovaleryl (**35**) analogues were obtained in *E*/*Z* ratios of 3:2 and 3:1, respectively.

The 1,3-dienol **37** derived from 1,2-diol **25** would have contained a useful synthetic handle; however, its failure to participate in the rearrangement could be mitigated as shown below in Scheme 7. Treatment of **15** with ethyl propiolate gave

Scheme 7. Acid-Catalyzed Rearrangement of 1,2-Diol 38



the enol ester **38**, which when treated with TFA gave thermodynamic diene **39** in 82% in an *E*/*Z* ratio of 94:6 and with a 1,3-diene with a useful synthetic handle for further manipulation.

Mechanistically, the 2-oxonia Cope rearrangement follows the reports previously published (Scheme 8).[3,15] First, Lewis acid activation of benzaldehyde promotes the formation of the oxocarbenium ion **41** via **40**. This oxocarbenium ion **41** then undergoes a 2-oxonia Cope rearrangement to deliver the thermodynamic product **42**, with none of the Prins cyclization product **43** being detected or isolated. It is assumed[15,17] that the 2-oxonia Cope rearrangement goes via the corresponding chair transition states. The dominant stereoisomer in each rearrangement was of *E*-stereochemistry; however, in some cases, a small amount of the *Z*-stereoisomer could be detected by ^1H NMR spectroscopy, and this presumably occurs via

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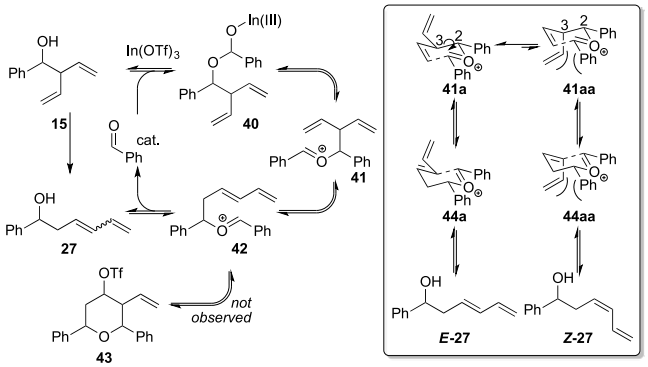
Scheme 8. Mechanism for the Kinetic to Thermodynamic Isomerization Using $In(OTf)_3$



bond rotation between C2−C3 within **41** as shown by **41a** and **41aa** (Scheme 8).

CONCLUSIONS

In summary, we have reported a two-step process for the synthesis of 1,3-dienols. A 2-oxonia Cope rearrangement was utilized to rearrange 1,4-dienols to their thermodynamic 1,3-dienol products, and this was facilitated by Lewis acid catalysis with a substoichiometric amount of the requisite aldehyde. This process has modest substrate scope but unfortunately failed with cinnamyl-substituted systems. However, it was demonstrated to be tolerant of alkynes, which in the context of our research programme should provide a suitable synthetic building for synthesizing fatty acid analogues.

EXPERIMENTAL PROCEDURES

General Procedure for Indium Addition with (*E*)-5-Bromopenta-1,3-diene. Aldehyde or ketone (1.00 mmol) and (*E*)-5-bromopenta-1,3-diene **13** (1.20 mmol) were added to absolute ethanol (6 mL) and allowed to stir at room temperature. Indium powder (1.50 mmol) was added slowly, so as not to increase the temperature of the reaction mixture, and then allowed to stir at room temperature for 72 h. The reaction mixture was diluted with diethyl ether and then filtered through a plug of silica. The solvent was then removed by evaporation under reduced pressure, and the crude product was purified by column chromatography.

*1-Phenyl-2-vinylbut-3-en-1-ol (**15**).*[8d] The title compound was isolated by column chromatography (4:1, light petroleum/ethyl acetate, R_f = 0.4) yielding a colorless liquid (157 mg, 0.90 mmol, 92%): ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.41−7.28 (m, 5H), 5.88 (ddd, J = 17.2, 10.4, 8.2 Hz, 1H), 5.71 (ddd, J = 17.2, 10.4, 7.2 Hz, 1H), 5.26 (dt, J = 9.6, 0.8 Hz, 1H), 5.22 (dt, J = 16.0, 1.2 Hz, 1H), 5.07 (dt, J = 10.4, 1.2 Hz, 1H), 5.04 (dt, J = 17.2, 1.2 Hz, 1H), 4.61 (dd, J = 6.8, 2.0 Hz, 1H), 3.13 (dq, J = 7.2, 0.8 Hz, 1H), 2.27 (br s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 140.8, 135.8, 135.7, 127.1, 126.9, 125.7, 117.4, 116.1, 75.2, 55.2; IR (NaCl): 3079, 3066, 1634, 1603 cm^{-1}; HRMS (ESI): m/z [M + H]$^+$ calcd for $C_{12}H_{14}O$, 175.1123; found, 175.1126.

*1-(2-Bromophenyl)-2-vinylbut-3-en-1-ol (**16**).* The title compound was isolated by column chromatography (4:1, light petroleum/ethyl acetate, R_f = 0.4) yielding a colorless liquid (225 mg, 0.89 mmol, 89%): ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.50 (dd, J = 8.0, 1.2 Hz, 1H), 7.46 (d, J = 7.6 Hz, 1H), 7.31 (t, J = 15.2 Hz, 1H), 7.11 (dt, J = 7.6, 2.0 Hz, 1H), 5.95−5.83 (m, 2H), 5.21−5.01 (m, 5H), 3.20 (q, J = 6.8 Hz, 1H), 2.25 (s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 141.1, 137.1, 135.6, 132.7, 128.9, 129.6, 127.7, 122.6, 118.6, 117.0, 74.5, 54.5; IR (NaCl): 3427, 3077, 1636, 619 cm^{-1}; HRMS (ESI): m/z [M + H]$^+$ calcd for $C_{12}H_{12}O^{79}Br$, 251.0066; found, 251.0068.

*1-(3-Bromophenyl)-2-vinylbut-3-en-1-ol (**17**).* The title compound was isolated by column chromatography (4:1, light petroleum/ethyl acetate, R_f = 0.4) yielding a colorless liquid (180 mg, 0.71 mmol, 71%): ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.51−7.49 (m, 1H), 7.41 (dt, J = 6.8, 2.0 Hz, 1H), 7.26−7.19 (m, 2H), 5.83 (ddd, J = 17.2, 10.4, 8.0 Hz, 1H), 5.69 (ddd, J = 17.6, 10.4, 7.2 Hz, 1H), 5.27 (ddd, J = 10.4, 1.6, 0.8 Hz, 1H), 5.18 (dd, J = 17.2, 1.6, 0.8 Hz, 1H), 5.10 (dt, J = 10.4, 1.2 Hz, 1H), 5.04 (dt, J = 17.2, 1.2 Hz, 1H), 4.56 (d, J = 6.8 Hz, 1H), 3.07 (q, J = 7.2 Hz, 1H), 2.40 (br s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 144.2, 136.3, 136.2, 130.7, 129.9, 129.7, 125.6, 118.8, 117.6, 122.3, 75.5, 56.2; IR (NaCl): 3400, 3084, 1637, 739 cm^{-1}; HRMS (ESI): m/z [M + H]$^+$ calcd for $C_{12}H_{12}O^{79}Br$, 251.0066; found, 251.0058.

*1-(4-Bromophenyl)-2-vinylbut-3-en-1-ol (**18**).*[1a] The title compound was isolated by column chromatography (4:1, light petroleum/ethyl acetate, R_f = 0.4) yielding a colorless liquid (228 mg, 0.90 mmol, 90%): ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.44 (d, J = 8.0 Hz, 2H), 7.17 (d, J = 8.4 Hz, 2H), 5.80 (ddd, J = 18.0, 10.8, 8.4 Hz, 1H), 5.64 (ddd, J = 17.6, 10.8, 7.2 Hz, 1H), 5.25−5.13 (m, 2H), 5.07−4.97 (m, 2H), 4.54 (dd, J = 7.2, 3.2 Hz, 1H), 3.03 (q, J = 7.6 Hz, 1H), 2.24 (d, J = 3.2 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 140.8, 136.4, 136.3, 131.2, 128.6, 121.5, 118.8, 117.6, 75.5, 56.3; IR (NaCl): 3420, 3079, 1635, 623 cm^{-1}; HRMS (ESI): m/z [M + H]$^+$ calcd for $C_{12}H_{12}O^{79}Br$, 251.0066; found, 251.0068.

*1-(4-Methoxyphenyl)-2-vinylbut-3-en-1-ol (**19**).*[9b] The title compound was isolated by column chromatography (4:1, light petroleum/ethyl acetate, R_f = 0.3) yielding a dark yellow liquid (11 mg, 0.05 mmol, 5%): ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.22 (d, J = 8.0 Hz, 2H), 6.86 (d, J = 7.6 Hz, 2H), 5.84 (dt, J = 16.8, 9.2 Hz, 1H), 5.64 (dt, J = 16.8, 8.0 Hz, 1H), 5.21 (dd, J = 16.4, 10.0 Hz, 2H), 5.01 (t, J = 10.4 Hz, 2H), 4.52 (d, J = 7.2 Hz, 1H), 3.79 (s, 3H), 3.07 (q, J = 7.6 Hz, 1H), 2.16 (br s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 159.1, 137.1, 136.8, 134.0, 128.1, 118.3, 117.0, 113.6 (×2), 75.8, 56.3, 55.3; IR (NaCl): 3419 (br), 1634, 1219 cm^{-1}; HRMS (ESI): m/z [M + Na]$^+$ calcd for $C_{13}H_{16}O$, 227.1048; found, 227.1037.

*1(1-Naphthyl)-2-vinylbut-3-en-1-ol (**20**).* The title compound was isolated by column chromatography (4:1, light petroleum/ethyl acetate, R_f = 0.4) yielding a colorless liquid (192 mg, 0.86 mmol, 86%): ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.08 (d, J = 8.0 Hz, 1H), 7.86 (d, J = 8.0 Hz, 1H), 7.78 (d, J = 8.0 Hz, 1H), 7.60 (d, J = 7.2 Hz, 1H), 7.53−7.45 (m, 4H), 5.96−5.81 (m, 2H), 5.45 (dd, J = 6.0, 3.6 Hz, 1H), 5.22 (dd, J = 10.4, 0.8 Hz, 1H), 5.12−5.03 (m, 3H), 3.41−3.38 (m, 1H), 2.22 (d, J = 3.6 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 137.8, 137.6, 136.3, 133.9, 130.7, 129.1, 128.2, 126.1, 125.5, 125.3, 124.5, 123.3, 118.6, 116.8, 72.9, 54.8; IR (NaCl): 3583, 3084, 1677, 1421, 1265 cm^{-1}; HRMS (ESI): m/z [M + Na]$^+$ calcd for $C_{16}H_{16}O$, 247.1099; found, 247.1083.

*2-Phenylpent-4-en-2-ol (**21a**).*[8d] The title compound was isolated by column chromatography (4:1, light petroleum/ethyl acetate, R_f = 0.4) yielding a colorless liquid (142 mg, 0.76 mmol, 76%): ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.44−7.41 (m, 2H), 7.38−7.33 (m, 2H), 7.28−7.24 (m, 1H), 5.81 (ddd, J = 17.2, 10.4, 8.8 Hz, 1H), 5.74 (ddd, J = 17.6, 10.4, 7.2 Hz, 1H),

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5.20 (ddd, J = 10.4, 1.6, 0.4 Hz, 1H), 5.16−5.13 (m, 1H), 5.14−5.09 (m, 2H), 3.15 (t, J = 7.6 Hz, 1H), 2.17 (s, 1H), 1.57 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 146.4, 136.8, 136.3, 127.9, 126.7, 125.5, 118.1, 75.3, 29.8, 27.6; HRMS (ESI): m/z $[M + Na]^+$ calcd for $C_{13}H_{16}O$, 211.1099; found, 211.1087.

*1-(Cinnamyl)-2-vinylbut-3-en-1-ol (**22**).*[6b] The title compound was isolated by column chromatography (4:1, light petroleum/ethyl acetate, R_f = 0.3) yielding a dark yellow liquid (120 mg, 0.60 mmol, 60%): ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.46−7.41 (m, 2H), 7.38−7.34 (m, 2H), 7.31−7.26 (m, 1H), 6.65 (dd, J = 16.0, 0.8 Hz, 1H), 6.27 (dd, J = 16.0, 6.4 Hz, 1H), 5.97−5.88 (m, 1H), 5.92−5.86 (m, 1H), 5.29−5.19 (m, 4H), 4.30 (t, J = 6.0 Hz, 1H), 3.08−3.02 (tq, J = 7.2, 1.2 Hz, 1H), 2.12 (br s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 136.8, 136.6, 131.6, 129.7, 128.6, 127.7, 126.6, 118.0, 117.7, 76.8, 55.0; IR (NaCl): 3400, 3061, 1636 cm^{-1}; HRMS (ESI): m/z $[M + H]^+$ calcd for $C_{14}H_{16}O$, 201.1279; found, 201.1273.

*1-Cyclohexyl-2-vinylbut-3-en-1-ol (**23**).*[8d] The title compound was isolated by column chromatography (4:1, light petroleum/ethyl acetate, R_f = 0.5) yielding a colorless liquid (137 mg, 0.76 mmol, 76%): ^{1}H NMR ($CDCl_3$, 400 MHz): δ 5.85 (ddd, J = 16.4, 10.0, 8.4 Hz, 1H), 5.85−5.77 (m, 1H), 5.17 (dd, J = 10.0, 1.6 Hz, 1H), 5.12 (ddd, J = 10.8, 2.0, 1.2 Hz, 1H), 5.12−5.10 (m, 1H), 5.09−5.07 (m, 1H), 3.29−3.25 (m, 1H), 2.95 (q, J = 7.2 Hz, 1H), 1.88−1.79 (m, 1H), 1.78−1.69 (m, 2H), 1.68−1.57 (m, 2H), 1.48−1.37 (m, 1H), 1.29−1.00 (m, 5H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 136.5, 135.3, 115.4, 114.2, 75.3, 49.7, 38.4, 27.9, 24.9, 24.5, 24.4, 24.2; IR (NaCl): 3435 (br), 3077, 1633 cm^{-1}; HRMS (ESI): m/z $[M + Na]^+$ calcd for $C_{12}H_{20}O$, 203.1412; found, 203.1406.

*6-Methyl-3-vinylhept-1-en-4-ol (**24**).*[18] The title compound was isolated by column chromatography (4:1, light petroleum/ethyl acetate, R_f = 0.4) yielding a colorless liquid (106 mg, 0.69 mmol, 69%): ^{1}H NMR ($CDCl_3$, 400 MHz): δ 5.86 (ddd, J = 10.0, 8.0, 4.8 Hz, 1H), 5.81 (ddd, J = 12.8, 7.6, 4.4 Hz, 1H), 5.21 (dd, J = 10.4, 1.2 Hz, 1H), 5.18−5.15 (m, 1H), 5.16−5.14 (m, 1H), 5.13 (ddd, J = 5.6, 2.4, 0.8 Hz, 1H), 3.65 (dt, J = 9.6, 4.4 Hz, 1H), 2.79 (q, J = 7.6 Hz, 1H), 1.89−1.79 (m, 1H), 1.65 (d, J = 4.4 Hz, 1H), 1.36−1.29 (m, 2H), 0.95 (d, J = 6.8 Hz, 3H), 0.92 (d, J = 6.4 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 137.6, 136.9, 117.6, 116.9, 71.2, 55.4, 43.4, 24.6, 23.8, 21.7; IR (NaCl): 3368 (br), 3079, 1635 cm^{-1}; HRMS (ESI): m/z $[M + H]^+$ calcd for $C_{10}H_{18}O$, 155.1436; found, 155.1429.

*3-Vinylpent-4-ene-1,2-diol (**25**).* The title compound was isolated by column chromatography (4:1, light petroleum/ethyl acetate, R_f = 0.2) yielding a colorless oil (92 mg, 0.72 mmol, 72%): ^{1}H NMR ($CDCl_3$, 400 MHz): δ 5.86 (ddd, J = 16.8, 10.8, 8.0 Hz, 1H), 5.77 (ddd, J = 16.8, 10.8, 8.0 Hz, 1H), 5.21−5.16 (m, 2H), 5.15−5.11 (m, 2H), 3.71−3.62 (m, 2H), 3.55−3.47 (m, 1H), 3.23 (br s, 1H), 3.15 (m, 1H), 2.88 (q, J = 8.0 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 136.8, 136.7, 117.5, 117.1, 73.6, 64.6, 51.7; IR (NaCl): 3365 (br), 3003, 1637 cm^{-1}; HRMS (ESI): m/z $[M + Na]^+$ calcd for $C_7H_{12}O_2$, 151.0735; found, 151.0729.

*1-(Trimethylsilyl)-4-vinylhex-5-en-1-yn-3-ol (**14**).* Aldehyde **12** (1.51 g, 12.00 mmol) and (*E*)-5-bromopenta-1,3-diene **13** (2.12 g, 14.40 mmol) were added to absolute ethanol (20 mL) and allowed to stir at room temperature. Indium powder (2.05 g, 18.00 mmol) was added in portions, so as not to increase the temperature of the reaction mixture and then allowed to stir at room temperature for 72 h. The reaction mixture was diluted with diethyl ether and then filtered through a plug of silica. The solvent was then removed by evaporation under reduced pressure, and the crude product was purified by column chromatography. The title compound was isolated by column chromatography (4:1, light petroleum/ethyl acetate, R_f = 0.6) yielding a pale yellow oil (1.87 g, 9.60 mmol, 80%): ^{1}H NMR ($CDCl_3$, 400 MHz): δ 5.91 (ddd, J = 17.2, 10.4, 8.0 Hz, 2H), 5.28−5.18 (m, 4H), 4.33 (dd, J = 7.2, 5.6 Hz, 1H), 3.07−3.02 (m, 1H), 2.10 (d, J = 7.2 Hz, 1H), 0.19 (s, 9H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 136.1, 135.7, 118.7, 118.2, 104.6, 91.2, 65.3, 54.7, 0.01; IR (NaCl): 3429 (br), 3008, 2173, 1638 cm^{-1}; HRMS (ESI): m/z $[M + Na]^+$ calcd for $C_{11}H_{18}OSi$, 217.1019; found, 217.1020.

General Procedure for the Rearrangement from Branched to Straight Chain Diene. Branched chain diene (1.0 mmol) in dichloromethane (2.0 mL/mmol) was added to indium trifluoromethanesulfonate (10 mol %) and the aldehyde (10 mol %) and allowed to stir at room temperature for 24 h. The reaction mixture was then transferred to a separating funnel, diluted with further dichloromethane, and washed with distilled water. The organic extracts were retained, dried (Na_2SO_4), and filtered, and the solvent was removed by evaporation under reduced pressure. The title compound was isolated by column chromatography. The following compounds were synthesized using this method.

*(E)-1-Phenylhexa-3,5-dien-1-ol (**27**).* The title compound was isolated by column chromatography (4:1, light petroleum/ethyl acetate, R_f = 0.3) yielding a colorless liquid (116 mg, 0.67 mmol, 67%): ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.42−7.29 (m, 5H), 6.35 (td, J = 16.8, 10.0 Hz, 1H), 6.22 (dd, J = 15.2, 10.4 Hz, 1H), 5.71 (dt, J = 15.2, 7.2 Hz, 1H), 5.18 (d, J = 16.4 Hz, 1H), 5.06 (d, J = 10.0 Hz, 1H), 4.80−4.74 (m, 1H), 2.60−2.56 (m, 2H), 2.13 (d, J = 3.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 143.9, 136.8, 134.4, 130.1, 128.5, 127.7, 125.8, 116.3, 73.7, 42.6; IR (NaCl): 3411, 3080, 3030, 1634, 1603 cm^{-1}; HRMS (ESI): m/z $[M - H^+]$ calcd for $C_{12}H_{13}O$, 173.0966; found, 173.0961.

*(E)-1-(2-Bromophenyl)hexa-3,5-dien-1-ol (**28**).* The title compound was isolated by column chromatography (4:1, light petroleum/ethyl acetate, R_f = 0.3) yielding a colorless liquid 182 mg, 0.72 mmol, 71%): ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.82 (d, J = 7.6 Hz, 1H), 7.64 (dd, J = 8.0, 1.2 Hz, 1H), 7.18−7.08 (m, 2H), 6.07 (d, J = 1.2 Hz, 1H), 5.95−5.84 (m, 1H), 5.71 (dd, J = 16.0, 5.6 Hz, 1H), 5.29 (dd, J = 5.6, 2.4 Hz, 1H), 4.58 (dd, J = 10.8, 5.6 Hz, 1H), 2.64−2.53 (m, 1H), 2.39−2.28 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 142.7, 133.1, 132.7, 132.6, 130.5, 128.5, 121.2, 100.6, 78.0, 77.2, 72.1, 40.6; IR (NaCl): 3428, 3077, 1636, 619 cm^{-1}; HRMS (ESI): m/z $[M - H^+]$ calcd for $C_{12}H_{12}O^{79}Br$, 251.0072; found, 251.0065.

*(E)-1-(3-Bromophenyl)hexa-3,5-dien-1-ol (**29**).* The title compound was isolated by column chromatography (4:1, light petroleum/ethyl acetate, R_f = 0.3) yielding a colorless liquid (175 mg, 0.69 mmol, 69%): ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.57−7.54 (m, 1H), 7.45−7.41 (m, 1H), 7.31−7.22 (m, 2H), 6.34 (td, J = 16.8, 10.0 Hz, 1H), 6.20 (dd, J = 15.2, 10.4 Hz, 1H), 5.68 (dt, J = 15.2, 7.6 Hz, 1H), 5.19 (d, J = 16.8 Hz, 1H), 5.08 (d, J = 10.0 Hz, 1H), 4.75−4.71 (m, 1H), 2.59−2.46 (m, 2H), 2.11 (d, J = 3.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 146.2, 136.6, 134.9, 132.8, 130.6, 130.0, 129.4, 124.4, 122.6, 116.7, 72.9, 42.7; IR (NaCl): 3391, 3084, 1637, 704 cm^{-1}; HRMS (ESI): m/z $[M - H^+]$ calcd for $C_{12}H_{12}O^{79}Br$, 251.0072; found, 251.0059.

*(E)-1-(4-Bromophenyl)hexa-3,5-dien-1-ol (**30**).* The title compound was isolated by column chromatography (4:1, light petroleum/ethyl acetate, R_f = 0.3) yielding a colorless liquid

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(180 mg, 0.71 mmol, 72%): ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.46 (d, J = 8.0 Hz, 2H), 7.22 (d, J = 8.4 Hz, 2H), 6.30 (td, J = 16.8, 10.8 Hz, 1H), 6.15 (dd, J = 15.6, 10.4 Hz, 1H), 5.63 (dt, J = 14.4, 8.0 Hz, 1H), 5.15 (dd, J = 16.8, 7.6 Hz, 1H), 5.07−5.01 (m, 1H), 4.74−4.66 (m, 1H), 2.55−2.43 (m, 2H), 2.00 (d, J = 3.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 142.8.136.6, 134.9, 131.6, 129.4, 127.6 (×2), 121.4, 116.6, 70.0, 42.7; IR (NaCl): 3419, 3079, 1635, 623 cm^{-1}; HRMS (ESI): m/z [M − H$^+$] calcd for $C_{12}H_{12}O^{79}Br$, 251.0072; found, 251.0066.

*(E)-1-(1-Naphthyl)hexa-3,5-dien-1-ol (**14**) (**32**).* The title compound was isolated by column chromatography (4:1, light petroleum/ethyl acetate, R_f = 0.3) yielding a colorless liquid (152 mg, 0.68 mmol, 72%): ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.06 (d, J = 8.8 Hz, 1H), 7.88−7.86 (m, 1H), 7.78 (d, J = 7.6 Hz, 1H), 7.66 (d, J = 7.2 Hz, 1H), 7.65−7.46 (m, 3H), 6.34 (dt, J = 16.8, 10.4 Hz, 1H), 6.22 (dd, J = 14.8, 10.4 Hz, 1H), 5.81 (pent, J = 7.6 Hz, 1H), 5.52 (dd, J = 8.4, 3.2 Hz, 1H), 5.19−5.16 (m, 1H), 5.08−5.04 (m, 1H), 2.84−2.75 (m, 1H), 2.66−2.59 (m, 1H), 2.13 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 139.5, 136.8, 134.4, 133.9, 130.5, 130.3, 129.1, 128.1, 126.2, 125.6, 125.6, 123.0, 122.9, 116.4, 70.5, 41.8; HRMS (ESI) m/z [M + Na$^+$] calcd for $C_{16}H_{16}O$, 247.1099; found, 247.1083.

*(E)-1-Cyclohexylhexa-3,5-dien-1-ol (**34**).* The title compound was isolated by column chromatography (4:1, light petroleum/ethyl acetate, R_f = 0.4) yielding a colorless liquid (108 mg, 0.60 mmol, 60%): ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.31 (td, J = 17.2, 10.4 Hz, 1H), 6.18−6.08 (m, 1H), 5.70 (q, J = 8.0 Hz, 1H), 5.11 (d, J = 16.4 Hz, 2H), 3.42−3.34 (m, 1H), 2.38−2.29 (m, 2H), 2.22−2.13 (m, 1H), 1.40−0.98 (m, 10H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 136.9, 134.0, 131.3, 115.8, 75.3, 41.4, 29.9, 29.7, 26.6, 26.4, 26.3, 22.7; IR (NaCl): 3457, 3088, 2928, 1650 cm^{-1}; HRMS (ESI) m/z [M − H$^+$] calcd for $C_{12}H_{19}O$, 179.1436; found, 179.1429.

*(E)-1-Isovalerylhexa-3,5-dien-1-ol (**35**).* The title compound was isolated by column chromatography (4:1, light petroleum/ethyl acetate, R_f = 0.4) yielding a colorless liquid (97 mg, 0.63 mmol, 63%): ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.31 (dt, J = 16.8, 10.4 Hz, 1H), 6.12 (dd, J = 15.2, 10.8 Hz, 1H), 5.70 (pent, J = 7.6 Hz, 1H), 5.13 (d, J = 12.4 Hz, 1H), 5.00 (dd, J = 8.8, 1.2 Hz, 1H), 3.72−3.68 (m, 1H), 2.36−2.25 (m, 1H), 2.19−2.11 (m, 1H), 1.86−1.72 (m, 1H), 1.49 (br s, 1H), 1.42−1.36 (m, 1H), 1.27−1.19 (m, 1H), 0.91−0.88 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 136.9, 134.3, 130.7, 116.0, 69.2, 46.2, 41.3, 24.7, 26.5, 22.1; IR (NaCl): 3584, 3086, 2927, 1651, 1467, 1367, 1004 cm^{-1}; HRMS (ESI) m/z [M + Na$^+$] calcd for $C_{10}H_{18}O$, 177.1255; found, 177.1241.

*(E)-1-(Trimethylsilyl)octa-5,7-dien-1-yn-3-ol (**36**).* The title compound was isolated by column chromatography (4:1, light petroleum/ethyl acetate, R_f = 0.5) yielding a pale yellow liquid (110 mg, 0.53 mmol, 53%): ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.37 (td, J = 16.8, 10.8 Hz, 1H), 6.26−6.19 (m, 1H), 5.77 (td, J = 14.8, 7.6 Hz, 1H), 5.19 (dd, J = 16.8, 0.8 Hz, 1H), 5.09 (dd, J = 10.4, 1.2 Hz, 1H), 4.43 (q, J = 6.0 Hz, 1H), 2.52 (t, J = 6.4 Hz, 2H), 0.18 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 137.0, 135.0, 128.5, 116.5, 105.9, 90.0, 62.2, 40.9, 0.1; IR (NaCl): 3400, 2999, 2152, 1618 cm^{-1}; HRMS (ESI) m/z [M + H$^+$] calcd for $C_{11}H_{18}OSi$, 195.1205; found, 195.1200.

*Ethyl (E)-3-([1-Phenyl-2-vinylbut-3-en-1-yl]oxy)acrylate (**38**).* To a solution of diene **15** (192 mg, 1.10 mmol), THF (3.00 mL) was added DABCO (12 mg, 0.10 mmol) and the resulting solution was stirred under N_2 and cooled to 0 °C. To this was added ethyl propiolate (0.10 mL, 1.00 mmol) drop wise over 5 min and the reaction mixture then allowed to warm to room temperature and stirred overnight. The reaction mixture was then concentrated in vacuo, and the resultant oil was purified by column chromatography (4:1, light petroleum/ethyl acetate, R_f = 0.8) yielding a colorless liquid (284 mg, 0.95 mmol, 95%): ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.48 (d, J = 12.8 Hz, 1H), 7.35−7.25 (m, 3H), 7.22−7.18 (m, 2H), 5.80 (ddd, J = 17.2, 10.4, 7.6 Hz, 1H), 5.69 (ddd, J = 17.2, 10.0, 7.2 Hz, 1H), 5.18 (d, J = 12.4 Hz, 1H), 5.15−5.04 (m, 2H), 5.05−4.98 (m, 2H), 4.83 (d, J = 6.0 Hz, 1H), 4.14−4.09 (m, 2H), 3.24−3.18 (m, 1H), 1.20 (t, J = 6.8 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 167.8, 161.5, 137.6, 136.0, 135.6, 128.4, 128.3, 127.0, 118.0, 117.7, 98.7, 86.4, 59.8, 54.2, 14.4; IR (NaCl): 3584, 2981, 1731, 1651, 1373 cm^{-1}; HRMS (ESI): m/z [M + Na]$^+$ calcd for $C_{17}H_{20}O_3$, 295.1310; found, 295.1293.

*Ethyl (E)-3-Hydroxyocta-5,7-dienoate (**39**).* To a solution of **38** (100 mg, 0.37 mmol) in CH_2Cl_2 (2.00 mL) under a N_2 atmosphere at 0 °C was added TFA (0.03 mL, 0.41 mmol), and the resultant reaction mixture was allowed to warm to room temperature and stirred overnight. After this period, $NaHCO_3$ (2 mL) was added to the reaction mixture, the reaction mixture was then transferred to a separating funnel with additional CH_2Cl_2 (20 mL) and water (20 mL), the layers separated, and the aqueous layer extracted with a further portion of CH_2Cl_2 (20 mL). The combined organic extracts were then dried (Na_2SO_4) and filtered, and the solvent was removed under vacuum and the crude oil was purified by column chromatography (4:1, light petroleum/ethyl acetate, R_f = 0.3) yielding a colorless liquid (56 mg, 0.30 mmol, 82%): ^{1}H NMR ($CDCl_3$, 400 MHz): δ 6.30 (dt, J = 16.8, 10.4 Hz, 1H), 6.12 (dd, J = 15.2, 10.8 Hz, 1H), 5.69 (pent, J = 7.2 Hz, 1H), 5.12 (d, J = 16.8 Hz, 1H), 5.00 (d, J = 9.6 Hz, 1H), 4.15 (q, J = 7.6 Hz, 1H), 4.11−4.04 (m, 1H), 2.98 (d, J = 3.6 Hz, 1H), 2.50 (dd, J = 16.8, 4.0 Hz, 1H), 2.40 (dd, J = 16.4, 8.8 Hz, 1H), 2.36−2.23 (m, 2H), 1.25 (t, J = 7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 171.9, 136.8, 134.3, 129.7, 116.3, 67.7, 60.8, 40.7, 39.7, 14.3; IR (NaCl): 3583, 2983, 2253, 1719, 1374 cm^{-1}; HRMS (ESI): m/z [M + Na]$^+$ calcd for $C_{10}H_{16}O_3$, 207.0997; found, 207.0983.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acsomega.8b03118.

Copies of ^{1}H and ^{13}C spectra of all products (PDF)

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The authors declare no competing financial interest.

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