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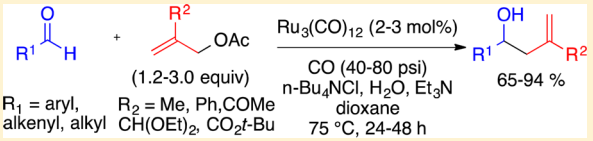
Catalytic, Nucleophilic Allylation of Aldehydes with 2-Substituted Allylic Acetates: Carbon−Carbon Bond Formation Driven by the Water−Gas Shift Reaction

Scott E. Denmark* and Zachery D. Matesich

Roger Adams Laboratory, Department of Chemistry, University of Illinois, Urbana, Illinois 61801, United States

Supporting Information

ABSTRACT: The ruthenium-catalyzed allylation of aldehydes with allylic acetates has been expanded to incorporate substituents at the 2-position of the allylic components. Allylic acetates bearing a variety of substituents (CO_2-*t*-Bu, COMe, Ph, $CH(OEt)_2$, and Me) undergo high-yielding additions with aromatic, α,β-unsaturated, and aliphatic aldehydes. The conditions of the reaction were found to be mild (75 °C, 24−48 h) and only required the use of 2−3 mol % of the triruthenium dodecacarbonyl catalyst under 40−80 psi of CO. The stoichiometries of water and allylic acetate employed were found to be critical to reaction efficiency.



INTRODUCTION

The importance of synthetic methods that form carbon−carbon bonds from carbonyl substrates cannot be overstated. One of the most commonly employed methods to generate carbon−carbon bonds is the metal-mediated allylation of aldehydes.[1−5] The capacity to form a homoallylic alcohol and two new stereogenic centers makes allylations an especially powerful transformation in building complexity. Technologies that afford both diastereo- and enantiomerically enriched products with excellent selectivity and yield have been developed.[6−8]

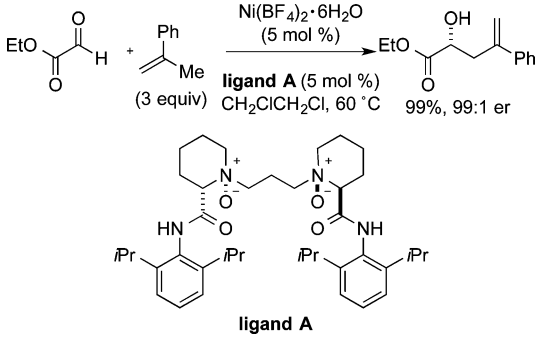
The major drawback with many of the aforementioned methods is the requirement of stoichiometric amounts of metal reagents or additives. In response to this shortcoming, efforts have been directed to develop reactions that are catalytic in metal.[9−14] One such method is the ruthenium-catalyzed allylation reaction, recently reported from these laboratories, which uses carbon monoxide as the stoichiometric reductant and produces only AcOH and CO_2 as the stoichiometric, environmentally benign byproducts.[15]

BACKGROUND

1. Current Methods for the Metal-Catalyzed Carbonyl Allylation Reaction. The interest in metal-catalyzed allylation reactions is driven by the desire to avoid the generation of inorganic wastes streams that can be difficult to remove from the desired product. The carbonyl-ene reaction has emerged as one method for the production of homoallylic alcohols which is efficient as well as being general and highly selective.[13,16] Moreover, highly enantioselective variants have been developed (Scheme 1).[17]

The use of catalytic amounts of palladium and rhodium has found use in the formation of homoallylic alcohols.[18−20] Although the majority of these cases employ stoichiometric amounts of tin, which is undesirable due to its toxicity and difficultly in removal from the products, other allyl sources have been employed in the allylation reactions.[21] For example, it is possible to substitute boron for tin in the allylation of aldehydes, as shown in the works of Szabó (eq 1) and Murakami (eq 2) (Scheme 2).[22,23]

Scheme 1



Krische and co-workers have developed a catalytic, enantioselective allylation of aldehydes that employs an iridium-based transfer hydrogenation catalyst to produce homoallylic alcohols in high yield and enantioselectivity starting from allylic acetates, dienes, or allenes.[24] This chemistry has been successfully employed in the synthesis of various polyketide natural products.[25] In these reactions, the reducing agent is either the alcohol precursor to the aldehyde electrophile or a sacrificial alcohol with an aldehyde (Scheme 3, eq 1 and eq 2). This method has found further application in the formal allylation of epimerizable aldehydes though the alcohol oxidation state (Scheme 3, eq 3).[26] The transient nature of the aldehyde that is formed reduces the opportunity for epimerization to occur. Furthermore, only allylation of the primary alcohol is observed, allowing for selective reactions on

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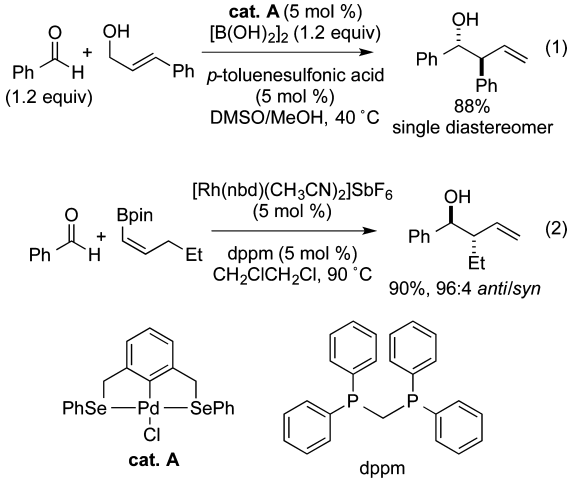
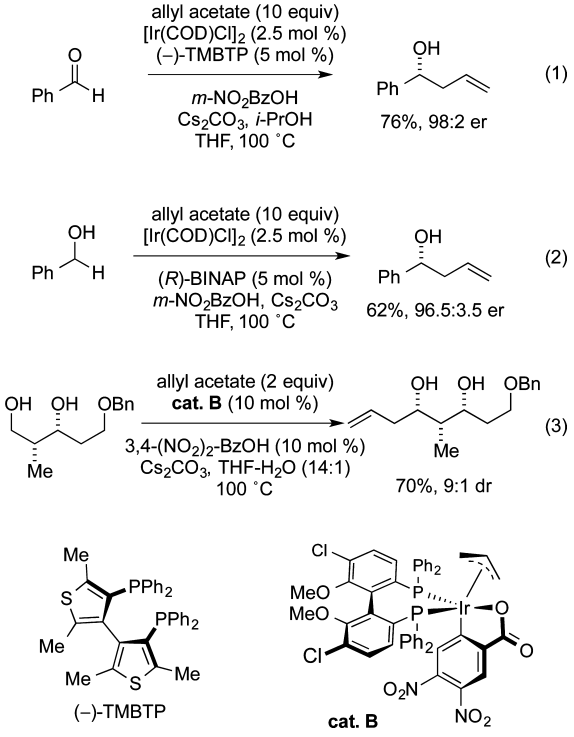
Scheme 2



Scheme 3

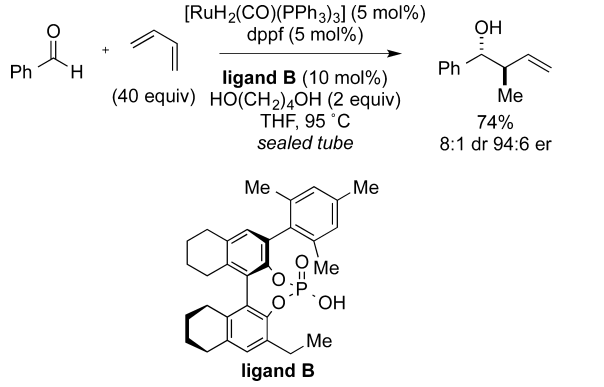


compounds that contain secondary alcohols, thereby eliminating the need for protecting groups.

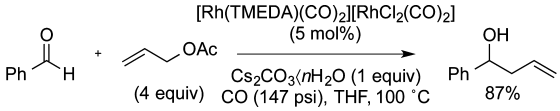
Progress has also been made by Krische and co-workers in employing other metal catalysts in this method, specifically ruthenium, while maintaining the reactivity profile of the iridium catalysts in the allylation reactions of allenes and dienes with aldehydes.[27,28] The ruthenium-catalyzed reactions have also been rendered diastereo- and enantioselective through the use of a chiral Brønsted acid cocatalyst (Scheme 4).[29]

Alper and co-workers have recently shown that a rhodium-catalyzed allylation reaction is also possible (Scheme 5).[14] Through the use of an ionic diamine carbonyl rhodium complex and a stoichiometric amount of Cs_2CO_3, several aromatic and α,β-unsaturated aldehydes were successfully allylated.

Scheme 4

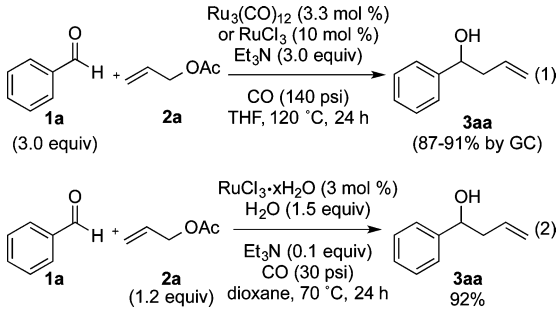


Scheme 5



2. Catalytic Nucleophilic Allylation of Aldehydes Employing CO as the Reductant. A prior disclosure from these laboratories described the potential for the use of ruthenium catalytically in the allylation of aldehydes employing allyl acetate (**2a**) and CO.[15] This development was inspired by an early report form Watanabe et al., who reported the formation of homoallylic alcohols under catalysis by ruthenium and using a trialkylamine as the reducing agent. However, this process suffered from the need for high temperatures and pressures of CO, in addition to superstoichiometric amounts of aldehyde (Scheme 6, eq 1).[30] The discovery that the addition of 1.5 equiv of water allowed both the reaction temperature and CO pressure to be significantly decreased enabled the development of a superior process (Scheme 6, eq 2). Furthermore, the aldehyde became the limiting reagent, greatly increasing the practicality of the reaction.

Scheme 6



The original reaction conditions described by Watanabe relied on a superstoichiometric amount of Et_3N whereas the new conditions required only 0.1 equiv, suggesting that the mechanisms are likely different.[31] Although a secondary or tertiary amine base is required, it does not act as the reducing agent. Instead, the reducing potential in this variant of the reaction is provided by the combination of water and CO, namely through the agency of the water–gas shift reaction.[32−34]

Interestingly, further studies performed in these laboratories revealed that the presence of a halide was critical for reaction efficiency. Replacing $RuCl_3{\cdot}xH_2O$ with $Ru_3(CO)_{12}$ afforded the

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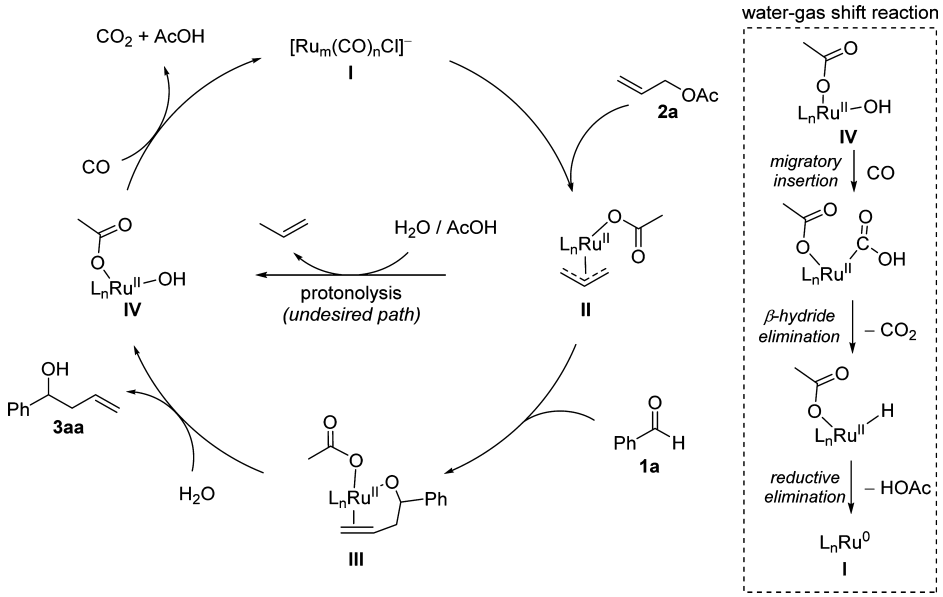
Scheme 7



allylation product in significantly lower yield. However, the addition of a soluble halide source resulted in yields comparable to those seen in the $RuCl_3 \cdot xH_2O$ reactions.[15] The presence of a halide may act as a ligand on ruthenium(0), resulting in the formation of an anionic ruthenium complex. This species would be expected to have increased nucleophilic character, allowing for a more facile oxidative addition.[35,36]

On the basis of these observations, a catalytic cycle for this reaction was formulated (Scheme 7). Following initial reduction of ruthenium(III) (in the case of $RuCl_3$) to the ruthenium(0) species (**I**) by CO, oxidative addition (OA) to acetate **2a** occurs to afford the ruthenium(II) π-allyl species (**II**). The nucleophilic allyl metal species (**II**) next inserts into the aldehyde **1a** via coordination of the carbonyl group to the ruthenium(II) center (via the η^1 form of **II**) to generate (**III**). Hydrolysis of the alkoxide (**III**) then releases the homoallylic alcohol product **3** and generates a ruthenium(II) hydroxide species (**IV**). By means of the water–gas shift reaction, CO undergoes a migratory insertion into the ruthenium(II)–OH bond, followed by β-hydride elimination to release CO_2 (as shown in the inset). Subsequent reductive elimination of the ruthenium(II) hydride intermediate regenerates the ruthenium(0) complex (**I**).

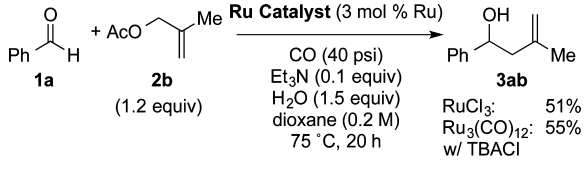
3. Use of Substituted Allyl Sources. The majority of the current carbonyl allylation methods employ only simple, unsubstituted allyl sources. This clearly limits the potential for the incorporation of more complex and functionalized building blocks. The few examples that do employ substituted allyl sources require superstoichiometric amounts of a metallic reducing agent or involve the preformation of an allylic metal species.[7,37] Ideally, the substituted allyl should be available as a shelf-stable reagent that requires only a substoichiometric amount of metal in the addition to carbonyl compounds. This value added process has been demonstrated recently in the generation of α-exomethylene γ-butyrolactones with the use of an allylic acetate containing an ester substituent.[38] Clearly, the potential for greater synthetic utility would be realized if a more general process were developed to allow the use of variety of functional groups as allyl substituents in the addition reaction. The research described herein demonstrates incorporation of various substituents at the 2-position of allylic acetates in the ruthenium-catalyzed allylation reaction. As the proposed catalytic cycle for the reaction involves the formation of a ruthenium(II) π-allyl species (**II**), the use of substituents with varying electronic and steric properties could offer insights into the reactivity characteristics of the allyl group on the reaction. In addition, various nucleofuges on the allyl donor were used to further optimize the catalytic process.

RESULTS

1. Catalytic Nucleophilic Allylation with 2-Methallyl Acetate. *1.1. Optimization of Reaction Conditions.* The investigations began with 2-methallyl acetate **2b** as the methyl substituent creates a slightly more electron-rich ruthenium π-allyl than allyl acetate (**2a**) without significantly changing the steric bulk or involving additional functional groups. In an orienting study to determine a suitable ruthenium source for the reaction, two catalysts ($RuCl_3$ and $Ru_3(CO)_{12}$) that were used previously were examined using the original reaction conditions (Scheme 8).[15] A higher yield of product **3ab** was observed with $Ru_3(CO)_{12}$ as compared to $RuCl_3$, 55% and 51% respectively. In both cases, unreacted benzaldehyde **1a** and methallyl acetate **2b** were recovered from the reactions, indicating the low yield results from incomplete conversion of the aldehyde, not the formation of byproducts.[39]

Surprisingly, the use of either of the two ruthenium catalysts produced **3ab** in lower yield than what was previously observed for the generation of **3aa** from allyl acetate (Scheme 6, eq 2).[15] This observation, combined with the presence of unreacted **2b**, suggested that acetate **2b** is significantly less reactive than allyl acetate **2a**. This property may be due in part to the decreased

Scheme 8



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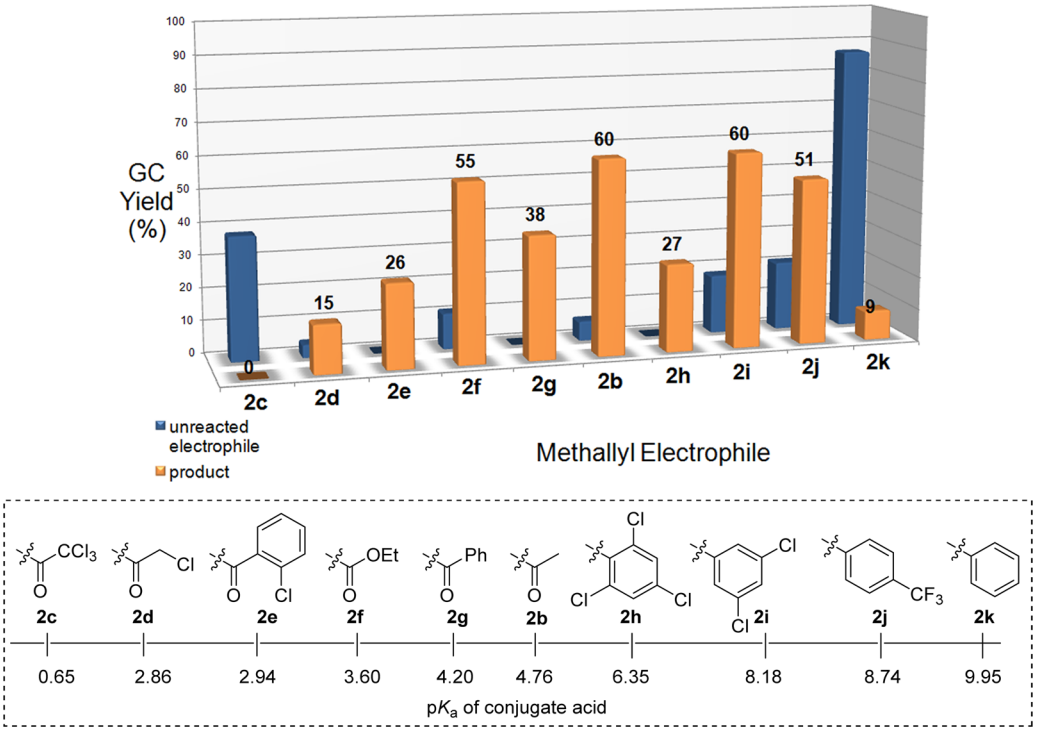
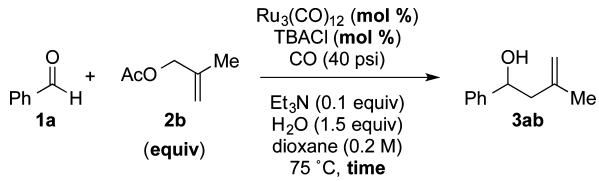


Figure 1. Survey of methallyl electrophile nucleofuges in the allylation of benzaldehyde. pK_a values of nucleofuge conjugate acids shown below the line. All yields measured by GC analysis with tetradecane as the internal standard.

electrophilic character of **2b**. Exchanging the acetate leaving group of **2b** for a leaving group that would increase the electrophilic character could improve the yield of **3ab** by increasing the rate of formation of the ruthenium π-allyl. A variety of 2-methallyl electrophiles, selected on the basis of the pK_a in water of the conjugate acid of the nucleofuge (reference: pK_a of AcOH is 4.76), were examined and the yields of **3ab** are compared in increasing order of pK_a in Figure 1.[40] In general, lower product **3ab** yields were observed as the pK_a values of the nucleofuges decreased (trichloroacetate **2c**, chloromethyl acetate **2d**, and *ortho*-chlorobenzoate **2e**). The use of methallyl phenyl ether (**2k**), which had the highest pK_a value, also resulted in a low product yield with a significant amount of unreacted electrophile. Nucleofuges with pK_a values most similar to acetate had product yields similar to acetate, with a maximum of 60% for 3,5-chlorophenol (**2i**). The benzoate (**2g**) and 2,4,6-*tri*-chlorophenol nucleofuges (**2h**) led to low product yields (38% and 27% respectively) despite having pK_a values closer to that of acetic acid, indicating that there may be additional factors to consider in the use of these groups. Whereas **2i** afforded comparable product yields and less unproductive consumption when compared to **2b**, acetate was selected as the leaving group for all subsequent studies due to ease of substrate preparation and the formation of acetic acid as the stoichiometric byproduct.

The reaction of acetate **2b** with benzaldehyde (**1a**) was optimized with respect to substrate and catalyst loading and reaction time (Table 1). Increasing the equivalents of **2b** resulted in higher yield of **3ab** (Table 1, entries 1−2 and entries 5−7). Increasing the loading of catalyst to 2 mol % also increased the yield (Table 1, entry 7). Extended reaction times did not offer any benefit, as those reactions that were performed for 40 h did not show any marked increase in yield when compared to the 20 h experiments (Table 1, entries 1−4, and entries 6 and 8). The use of 2 mol % of the catalyst and 3.0 equiv **2b** at 20 h was found to be the most effective in the production of **3ab**, albeit still in moderate yield (Table 1, entry 7).

Table 1. Effect of 2ab Equivalents, Catalyst Loading, and Time on Yield of 3ab



entry	$Ru_3(CO)_{12}$[a] (mol %)	time (h)	**2b** (equiv)	**2b** recovery[b,c] (%)	**3ab** yield[b] (%)
1	1	20	1.2	0	53
2	1	20	2.0	6	60
3	1	40	1.4	2	49
4	1	40	2.0	0	52
5	2	20	1.2	0	39
6	2	20	2.0	10	55
7	2	20	3.0	36	61
8	2	40	2.0	11	53

[a]TBACl loading 3 mol % with respect to $Ru_3(CO)_{12}$. [b]Determined by GC using tetradecane as the internal standard. [c]Percentage recovered with respect to the total equivalents of **2b**.

1.2. Aldehyde Scope for Allylation Reactions. Using the optimized conditions of 2 mol % of catalyst and 3.0 equiv of **2b**, found in Table 1, acetate **2b** was reacted with a set of aldehydes (Table 2). The reaction of aromatic (**1a**), α,β-unsaturated (**1b**), and aliphatic (**1c**) aldehydes with acetate **2b** afforded the desired products in good yields. The reaction concentration was increased to 0.4 M from 0.2 M, and the equivalents of H_2O

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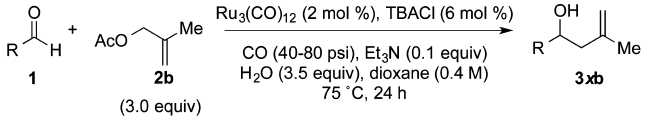
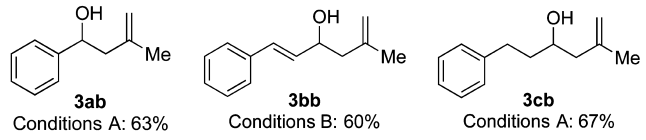
were increased to 3.5 equiv as other experiments revealed significant increases in yield with these changes (*vide infra*). The use of (*E*)-cinnamaldehyde required the use of 80 psi of CO to maintain the same level of aldehyde conversion as **1a** and **1c**. Under these conditions, product **3bb** from (*E*)-cinnamaldehyde was partially reduced to **3cb**, yielding an inseparable mixture of **3bb**/**3cb** in a 94:6 ratio.

Table 2. Additions with 2-Methallyl Acetate (2b)[a,b]

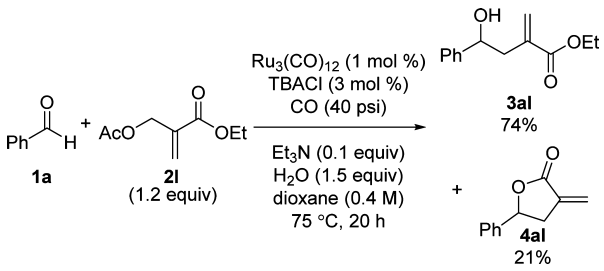




[a]Reaction conditions: (A) 40 psi CO; (B) 80 psi CO. [b]Yield of isolated product.

2. Catalytic Nucleophilic Allylation with *tert*-Butyl 2-(Acetoxymethyl)acrylate. *2.1. Optimization of Reaction Conditions.* Ethyl 2-(acetoxymethyl)acrylate **2l**, which possesses an electron-withdrawing group, was next employed as the allyl source, as ester substituted allyl reagents have been successfully employed in other carbonyl allylation reactions.[38] When **2l** was combined with **1a**, full conversion of the aldehyde was observed. However, upon isolation, in addition to the expected homoallylic alcohol product (**3al**), an α-exomethylene γ-butyrolactone (**4al**) (resulting from cyclization of **3al**) was formed (Scheme 9).

Scheme 9



To avoid this undesired lactonization, *tert*-butyl 2-(acetoxymethyl)acrylate (**2m**) was employed instead. This modification suppressed the formation of the lactone to a significant extent. To establish the reactivity pattern of **2m**, a set of aldehydes was examined in combination with **2m** using conditions similar those with **2a** (see Supporting Information). These initial conditions did not allow for the full conversion of the aldehydes whereas the use of 2 mol % of $Ru_3(CO)_{12}$ did allow for uniformly high (>90%) conversions in reasonable reaction times (20 h). Additional optimization determined that an increase in concentration to 0.4 M resulted in a significant rate increase and as such, the 0.4 M concentration was used for all further reactions (see Supporting Information).

2.2. Aldehyde Scope for Allylation Reactions. Using the optimal conditions of 0.4 M and 2 mol % catalyst, the scope of aldehyde in additions with acetate **2m** was examined on a preparative scale (1.0 mmol) (Table 3). The number of equivalents of **2m** employed in these reactions was the minimum required for full conversion of **1**. Acetate **2m** is relatively insensitive to the electronic properties of aromatic aldehydes, as both electron-rich (**1a** and **1f**) and electron-poor substrates (**1e**) reacted in good yield. Although 4-nitrobenzaldehyde (**1d**) provided a lower yield, it is possible that some decomposition of product **3dm** may have occurred. Aliphatic and α,β-unsaturated aldehydes also reacted smoothly (**1c** and **1b**). Slightly lower yields for the more bulky substrates (**1g** and **1i**) were observed whereas the branched aldehyde (**1h**) afforded the product in good yield. Finally, heteroaromatic aldehyde (**1j**) produced the desired homoallylic alcohol (**3jm**) in a very good yield.

3. Catalytic Nucleophilic Allylation 2-Methylene-3-oxobutyl Acetate. *3.1. Optimization of Reaction Conditions.* The compatibility of esters under the reaction conditions encouraged the investigation of ketones as reaction partners as part of the allylating reagent. Test nucleophile 2-methylene-3-oxobutyl acetate **2n** was examined to further expand the scope of compatible functional groups. The effects of loading of **2n**, catalyst, and reaction time were investigated (Table 4). Increasing the loading of acetate **2n** improved the yield of **3an** from 51% with 1.2 equiv to 73% with 2.0 equiv (Table 4, entries 1−3). Despite some unreacted acetate **2n** remaining at 20 h, extending the reaction time to 40 h did not increase product yield (Table 4, entries 3 and 4). However, an increase in the $Ru_3(CO)_{12}$ loading from 1 mol % to 2 mol % led to a 94% yield of product after 20 h (Table 4, entry 4 and 5).

In the reactions of **2n** with **1b** and **1c** for the formation of the α,β-unsaturated and aliphatic addition products, **3bn** and **3cn**, significant amounts of unreacted aldehyde were observed. One possibility for incomplete consumption of **2n** is an insufficient amount of H_2O in the reaction. Without a sufficient amount of H_2O, the catalytic turnover would be inhibited. To examine this possibility, an investigation into the loading of H_2O was performed (Table 5). Increasing the number of equivalents of H_2O in the formation of **3bn** appeared to have little effect at 24 h, but at 48 h the conversion of **1b** significantly increased (Table 5, entries 1−4). Increasing the number of H_2O equivalents to 3.5 allowed for nearly complete conversion of **1c** in 24 h for **3cn** (Table 5, entries 5 and 6).

3.2. Aldehyde Scope for Allylation Reactions. The representative set of aldehydes was employed in reaction with acetate **2n** on a preparative scale (1.0 mmol) using the conditions obtained in the optimization (Table 6). These aldehydes reacted with acetate **2n** in good yields to generate the aromatic (**3an**), α,β-unsaturated (**3bn**), and aliphatic (**3cn**) products.

4. Catalytic Nucleophilic Allylation 2-Phenylallyl Acetate. *4.1. Reaction Optimization.* The use of 2-phenylallyl acetate **2o** was next investigated to explore the suitability for the installation of an aryl ring, a common structural motif, in the product. The phenyl substituent should result in a less electron-rich allyl species through induction and a removal of electron density from the allyl, lowering the LUMO. This should allow for a more facile oxidative addition, though to a lesser extent than the ester substituent. The effects of concentration, time, catalyst loading, and acetate **2o** equivalents were examined (Table 7). Under the initial reaction conditions based on acetate **2a**, significant amounts of benzaldehyde were recovered (Table 7, entry 1). Increases in reaction time and acetate **2o** equivalents produced higher conversions of **1a**

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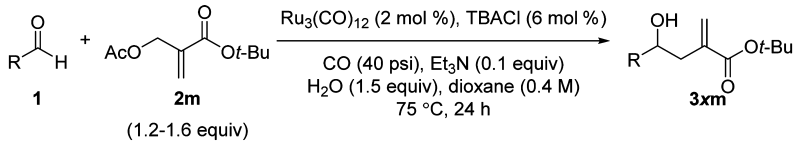
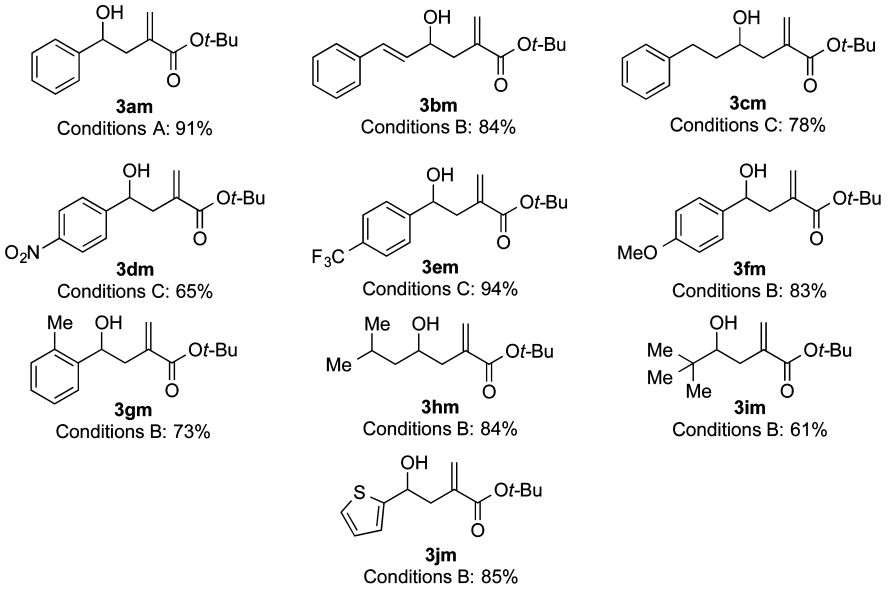
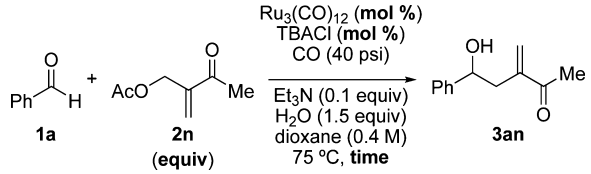
Table 3. Additions with *tert*-Butyl 2-(Acetoxymethyl)acrylate (2m)[a,b]





[a]Reaction conditions: (A) 1.6 equiv of acetate **2m**; (B) 1.4 equiv of acetate **2m**; (C) 1.2 equiv of acetate **2m**. [b]Yield of isolated product.

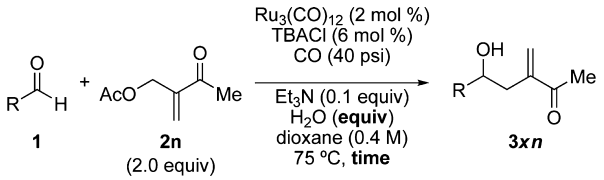
Table 4. Effect of Catalyst Loading, Reaction Time, and Equivalents of 2n on Allylation of 1a

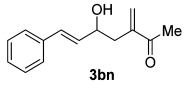
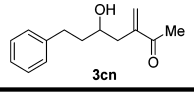


entry	$Ru_3(CO)_{12}$[a] (mol %)	time (h)	**2n** (equiv)	**2n** recovery[b,c] (%)	**3an** yield[b] (%)
1	1	20	1.2	0	51
2	1	20	1.6	18	58
3	1	20	2.0	28	73
4	1	40	2.0	24	71
5	2	20	2.0	23	94

[a]TBACl loading 3 mol % with respect to $Ru_3(CO)_{12}$. [b]Determined by GC analysis using tetradecane as the internal standard. [c]Percentage recovered is with respect to the total equivalents of **2n**.

Table 5. Effect of H_2O Loading on Allylation with 2n[a]



entry	product **3xn**	H_2O (equiv)	time (h)	**1** recovery (%)[a,b]	**2n** recovery (%)[b,c]
1		2.5	48	20	14
2		3.0	24	40	26
3		3.5	24	39	24
4		3.5	48	18	8
5		3.0	24	11	4
6		3.5	24	2	15

[a]The products for the reactions were not isolated and as such, the consumption of the starting aldehyde was used as a qualitative measurement of reaction efficiency. [b]Determined by GC analysis using tetradecane as the internal standard. [c]Percentage recovered is with respect to the total equivalents of **2n** added.

(Table 7, entry 2). An increase in reaction concentration (w.r.t **1a**) further increased the conversion of benzaldehyde (Table 7, entry 3). Increasing the catalyst loading to 2 mol % and acetate **2o** equivalents to 1.8 resulted in nearly the same benzaldehyde conversion and a decreased reaction time of 20 h (Table 7, entry 4). However, a small amount of **2o** remained unreacted. The observation of α-methylstyrene in the GC traces revealed that the protonolysis pathway was an active means of unproductively consuming **2o.**

Here again, increasing the number of equivalents of H_2O allowed for increased conversion of **1a** with **2n** (Table 5). To investigate whether a similar effect could be realized for acetate **2o**, the amounts of H_2O in the allylation of **1** with acetate **2o** was varied (Table 8). In general, increases in the amount of H_2O led to higher product yields (Table 8, entries 1 and 3). An increase in reaction time did not affect much change in the yields of **3ao** (Table 8, entries 2 and 4). Significantly higher amounts of H_2O than **2o** resulted in total consumption of acetate and lower yields as compared to those reactions with more similar ratios of H_2O to **2o** (Table 8, entries 5 and 6). With (*E*)-cinnamaldehyde, altering the reaction time, amount

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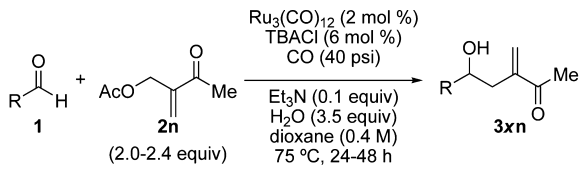
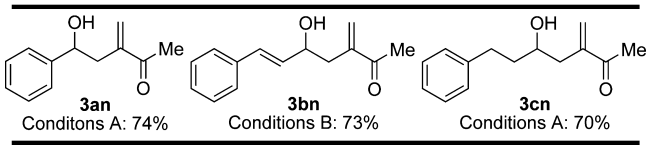
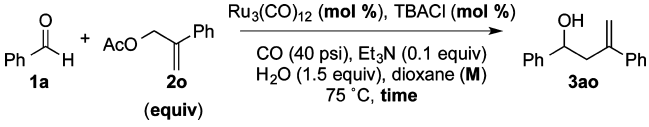
Table 6. Additions with 2-Methylene-3-oxobutyl Acetate (2n)[a,b]





[a]Reaction conditions: (A) 2.0 equiv **2n**, 24 h; (B) 2.4 equiv **2n**, 48 h. [b]Yield of isolated product.

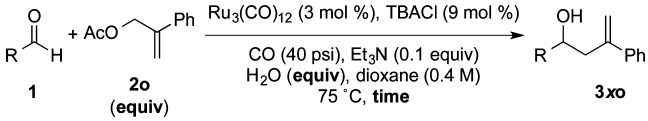
Table 7. Effect of Concentration, Time, Catalyst, and 2o Loading on the Allylation of 1a[a]



entry	$Ru_3(CO)_{12}$[b] (mol %)	1a conc (M)	time (h)	2o (equiv)	1a recovery[a,c] (%)	2o recovery[c,d] (%)
1	1	0.2	20	1.2	47	0
2	1	0.2	40	1.5	25	0
3	1	0.4	40	1.5	18	1
4	2	0.4	20	1.8	23	26

[a]The products for the reactions were not isolated, and as such, the consumption of the starting aldehyde was used as a qualitative measurement of reaction efficiency. [b]TBACl loading 3 mol % with respect to $Ru_3(CO)_{12}$. [c]Determined by GC analysis using tetradecane as the internal standard. [d]Percentage recovered is with respect to the total equivalents of **2o** added.

Table 8. Effect of Time and H_2O and 2o Loading on Allylation of 1[a]



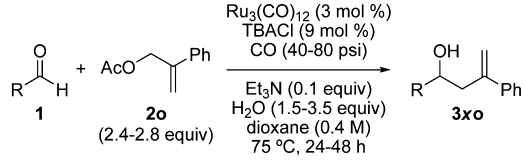
entry	product 3xo	H_2O (equiv)	2o (equiv)	time (h)	1 recovery (%)[b]	2o recovery (%)[b,c]
1		2.0	2.8	24	16	40
2		2.0	2.8	48	17	37
3		2.5	2.8	24	12	11
4	3ao	2.5	2.8	48	11	7
5		3.0	2.4	24	17	0
6		3.5	2.4	24	19	1
7		2.5	2.8	24	22	12
8		3.5	2.4	24	18	0
9	3bo	3.5	2.8	24	22	0
10		3.5	2.8	48	18	0

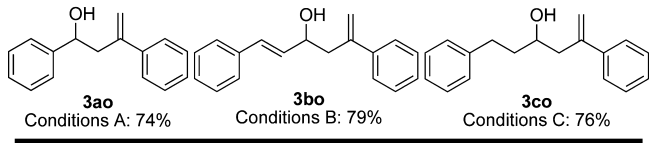
[a]The products for the reactions were not isolated, and as such, the consumption of the starting aldehyde was used as a qualitative measurement of reaction efficiency. [b]Determined by GC analysis using tetradecane as the internal standard. [c]Percentage recovered is with respect to the total equivalents of **2o** added.

of H_2O, or the amount of **2o** had little effect on the yield of **3bo** (Table 8, entries 7−10).

4.2. Aldehyde Scope for Allylation Reactions. Using the conditions identified in the optimization, the allylation of the representative aldehydes on a preparative scale (1.0 mmol) was next performed with acetate **2o** (Table 9). Thus, **1a**, **1b**, and **1c** reacted with **2o** to give the desired products in good yields. For (*E*)-cinnamaldehyde, a higher pressure of CO (80 psi) was required to maintain the same level of conversion as with **1a** and **1c**. Under these conditions, product **3bo** from (*E*)-cinnamaldehyde was partially reduced to **3co**, yielding an inseparable mixture of **3bo**/**3co** in an 88:12 ratio.

Table 9. Addition with 2-Phenylallyl Acetate (2o)[a,b]

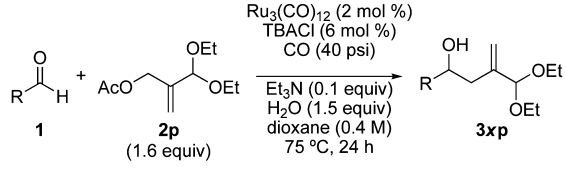


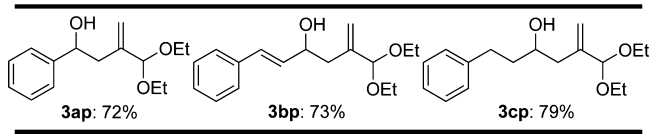


[a]Reaction conditions: (A) 2.8 equiv of **2o**, 2.5 equiv of H_2O, 40 psi CO, 48 h; (B) 2.8 equiv of **2o**, 3.5 equiv of H_2O, 80 psi CO, 24 h; (C) 2.4 equiv of **2o**, 1.5 equiv of H_2O, 40 psi CO, 24 h. [b]Yield of isolated product.

5. Catalytic Nucleophilic Allylation 2-(Diethoxymethyl)allyl Acetate. *5.1. Aldehyde Scope for Allylation Reactions.* The aldehyde chemoselectivity of the carbonyl allylation reaction has been clearly established based upon the previously employed allylic acetates. However, it is desirable to maintain an aldehyde functional group in the compound after the addition. Thus, an allyl source containing a protected aldehyde was prepared (**2p**). Using the conditions obtained in the optimization for acetate **2m**, the allylation of the model set of aldehydes on a preparative scale (1.0 mmol) was performed (Table 10). The aromatic (**1a**), *α,β*-unsaturated (**1b**), and aliphatic (**1c**) aldehydes reacted with **2p** in good yield. Under these conditions, product **3bp** from (*E*)-cinnamaldehyde was partially reduced to **3cp**, yielding an inseparable mixture of **3bp**/**3cp** in an 88:12 ratio.

Table 10. Addition with 2-(Diethoxymethyl)allyl Acetate (2p)[a]





[a]Yield of isolated product.

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DISCUSSION

1. Effect of Substitution at 2-Position of Allyl Acetates. A variety of 2-substituted allylic acetates (**2**) were found to effectively engage in the carbonyl allylation reaction. In general, those allylic acetates containing electron-withdrawing substituents at the 2-position (i.e., *tert*-butyl ester, methyl ketone, phenyl, and diethoxy acetal) were able to produce the expected homoallylic alcohol products in high yields. The use of an electron donating substituent (i.e., methyl) also led to the formation of the desired products, but in somewhat diminished yield. This clearly points to the effect that the electronic nature of the substituent plays on the reaction. It is likely that either conjugation or close proximity of electron-deficient elements in these substituents lowers the LUMO of the allylic acetate. Therefore, the activation barrier toward formation of the ruthenium(II) π-allyl complex (**II**) should be lowered, allowing for a greater rate of formation. The methyl group at the 2-position of 2-methallyl acetate (**2b**) donates electron density into the allyl group though hyperconjugation and causes the allyl acetate to be less electrophilic, raising the LUMO of the allylic acetate.

The use of the 2-substituted allylic acetates further illustrates the functional group compatibility of the ruthenium-catalyzed allylation reaction. Specifically, the use of the methyl ketone and ester moieties reveals the chemoselectivity of the reaction for the aldehyde, even when the ketone or ester component was present in a much higher relative ratio (as high as 1:2.4). In no cases was any addition product from self-condensation observed. While the unintended formation of the α-exomethylene γ-butyrolactones was observed when an ethyl ester was employed, the use of a *tert*-butyl ester avoided the formation of this byproduct. It was also shown that the aldehyde oxidation state can be retained in the addition product by way of the diethoxy acetal. Even under the reaction conditions which are acidic due to the stoichiometric formation of acetic acid, no product from hydrolysis was observed.

2. Effects of H_2O Loading. From consideration of the proposed catalytic cycle, H_2O plays two roles: (1) the hydrolysis of ruthenium(II) complex **III** yielding **3** and (2) as the proton source for the unproductive consumption of the allyl acetate. Therefore, beyond the necessary equivalents for the turnover of the catalyst and this unproductive pathway, additional equivalents of H_2O should have little influence on the reaction. Yet, the addition of H_2O beyond the theoretically required amounts was shown to increase the conversion of aldehydes **1** (Table 5, entries 5 and 6). This observation suggests a further role for H_2O in the catalytic cycle. A potential additional role for H_2O in the reaction is that of a proton relay during the water–gas shift reaction. A DFT study of several possible mechanisms for the water–gas shift reaction indicates that several transition states are lowered in energy when additional H_2O molecules are included.[41]

An alternative explanation for the salutary effects of H_2O in the reaction is the inclusion of an off-cycle water–gas shift reaction, in the production of H_2. In addition to the productive pathway whereby ruthenium(II) is reduced to ruthenium(0), it is also possible for $Ru_3(CO)_{12}$ to catalyze the water–gas shift reaction without undergoing oxidative addition (OA) with an allylic acetate. Instead, it undergoes a more typical water–gas shift reaction mechanism and reduces H_2O to form hydrogen gas.[42] This factor could account for the slight increase in yield when an increase in the amount of H_2O was made. The H_2 thus generated could also account for the appearance of the reduction products observed in the products from additions with (*E*)-cinnamaldehyde. In addition to acting as the water–gas shift reaction catalyst, ruthenium is known to undergo hydrogenation of alkenes.[43] It is unlikely that the (*E*)-cinnamaldehyde is being reduced before the allylation reaction because the reduced product was not observed in all reactions between (*E*)-cinnamaldehyde and the 2-substituted allyl acetates. Curiously, when 2-methylene-3-oxobutyl acetate (**2n**) was employed, only the desired product from the addition to (*E*)-cinnamaldehyde was observed and while the reduction product was observed with **2m**, it was to a very small extent. As both of these allylic acetates contain a carbonyl functional group, it is possible that the carbonyl binds to the ruthenium metal which could deactivate the reduction pathway while still allowing for the formation of the homoallylic alcohol products.

3. Effects of Acetate Stoichiometry. Differing amounts of acetates **2** also had a small, but reproducible effect on product yields, even after the addition of sufficient allylic acetate to make up for unproductive consumption was taken into account. An increase in the relative concentration of allylic acetate could correspond to an increased rate of the formation of ruthenium(II) π-allyl complex **II**, thereby allowing for an increased yield within the time of the reaction.

Another possible effect of increased amounts of **2** on the catalytic cycle involves the formation of AcOH, the byproduct of the water–gas shift reaction. As the allylation reaction progresses, it is likely that AcOH causes the further protonolysis of the π-allyl complex **II**. Upon formation of the π-allyl complex **II**, one of two pathways are available: (1) the productive pathway that involves insertion of the π-allyl complex **II** into the aldehyde which ultimately leads to the formation of **3** or (2) the unproductive protonolysis pathway that consumes **2**. If these two pathways occur at roughly the same rates, 2.0 equiv of **2** should be required to both fully consume the aldehyde and account for protonolysis. In the early stages of the reaction, the productive pathway is likely more rapid as the complete consumption of the aldehydes with less than 2 equiv of acetates **2** is observed. If the protonolysis pathway is more rapid, at least 2 equiv of acetate **2** would always be required for full conversion of the aldehydes. As the reaction progresses; however, increased concentrations of AcOH could increase the ability of the protonolysis reaction to compete with the productive pathway. The total consumption of aldehyde with less than 2.0 equiv of acetate, as in the case of *tert*-butyl 2-(acetoxymethyl)acrylate (**2m**) and 2-(diethoxymethyl)allyl acetate (**2p**), reveals that the productive pathway is more rapid throughout the course of these reactions.

4. Effects of Nucleofuge on Reactivity of the 2-Methallyl Subunit. The choice of leaving group on the methallyl subunit was shown to have a profound effect on the production of homoallylic alcohol product. The yield of **3ab** decreases as the pK_a of the conjugate acid of the nucleofuge becomes either less than or greater than acetate, indicating that two mechanisms may be operative. Those 2-methallyl electrophiles with conjugate acid pK_a values higher than AcOH appear to be operating under OA as the turnover-limiting step (TLS). Their lower reactivity can be understood on the basis of their poorer leaving group ability compared to acetate. The large amount of unreacted electrophile remaining when compared to the other allyl sources also supports this conclusion. However,

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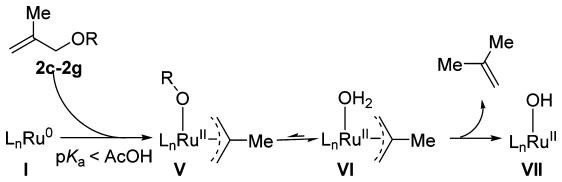
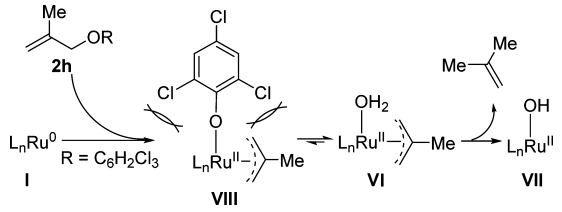
the 2-methallyl electrophiles with conjugate acid pK_a values lower than acetate also led to lower yields, despite containing good leaving groups. Therefore, these substrates may react by a mechanism in which the TLS follows the OA and the formation of homoallylic alcohol product is hampered, but allows for the consumption of the ruthenium π-allyl complex **V**. For example, the nucleofuges for these substrates are poor ligands for ruthenium(II) owing to their lower basicity. After OA, the nucleofuge may bind weakly to the ruthenium catalyst and could be easily displaced by H_2O, allowing the ruthenium(II) π-allyl complex **V** to undergo a facile protonolysis, resulting in the high levels of unproductive consumption of 2-methallyl electrophile observed (Scheme 10). If the TLS occurs after the formation of **V**, the decreased nucleophilicity of the ruthenium(II) π-allyl complex **V** may decrease the rate of the insertion of complex **V** into aldehyde **1**. The protonolysis pathway may then become more accessible than the formation of the homoallylic alcohol product. The difference in the amounts of consumed electrophile and generated product is likely due to an unproductive consumption of the electrophiles.

Scheme 10



A similar case can be posited for the unproductive consumption of 2-methallyl 2,4,6-trichlorophenol (**2h**), despite the higher pK_a of its conjugate acid as compared to AcOH. In this case, the weak binding to ruthenium(II) could arise from steric interactions (Scheme 11). After the formation of the ruthenium π-allyl complex **VIII**, the *ortho*-chlorine atoms on the phenol ligand would create unfavorable steric repulsion with the ruthenium metal and ligands, allowing for the displacement of the phenol by H_2O and subsequent protonolysis of the H_2O-bound ruthenium π-allyl.

Scheme 11



5. Aldehyde Scope. As part of the investigation of different allylic acetates, a variety of aldehyde substrates were examined. In several of the cases, a minor change was required in the reaction conditions to obtain high or complete conversion of the slower acting aldehydes such as an increase in reaction time (48 h) or an increase in CO pressure (80 psi). It has been previously demonstrated that the use of (*E*)-cinnamaldehyde may require more forcing conditions to react as rapidly as the other aldehydes.[14] In general, the allylation reaction preferably engages unhindered aldehydes. With sterically hindered aldehydes, however, a moderate yield is still produced, 61% for **2m** with pivalaldehyde and 73% for **2m** with 2-tolualdehyde (Table 3, **3im** and **3gm**). The decrease in yield for the aldehydes with high steric hindrance can be attributed to the difficulty for approach of the π-allyl **II** to the aldehyde. With regard to aromatic aldehydes, a slight difference in yield between electron-rich and electron-deficient aldehydes was noted for the addition with **2m**. The use of electron-rich aldehydes **1f** and **1g** afforded lower yields than the electron-neutral or electron-poor aldehydes **1a** and **1e**. Decreased electron density in the aldehyde lowers the LUMO and thereby reduces the energy of activation barrier for the addition.

■ CONCLUSIONS

The ruthenium-catalyzed, nucleophilic allylation of aldehydes has been successfully expanded to include allylic acetates with substituents at the 2-position. This substitution has allowed for the introduction of additional functionality in the homoallylic alcohol products, significantly expanding the synthetic utility of this reaction. Allylic acetates with electron-withdrawing substituents are more effective in the generation of products from a variety of aromatic, α,β-unsaturated, and aliphatic aldehydes. Electron-donating substituents on the allylic acetate are less effective, despite extensive optimization.

During the course of this optimization, several variables were discovered to have significant influence on the efficiency of formation of the homoallylic alcohols. A delicate balance between the amounts of H_2O and acetate beyond the quantities employed in the original reaction conditions was critical for the allylation reaction because both components participate in unproductive, off-cycle reactions to consume the acetate. Further studies on the development of stereoselective variants of this reaction are underway and will be reported in due course.

■ EXPERIMENTAL SECTION

General Allylation Procedure for Allylation Reactions of 2-Substituted Allylic Acetates. In a glovebox, to a 10 mL, flat-bottomed, glass tube (1.5 × 6.5 cm) containing a Teflon-coated, magnetic stir bar were added $Ru_3(CO)_{12}$ (1, 2, or 3 mol %) and TBACl (3, 6, or 9 mol %). The tube was covered with a rubber septum before being removed from the glovebox. Outside the glovebox, the tube was charged sequentially with 1,4-dioxane (2.5 mL), H_2O (1.5, 2.5, or 3.5 equiv), Et_3N (13.9 μL, 0.10 mmol, 0.1 equiv), allyl donor **2** (1.2, 1.4, 1.6, 2.0, 2.4, 2.8, or 3.0 equiv), and aldehyde **1** (1.00 mmol, 1.0 equiv) via syringe. The tube was placed in a six-well autoclave that allows six separate reactions to be conducted at the same time. The autoclave was sealed and connected to a carbon monoxide gas cylinder. The autoclave was charged with CO gas (100 psi), and pressure was released to a vented hood four times before the CO gas was maintained at the specified pressure (40 or 80 psi) and the valves for each cell were closed. The autoclave was mounted onto a magnetic stirrer with a temperature probe inserted into the metal block of the autoclave. The temperature was set at 75 °C, and stirring was started. The temperature reached 75 °C within 30 min and was maintained for the time specified (24 or 48 h). The autoclave was removed from the stirrer and chilled in an ice/water bath. The temperature reached ~20 °C within 40 min. The outlet was connected to a vented hood, and the pressure in the autoclave was gently released. The inlet was then connected to a nitrogen line, and the system was purged by N_2 (which was passed through a drying tube filled with Drierite) for 15 min before the autoclave was opened. The reaction mixture was transferred to a 20 mL, glass scintillation vial with the aid of 3 mL of diethyl ether. The solvent was removed under reduced pressure by rotary evaporation (25 °C, 20 mmHg).

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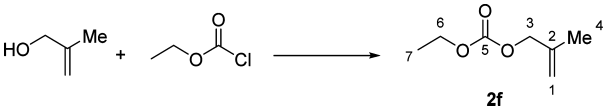
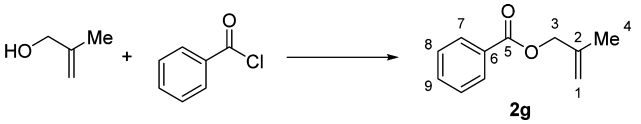
Preparation of 2-Substituted Allylic Electrophiles.

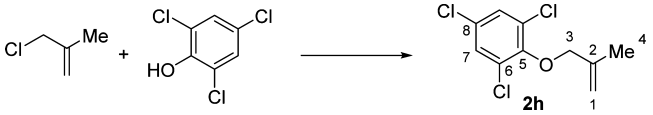
*Preparation of 2-Methylallyl 2-Chlorobenzoate (**2e**).* In a 100 mL, round-bottomed, three-neck flask (equipped with an Ar inlet, septum, Teflon-coated stir bar, and glass stopper) in an ice/water bath at 0 °C was added dropwise 2-chlorobenzoyl chloride (1.27 mL, 10 mmol, 1.0 equiv) via syringe to a solution of CH_2Cl_2 (50 mL) containing 2-methallyl alcohol (0.721 g, 0.841 mL, 10 mmol) and pyridine (1.05 mL, 13 mmol, 1.3 equiv) over the course of 15 min. The reaction mixture was warmed to room temperature and stirred for 19 h. The reaction mixture was washed with aqueous HCl (3 M, 4.33 mL), the layers were separated, and the aqueous layer was extracted with CH_2Cl_2 (1 × 30 mL). The combined organic layers were washed with $NaHCO_3$ (7 × 10 mL), dried ($MgSO_4$), and filtered, and the solvent was removed under reduced pressure. The residue was purified via MPLC silica gel chromatography (24 g SiO_2, hexane (100%) for 5 column volumes, then increased to CH_2Cl_2/hexane (1:9) over 8 column volumes, then CH_2Cl_2 (100%) for 3 column volumes) to afford **2e** (0.705 g, 33%) as a clear, colorless oil. Data for **2e**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.86 (dd, J = 7.8, 1.7 Hz, 1H, C(11)H), 7.46 (dd, 1H, J = 8.1, 1.4 Hz C(8)H), 7.42 (td, 1H, J = 8.1, 7.5, 1.7 Hz, C(9)H), 7.32 (td, J = 7.8, 7.5, 1.4 Hz, 1H, C(10)H), 5.10 (d, J = 1.3 Hz, 1H, C(1a)H), 5.00 (d, J = 1.3 Hz, 1H, C(1b)H), 4.76 (s, 2H, C(3)H_2), 1.85 (s, 3H, C(4)H_3); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 165.5 (C5), 139.7 (C2), 133.9 (C7), 132.7 (C9), 131.6 (C11), 131.2 (C8), 130.2 (C6), 126.7 (C10), 113.8 (C1), 69.0 (C3), 19.8 (C4); IR (neat) 3080 (w), 2975 (w), 2943 (w), 1731 (m), 1660 (w), 1593 (w), 1473 (w), 1436 (w), 1378 (w), 1363 (w), 1296 (m), 1243 (m), 1163 (w), 1116 (m), 1048 (m), 984 (w), 946 (w), 906 (w), 816 (w), 791 (w), 744 (s), 723 (w), 691 (w), 649 (w), 571 (w); MS (EI$^+$, TOF, 70 eV) 210.0 (M^+, 3), 141.0 (32), 139.0 (100), 111.0 (15); HRMS (EI$^+$, TOF) calcd for $C_{11}H_{11}O_2Cl$ 210.0448, found 210.0451; TLC R_f 0.48 (EtOAc/hexane, 1:4) [UV, PA].



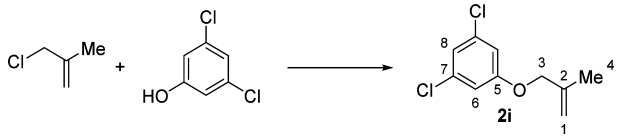
*Preparation of Ethyl (2-Methylallyl) Carbonate (**2f**).* In a 100 mL, round-bottomed, three-neck flask (equipped with an Ar inlet, septum, Teflon-coated stir bar, and glass stopper) in an ice/water bath at 0 °C was added dropwise ethyl chloroformate (1.30 mL, 14.5 mmol, 1.45 equiv) via syringe to a solution of CH_2Cl_2 (25 mL) containing 2-methallyl alcohol (0.721 g, 0.841 mL, 10 mmol) and pyridine (1.17 mL, 14.5 mmol, 1.45 equiv) over the course of 15 min. The reaction mixture was warmed to room temperature and stirred for 3.5 h. The reaction mixture was washed with aqueous HCl (1 M, 2 × 20 mL), the layers were separated, and the aqueous layer was extracted with CH_2Cl_2 (1 × 20 mL). The combined organic layers were washed with $NaHCO_3$ (3 × 10 mL), dried ($MgSO_4$), and filtered, and the solvent was removed under reduced pressure. The residue was purified via bulb-to-bulb distillation (85 °C ABT, ~4 mmHg) to afford **2f** (1.138 g, 79%) as a clear, colorless oil. The spectroscopic data matched those from literature, and the sample was free of any major impurities.[44]



*Preparation of 2-Methylallyl Benzoate (**2g**).* In a 100 mL, round-bottomed, three-neck flask (equipped with an Ar inlet, septum, Teflon-coated stir bar, and glass stopper) in an ice/water bath at 0 °C was added dropwise benzoyl chloride (1.74 mL, 15 mmol, 1.5 equiv) via syringe to a solution of CH_2Cl_2 (50 mL) containing 2-methallyl alcohol (0.721 g, 0.841 mL, 10 mmol) and pyridine (1.05 mL, 13 mmol, 1.3 equiv) over the course of 15 min. The reaction mixture was warmed to room temperature and stirred for 2 h. The reaction mixture was washed with aqueous HCl (3 M, 4.33 mL), the layers were separated, and the aqueous layer was extracted with CH_2Cl_2 (3 × 20 mL). The combined organic layers were washed with $NaHCO_3$ (7 × 10 mL), dried ($MgSO_4$), and filtered, and the solvent was removed under reduced pressure. The residue was purified via bulb-to-bulb distillation (80 °C ABT, ~1.3 mmHg) and then further purified via MPLC silica gel chromatography (25 g SiO_2, hexane (100%) for 5 column volumes, then increase to CH_2Cl_2/hexane (1:9) over 8 column volumes) to afford **2g** (1.225 g, 70%) as a clear, colorless oil. The spectroscopic data matched those from literature, and the sample was free of any major impurities.[45]



*Preparation of 1,3,5-Trichloro-2-((2-methylallyl)oxy)benzene (**2h**).* In a 50 mL, round-bottomed, three-neck flask (equipped with a reflux condenser w/Ar inlet, septum, Teflon-coated stir bar, and glass stopper) was added dropwise 3-chloro-2-methylprop-1-ene (0.979 mL, 10 mmol, 2 equiv) via syringe to a solution of acetone (15 mL), K_2CO_3 (864 mg, 6.25 mmol, 1.25 equiv), KI (83 mg, 0.5 mmol, 0.1 equiv), and 2,4,6-trichlorophenol (987 mg, 5 mmol) over the course of 10 min. The septa was replaced with a glass stopper and the flask placed into an oil bath (65 °C). Water was run through the reflux condenser and the reaction stirred for 15 h. The reaction washed through a Celite pad (1.0 cm × 3 cm) using acetone (20 mL). The solvent was removed under reduced pressure. The residue was taken back up into EtOAc (25 mL), washed with deionized water (25 mL) and brine (15 mL), dried ($MgSO_4$), and filtered, and solvent was removed under reduced pressure. The residue was purified via silica gel chromatography via MPLC (40 g SiO_2, 5 column volumes hexane (100%)) to afford **2h** (1.10 g, 87%) as a white solid. Data for **2h**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.31 (d, J = 0.6 Hz, 2H, C(7)H), 5.15 (dd, J = 2.0, 1.2 Hz, 1H, C(1a)H), 5.03 (dd, J = 2.0, 1.2 Hz, 1H, C(1b)H), 4.40 (s, 2H, C(3)H_2), 1.94 (d, J = 1.2 Hz, 3H, C(4)H_3); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 150.5 (C5), 140.7 (C2), 130.3 C(6) × 2, 129.6 C(8), 128.9 C(7) × 2, 114.4 (C1), 77.2 C(3), 19.8 C(4); MS (EI$^+$, 70 eV) 250.0 (M^+, 78), 219.0 (15), 217.0 (61), 216.0 (15), 215.0 (100), 201.0 (15), 199.9 (29), 198.9 (12), 197.9 (95), 196.9 (29), 195.9 (99), 194.9 (35), 192.9 (13), 181.9 (12), 179.9 (12), 170.9 (17), 168.9 (55), 166.9 (57), 161.9 (10), 159.9 (15), 149.0 (10), 145.0 (12), 143.0 (12), 134.0 (17), 132.0 (27), 109.0 (11), 108.9 (18), 106.9 (29), 99.0 (21), 97.0 (65), 96.0 (10), 82.9 (10), 62.0 (16); HRMS (EI$^+$, TOF) calcd for $C_{10}H_9OCl_3$ 249.9719, found 249.9718; TLC R_f 0.72 (EtOAc/hexane, 1:4) [UV, PA].



*Preparation of 1,3-Dichloro-5-((2-methylallyl)oxy)benzene (**2i**).* In a 50 mL. round-bottomed, three-neck flask (equipped with a reflux condenser w/Ar inlet, septum, Teflon-coated stir bar, and glass stopper) was added dropwise 3-chloro-2-methylprop-1-ene (0.979 mL, 10 mmol, 2 equiv) via syringe to a solution of acetone (15 mL), K_2CO_3 (864 mg, 6.25 mmol, 1.25 equiv), KI (83 mg, 0.5 mmol, 0.1 equiv), and 3,5-dichlorophenol (815 mg, 5 mmol) over the course of 10 min. The septa was replaced with a glass stopper and the flask placed into an oil bath (65 °C). Water was run through the reflux condenser and the reaction stirred for 15 h. The reaction mixture was washed through a Celite pad (1.0 cm × 3 cm) using acetone (20 mL). The solvent was removed under reduced pressure. The residue was taken back up into EtOAc (25 mL), washed with deionized water (25 mL) and brine (15 mL), dried ($MgSO_4$), and filtered, and solvent was removed under reduced pressure. The residue was purified via silica gel chromatography via MPLC (40 g SiO_2, 5 column volumes hexane (100%)) to afford **2i** (1.07 g, 98%) as a clear, colorless oil. Data for **2i**:

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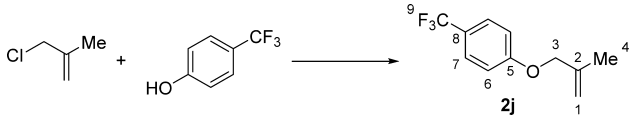
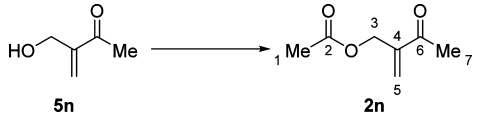
^{1}H NMR (500 MHz, $CDCl_3$) δ 6.95 (t, J = 1.8 Hz, 1H, C(8)H), 6.81 (d, J = 1.8 Hz, 2H, C(6)H), 5.07 (d, J = 0.8 Hz, 1H, C(1a)H), 5.01 (d, J = 0.8 Hz, 1H, C(1b)H), 4.40 (s, 2H, C(3)H_2), 1.81 (s, 3H, C(4)H_3); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 159.9 C(5), 140.0 C(2), 135.4 C(7) × 2, 121.3 C(8), 114.0 C(6) × 2, 113.5 C(1), 72.3 C(3), 19.4 C(4); MS (EI$^+$, 70 eV) 216.0 (80), 203.0 (64), 201.0 (100), 181.0 (32), 164.0 (18), 162.0 (30), 133.0 (12), 109.0 (10), 63.0 (15); HRMS (EI$^+$, TOF) calcd for $C_{10}H_{10}OCl_2$ 216.0109, found 216.0107; TLC R_f 0.63 (EtOAc/hexane, 1:4) [UV, PA].



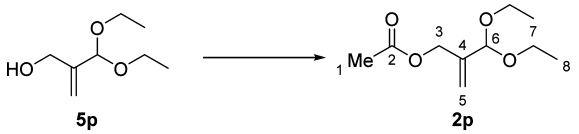
2j

*Preparation of 1-((2-Methylallyl)oxy)-4-(trifluoromethyl)benzene (**2j**).* In a 50 mL, round-bottomed, three-neck flask (equipped with a reflux condenser w/Ar inlet, septum, Teflon-coated stir bar, and glass stopper) was added dropwise 3-chloro-2-methylprop-1-ene (0.979 mL, 10 mmol, 2 equiv) via syringe to a solution of acetone (15 mL), K_2CO_3 (864 mg, 6.25 mmol, 1.25 equiv), KI (83 mg, 0.5 mmol, 0.1 equiv), and 4-trifluoromethylphenol (811 mg, 5 mmol) over the course of 10 min. The septa was replaced with a glass stopper and the flask placed into an oil bath (65 °C). Water was run through the reflux condenser and the reaction stirred for 15 h. The reaction was washed through a Celite pad (1.0 cm × 3 cm) using acetone (20 mL). The solvent was removed under reduced pressure. The residue was taken back up into EtOAc (25 mL), washed with deionized water (25 mL) and brine (15 mL), dried ($MgSO_4$), and filtered, and solvent was removed under reduced pressure. The residue was purified via silica gel chromatography via MPLC (40 g SiO_2, 5 column volumes hexane (100%)) to afford **2j** (918 mg, 85%) as a clear, colorless oil. Data for **2j**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.54 (d, 2H, C(7)H), 6.98 (d, 2H, C(6)H), 5.11 (d, J = 1.4 Hz, 1H, C(1a)H), 5.04 (d, J = 1.4 Hz, 1H, C(1b)H), 4.50 (s, 2H, C(3)H_2), 1.86 (s, 3H, C(4)H_3); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 161.3 C(5), 140.3 C(2), 127.0 (q, J = 3.8 Hz, C(7)), 124.6 (q, J = 271.1 Hz, C(9)), 123.06 (q, J = 32.7 Hz, C(8)), 114.86 C(6), 113.4 C(1), 72.0 C(3), 19.5 C(4); MS (EI$^+$, 70 eV) 216.1 (M$^+$, 100), 202.1 (10), 201.1 (90), 197.1 (14), 162.0 (30), 145.0 (23), 143.0 (13), 133.0 (10), 113.0 (10), 55.1 (84); HRMS (EI$^+$, TOF) calcd for $C_{11}H_{11}OF_3$ 216.0762, found 216.0759; TLC R_f 0.62 (EtOAc/hexane, 1:5) [UV, PA].



5n **2n**

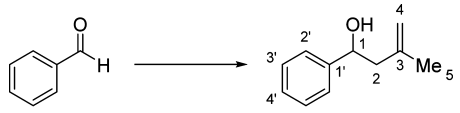
*Preparation of 2-Methylene-3-oxobutyl acetate (**2n**).* In a 250 mL, round-bottomed, three-necked flask (equipped with an Ar inlet, septum, and glass stopper) in an ice/water bath at 0 °C was added dropwise acetyl chloride (1.86 mL, 26 mmol, 1.3 equiv) via syringe to a solution of CH_2Cl_2 (100 mL) containing **5n** (4.0 g, 1.89 mL, 20 mmol) and pyridine (2.1 mL, 26 mmol, 1.3 equiv) over the course of 10 min. The reaction mixture was warmed to room temperature and stirred for 1 h. The reaction was quenched with aqueous HCl (1 M, 26 mL), layers were separated, and the aqueous layer was extracted with CH_2Cl_2 (1 × 30 mL). The combined organic layers were washed with $NaHCO_3$ (1 × 20 mL), dried ($MgSO_4$), and filtered, and the solvent was removed under reduced pressure. The residue was purified via silica gel chromatography via MPLC (120 g SiO_2 100% hexane for 13 column volumes then increase to EtOAc/hexane (1:9) for 17 column volumes) and then further purified via Kugelrohr distillation to afford **2n** (2.3 g, 81%) as a clear, colorless oil. Data for **2n**: bp 125 °C (ABT, 2.1 mmHg), ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.13 (d, J = 1.1 Hz, 1H, C(5a)H), 5.95 (t, J = 1.6 Hz, 1H, C(5b)H), 4.72 (t, J = 1.6 Hz, 2H C(3)H), 2.29 (s, 3H, C(7)H), 2.02 (s, 3H, C(1)H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 198.0 C(6), 170.0 C(2), 143.2 C(4), 126.7 C(5), 61.9 (C3), 25.8 C(7), 20.8 C(1); IR (neat) 3335 (w), 3109 (w), 3004 (m), 2951 (m), 2358 (w), 2334 (w), 1752 (s), 1742 (s), 1736 (s), 1686 (s), 1676 (s), 1637 (m), 1438 (m), 1403 (m), 1369 (s), 1322 (m), 1300 (s), 1229 (s), 1144 (m), 1129 (m), 1049 (s), 1035 (m), 977 (m), 950 (m), 903 (w), 842 (w), 642 (w), 605 (w), 578 (w); MS (EI$^+$, 70 eV) 142.1 (M$^+$, 5), 100.1 (35), 99.1 (100), 85.1 (30); TLC R_f 0.19 (EtOAc/hexane, 1:4) [$KMnO_4$]. Anal. Calcd for $C_7H_{10}O_3$ (142.15): C, 59.15; H, 7.09. Found: C, 58.94; H, 7.10.



5p **2p**

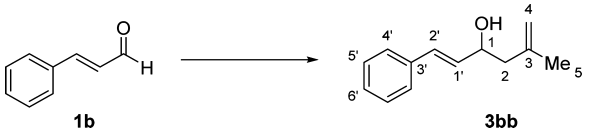
*Preparation of 2-(Diethoxymethyl)allyl Acetate (**2p**).* In a 100 mL, round-bottomed, three-neck flask (equipped with an Ar inlet, septum, Teflon-coated stir bar, and glass stopper) in an ice/water bath at 0 °C, acetyl chloride (0.562 mL, 7.56 mmol, 1.05 equiv) was added dropwise via syringe to a solution of CH_2Cl_2 (38 mL) containing **5p** (1.2 g, 7.49 mmol) and pyridine (0.788 mL, 9.74 mmol, 1.3 equiv) over the course of 10 min. The reaction mixture was warmed to room temperature and stirred for 1 h. The reaction was washed with $CuSO_4$ (satd, 3 × 20 mL), the layers were separated, and the aqueous layer was extracted with CH_2Cl_2 (1 × 30 mL). The combined organic layers were dried ($MgSO_4$) and filtered, and the solvent was removed under reduced pressure. The residue was purified via silica gel chromatography (130 g SiO_2, 4.5 × 22 cm column, hexane (100%) → Et_2O/hexane (1:7)) and then further purified via Kugelrohr distillation to afford **2p** (1.17 g, 77%) as a clear, colorless oil. Data for **2p**: bp 125 °C (ABT, 15 mmHg); ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.38 (d, J = 2.0 Hz, 1H, C(5a)H), 5.26 (dd, J = 2.0, 1.2 Hz, 1H, C(5b)H), 4.89 (s, 1H, C(6)H), 4.63 (t, J = 1.2 Hz, 2H, C(3)H_2), 3.61 (dq, J = 9.4, 7.0 Hz, 2H, C(7a)H_2), 3.48 (dq, J = 9.4, 7.0 Hz, 2H, C(7b)H_2), 2.09 (s, 3H, C(1)H_3), 1.22 (t, J = 7.0 Hz, 6H, C(8)H_3 × 2); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 170.7 C(2), 141.1 C(4), 115.4 C(5), 101.2 C(6), 63.5 C(3), 61.7 C(7), 21.0 C(1), 15.2 C(8); IR (neat) 2977 (w), 2937 (w), 2879 (w), 1744 (m), 1444 (w), 1391 (w), 1371 (w), 1328 (w), 1269 (w), 1226 (m), 1118 (m), 1051 (m), 1028 (m), 1007 (m), 920 (w), 840 (w), 606 (w); MS (ESI) 225.2 (MNa$^+$, 100), 158.2 (10), 157.2 (98), 143.1 (81), 129.2 (20); TLC R_f 0.42 (EtOAc/hexane, 1:4) [PA]. Anal. Calcd for $C_{10}H_{18}O_4$ (202.25): C, 59.39; H, 8.97. Found: C, 59.42; H, 9.24.

Preparation of Homoallylic Alcohols.



1a **3ab**

*Preparation of 3-Methyl-1-phenylbut-3-en-1-ol (**3ab**).* Following the general allylation procedure, **1a** (102 μL, 1.0 mmol), $Ru_3(CO)_{12}$ (12.8 mg, 0.02 mmol, 0.02 equiv), TBACl (16.7 mg, 0.06 mmol, 0.06 equiv), **2b** (374 μL, 3.0 mmol, 3.0 equiv), H_2O (63 μL, 3.5 mmol, 3.5 equiv), Et_3N (14 μL, 0.1 mmol, 0.1 equiv), and dioxane (2.5 mL) were combined under 40 psi of CO at 75 °C for 24 h. Workup and purification by silica gel column chromatography (47 g SiO_2, 3.5 × 12.5 cm column, hexane (100%) then Et_2O/hexane (1:9)) provided **3ab** (102 mg, 63%) as a colorless oil, which became a white solid in the freezer (−27 °C). The spectroscopic data matched those from literature and was free of any major impurities.[46] Data for **3ab**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.40−7.34 (m, 4H, C(2′,3′)H), 7.30−7.26 (m, 1H, C(4′)H), 4.93 (s, 1H, C(4a)H), 4.87 (s, 1H, C(4b)H), 4.82 (t, 1H, J = 6.8 Hz, C(1)H), 2.44 (d, 2H, J = 6.8 Hz, C(2)H), 2.14 (s, 1H, OH), 1.77 (s, 3H, C(5)H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 144.2, 142.5, 128.5, 127.6, 125.9, 114.3, 71.5, 48.5, 22.5; MS (EI$^+$, TOF, 70 eV) 162.1 (M$^+$, 2), 145.1 (3), 128.1 (4), 107.1 (100), 79.1 (53), 77 (25); TLC R_f 0.31 (EtOAc/hexane, 1:4) [UV, $KMnO_4$].

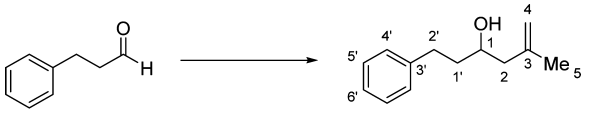


1b **3bb**

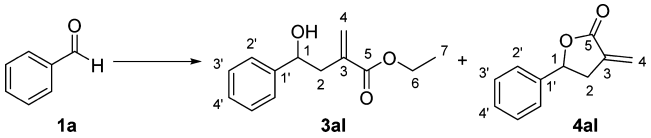
*Preparation of (E)-5-Methyl-1-phenylhexa-1,5-dien-3-ol (**3bb.**).* Following the general allylation procedure, **1b** (126 μL, 1.0 mmol),

dx.doi.org/10.1021/jo501004j | J. Org. Chem. 2014, 79, 5970−5986

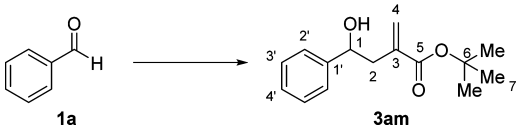
$Ru_3(CO)_{12}$ (6.4 mg, 0.01 mmol, 0.01 equiv), TBACl (8.3 mg, 0.03 mmol, 0.03 equiv), **2b** (158 μL, 1.2 mmol, 1.2 equiv), H_2O (27 μL, 1.5 mmol, 1.5 equiv), Et_3N (14 μL, 0.1 mmol, 0.1 equiv), and dioxane (2.5 mL) were combined under 80 psi of CO at 75 °C for 24 h. Workup and purification by silica gel column chromatography (51 g SiO_2, 3.5 × 13.5 cm column, hexane (100%) then Et_2O/hexane (1:9 → 1:4)) provided an inseparable mixture of **3bb**/**3cb** in a 94:6 ratio (113 mg, 60%) as a colorless oil. The spectroscopic data for **3bb** matched those from literature when the peaks for **3cb** were accounted for.[46] Data for **3bb**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.40−7.38 (m, 2H, C(4′)H), 7.32 (dd, *J* = 8.4, 6.8 Hz, 2H, C(5′)H), 7.26−7.22 (m, 1H, C(6′)H), 6.64 (dd, 1H, *J* = 15.9, 1.3 Hz, C(2′)H), 6.24 (dd, *J* = 15.9, 6.2 Hz, C(1′)H), 4.93 (t, *J* = 1.7 Hz, 1H, C(4a)H), 4.87 (dd, *J* = 1.7, 1.0 Hz, 1H, C(4b)H), 4.50−4.41 (m, 1H, C(1)H), 2.40−2.30 (m, 2H, C(2)H), 1.91 (s, 1H, OH), 1.82 (s, 1H, C(5)H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 142.1, 142.1, 136.9, 131.9, 130.2, 130.2, 128.7, 128.7, 127.7, 127.7, 126.6, 126.6, 114.2, 70.1, 46.4, 22.7; MS (EI$^+$, TOF, 70 eV) 188.1 (M$^+$, 2), 170.1 (38), 155.1 (48), 133.1 (100), 115.1 (38), 91.1 (57); TLC R_f 0.28 (EtOAc/hexane, 1:4) [UV, $KMnO_4$].



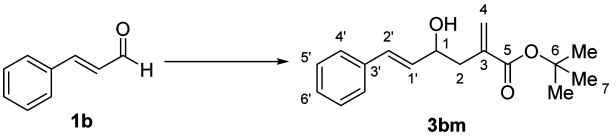
*Preparation of 5-Methyl-1-phenylhex-5-en-3-ol (**3cb**).* Following the general allylation procedure, **1c** (132 μL, 1.0 mmol), $Ru_3(CO)_{12}$ (12.8 mg, 0.02 mmol, 0.02 equiv), TBACl (16.7 mg, 0.06 mmol, 0.06 equiv), **2b** (374, 3.0 mmol, 3.0 equiv), H_2O (63 μL, 3.5 mmol, 3.5 equiv), Et_3N (14 μL, 0.1 mmol, 0.1 equiv), and dioxane (2.5 mL) were combined under 40 psi of CO at 75 °C for 24 h. Workup and purification by silica gel column chromatography (49 g SiO_2, 3.5 × 13 cm column, hexane (100%) then Et_2O/hexane (1:9 → 1:4)) provided **3cb** (128 mg, 67%) as a colorless oil. The spectroscopic data matched those from literature and was free of any major impurities.[46] Data for **3cb**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.30 (t, *J* = 7.6 Hz, 2H, C(5′)H), 7.25−7.16 (m, 3H, C(6′,4′)H), 4.90 (t, *J* = 1.8 Hz, 1H, C(4a)H), 4.82 (s, 1H, C(4b)H), 3.81−3.74 (m, 1H, C(1)H), 2.85 (dt, *J* = 13.7, 7.8 Hz, 1H, C(2′a)H), 2.72 (dt, *J* = 13.7, 8.1 Hz, 1H, C(2′b)H), 2.24 (dd, *J* = 13.7, 3.9 Hz, 1H, C(2a)H), 2.15 (dd, *J* = 13.7, 9.2 Hz, 1H, C(2b)H), 1.83−1.77 (m, 3H, OH and C(1′)H_2), 1.75 (s, 1H, C(5)H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 142.8, 128.6, 128.5, 125.9, 113.7, 68.2, 46.4, 38.9, 32.3, 22.6; MS (EI$^+$, TOF, 70 eV) 190.1 (M$^+$, 4), 135.1 (11), 134.1 (37), 117.1 (12), 92.1 (32), 91.0 (100); TLC R_f 0.30 (EtOAc/hexane, 1:4) [UV, $KMnO_4$].



*Preparation of Ethyl 4-Hydroxy-2-methylene-4-phenylbutanoate (**3al**).* Following the general allylation procedure, **1a** (81.6 μL, 0.8 mmol), $Ru_3(CO)_{12}$ (5.1 mg, 0.008 mmol, 0.01 equiv), TBACl (6.6 mg, 0.024 mmol, 0.03 equiv), **2l** (78.0 μL, 0.48 mmol, 1.2 equiv), H_2O (21.6 μL, 1.2 mmol, 1.5 equiv), Et_3N (11.2 μL, 0.08 mmol, 0.1 equiv), and dioxane (2.0 mL) were combined under 40 psi of CO at 75 °C for 20 h. Workup and purification by silica gel column radial silica gel chromatography 2 mm Et_2O/CH_2Cl_2 (7% Et_2O)) provided **3al** (130 mg, 74%) as a colorless oil and **4al** (36 mg, 21%) as an impure white solid. The spectroscopic data matched those from literature and was free of any major impurities in the case of **3al**.[47,48] Data for **3al**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.23−7.37 (m, 5H, C(aryl)H), 6.22 (d, *J* = 1.2 Hz, 1H, C(4)H), 5.58 (d, *J* = 1.2 Hz, 1H, C(4′)H), 4.87 (ddd, *J* = 8.4, 4.2, 3.6 Hz, 1H, C(1)H), 4.20 (q, *J* = 7.2 Hz, 2H, C(6)H), 2.92 (d, *J* = 3.6 Hz, 1H, C(OH)), 2.78 (dd, *J* = 14.1, 4.2 Hz, 1H, C(2a)H), 2.66 (dd, *J* = 14.1, 8.4 Hz, 1H, C(2b)H), 1.32 (t, *J* = 7.2 Hz, 3H, C(7)H); MS (ESI) 221.0 (MH$^+$, 17), 204.0 (14), 203.0 (100); TLC R_f 0.292 (Et_2O/CH_2Cl_2, 5% Et_2O) [UV, PA]. Data for **4al**: TLC R_f 0.71 (Et_2O/CH_2Cl_2 5% Et_2O) [UV, PA].



*Preparation of tert-Butyl 4-Hydroxy-2-methylene-4-phenylbutanoate (**3am**).* Following the general allylation procedure, **1a** (102 μL, 1.0 mmol), $Ru_3(CO)_{12}$ (12.8 mg, 0.020 mmol, 0.02 equiv), TBACl (16.9 mg, 0.060 mmol, 0.06 equiv), **2m** (320.4 mg, 1.60 mmol, 1.6 equiv), H_2O (27 μL, 1.5 mmol, 1.5 equiv), Et_3N (14 μL, 0.1 mmol, 0.1 equiv), and dioxane (2.5 mL) were combined under 40 psi of CO at 75 °C for 24 h. Workup and purification by silica gel column chromatography (radial silica gel chromatography 2 mm, EtOAc/hexane (1:7) then radial silica gel chromatography 2 mm, Et_2O/CH_2Cl_2 (5% Et_2O) then 7.2 g SiO_2, 1 × 19.5 cm column, Et_2O/hexane (3% Et_2O)) and then further purification via Kugelrohr distillation afforded **3am** (227 mg, 91%) as a clear, colorless oil. Data for **3am**: bp 100 °C (ABT, 10^{-5} mm Hg); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.38−7.35 (m, 2H, C(3′)H), 7.35−7.31 (m, 2H, C(2′)H), 7.26 (tt, *J* = 6.2, 1.7 Hz, 1H, C(4′)H), 6.15 (d, *J* = 1.6 Hz, 1H, C(4a)H), 5.52 (d, *J* = 1.6 Hz, 1H, C(4b)H), 4.87 (dt, *J* = 8.6, 4.0 Hz, 1H, C(1)H), 2.95 (d, *J* = 3.2 Hz, 1H, OH), 2.75 (ddd, *J* = 14.0, 4.0, 1.1 Hz, 1H, C(2a)H), 2.62 (ddd, *J* = 14.0, 8.6, 0.9 Hz, 1H, C(2b)H), 1.51 (s, 9H, C(7)H_3 × 3); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 167.2 C(5), 144.2 C(1′), 138.7 C(3), 128.5 C(2′), 127.6 C(4′), 127.5 C(4), 125.8 C(3′), 81.4 C(6), 73.4 C(1), 42.9 C(2), 28.2 C(7); IR (neat) 3438 (m), 3062 (w), 3029 (w), 3004 (w), 2977 (m), 2931 (m), 2359 (w), 2338 (w), 1708 (s), 1603 (m), 1493 (w), 1479 (w), 1453 (m), 1392 (m), 1368 (s), 1339 (m), 1313 (m), 1254 (m), 1214 (m), 1146 (s), 1050 (m), 950 (w), 912 (w), 879 (w), 850 (m), 817 (w), 755 (m), 737 (w), 70 (m), 637 (w); MS (CI$^+$, 70 EV) 249.1 (MH$^+$, 10), 193.0 (24), 175.0 (100), 129.0 (10), 107.0 (41), 79.0 (20), 77.0 (18); TLC R_f 0.30 (EtOAc/hexane, 1:4) [UV, $KMnO_4$]. Anal. Calcd for $C_{15}H_{20}O_3$ (248.32): C, 72.55; H, 8.12. Found: C, 72.30; H, 8.11.



*Preparation of (E)-tert-Butyl 4-Hydroxy-2-methylene-6-phenylhex-5-enoate (**3bm**).* Following the general allylation procedure, **1b** (125.9 μL, 1.0 mmol), $Ru_3(CO)_{12}$ (12.79 mg, 0.02 mmol, 0.02 equiv), TBACl (16.7 mg, 0.06 mmol, 0.06 equiv), **2m** (280.3 mg, 1.4 mmol, 1.4 equiv), H_2O (27 μL, 1.5 mmol, 1.5 equiv), Et_3N (14 μL, 0.1 mmol, 0.1 equiv), and dioxane (2.5 mL) were combined under 40 psi of CO at 75 °C for 24 h. Workup and purification by silica gel column chromatography (62 g SiO_2, 3.5 × 17 cm column, CH_2Cl_2 (100%) → Et_2O/CH_2Cl_2 (1% → 4% Et_2O) then 30 g SiO_2, 2.5 × 17 cm column, CH_2Cl_2 (100%) → Et_2O/CH_2Cl_2 (3% Et_2O)) provided **3bm** (230 mg, 84%) as a clear, slightly yellow oil. Data for **3bm**: bp 150 °C (ABT, 10^{-5} mm Hg); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.40−7.34 (m, 2H, C(4′)H), 7.34−7.27 (m, 2H, C(5′)H), 7.27−7.19 (m, 1H, C(6′)H), 6.65−6.57 (m, 1H, C(2′)H), 6.23 (dd, *J* = 15.9, 6.2 Hz, 1H, C(1′)H), 6.19 (dd, *J* = 1.6, 0.6 Hz, 1H, C(4a)H), 5.63 (dt, *J* = 1.6, 1.0 Hz, 1H, C(4b)H), 4.47 (dqd, *J* = 8.7, 4.3, 2.1 Hz, 1H, C(1)H), 2.69 (ddd, *J* = 13.9, 4.3, 1.1 Hz, 1H, C(2a)H), 2.59−2.47 (m, 2H, OH and C(2b)H) 1.49 (s, 9H, C(7)H_3 × 3); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 167.2 C(5), 138.5 C(3), 136.9 C(3′), 131.8 C(2′), 130.2 C(1′), 128.6 C(5′), 127.7 C(6′), 127.5 C(4), 126.6 C(4′), 81.4 C(6), 71.9 C(1), 40.7 C(2), 28.2 C(7); IR (neat) 3420 (m), 3024 (m), 2977 (s), 2930 (m), 2871 (w), 1706 (s), 1629 (m), 1494 (m), 1476 (m), 1449 (m), 1392 (m), 1368 (s), 1337 (m), 1314 (s), 1255 (m), 1215 (m), 1148 (s), 1098 (m), 1070 (w), 1032 (m), 965 (s), 876 (w), 850 (m), 817 (w), 749 (s), 693 (s); MS (ESI) 297.2 (MNa$^+$, 100), 242.2 (14), 201.0 (20); TLC R_f 0.25 (EtOAc/hexane, 1:4) [UV, $KMnO_4$]. Anal. Calcd for $C_{17}H_{22}O_3$ (274.36): C, 74.42; H, 8.08. Found: C, 74.48; H, 8.35.

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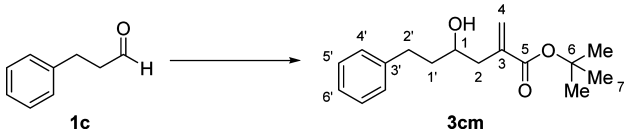
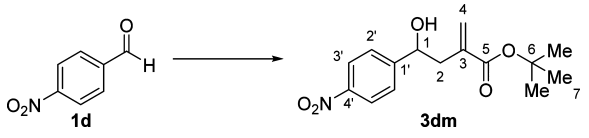
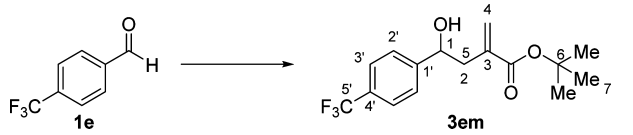


*Preparation of tert-Butyl 4-Hydroxy-2-methylene-6-phenylhexanoate (**3cm**).* Following the general allylation procedure, **1c** (131.7 μL, 1.0 mmol), $Ru_3(CO)_{12}$ (12.8 mg, 0.020 mmol, 0.02 equiv), TBACl (16.9 mg, 0.060 mmol, 0.06 equiv), **2m** (240.3 mg, 1.20 mmol, 1.2 equiv), H_2O (27 μL, 1.5 mmol, 1.5 equiv), Et_3N (14 μL, 0.1 mmol, 0.1 equiv), and dioxane (2.5 mL) were combined under 40 psi of CO at 75 °C for 24 h. Workup and purification by silica gel column chromatography (radial silica gel chromatography 2 mm, EtOAc/hexane (1:9) then 25 g SiO_2, 2 × 14 cm column, Et_2O/CH_2Cl_2 (3% Et_2O)) provided **3cm** (216 mg, 78%) as a colorless oil. Data for **3cm**: bp 125 °C (ABT, 10^{-5} mm Hg); ^1H NMR (500 MHz, $CDCl_3$) δ 7.31−7.25 (m, 2H, C(5′)H), 7.24−7.20 (m, 2H, C(4′)H), 7.20−7.15 (m, 1H, C(6′)H) 6.15 (d, *J* = 1.7 Hz, 1H, C(4a)H), 5.57 (d, *J* = 1.7 Hz, 1H, C(4b)H), 3.76 (dddd, *J* = 8.3, 6.0, 4.1, 2.4 Hz, 1H, C(2)H), 2.83 (dt, *J* = 13.8, 7.7 Hz, 1H, C(2′a)H), 2.70 (dt, *J* = 13.8, 8.2 Hz, 1H, C(2′b)H), 2.57 (ddd, *J* = 13.9, 3.5, 1.1 Hz, 1H, C(2a)H), 2.49 (d, *J* = 4.1 Hz, 1H, OH), 2.36 (ddd, *J* = 13.9, 8.3, 0.9 Hz, 1H, C(2b)H), 1.78 (td, *J* = 8.2, 6.0 Hz, 2H, C(1′)H_2), 1.48 (s, 9H, C(7)H_3 × 3); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 167.2 C(5), 142.3 C(3′), 139.1 C(3), 128.6 C(4′), 128.5 C(5′), 127.0 C(4), 125.9 C(6′), 81.3 C(6), 70.2 C(1), 40.7 C(2), 39.1 C(1′), 32.2 C(2′), 28.1 C(7); IR (neat) 3426 (m), 3085 (w), 3062 (w), 3026 (w), 2977 (m), 2930 (m), 2863 (w), 1709 (s), 1630 (m), 1603 (w), 1495 (w), 1478 (w), 1541 (m), 1392 (m), 1368 (s), 1336 (m), 1313 (m), 1254 (m), 1217 (m), 1151 (s), 1078 (w), 1052 (w), 1031 (w), 946 (w), 849 (w), 819 (w), 747 (w), 700 (m); MS (CI^+, 70 eV) 277.2 (MH^+, 6), 221.1 (63), 203.1 (100), 185.1 (48), 157.1 (84), 125.1 (12), 117.1 (28), 91.1 (34); TLC R_f 0.33 (EtOAc/hexane, 1:4) [UV, $KMnO_4$]. Anal. Calcd for $C_{17}H_{24}O_3$ (264.38): C, 73.88; H, 8.75. Found: C, 73.60; H, 8.84.



*Preparation of tert-Butyl 4-Hydroxy-2-methylene-4-(4-nitrophenyl)butanoate (**3dm**).* Following the general allylation procedure, **1d** (151.1 mg, 1.0 mmol), $Ru_3(CO)_{12}$ (12.8 mg, 0.020 mmol, 0.02 equiv), TBACl (16.9 mg, 0.060 mmol, 0.06 equiv), **2m** (240.3 mg, 1.20 mmol, 1.2 equiv), H_2O (27 μL, 1.5 mmol, 1.5 equiv), Et_3N (14 μL, 0.1 mmol, 0.1 equiv), and dioxane (2.5 mL) were combined under 40 psi of CO at 75 °C for 24 h. Workup and purification by silica gel column chromatography (62 g, 3.5 × 17 cm column, EtOAc/hexane (1:9 → 1:7 → 1:4) then Et_2O/CH_2Cl_2 (3% Et_2O)) and then further purification via Kugelrohr distillation afforded **3dm** (190 mg, 65%) as a clear, yellow viscous oil. Data for **3dm**: bp 200 °C (ABT, 10^{-5} mm Hg); ^1H NMR (500 MHz, $CDCl_3$) δ 8.20 (dd, *J* = 8.7, 1.8 Hz, 2H, C(3′)H), 7.54 (dd, *J* = 8.7, 1.8 Hz, 1H, C(2′)H), 6.15 (t, *J* = 1.5 Hz, 1H, C(4a)H), 5.51 (t, *J* = 1.2 Hz, 1H, C(4b)H), 5.00 (dt, *J* = 7.6, 3.6 Hz, 1H, C(1)H), 3.50 (d, *J* = 3.5 Hz, 1H, OH), 2.80 (ddt, *J* = 14.1, 3.6, 1.0 Hz, 1H, C(2a)H), 2.58 (m, 1H, C(2b)H), 1.52 (d, *J* = 1.5 Hz, 9H, C(7)H_3 × 3); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 167.5 C(5), 151.5 C(1′), 147.3 C(4′), 137.9 C(3), 128.5 C(4), 126.6 C(2′), 123.7 C(3′), 82.1 C(6), 72.7 C(1), 42.9 C(2), 28.2 C(7); IR (neat) 3444 (m), 3078 (w), 2979 (s), 2932 (m), 2870 (w), 2451 (w), 1929 (w), 1807 (w), 1705 (s), 1630 (m), 1602 (s), 1522 (s), 1492 (m), 1478 (m), 1457 (m), 1431 (m), 1393 (s), 1368 (s), 1345 (s), 1314 (s), 1255 (s), 1217 (s), 1148 (s), 1109 (m), 1063 (s), 1013 (m), 954 (m), 880 (m), 853 (s), 820 (m), 751 (m), 737 (m), 701 (m), 659 (w), 616 (w); MS (EI^+, 70 eV) 294.1 (MH^+, 31), 238.1 (76), 220.0 (100), 152.0 (24), 142.1 (42), 135.0 (25), 106.0 (11), 105.0 (11), 86.1 (36); TLC R_f 0.15 (EtOAc/hexane, 1:4) [UV, $KMnO_4$]. Anal. Calcd for $C_{15}H_{19}NO_5$ (293.32): C, 61.42; H, 6.53; N, 4.78. Found: C, 61.64; H, 6.51; N, 4.81.



*Preparation of tert-Butyl 4-Hydroxy-2-methylene-4-(4-(trifluoromethyl)phenyl)butanoate (**3em**).* Following the general allylation procedure, **1e** (136.6 μL, 1.0 mmol), $Ru_3(CO)_{12}$ (12.8 mg, 0.020 mmol, 0.02 equiv), TBACl (16.9 mg, 0.060 mmol, 0.06 equiv), **2m** (240.3 mg, 1.20 mmol, 1.2 equiv), H_2O (27 μL, 1.5 mmol, 1.5 equiv), Et_3N (14 μL, 0.1 mmol, 0.1 equiv), and dioxane (2.5 mL) were combined under 40 psi of CO at 75 °C for 24 h. Workup and purification by silica gel column chromatography (radial silica gel chromatography 2 mm, EtOAc/hexane (1:4) then 16 g SiO_2, 2.5 × 8.5 cm column, Et_2O/hexane (1:7)) and then further purification via Kugelrohr distillation afforded **3em** (296 mg, 94%) as a white solid. Data for **3em**: bp 125 (ABT, 10^{-5} mm Hg); mp 51−52 °C; ^1H NMR (500 MHz, $CDCl_3$) δ 7.60 (d, *J* = 8.2 Hz, 2H, C(3′)H), 7.48 (d, *J* = 8.2 Hz, 2H, C(2′)), 6.16 (d, *J* = 1.5 Hz, 1H, C(4a)H), 5.53 (d, *J* = 1.5 Hz, 1H, C(4b)H), 4.94 (dt, *J* = 7.8, 3.5 Hz, 1H, C(1)H), 3.22 (d, *J* = 3.5 Hz, 1H, OH), 2.83−2.72 (m, 1H, C(2a)H), 2.65−2.53 (m, 1H, C(2b)H), 1.51 (s, 9H, C(7)H_3 × 3; $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 167.3 C(5), 148.2 C(1′), 138.2 C(3), 129.59 (q, *J* = 32.3 Hz, C(4′)), 128.11 C(4), 126.13 C(2′), 125.34 (q, *J* = 3.9 Hz, C(3′)), 124.4 (q, *J* = 271.9 Hz, C(5′)), 81.72 C(6), 72.9 C(1), 42.8 C(2), 28.1 C(7).; ^{19}F NMR (376 MHz, $CDCl_3$) δ −62.9 (versus external BF_3·OEt_2 standard); IR (neat) 3417 (w), 3006 (w), 2984 (w), 2931 (w), 1703 (s), 1633 (w), 1619 (w), 1422 (w), 1417 (w), 1408 (w), 1391 (w), 1370 (m), 1330 (s), 1257 (w), 1226 (w), 1162 (s), 1149 (s), 1126 (s), 1106 (m), 1068 (m), 1052 (w), 1015 (w), 955 (w), 948 (w), 875 (w), 849 (w), 835 (m), 819 (w), 756 (w), 689 (w), 654 (w), 605 (w); MS (EI^+, 70 eV) 317.0 (MH^+,4), 260.9 (32), 242.9 (100), 240.9 (42), 231.0 (15), 222.9 (16), 196.9 (19), 177.0 (15), 174.9 (96), 173.0 (24), 145.0 (20), 142.0 (52), 128.0 (20), 127.0 (75), 86.0 (48), 68.0 (18); TLC R_f 0.26 (EtOAc/hexane, 1:4) [UV, $KMnO_4$]. Anal. Calcd for $C_{16}H_{19}F_3O_3$ (316.32): C, 60.75; H, 6.05. Found: C, 60.44; H, 6.01.

*Preparation of tert-Butyl 4-Hydroxy-4-(4-methoxyphenyl)-2-methylenebutanoate (**3fm**).* Following the general allylation procedure, **1f** (121.7 μL 1.0 mmol), $Ru_3(CO)_{12}$ (12.8 mg, 0.020 mmol, 0.02 equiv), TBACl (16.9 mg, 0.060 mmol, 0.06 equiv), **2m** (240.3 mg, 1.20 mmol, 1.2 equiv), H_2O (27 μL, 1.5 mmol, 1.5 equiv), Et_3N (14 μL, 0.1 mmol, 0.1 equiv), and dioxane (2.5 mL) were combined under 40 psi of CO at 75 °C for 24 h. Workup and purification by silica gel column chromatography (radial silica gel chromatography 2 mm, Et_2O/CH_2Cl_2 (3% Et_2O) then radial silica gel chromatography 2 mm, Et_2O/CH_2Cl_2 (3% Et_2O) then 7.2 g SiO_2, 1 × 15.5 cm column, CH_2Cl_2 (100%) → Et_2O/CH_2Cl_2 (3% Et_2O)) and then further purification via Kugelrohr distillation afforded **3fm** (232 mg, 83%) as a clear, colorless oil. Data for **3fm**: bp 175 °C (ABT, 10^{-5} mm Hg); ^1H NMR (500 MHz, $CDCl_3$) δ 7.29 (d, *J* = 8.7 Hz, 2H, C(2′)H), 6.88 (d, *J* = 8.7 Hz, 2H, C(3′)H), 6.14 (d, *J* = 1.7 Hz, 1H, C(4a)H), 5.52 (d, *J* = 1.7 Hz, 1H, C(4b)H), 4.82 (dd, *J* = 8.4, 3.4 Hz, 1H, C(1)H), 3.80 (s, 3H, C(5′)H_3), 2.75−2.69 (m, 2H, OH and C(2a)H), 2.62 (ddd, *J* = 13.9, 8.5, 0.9 Hz, 1H, C(2b)H), 1.51 (s, 9H, C(7)H_3 × 3); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 167.2 C(5), 159.1 C(4′), 138.9 C(3), 136.4 C(1′), 127.4 C(4), 127.1 C(2′), 113.9 C(3′), 81.3 C(6), 73.09 C(1), 55.4 C(5′), 42.8 C(2), 28.2 C(7); IR (neat) 3443 (m), 2996 (m), 2977 (s), 2931 (m), 2832 (m), 1710 (s), 1629 (m), 1613 (s), 1586 (m), 1513 (s), 1456 (m), 1439 (m), 1393 (m), 1368 (s), 1335 (m), 1303 (s), 1247 (s), 1214 (m), 1146 (s), 1109 (m), 1036 (s), 952 (w), 879 (w), 847 (m), 832 (m), 817 (m), 775 (w), 758 (w); MS (ESI) 301.2 (MNa^+, 100), 242.2 (40), 205.0 (35), 102.1 (23); TLC R_f 0.18 (EtOAc/hexane, 1:4) [UV, $KMnO_4$]. Anal. Calcd for $C_{16}H_{22}O_4$ (278.35): C, 69.04; H, 7.97. Found: C, 68.75; H, 8.13.

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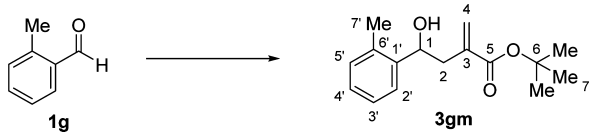
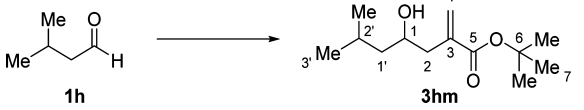


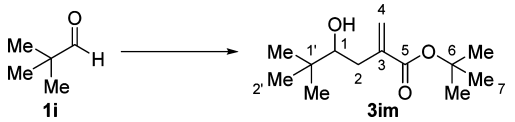
1g 3gm

*Preparation of tert-Butyl 4-Hydroxy-2-methylene-4-(2-tolyl)-butanoate (**3gm**).* Following the general allylation procedure, **1g** (115.6 μL, 1.0 mmol), $Ru_3(CO)_{12}$ (12.79 mg, 0.02 mmol, 0.02 equiv), TBACl (16.7 mg, 0.06 mmol, 0.06 equiv), **2m** (280.3 mg, 1.4 mmol, 1.4 equiv), H_2O (27 μL, 1.5 mmol, 1.5 equiv), Et_3N (14 μL, 0.1 mmol, 0.1 equiv), and dioxane (2.5 mL) were combined under 40 psi of CO at 75 °C for 24 h. Workup and purification by silica gel column chromatography (radial silica gel chromatography 2 mm, EtOAc/hexane (1:7) then radial silica gel chromatography 2 mm, Et_2O/CH_2Cl_2 (5% Et_2O) then 7.2 SiO_2, 1 × 19.5 cm column, Et_2O/CH_2Cl_2 (3% Et_2O)) and then further purification via Kugelrohr distillation provided **3gm** (192 mg, 73%) as a clear, colorless oil. Data for **3gm**: bp 125 °C (ABT, 10^{-5} mm Hg); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.51 (dd, *J* = 7.5, 1.4 Hz, 1H), 7.23 (td, *J* = 7.5, 1.6 Hz, 1H, C(3′)H), 7.16 (td, *J* = 7.5, 1.4 Hz, 1H, C(4′)H), 7.12 (dd, *J* = 7.5, 1.6 Hz, 1H, C(5′)H), 6.16 (d, *J* = 1.6 Hz, 1H, C(4a)H), 5.56 (d, *J* = 1.6 Hz, 1H, C(4b)H), 5.15−5.01 (m, 1H, C(1)H), 2.88 (s, 1H, OH), 2.72 (ddd, *J* = 14.0, 3.5, 1.1 Hz, 1H, C(2a)H), 2.57 (ddd, *J* = 14.0, 8.8, 0.9 Hz, 1H, C(2b)H), 2.36 (s, 3H, C(7′)H_3), 1.51 (s, 9H, C(7)H_3 × 3); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 167.3 C(5), 142.4 C(6′), 139.0 C(3), 134.4 C(1′), 130.4 C(5′), 127.5 C(4), 127.3 C(4′), 126.3 C(3′), 125.3 C(2′), 81.4 C(6), 69.9 C(1), 41.6 C(2), 28.2 C(7), 19.2 C(7′); IR (neat) 3441 (m), 3052 (w), 2977 (s), 2931 (m), 1914 (w), 1712 (s), 1630 (m), 1605 (w), 1479 (m), 1461 (m), 1393 (s), 1368 (s), 1337 (s), 1316 (s), 1281 (m), 1255 (s), 1215 (s), 1146 (s), 1111 (m), 1045 (s), 1011 (m), 946 (m), 879 (w), 850 (m), 818 (w), 754 (m), 726 (m), 676 (w), 632 (w), 607 (w); MS (EI$^+$, 70 eV) 262.1 (M^+, 1), 206.1 (11), 189.1 (11), 212.0 (12), 121.1 (100), 93.1 (24), 91.0 (17), 77.1 (13); TLC R_f 0.31 (EtOAc/hexane, 1:4) [UV, $KMnO_4$]. Anal. Calcd for $C_{16}H_{22}O_3$ (262.34): C, 73.25; H, 8.45. Found: C, 73.19; H, 8.26.



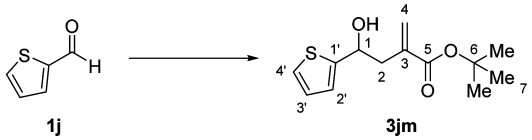
1h 3hm

*Preparation of tert-Butyl 4-Hydroxy-6-methyl-2-methylenehep-tanoate (**3hm**).* Following the general allylation procedure, **1h** (107.3 μL, 1.0 mmol), $Ru_3(CO)_{12}$ (12.79 mg, 0.02 mmol, 0.02 equiv), TBACl (16.7 mg, 0.06 mmol, 0.06 equiv), **2h** (280.3 mg, 1.4 mmol, 1.4 equiv), H_2O (27 μL, 1.5 mmol, 1.5 equiv), Et_3N (14 μL, 0.1 mmol, 0.1 equiv), and dioxane (2.5 mL) were combined under 40 psi of CO at 75 °C for 24 h. Workup and purification by silica gel column chromatography (48 g SiO_2 3.5 × 13.5 cm column, hexane (100%) → Et_2O/hexane (1:7) then 20 g SiO_2 2.5 × 11 cm column, CH_2Cl_2 (100%) → Et_2O/CH_2Cl_2 (3% Et_2O)) provided **3hm** (192 mg, 84%) as a clear, colorless oil. Data for **3hm**: bp 75 °C (ABT, 0.18 mmHg); ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.15 (d, *J* = 1.7 Hz, 1H, C(4a)H), 5.57 (d, *J* = 0.9 Hz, 1H, C(4b)H), 3.80 (tt, *J* = 8.3, 3.9 Hz, 1H, C(1)H), 2.53 (ddd, *J* = 13.9, 3.4, 1.1 Hz, 1H, C(2a)H), 2.27 (ddd, *J* = 13.9, 8.4, 0.9 Hz, 1H, C(2b)H), 2.15 (s, 1H, OH), 1.80 (dddd, *J* = 13.2, 12.2, 8.7, 6.6 Hz, 1H, C(2′)H), 1.50 (s, 9H, C(7)H_3 × 3), 1.42 (ddd, *J* = 14.1, 8.7, 5.6 Hz, 1H, C(1′a)H), 1.23 (ddd, *J* = 13.4, 8.7, 4.4 Hz, 1H, C(1′b)H), 0.92 (dd, *J* = 8.9, 6.6 Hz, 6H, C(3′)H_3 × 2); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 167.2 C(5), 139.3 C(3), 126.8 C(4), 81.2 C(6), 68.8 C(1), 46.6 C(1′), 41.1 C(2), 28.2 C(7), 24.7 C(2′), 23.5 C(3′a), 22.2 C(3′b); IR (neat) 3443 (m), 2955 (s), 2930 (s), 2870 (m), 1886 (w), 1711 (s), 1631 (m), 1469 (m), 1455 (m), 1392 (m), 1368 (s), 1338 (s), 1314 (s), 1255 (m), 1214 (s), 1150 (s), 1070 (m), 1031 (m), 988 (w), 944 (m), 876 (w), 851 (m), 818 (w), 759 (w), 738 (w), 692 (w), 621 (w); MS (CI$^+$, 70 eV) 229.2 (MH^+, 36), 174.1 (13), 173.1 (97), 155.1 (92), 153.1 (10), 137.1 (39), 115.0 (19), 109.1 (100), 69.1 (10), 57.0 (82); TLC R_f 0.28 (EtOAc/hexane, 1:4) [UV, $KMnO_4$]. Anal. Calcd for $C_{13}H_{24}O_3$ (228.33): C, 68.38; H, 10.59. Found: C, 68.56; H, 10.54.



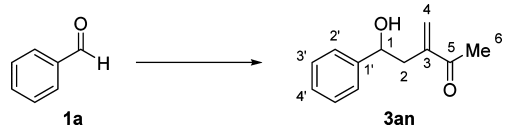
1i 3im

*Preparation of tert-Butyl 4-Hydroxy-5,5-dimethyl-2-methylene-hexanoate (**3im**).* Following the general allylation procedure, **1i** (108.6 μL, 1.0 mmol), $Ru_3(CO)_{12}$ (12.79 mg, 0.02 mmol, 0.02 equiv), TBACl (16.7 mg, 0.06 mmol, 0.06 equiv), **2m** (280.3 mg, 1.4 mmol, 1.4 equiv), H_2O (27 μL, 1.5 mmol, 1.5 equiv), Et_3N (14 μL, 0.1 mmol, 0.1 equiv), and dioxane (2.5 mL) were combined under 40 psi of CO at 75 °C for 24 h. Workup and purification by silica gel column chromatography (31 g SiO_2 3.5 × 8.5 cm column, Et_2O/hexane (1:7) then 24.5 g SiO_2 2.5 × 14 cm column, CH_2Cl_2 (100%) → Et_2O/CH_2Cl_2 (3% Et_2O)) provided **3im** (140 mg, 61%) as a clear, colorless oil. Data for **3im**: bp 75 °C (ABT, 10^{-5} mm Hg); ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.15 (d, *J* = 1.7 Hz, 1H, C(4a)H), 5.58 (dt, *J* = 1.7, 1.0 Hz, 1H, C(4b)H), 3.30 (ddd, *J* = 10.4, 4.3, 2.0 Hz, 1H, C(1)H), 2.59 (ddd, *J* = 13.8, 2.0, 1.2 Hz, 1H, C(2a)H), 2.26 (d, *J* = 4.3 Hz, 1H, OH), 2.16 (ddd, *J* = 13.8, 10.4, 0.8 Hz, 1H, C(2b)H), 1.50 (s, 9H, C(7)H_3 × 3), 0.94 (s, 9H, C(2′)H_3 × 3); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 167.4 C(5), 140.4 C(3), 126.6 C(4), 81.3 C(6), 78.9 C(1), 35.2 C(2), 35.1 C(1′), 28.2 C(7), 25.8 C(2′); IR (neat) 3475 (m), 3004 (m), 2961 (s), 2907 (m), 2870 (m), 1709 (s), 1631 (m), 1479 (m), 1460 (m), 1432 (w), 1393 (m), 1367 (s), 1337 (m), 1318 (m), 1288 (m), 1250 (m), 1223 (m), 1148 (s), 1068 (m), 1043 (w), 1009 (m), 944 (m), 910 (w), 864 (w), 850 (m), 818 (w), 756 (w), 675 (w), 628 (w); MS (CI$^+$, 70 eV) 229.2 (MH^+, 5), 156.0 (12), 155.1 (100), 137.1 (84), 109.1 (52), 101.1 (24), 89.1 (16), 87.0 (15); TLC R_f 0.37 (EtOAc/hexane, 1:4) [UV, $KMnO_4$]. Anal. Calcd for $C_{13}H_{24}O_3$ (228.33): C, 68.38; H, 10.59. Found: C, 68.03; H, 10.74.



1j 3jm

*Preparation of tert-Butyl 4-Hydroxy-4-(4-methoxyphenyl)-2-methylenebutanoate (**3jm**).* Following the general allylation procedure, **1j** (93.5 mg, 1.0 mmol), $Ru_3(CO)_{12}$ (12.8 mg, 0.020 mmol, 0.02 equiv), TBACl (16.9 mg, 0.060 mmol, 0.06 equiv), **2m** (240.3 mg, 1.20 mmol, 1.2 equiv), H_2O (27 μL, 1.5 mmol, 1.5 equiv), Et_3N (14 μL, 0.1 mmol, 0.1 equiv), and dioxane (2.5 mL) were combined under 40 psi of CO at 75 °C for 24 h. Workup and purification by silica gel column chromatography (57 g SiO_2, 3.5 × 15 cm column, hexane (100%) → TBME/hexane (1:9 → 1:7) then 27 g SiO_2, 2 × 27 cm column, CH_2Cl_2 (100%) → Et_2O/CH_2Cl_2 (3% Et_2O)) and then further purification via Kugelrohr distillation afforded **3jm** (215 mg, 85%) as a clear, colorless oil. Data for **3jm**: bp 150 °C (ABT, 10^{-5} mm Hg); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.24−7.21 (m, 1H, C(4′)H), 7.01−6.90 (m, 2H, C(3′)H and C(2′)H), 6.17 (t, *J* = 1.2 Hz, 1H, C(4a)H), 5.59 (t, *J* = 1.3 Hz, 1H, C(4b)H), 5.19−5.05 (m, 1H, C(1)H), 3.01 (dd, *J* = 4.0, 0.9 Hz, 1H, OH), 2.86 (ddd, *J* = 14.0, 4.2, 1.0 Hz, 1H, C(2a)H), 2.75 (ddd, *J* = 14.0, 8.5, 0.9 Hz, 1H, C(2b)H), 1.51 (d, *J* = 0.8 Hz, 9H, C(7)H_3 × 3); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 167.1 C(5), 148.3 C(1′), 138.2 C(3), 127.9 C(4), 126.7 C(3′), 124.4 C(4′), 123.5 C(2′), 81.5 C(6), 69.7 C(1), 42.9 C(2), 28.2 C(7); IR (neat) 3431 (m), 2977 (m), 2926 (m), 1704 (s), 1632 (m), 1393 (m), 1368 (s), 1340 (m), 1316 (m), 1255 (m), 1222 (m), 1152 9s), 1037 (m), 951 (m), 876 (w), 850 (m), 818 (m), 751 (w), 698 (m); MS (ESI) 277.1 (MNa^+, 100), 242.3 (33), 181.0 (10); TLC R_f 0.31 (EtOAc/hexane, 1:4) [UV, $KMnO_4$]. Anal. Calcd for $C_{13}H_{18}O_3S$ (254.34): C, 61.39; H, 7.13. Found: C, 61.33; H, 7.07.



1a 3an

*Preparation of 5-Hydroxy-3-methylene-5-phenylpentan-2-one (**3an**).* Following the general allylation procedure, **1a** (102 μL, 1.0 mmol), $Ru_3(CO)_{12}$ (12.8 mg, 0.02 mmol, 0.02 equiv), TBACl (16.7

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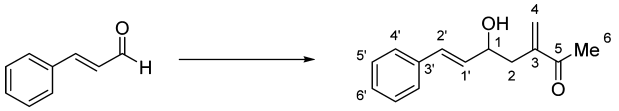
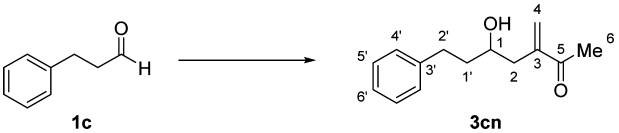
mg, 0.06 mmol, 0.06 equiv), **2n** (284.1 mg, 2.0 mmol, 2.0 equiv), H_2O (63 μL, 3.5 mmol, 3.5 equiv), Et_3N (14 μL, 0.1 mmol, 0.1 equiv), and dioxane (2.5 mL) were combined under 40 psi of CO at 75 °C for 24 h. Workup and purification by silica gel column chromatography (50 g SiO_2, 2.5 × 27 cm column, EtOAc/hexane (1:9 w/1% Et_3N → 1:5 → 1:4) then radial silica gel chromatography 2 mm Et_2O/CH_2Cl_2 (15% Et_2O)) provided **3an** (141 mg, 74%) as a colorless oil. Data for **3an**: ^1H NMR (500 MHz, $CDCl_3$) δ 7.39−7.32 (m, 4H, C(3′H and C(2′)H), 7.30−7.24 (m, 1H, C(4′)H), 6.10 (s, 1H, C(4a)H), 5.82 (d, *J* = 1.0 Hz, 1H, C(4b)H), 4.83 (dt, *J* = 8.1, 3.7 Hz, 1H, C(1)H), 2.90 (d, *J* = 3.7 Hz, 1H, OH), 2.77 (ddd, *J* = 13.9, 4.0, 1.0 Hz, 1H, C(2a)H), 2.65 (ddd, *J* = 13.9, 8.4, 0.9 Hz, 1H, C(2b)H), 2.38 (s, 3H, $C(6)H_3$); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 201.3 C(5), 145.7 C(3), 144.3 C(1′), 128.8 C(4), 128.4 C(2′), 127.5 C(4′), 125.8 C(3′), 73.4 C(1), 41.6 C(2), 25.9 C(6); IR (neat) 3411 (w), 3088 (w), 3063 (w), 3030 (w0, 2925 (w), 1671 (m), 1628 (w), 1494 (w), 1453 (w), 1426 (w), 1365 (w), 1325 (w), 1186 (w), 1126 (w), 1081 (w), 1052 (w), 1027 (w), 1016 (w), 947 (w), 876 (w), 760 (w), 699 (m), 652 (w), 609 (w); MS (EI^+, 70 eV) 190.1 (M^+, 25), 173.1 (38), 172.1 (18), 129.1 (21), 128.1 (15), 108.1 (18), 107.1 (100), 105.0 (44), 85.1 (34), 84.1 (34), 79.1 (98), 78.1 (16), 77.1 (78), 69.0 (67), 50.7 (25); HRMS (CI^+, TOF) calcd for $C_{12}H_{14}O_2$ 190.0994, found 190.0995; TLC R_f 0.09 (EtOAc/hexane, 1:4) [UV, PA].



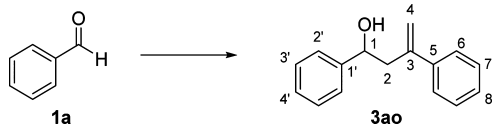
1b **3bn**

*Preparation of (E)-5-Hydroxy-3-methylene-7-phenylhept-6-en-2-one (**3bn**).* Following the general allylation procedure, **1b** (126 μL, 1.0 mmol), $Ru_3(CO)_{12}$ (12.8 mg, 0.02 mmol, 0.02 equiv), TBACl (16.7 mg, 0.06 mmol, 0.06 equiv), **2n** (340.9 mg, 2.4 mmol, 2.4 equiv), H_2O (63 μL, 3.5 mmol, 3.5 equiv), Et_3N (14 μL, 0.1 mmol, 0.1 equiv), and dioxane (2.5 mL) were combined under 40 psi of CO at 75 °C for 48 h. Workup and purification by silica gel column chromatography (55 g SiO_2, 2.5 × 31 cm column, EtOAc/hexane (1:9 w/1% Et_3N → 1:9 → 1:3 → 1:2) then radial silica gel chromatography 2 mm Et_2O/CH_2Cl_2 (5% → 7% Et_2O)) provided **3bn** (158 mg, 73%) as a colorless oil. Data for **3bn**: ^1H NMR (500 MHz, $CDCl_3$) δ 7.37 (dd, *J* = 8.2, 1.3 Hz, 2H, C(4′)H), 7.31 (dd, *J* = 8.2, 6.8 Hz, 2H, C(5′)H), 7.23 (tt, *J* = 6.8, 1.3 Hz, 1H, C(6′)H), 6.59 (d, *J* = 15.0 Hz, 1H C(2′)H), 6.20 (dd, *J* = 15.0, 6.2 Hz, 1H, C(1′)H), 6.15 (s, 1H, C(4a)H), 5.95 (s, 1H, C(4b)H), 4.41 (tt, *J* = 6.2, 3.1 Hz, 1H, C(1)H), 2.69 (ddd, *J* = 13.8, 4.4, 0.9 Hz, 1H, C(2a)H), 2.59−2.48 (m, 2H, OH and C(2b)H), 2.37 (s, 3H, $C(6)H_3$); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 201.2 C(5), 145.5 C(3), 136.8 C(3′), 131.8 C(1′), 130.2 C(2′), 128.9 C(4), 128.7 C(5′), 127.7 C(6′), 126.6 (4′), 71.8 C(1), 39.5 C(2), 26.0 C(6); IR (neat) 3410 (w), 3026 (w), 1671 (w), 1628 (w), 1600 (w), 1494 (w), 1449 (w), 1428 (w), 1395 (w), 1366 (w), 1326 (w), 1182 (w), 1130 (w), 1098 (w), 1071 (w), 1024 (w), 967 (m), 944 (w), 873 (w), 750 (m), 693 (m); MS (EI^+, 70 eV) 216.1 (M^+, 18), 198.1 (11), 155.1 (11), 134.1 (10), 133.1 (100), 132.1 (11), 131.0 (42), 115.1 (40), 105.1 (20), 104.1 (11), 103.1 (17), 91.1 (28), 85.1 (13), 79.1 (10), 77.1 (24), 69.0 (11), 54.9 (2), 50.7 (11); TLC R_f 0.07 (EtOAc/hexane, 1:4) [UV, PA]. Anal. Calcd for $C_{14}H_{16}O_2$ (216.28): C, 77.75; H, 7.46. Found: C, 77.79; H, 7.33.



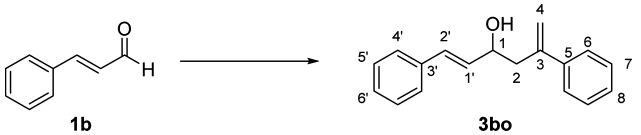
1c **3cn**

*Preparation of 5-Hydroxy-3-methylene-7-phenylheptan-2-one (**3cn**).* Following the general allylation procedure, **1c** (132 μL, 1.0 mmol), $Ru_3(CO)_{12}$ (12.8 mg, 0.02 mmol, 0.02 equiv), TBACl (16.7 mg, 0.06 mmol, 0.06 equiv), **2n** (284.1 mg, 2.0 mmol, 2.0 equiv), H_2O (63 μL, 3.5 mmol, 3.5 equiv), Et_3N (14 μL, 0.1 mmol, 0.1 equiv), and dioxane (2.5 mL) were combined under 40 psi of CO at 75 °C for 24 h. Workup and purification by silica gel column chromatography (49 g SiO_2, 2.5 × 28 cm column, EtOAc/hexane (1:9 w/1% Et_3N → 1:5 → 1:3) then radial silica gel chromatography 2 mm Et_2O/CH_2Cl_2 (7% Et_2O)) provided **3cn** (152 mg, 70%) as a colorless oil. Data for **3cn**: ^1H NMR (500 MHz, $CDCl_3$) δ 7.28 (t, *J* = 7.6 Hz, 2H, C(5′)H), 7.24−7.15 (m, 3H, C(6′)H and C(4′)H), 6.13 (s, 1H, C(4a)H), 5.91 (s, 1H, C(4b)H), 3.70 (tq, *J* = 8.1, 4.3 Hz, 1H, C(1)H), 2.82 (ddd, *J* = 13.8, 9.0, 6.7 Hz, 1H, C(2′a)H), 2.68 (ddd, *J* = 13.8, 9.1, 7.1 Hz, 1H,C(2′b)H), 2.57 (ddd, *J* = 13.8, 3.5, 1.0 Hz, 1H, C(2a)H), 2.42−2.31 (m, 5H, OH, C(2b)H, and $C(6)H_3$), 1.76 (ddd, *J* = 10.6, 9.1, 3.5 Hz, 2H, $C(1')H_2$); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 201.3 C(5), 146.2 (3), 142.3 C(3′), 128.6 C(4), 128.5 C(4′), 128.4 C(5′), 125.9 C(6′), 70.5 C(1), 39.5 C(2), 39.3 C(1′), 32.2 C(2′), 25.9 C(6); IR (neat) 3435 (w), 3027 (w), 2926 (w), 2857 (w), 1674 (w), 1627 (w), 1603 (w), 1496 (2), 1454 (w), 1430 (w), 1366 (w), 1324 (w), 1154 (w), 1126 (w), 1076 (w), 1053 (w), 1030 (w), 943 (w), 866 (w), 748 (w), 601 (m), 650 (w), 565 (w); MS (EI^+, 70 eV) 218.1 (M^+, 5), 200.1 (39), 117.1 (35), 109.1 (15), 105.1 (11), 96.1 (17), 95.1 (12), 91.1 (100), 85.1 (20), 84.1 (23), 79.1 (12), 77.1 (14), 69.0 (35), 65.0 (21); HRMS (CI^+, TOF) calcd for $C_{14}H_{18}O_2$, 218.1307; found, 218.1305; TLC R_f 0.08 (EtOAc/hexane, 1:4) [UV, PA].



1a **3ao**

*Preparation of 1,3-Diphenylbut-3-en-1-ol (**3ao**).* Following the general allylation procedure, **1a** (101.9 μL, 1.0 mmol), $Ru_3(CO)_{12}$ (19.2 mg, 0.03 mmol, 0.03 equiv), TBACl (25.0 mg, 0.09 mmol, 0.09 equiv), **2o** (493.3 mg, 2.8 mmol, 2.8 equiv), H_2O (45 μL, 2.5 mmol, 2.5 equiv), Et_3N (14 μL, 0.1 mmol, 0.1 equiv), and dioxane (2.5 mL) were combined under 40 psi of CO at 75 °C for 48 h. Workup and purification by silica gel column chromatography (62 g SiO_2, 3.5 × 18.5 cm column, hexane (100%) then EtOAc/hexane (1:9)) provided **3ao** (166 mg, 74%) as a white solid. The spectroscopic data matched those from literature, and the sample was free of any major impurities.[49] Data for **3ao**: ^1H NMR (500 MHz, $CDCl_3$) δ 7.45−7.38 (m, 2H, C(4′, 8)H), 7.36−7.18 (m, 8H, C(2′, 3′, 6, 7), 5.37 (d, *J* = 1.4 Hz, 1H, C(4a)H), 5.12 (d, *J* = 1.4 Hz, 1H, C(4b)H), 4.68 (ddd, *J* = 9.0, 4.3, 2.3 Hz, 1H, C(1)H), 2.96 (ddd, *J* = 14.3, 4.3, 1.3 Hz, 1H, C(2a)H), 2.81 (ddd, *J* = 14.3, 9.0, 0.9 Hz, 1H, C(2b)H), 2.06 (d, *J* = 2.3 Hz, 1H, OH); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 145.1, 144.0, 140.4, 128.6, 128.5, 127.9, 127.9, 126.4, 125.9, 115.8, 72.2, 46.1; MS (EI^+, 70 eV) 224.1 (M^+, 1), 207.1 (11), 206.1 (67), 205.1 (35), 204.1 (13), 203.1 (16), 202.1 (13), 191.1 (28), 190.1 (10), 165.1 (10), 129.1 (14), 128.1 (25), 119.1 (10), 118.1 (100), 117.1 (27), 115.1 (32), 107.0 (83), 106.0 (14), 105.0 (21), 103.1 (17), 91.1 (41), 79.1 (51), 78.0 (20), 77.0 (58), 51.0 (18); TLC R_f 0.25 (EtOAc/hexane, 1:5) [UV, PA].



1b **3bo**

*Preparation of (E)-1,5-Diphenylhexa-1,5-dien-3-ol (**3bo**).* Following the general allylation procedure, **1b** (126 μL, 1.0 mmol), $Ru_3(CO)_{12}$ (19.2 mg, 0.03 mmol, 0.03 equiv), TBACl (25.0 mg, 0.09 mmol, 0.09 equiv), **2o** (493.3 mg, 2.8 mmol, 2.8 equiv), H_2O (63 μL, 3.5 mmol, 3.5 equiv), Et_3N (14 μL, 0.1 mmol, 0.1 equiv), and dioxane (2.5 mL) were combined under 80 psi of CO at 75 °C for 24 h. Workup and purification by silica gel column chromatography (58 g SiO_2, 3.5 × 17 cm column, Et_2O/hexane (1:9 → 1:5 → 1:3 → 1:2)) provided an inseparable mixture of **3bo**/**3co** in an 88:12 ratio (166 mg, 74%) as a colorless oil. The spectroscopic data for **3bo** matched those from literature when the peaks for **3co** were accounted for.[50] Data for **3bo**: ^1H NMR (500 MHz, $CDCl_3$) δ 7.48−7.40 (m, 2H, C(6′, 8)H), 7.41−7.15 (m, 10H, C(5′, 4′, 6, 7)H), 6.54 (dd, *J* = 15.9, 1.1 Hz, 1H, C(2′)H), 6.22 (ddd, *J* = 15.9, 6.4, 0.7 Hz, 1H, C(1′)H), 5.43 (d, *J* = 1.4 Hz, 1H, C(4a)H), 5.22 (d, *J* = 1.2 Hz, 1H, C(4b)H), 4.36 (dddd, *J* = 8.0, 6.3, 5.0, 1.2 Hz, 1H, C(1)H), 2.91 (ddd, *J* = 14.1, 5.0, 1.1 Hz, 1H, C(2a)H), 2.79 (ddd, *J* = 14.1, 8.0, 0.9 Hz, 1H,

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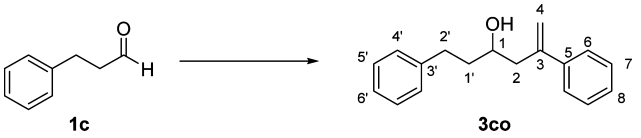
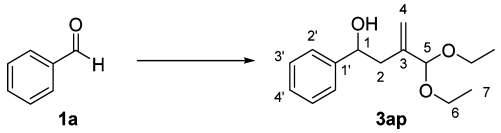
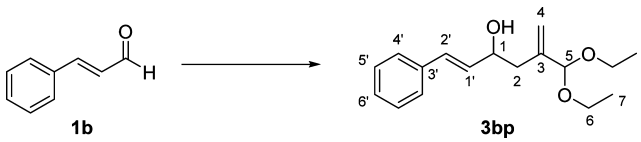
C(2b)H), 1.87 (s, 1H, br OH); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 144.6, 140.3, 136.6, 131.4, 130.1, 128.4, 128.4, 127.6, 127.5, 126.3, 126.2, 115.7, 70.5, 43.8; MS (EI$^+$, 70 eV) 250.1 (M$^+$, 4), 233.1 (15), 232.1 (83), 231.1 (12), 217.1 (15), 216.1 (11), 215.1 (19), 202.1 (12), 154.1 (12), 153.1 (12), 143.1 (12), 141.1 (35), 133.1 (74), 129.1 (11), 128.1 (25), 119.1 (11), 118.1 (55), 117.1 (31), 116.1 (11), 115.1 (49), 105.1 (10), 103.1 (21), 92.1 (14), 91.1 (100), 78.0 (15), 77.0 (24); TLC R_f 0.21 (EtOAc/hexane, 1:5) [UV, PA].



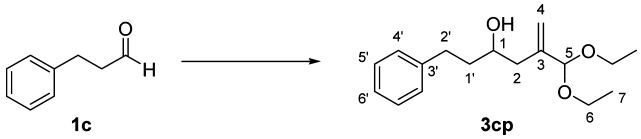
*Preparation of 1,5-Diphenylhex-5-en-3-ol (**3co**).* Following the general allylation procedure, **1c** (131.7 μL, 1.0 mmol), Ru3(CO)12 (19.2 mg, 0.03 mmol, 0.03 equiv), TBACl (25.0 mg, 0.09 mmol, 0.09 equiv), **2o** (422.8 mg, 2.4 mmol, 2.4 equiv), H_2O (27 μL, 1.5 mmol, 1.5 equiv), Et_3N (14 μL, 0.1 mmol, 0.1 equiv), and dioxane (2.5 mL) were combined under 40 psi of CO at 75 °C for 24 h. Workup and purification by silica gel column chromatography (64 g SiO_2, 3.5 × 19 cm column, hexane (100%) then Et_2O/hexane (1:9 → 1:4)) provided **3co** (198 mg, 78%) as a clear, colorless oil. The spectroscopic data matched those from literature and was free of any major impurities.[51] Data for **3co**: ^1H NMR (500 MHz, $CDCl_3$) δ 7.39 (dt, J = 8.2, 1.2 Hz, 2H, C(aryl)H), 7.33 (dd, J = 8.4, 6.4 Hz, 2H, C(aryl)H), 7.31−7.24 (m, 3H, C(aryl)H), 7.20−7.15 (m, 3H, C(aryl)H), 5.42 (t, J = 1.1 Hz, 1H, C(4a)H), 5.17 (t, J = 1.1 Hz, 1H, C(4b)H), 3.71 (m, 1H, C(1)H), 2.85−2.76 (m, 2H, C(2′a, 2a)H), 2.66 (ddd, J = 14.1, 9.3, 6.9 Hz, 1H, C(2′b)H), 2.58 (dd, J = 14.1, 8.1 Hz, 1H, C(2b)H), 1.82 (dtd, J = 9.3, 6.7, 5.9, 2.7 Hz, 2H, C(1′)H_2), 1.68 (d, J = 1.6 Hz, 1H, OH); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 145.5, 142.2, 140.7, 128.6, 128.5, 127.9, 126.4, 125.9, 115.5, 69.2, 44.0, 38.8, 32.2; MS (EI$^+$, 70 eV) 252.0 (M$^+$, 6), 234.0 (12), 147.0 (28), 119.0 (31), 118.0 (100), 117.0 (40), 115.0 (18), 105.0 (16), 103.0 (15), 92.0 (23), 91.0 (100), 78.0 (21), 77.0 (17), 65.0 (13); TLC R_f 0.23 (EtOAc/hexane, 1:5) [UV, PA].



*Preparation of 3-(Diethoxymethyl)-1-phenylbut-3-en-1-ol (**3ap**).* Following the general allylation procedure, **1a** (101.9 μL, 1.0 mmol), $Ru_3(CO)_{12}$ (12.79 mg, 0.02 mmol, 0.02 equiv), TBACl (16.7 mg, 0.06 mmol, 0.06 equiv), **2p** (323.8 mg, 1.6 mmol, 1.6 equiv), H_2O (27 μL, 1.5 mmol, 1.5 equiv), Et_3N (14 μL, 0.1 mmol, 0.1 equiv), and dioxane (2.5 mL) were combined under 40 psi of CO at 75 °C for 24 h. Workup and purification by silica gel column chromatography (38 g SiO_2, 2.5 × 21.5 cm column, Et_2O/hexane (1:9 w/1% Et_3N → 1:5 → 1:3)) provided **3ap** (180 mg, 72%) as a colorless oil. Data for **3ap**: bp 100 °C (ABT, 10^{-5} mm Hg); ^1H NMR (500 MHz, $CDCl_3$) δ 7.43−7.37 (m, 2H, C(3′)H), 7.33 (dd, J = 8.3, 6.9 Hz, 2H, C(2′)H), 7.28−7.21 (m, 1H, C(4′)H), 5.26 (d, J = 1.2 Hz, 1H, C(4a)H), 5.11 (d, J = 1.2 Hz, 1H, C(4b)H), 4.89−4.84 (m, 1H, C(1)H), 4.74 (s, 1H, C(5)H), 3.78−3.62 (m, 3H, OH and C(6a)H_2), 3.51 (ddq, J = 21.8, 9.4, 7.0 Hz, 2H, C(6b)H_2), 2.57 (ddd, J = 14.2, 3.4, 1.0 Hz, 1H, C(2a)H), 2.50 (ddt, J = 14.2, 9.3, 0.8 Hz, 1H, C(2b)H), 1.26 (dt, J = 11.7, 7.0 Hz, 6H, C(7)H_3 × 2); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ ; 144.7 C(1′), 143.4 C(3), 128.4 C(2′), 127.3 C(4′), 125.9 C(3′), 117.8 C(4), 104.7 C(5), 73.8 C(1), 63.0 C(6a), 62.6 C(6b), 42.1 (2), 15.22 C(7a), 15.18 C(7b); IR (neat) 3429 (w), 3029 (w), 2976 (w), 2878 (w), 1651 (w), 1606 (w), 1494 (w), 1453 (w), 1393 (w), 1329 (w), 1162 (w), 1111 (w), 1053 (m), 1007 (w), 976 (w), 916 (w), 757 (w), 699 (m); MS (ESI) 273.3 (MNa$^+$, 4), 147.2 (14), 146.2 (32), 123.3 (11), 116.3 (16), 115.3 (100), 107.1 (95); TLC R_f 0.24 (EtOAc/hexane, 1:4) [UV, PA]. Anal. Calcd for $C_{15}H_{22}O_3$ (250.34): C, 71.97; H, 8.86. Found: C, 72.17; H, 8.87.



*Preparation of (E)-5-(Diethoxymethyl)-1-phenylhexa-1,5-dien-3-ol (**3bp**).* Following the general allylation procedure, **1b** (126 μL, 1.0 mmol), $Ru_3(CO)_{12}$ (12.79 mg, 0.02 mmol, 0.02 equiv), TBACl (16.7 mg, 0.06 mmol, 0.06 equiv), **2p** (323.8 mg, 1.6 mmol, 1.6 equiv), H_2O (27 μL, 1.5 mmol, 1.5 equiv), Et_3N (14 μL, 0.1 mmol, 0.1 equiv), and dioxane (2.5 mL) were combined under 40 psi of CO at 75 °C for 24 h. Workup entailed washing the reaction mixture with $NaHCO_3$ (3 × 5 mL) in a separatory funnel and extracting with Et_2O (2 × 5 mL) before drying over $MgSO_4$ and removing solvent. The residue was then purified via silica gel column chromatography (42.5 g SiO_2, 2.0 × 23.5 cm column, Et_2O/hexane (1:9 w/1% Et_3N → 1:6 → 1:3 → 1:1) providing a nearly inseparable mixture of **3bp**/**3cp** in an 88:12 ratio (203 mg, 73%) as a colorless oil. A small portion of **3bp** was successfully isolated via sacrificial purification (radial silica gel chromatography 2 mm, Et_2O/hexane (1:2 w/1% Et_3N → 1:2)), providing pure **3bp** (63 mg, 23%) with which all characterization data was obtained. Data for **3bp**: bp 125 °C (ABT, 10^{-5} mm Hg); ^1H NMR (500 MHz, $CDCl_3$) δ 7.38 (dd, J = 8.1, 1.4 Hz, 2H, C(4′)H), 7.30 (dd, J = 8.4, 6.8 Hz, 2H, C(5′)H), 7.22 (t, J = 7.3 Hz, 1H, C(6′)H), 6.64 (dd, J = 15.9, 1.4 Hz, 1H, C(2′)H), 6.25 (dd, J = 15.9, 6.0 Hz, 1H, C(1′)H), 5.27 (d, J = 1.8 Hz, 1H, C(4a)H), 5.17 (d, J = 1.8 Hz, 1H, C(4b)H), 4.75 (s, 1H, C(5)H), 4.47 (dtd, J = 8.0, 5.6, 4.9, 3.1 Hz, 1H, C(1)H), 3.68 (ddq, J = 18.4, 9.5, 7.1 Hz, 2H, C(6a)H_2), 3.52 (ddt, J = 11.3, 9.4, 7.0 Hz, 2H, C(6b)H_2), 3.46 (d, J = 3.4 Hz, 1H, OH), 2.53 (ddd, J = 14.2, 3.5, 1.1 Hz, 1H, C(2a)H), 2.39 (ddd, J = 14.1, 8.8, 0.8 Hz, 1H, C(2b)H), 1.25 (dd, J = 7.0 Hz, 6H, C(7)H_3 × 2; $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 143.1 C(3), 137.3 C(3′), 132.4 C(1′), 129.6 C(2′), 128.6 C(5′), 127.5 C(6′), 126.6 C(4′), 117.8 C(4), 104.7 C(5), 71.8 C(1), 62.9 C(6a), 62.7 C(6b), 40.0 C(2), 15.21 C(7a), 15.18 C(7b); IR (neat) 3423 (w), 3025 (w), 2976 (w), 2937 (w), 2877 (w), 1651 (w), 1600 (w), 1495 (w), 1448 (w), 1393 (w), 1372 (w), 1372 (w), 1329 (w), 1160 (w), 1109 (w), 1054 (m), 1009 (w), 966 (w), 916 (w), 748 (w), 693 (m); MS (ESI) 299.2 (MNa$^+$, 79), 291.3 (34), 283.2 (10), 264.2 (15), 219.2 (16), 218.2 (100), 213.1 (40), 186.1 (10), 185.1 (57), 184.1 (15), 169.1 (14), 168.1 (15), 167.1 (73), 157.1 (13); TLC R_f 0.46 (EtOAc/hexane, 1:4) [UV, PA]. Anal. Calcd for $C_{17}H_{24}O_3$ (276.38): C, 73.88; H, 8.75. Found: C, 74.23; H, 8.89.



*Preparation of 5-(Diethoxymethyl)-1-phenylhex-5-en-3-ol (**3cp**).* Following the general allylation procedure, **1c** (131.7 μL, 1.0 mmol), $Ru_3(CO)_{12}$ (12.79 mg, 0.02 mmol, 0.02 equiv), TBACl (16.7 mg, 0.06 mmol, 0.06 equiv), **2p** (323.8 mg, 1.6 mmol, 1.6 equiv), H_2O (27 μL, 1.5 mmol, 1.5 equiv), Et_3N (14 μL, 0.1 mmol, 0.1 equiv), and dioxane (2.5 mL) were combined under 40 psi of CO at 75 °C for 24 h. Workup and purification by silica gel column chromatography (37 g SiO_2, 2.5 × 21.5 cm column, Et_2O/hexane (1:9 w/1% Et_3N → 1:5 → 1:3)) provided **3cp** (221 mg, 79%) as a colorless oil. Data for **3cp**: bp 100 °C (ABT, 10^{-5} mm Hg); ^1H NMR (500 MHz, $CDCl_3$) δ 7.32−7.24 (m, 2H, C(4′)H), 7.24−7.20 (m, 2H, C(5′)H), 7.19−7.14 (m, 1H, C(6′)H), 5.22 (d, J = 1.7 Hz, 1H, C(4a)H), 5.10 (d, J = 1.7 Hz, 1H, C(4b)H), 4.70 (s, 1H, C(5)H), 3.77 (dddt, J = 9.2, 7.7, 4.8, 3.2 Hz, 1H, C(1)H), 3.65 (ddq, J = 19.6, 9.4, 7.0 Hz, 2H, C(6a)H_2), 3.48 (tq, J = 9.3, 7.0 Hz, 2H, C(6b)H_2), 3.22 (d, J = 3.2 Hz, 1H, OH), 2.83 (ddd, J = 13.7, 9.8, 5.9 Hz, 1H, C(2′a)H), 2.70 (ddd, J = 13.7, 9.7, 6.8 Hz, 1H, C(2′b)H), 2.43−2.32 (m, 1H, C(2a)H), 2.23 (ddd, J = 14.1, 9.2, 0.8 Hz, 1H, C(2b)H), 1.78 (tdd, J = 9.8, 7.7, 5.2 Hz, 2H, C(1′)H_2), 1.23 (td, J = 7.0, 5.7 Hz, 6H, C(7)H_3 × 2); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 143.7 C(3), 142.6 C(3′), 128.6 C(5′), 128.4 C(4′), 125.8 C(6′), 117.3 C(4), 104.8 C(5), 70.4 C(1), 63.0 C(6a),

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62.7 C(6b), 39.8 C(2), 39.3 C(1′), 32.4 C(2′), 15.20 C(7a), 15.16 C(7b); IR (neat) 3448 (w), 3029 (w), 2977 (w), 2930 (w), 2874 (w), 1648 (w), 1603 (w), 1496 (w), 1454 (w), 1395 (w), 1372 (w), 1329 (w), 1111 (w), 1055 (m), 1011 (w), 916 (w), 733 (w), 699 (m) MS (ESI) 301.4 (MNa^+, 100), 187.3 (38), 119.3 (14), 105.3 (12); TLC R_f 0.23 (EtOAc/hexane, 1:4) [UV, PA]. Anal. Calcd for $C_{17}H_{26}O_3$ (278.39): C, 73.35; H, 9.41. Found: C, 73.41; H, 9.48.

■ ASSOCIATED CONTENT

Supporting Information

Optimization studies, GC response factors/retention times, and ^1H and ^{13}C NMR spectra. This material is available free of charge via the Internet at http://pubs.acs.org.

■ AUTHOR INFORMATION

Corresponding Author

*Tel: (217) 333-0066. Fax: (217) 333-3984. E-mail: sdenmark@illinois.edu.

Notes

The authors declare no competing financial interest.

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