Chapter 1.

Ring-Opening Cross-Metathesis of Low-Strain Cycloolefins

Abstract

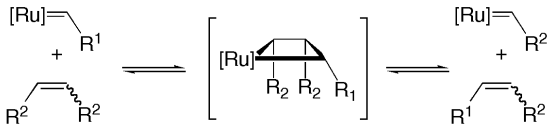
The ring-opening cross-metathesis (ROCM) of five- through eight-membered ring cycloolefins, catalyzed by a ruthenium alkylidene complex possessing an *N*-heterocyclic carbene ligand, was investigated. The ROCM of unsubstituted cycloolefins led to the formation of dienes that were symmetrically capped with the non-terminal alkene portion of the cross partner. Seven- and eight-membered ring substrates readily underwent ROCM with both electron-deficient and electron-rich alkenes, but five- and six-membered ring substrates required the use of electron-deficient cross partners. Trisubstituted cycloolefins underwent ROCM with α,β-unsaturated carbonyl compounds to regioselectively generate end-differentiated dienes, in which the carbonyl portion of the cross partner was located on the less-hindered side of the diene. For the ROCM of cycloolefins bearing allylic substitution, five- and six-membered ring substrates led to the sole formation of bis-carbonyl-capped dienes, but seven-membered ring substrates generated a mixture of two products: the bis-carbonyl-capped dienes and the same end-differentiated dienes that were observed during the ROCM of the trisubstituted cycloolefins. Of all the substituted cycloolefins investigated, only the trisubstituted eight-membered ring cycloolefins exhibited both high yields and high product selectivities. Mechanistic investigations indicated that the relative reactivity for these low-strain cycloolefins was cyclooctene > cycloheptene > cyclopentene > cyclohexene. These studies also indicated that (a) multiple propagating ruthenium alkylidenes were operative in these ROCM reactions, and (b) every step in these reactions was reversible.

1.1. Background

1.1.1. Ruthenium-catalyzed olefin metathesis

Ruthenium-catalyzed olefin metathesis is a carbon-carbon bond forming reaction that is widely used by both organic and polymer chemists.[1] In this reaction, a ruthenium alkylidene and an olefin interconvert to form a new olefin and alkylidene, presumably through the mechanism proposed by Chauvin (Scheme 1.1.1),[2] in which a metallacyclobutane intermediate forms via alternating [2 + 2] cycloadditions and cycloreversions.

Scheme 1.1.1. Chauvin mechanism for olefin metathesis.



Scheme 1.1.2 illustrates some common applications of olefin metathesis: ring-closing metathesis (RCM), acyclic diene metathesis (ADMET), ring-opening metathesis polymerization (ROMP), and cross-metathesis (CM).

Widespread use of ruthenium-catalyzed olefin metathesis has stemmed primarily from the development of catalysts **1** and **2** (Figure 1.1.1). Catalysts of this type are known for their relative ease of synthesis, high metathesis activity, and marked tolerance toward air, moisture,

Scheme 1.1.2. Common applications of olefin metathesis.

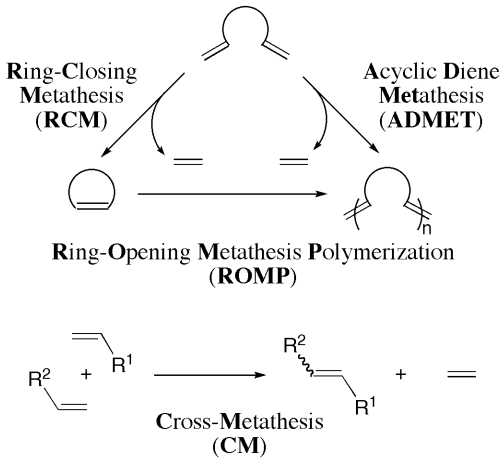
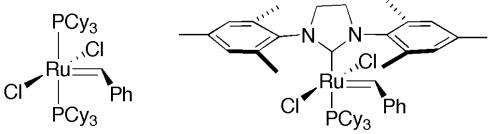


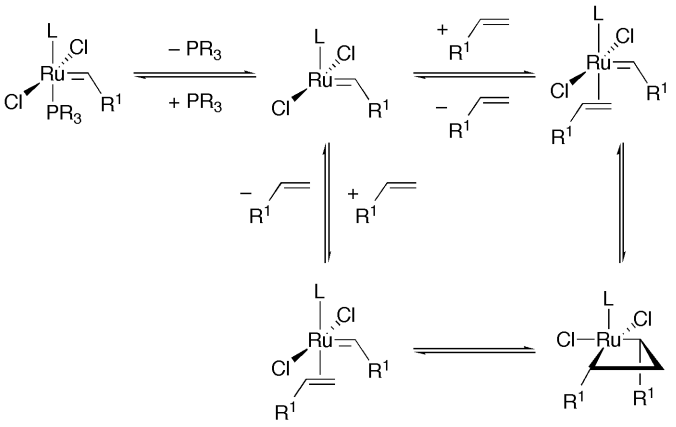
Figure 1.1.1. Most common ruthenium-based olefin metathesis catalysts (Cy = cyclohexyl).



1 **2**

and a variety of organic functional groups.[3] Our group has proposed the dissociative mechanism illustrated in Scheme 1.1.3[i] to describe olefin metathesis via catalysts **1**, **2**, and their derivatives.[4] Note that phosphine dissociation is required before the ruthenium species can enter into the catalytic cycle and that every step in the metathesis process is reversible. Catalyst **1**, first reported in 1995,[5] demonstrated unprecedented metathesis activity relative to previous ruthenium-based catalysts. This catalyst significantly increased the feasibility of organic applications of olefin metathesis, as evidenced by rapid growth in the fields of RCM[6] and CM.[7] Catalyst **2**, first reported in 1999,[8] exhibited activity far superior to that of **1**.

Scheme 1.1.3. Proposed mechanism for olefin metathesis via catalysts 1, 2, and their derivatives.

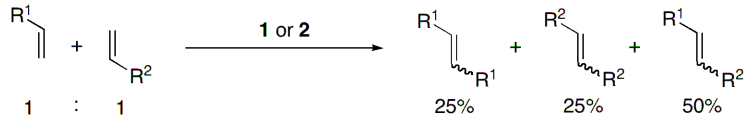


In addition to exhibiting superior activity in olefin metathesis reactions, catalyst **2** significantly broadened the scope of alkenes that were amenable to olefin metathesis. For the first time, substrates such as α,β-unsaturated carbonyl compounds[9] and geminally-disubstituted alkenes[10] could participate in these reactions. This development considerably enlarged the substrate scope of CM.[11] Scheme 1.1.4 illustrates the reason that the development of catalyst **2** had such a pronounced effect on

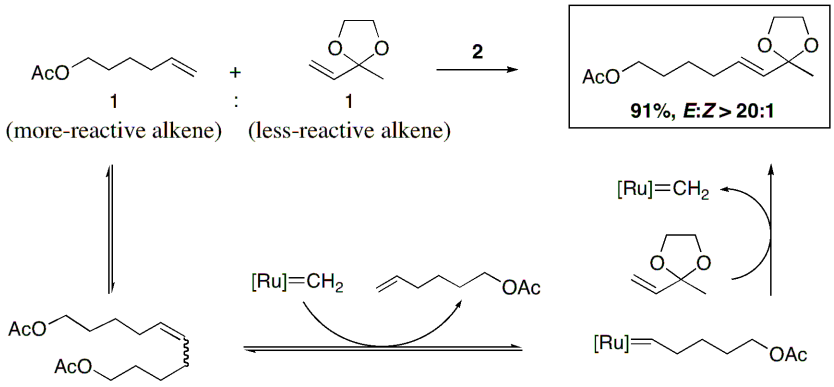
[i] The ruthenium coordination geometries shown in Scheme 1.1.3 are not meant to represent the actual geometries of the reactive species. Those specific geometries are, in fact, still an open topic of debate.

Scheme 1.1.4. Avoiding a statistical distribution of products in a CM reaction through the use of alkenes that greatly differ in reactivity.

1. Statistical distrubution of products: expected if the two cross partners possess similar reactivity



2. Selective CM: observed when the two cross partners greatly differ in reactivity[11]



CM. Since metathesis reactions are reversible and thus are under thermodynamic control, statistics predicts that a CM reaction can, at best, result in a 50% yield of the desired cross product, with the balance of the material forming homodimers of the two starting materials (Scheme 1.1.4, part 1). However, if the two cross partners greatly differ in reactivity toward the metathesis catalyst, three things occur. First, the less-reactive alkene homodimerizes at a much slower rate than does the more-reactive alkene. Second, the homodimer of the more-reactive alkene exhibits comparable reactivity to its parent alkene and can thus undergo further metathesis. Finally, the desired cross product is relatively unreactive toward subsequent metathesis, which introduces an essentially irreversible step into the CM reaction. As illustrated in part 2 of Scheme 1.1.4, this situation allows nearly all of the starting material to be converted into the desired cross product. In addition, high *E*-stereoselectivity is generally observed in these cases.

Our group has developed a general model to describe an alkene's reactivity toward CM.[11] In this model, the alkene is designated as either Type I, Type II, Type III, or Type IV. Type I alkenes undergo rapid homodimerization, and their homodimers are consumable. Type II alkenes undergo slow homodimerization, and their homodimers are sparingly consumable. Type III alkenes do not undergo homodimerization, and Type IV alkenes are spectators to CM. In this model, productive CM can only be expected to proceed in high yield if the two cross partners are of differing types from each other. In the above discussion, the more- and the less-reactive alkenes (Scheme 1.1.4, part 2) are Type I and Type III, respectively.[11]

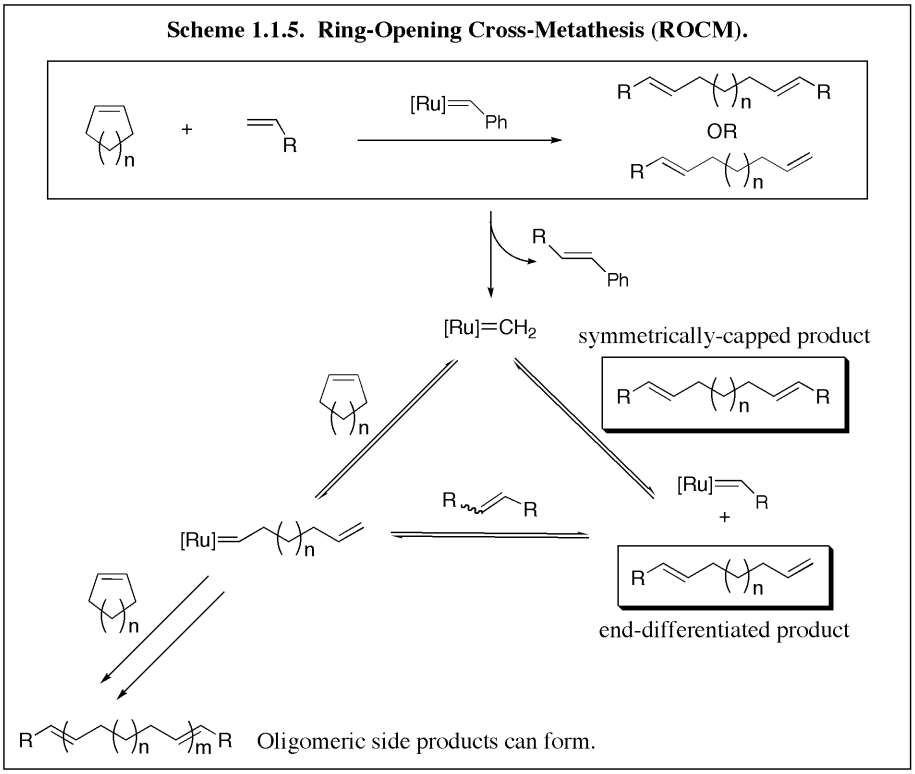
The reason that the development of catalyst **2** has markedly enhanced the usefulness of CM is that **2** allows a significantly wider variety of alkenes to qualify as Types I, II, and III. This broad substrate scope generates many more potential alkene combinations that will lead to efficient CM, as opposed to that of the earlier catalyst **1**, for which most alkenes qualify as either Type I or Type IV.[11] I joined the Grubbs group shortly after the initial discovery of catalyst **2**, and my early projects were geared toward exploring the new applications that had suddenly become possible in the area of small molecule synthesis, specifically the applications involving CM and its related metathesis reactions.

1.1.2. Ring-opening cross-metathesis

The first application that I explored, with the guidance and assistance of John P. Morgan, was ring-opening cross-metathesis (ROCM). This tandem reaction has become more prevalent as metathesis usage has increased,[12] along with other tandem metathesis sequences such as ring-opening/ring-closing metathesis (ROM/RCM).[13,14] These types of

reactions are desirable because they introduce multiple new functional groups into a molecule during a single reaction step. The ROCM reaction is illustrated in Scheme 1.1.5. It involves the initial opening of a cycloolefin ring by a metathesis catalyst, followed by the CM of another alkene (referred to herein as the "cross partner") onto each end of the opened ring, generating a diene. As shown in Scheme 1.1.5, either a symmetrically-capped diene or an end-differentiated diene can be produced. If the cycloolefin is readily polymerizable, or if a relatively small amount of the cross partner is used, then the reaction can undergo ROMP instead, forming telechelic polymers or oligomers.[15]

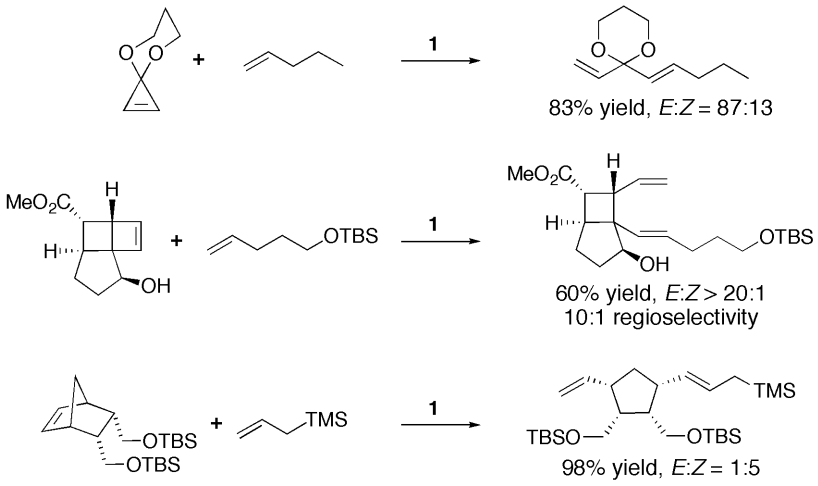
Scheme 1.1.5. Ring-Opening Cross-Metathesis (ROCM).



Prior to the discovery of catalyst **2**, ROCM reactions were carried out almost exclusively with catalyst **1**.[1e,12] These efforts focused on opening highly strained cycloolefins (cyclopropenes,[16] cyclobutenes,[17] and norbornenes[18]), using unhindered,

relatively electron-rich terminal alkenes as cross partners (Scheme 1.1.6). The cycloolefins employed in these reactions generally required bulky ring substituents in order to discourage the formation of oligomeric side products. Between the stringent requirements for suitable cycloolefins and the limited array of effective cross partners, the substrate scope available for ROCM reactions was quite limited.

Scheme 1.1.6. Previous ROCM reactions, which employed catalyst 1.[16,17a,18d]



Low-strain cycloolefins (five- to eight-membered rings) are much more desirable substrates for ROCM, due to their ease of synthesis relative to the highly strained ring systems. In addition, low-strain cycloolefins are stable enough toward ROMP to preclude the need for bulky ring substituents. However, the ROCM of low-strain cycloolefins with catalyst **1** results in either no reaction or little selectivity between diene formation and oligomerization, presumably due to the relatively slow rate at which catalyst **1** opens these ring systems.[12b] Catalyst **2**, however, with its significantly higher activity, is able to efficiently open such rings, as evidenced by reports of the ROMP of low-strain cycloolefins with **2**.[15b] In addition, the previously discussed broader substrate scope of catalyst **2**, relative to that of **1**, introduces a much larger variety of potential

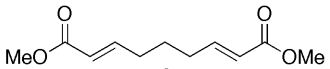
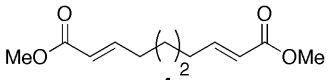
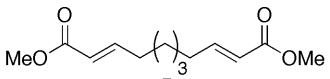
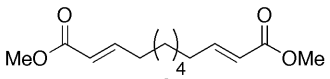
cross partners, whose properties could prove more capable of facilitating the ROCM of low-strain cycloolefins. Thus the purpose of our research during this project was to explore the ROCM, via catalyst **2**, of low-strain cycloolefins.

1.2. Unsubstituted Cycloolefins

1.2.1. Substrate scope

Our initial studies involved unsubstituted cycloolefins and α,β-unsaturated carbonyl compounds. The latter substrates had not been previously explored as cross partners for ROCM, due to their lack of reactivity with catalyst **1**.[11] Methyl acrylate was generally the cross partner of choice because of its relatively high stability and the ease of separation of its resultant side products (i.e., dimethyl fumarate and methyl cinnamate) from the reaction mixture. Table 1.2.1 lists the results of the ROCM of methyl acrylate with various unsubstituted low-strain cycloolefins using catalyst **2**.

Table 1.2.1. ROCM of unsubstituted cycloolefins with methyl acrylate.[a]

entry	cycloolefin	product[b]	isolated yield (%)	notebook page
1		 **3**	71	cm2-146
2		 **4**	44	cm2-60
3		 **5**	75	cm1-97
4		 **6**	95	cm2-125

[a] 0.2 mmol scale, 2-3 equiv methyl acrylate, 5 mol % **2**, CH_2Cl_2, reflux, cycloolefin = 0.1-0.2M.
[b] *E*:*Z* > 20:1 (^{1}H NMR).

Cycloheptene and cyclooctene required two or more equivalents of methyl acrylate to prevent oligomer formation, but cyclopentene and cyclohexene did not exhibit significant

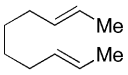
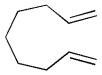
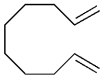
oligomerization, regardless of the reactant stoichiometry. Dimethyl fumarate was often observed as a side product when a large excess of methyl acrylate was employed, especially in the case of cyclohexene.

These reactions showed some notable trends with respect to both yield and selectivity. The yields were good-to-high in all cases except for that of cyclohexene. The trend for the product yield according to ring size was $8 > 7 \approx 5 > 6$. The relative ring strain of these four cycloolefins is $8 > 7 \approx 5 > 6$.[19] Thus these two trends match, suggesting that cycloolefins with relatively higher ring strain exhibit higher yields in ROCM reactions. The most interesting aspect of the results shown in Table 1.2.1, however, is that the only diene product observed in these reactions was the one containing an ester moiety on both ends. We never observed dienes that possessed terminal alkenes, even when the cycloolefin was used in excess. Presumably dienes containing terminal alkenes were only transient species in these ROCM reactions (Scheme 1.1.5), being too reactive toward subsequent metathesis to be isolated.

For comparison studies, we conducted similar ROCM experiments with the acyclic diene analogs of these four cycloolefins. Table 1.2.2 shows that the ROCM reactions of these dienes led to essentially identical products and yields as did the ROCM reactions of their cyclic analogs. This similarity implied that the opened- and the closed-forms of these cycloolefins were in rapid equilibrium with each other, and it was this equilibrium mixture that subsequently reacted with methyl acrylate. To test this hypothesis, the course of the reactions listed in entries 1 and 4 of Table 1.2.2 was observed by ^{1}H NMR spectroscopy. 1,6-heptadiene (entry 1) indeed exhibited at least a 50% conversion to cyclopentene prior to reaction with methyl acrylate. 1,8-nonadiene

(entry 4), however, showed little or no conversion to cycloheptene.[ii] A possible interpretation of these results is that the equilibrium mixture of cycloheptene favors its ring-opened form more so than that of cyclopentene.

Table 1.2.2. CM of acyclic dienes with methyl acrylate.[a]

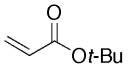
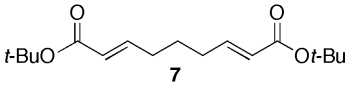
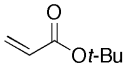
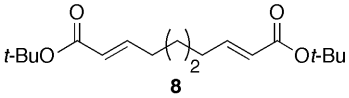
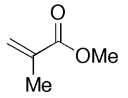
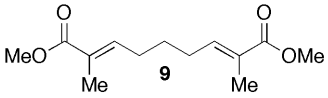
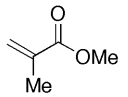
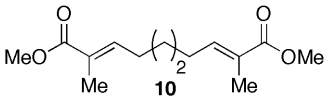
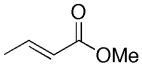
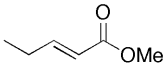
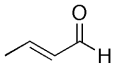
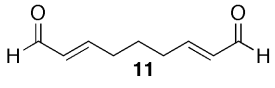
entry	diene	product[b]	isolated yield (%)	yield with cyclic analog (%)[c]	notebook page
1		**3**	79	71	cm2-139
2		**4**	31	44	cm2-136
3		**4**	15	44	cm1-89
4		**5**	79	75	cm1-81
5		**6**	92	95	cm2-138

[a] 0.2 mmol scale, 2-3 equiv methyl acrylate, 5 mol % **2**, CH_2Cl_2, reflux, diene = 0.2M.
[b] *E*:*Z* > 20:1 (^{1}H NMR). [c] Taken from Table 1.2.1.

The ROCM of cyclopentene and cyclohexene with other α,β-unsaturated carbonyl compounds was also investigated. The results of these studies are listed in Table 1.2.3. As observed with the use of methyl acrylate, the product dienes in all of these reactions possessed a carbonyl moiety on both ends. ROCM with *t*-butyl acrylate (entries 1-2) resulted in yields that were comparable to those obtained with methyl acrylate, while ROCM with methyl methacrylate (entries 3-4) exhibited yields that were significantly lower. Methyl methacrylate was a much less reactive cross partner, and, in fact, it had to be used as the reaction solvent before appreciable yields were observed at

[ii] Notebook pages: cm1-110 and cm1-120. It should be noted that these reactions were not completely valid representations of the actual reaction process because the closed NMR tube in which they were carried out stifled the evaporation of ethylene, which could potentially suppress both the ring closing- and the cross-metathesis reactions.

Table 1.2.3. ROCM of unsubstituted cycloolefins with other electron-deficient cross partners.[a]

entry	cycloolefin	cross partner	equiv cross partner	product[b]	isolated yield (%)	notebook page
1			3	 **7**	80	cm1-128
2			3	 **8**	40	cm2-61
3[c]			47	 **9**	37	cm1-141
4[c]			47	 **10**	26	cm2-58
5			3	**3**	35	cm2-164
6			3	**3**	< 7	cm1-117
7			2	 **11**	38[d,e]	cm1-19

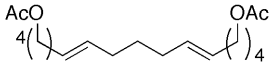
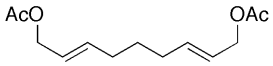
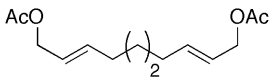
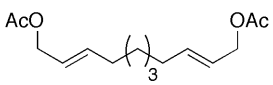
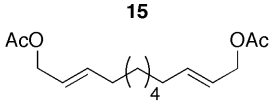
[a] 0.2-0.8 mmol scale, 5 mol % **2**, CH_2Cl_2, reflux, cycloolefin = 0.2M. [b] *E*:*Z* > 20:1 (^{1}H NMR). [c] Neat, 50 °C. [d] Approximately 23% of the aldehydes in this product became oxidized to carboxylic acids during silica gel chromatography. [e] 13% of the bis-aldehyde-capped dimer was isolated as well.

all. The ROCM of cyclopentene with β-substituted analogs of methyl acrylate was also examined (entries 5-6). Previous studies had indicated that phosphine-bound ruthenium alkylidenes possessing terminal alkenes (i.e., methylidenes) were significantly less active metathesis catalysts than were substituted alkylidenes.[4] We thus thought that use of these β-substituted methyl acrylate analogs would result in higher yields because they would preclude intermediate methylidene formation. Unfortunately these substrates led to significantly decreased yields relative to those obtained with methyl acrylate. We had observed a similar trend with the CM of methyl-substituted acyclic dienes (Table 1.2.2, compare entries 2 and 3). We concluded that the increased steric hindrance of the disubstituted alkenes led to these lower ROCM yields. Finally, crotonaldehyde also

underwent ROCM with cyclopentene (Table 1.2.3, entry 7), exhibiting a yield similar to that obtained with the use of methyl crotonate (entry 5).

We also explored the ROCM of these four cycloolefins with more electron-rich cross partners. As illustrated in Table 1.2.4, the yields obtained in these reactions were significantly lower than those obtained with the use of methyl acrylate in the cases of cyclopentene and cyclohexene (entries 1-3), but the yields were comparable to those obtained in the methyl acrylate reactions in the cases of cycloheptene and cyclooctene (entries 4-5). Therefore seven- and eight-membered ring cycloolefins were more versatile with respect to compatible cross partners in ROCM, as compared to five- and six-membered ring cycloolefins, which only underwent efficient ROCM with α,β-unsaturated carbonyl compounds.

Table 1.2.4. ROCM of unsubstituted cycloolefins with relatively electron-rich cross partners.[a]

entry	cycloolefin	cross partner	product[b]	isolated yield (%)	yield with methyl acrylate[c]	notebook page
1			 **12**	< 14	71	cm2-160
2			 **13**	40	71	cm1-132
3[d]			 **14**	12	44	cm2-33
4			 **15**	82	75	cm1-133
5			 **16**	73	95	cm2-141

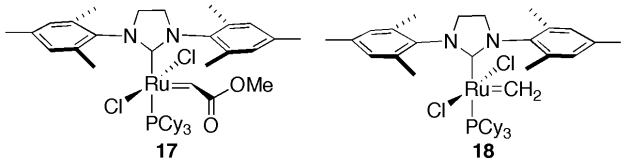
[a] 0.2 mmol scale, 3 equiv cross partner, unless otherwise noted, 5 mol % **2**, CH_2Cl_2, reflux, cycloolefin = 0.2M. [b] *E*:*Z* = ca. 7:1 (^{1}H NMR). [c] Taken from Table 1.2.1. [d] Neat in cyclohexene, 50 °C

1.2.2. Mechanism

We have postulated that ROCM involves the initial formation of an equilibrium mixture of the ring-opened and the ring-closed forms of a given cycloolefin (Scheme 1.1.5). The success of a ROCM reaction depends upon this equilibrium mixture favoring the ring-opened form, as the desired product only forms if an opened ring can react with the cross partner before closing again. Based upon our observation that cycloheptene and cyclooctene undergo efficient ROCM with a much more general class of cross partners relative to cyclopentene and cyclohexene, we hypothesized that the equilibrium mixtures for the former favor the ring-opened form, while those of the latter favor the ring-closed form. Qualitative observation, via ^{1}H NMR spectroscopy, of the relative propensities of these four cycloolefins to undergo oligomerization in the presence of catalyst **2** (without a cross partner present), also supported this postulate. In these studies, cycloheptene and cyclooctene oligomerized readily, but cyclopentene and cyclohexene did not oligomerize at all (under ROCM reaction conditions).

If the equilibrium mixture of cyclopentene and cyclohexene does not favor their ring-opened forms, then the success of their ROCM reactions should depend entirely upon the nature of the cross partner that is employed. Our results clearly indicated that electron-deficient alkenes such as methyl acrylate were suitable cross partners to effect ROCM reactions with these two cycloolefins, while more electron-rich alkenes were not (compare Tables 1.2.1 and 1.2.4). We suggest two possible explanations for this observation. Both explanations relate to the identity of the ruthenium alkylidene that promotes the initial ring-opening event in the ROCM reactions involving methyl acrylate, which is either ester carbene **17** or methylidene **18** (Figure 1.2.1). To our knowledge,

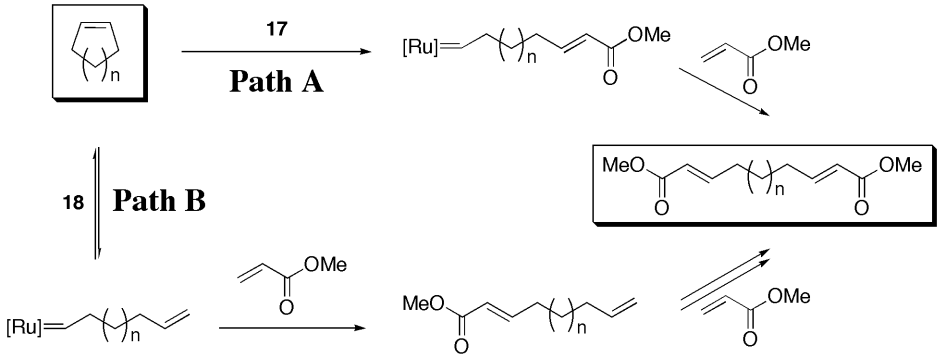
Figure 1.2.1. Possible propagating ruthenium alkylidenes for ROCM with methyl acrylate and catalyst 2.



alkylidene **17** has never been irrefutably observed during metathesis reactions or independently synthesized, but its existence has been inferred from the observed dimerization of acrylates.[9a] The bis-phosphine version of **17**, however, has been synthesized, and it is highly reactive and unstable.[20] Alkylidene **18** has been observed by NMR in numerous metathesis reactions, and it has been independently synthesized and studied.[4] Thus we assume that alkylidene **17** is much less stable than alkylidene **18**.

One possible explanation for the need for α,β-unsaturated carbonyl compounds as cross partners in the ROCM of cyclopentene and cyclohexene assumes that either alkylidene **17** or **18** can be responsible for opening the cycloolefin (Scheme 1.2.1). Just

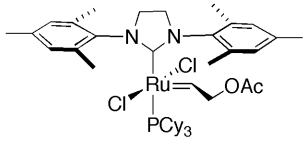
Scheme 1.2.1. Possible mechanisms for ROCM with methyl acrylate and catalyst 2.



as the release of ring-strain can drive a ROCM reaction toward product formation, the elimination of an energetically unfavorable ruthenium alkylidene such as **17** could also provide such a driving force. In such a situation, the initial ring-opening reaction would

not only be driven by the elimination of **17**, but the reaction should be essentially irreversible, since the reverse reaction would necessitate the re-formation of this highly unstable alkylidene (Scheme 1.2.1, Path A). For cyclopentene and cyclohexene, whose equilibrium mixture favors the ring-closed form, the introduction of this irreversible reaction step may be necessary in order for efficient ROCM to occur. We hypothesize that cyclopentene and cyclohexene can only be opened efficiently by the more reactive alkylidene **17** (Scheme 1.2.1, Path A), while cycloheptene and cyclooctene, whose ring-opened forms are more favored, can be opened by either **17** or **18** (Path A or Path B). This hypothesis explains the notable success of cross partners like methyl acrylate (Table 1.2.1), relative to the more electron-rich cross partners like *Z*-1,4-diacetoxy-2-butene (Table 1.2.4), in the ROCM of cyclopentene and cyclohexene. ROCM reactions involving *Z*-1,4-diacetoxy-2-butene would have to involve ring-opening by alkylidene **19** (Figure 1.2.2), which is expected to be significantly more stable than **17**,[4] thus rendering the ring-opening reaction completely reversible and allowing the cycloolefin to return to its more-favored ring-closed form before CM with *Z*-1,4-diacetoxy-2-butene can occur.

Figure 1.2.2. Propagating ruthenium alkylidene for ROCM reactions involving *Z*-1,4-diacetoxy-2-butene and catalyst 2.



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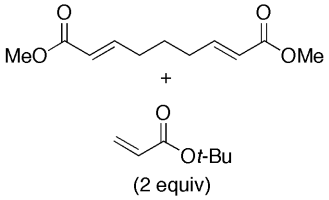
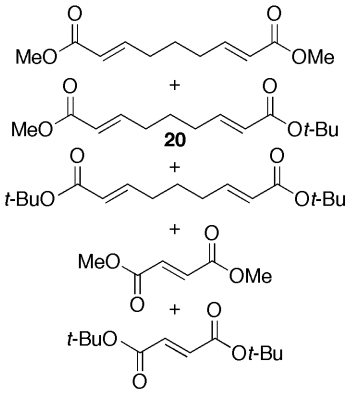
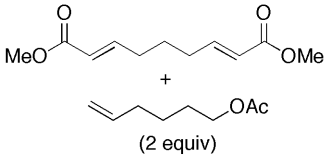
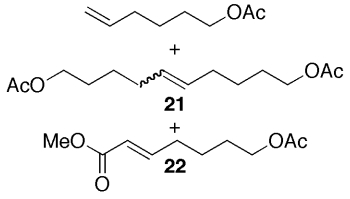
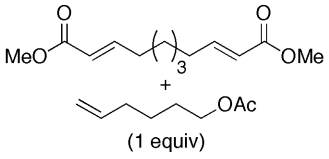
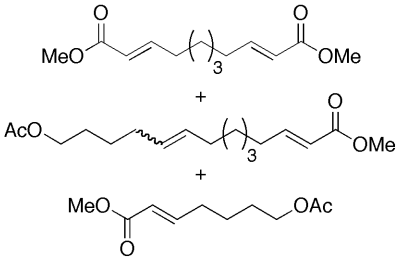
An alternative explanation assumes that alkylidene **17** is too unstable to participate in these ROCM reactions,[20] meaning that alkylidene **18** is solely responsible for opening the cycloolefin rings (Scheme 1.2.1, Path B). Because **18** is a relatively stable alkylidene, this ring-opening step should be completely reversible. However, because methyl acrylate acts as a Type II alkene in the presence of catalyst **2**,[11] its CM

product should be resistant to subsequent metathesis, thus, again, introducing an essentially irreversible step into the reaction and driving the ROCM reaction toward product formation (Scheme 1.2.1, Path B). This explanation also provides a reason for the superiority of methyl acrylate over *Z*-1,4-diacetoxy-2-butene as a cross partner in the ROCM of cyclopentene and cyclohexene, because *Z*-1,4-diacetoxy-2-butene acts as a Type I alkene in the presence of catalyst **2**.[11] Therefore the CM product derived from *Z*-1,4-diacetoxy-2-butene is highly reactive toward subsequent metathesis, creating a facile pathway for the cycloolefin to revert back to its ring-closed form. Conversely, *Z*-1,4-diacetoxy-2-butene would still be an effective cross partner in the ROCM of seven- and eight-membered ring cycloolefins, because the re-closing of these ring systems occurs less readily.

Both of the reaction mechanisms proposed in Scheme 1.2.1 assume that CM reactions involving α,β-unsaturated carbonyl compounds are essentially irreversible. In order to test the validity of this assumption, some of the isolated products from ROCM reactions involving methyl acrylate were resubjected to metathesis, via addition of fresh catalyst **2** and various cross partners. The results of these experiments are listed in Table 1.2.5. These reactions generated a large number of similar products, and they were difficult to analyze quantitatively. Thus the yields given in Table 1.2.5 are approximations. Nevertheless, these results demonstrate that the ROCM products of methyl acrylate are not entirely immune to subsequent metathesis, as both the opened cycloolefin and the carbonyl moiety were incorporated into new metathesis products. It was especially interesting that, for ROCM product derived from cyclopentene, the majority of its opened cycloolefin moiety was not recovered at all (Table 1.2.5, entries 1-

2). In entry 1, only 55% was recovered, and in entry 2, *none* of the cycloolefin was recovered. In these reactions, the lost material presumably converted back into cyclopentene and subsequently evaporated upon exposure to vacuum during the work-up procedure.

Table 1.2.5. Subsequent reaction of ROCM products.[a]

entry	ROCM product + cross partner	products	isolated yield (%)[b]	notebook page
1	 (2 equiv)	 **20**	10 30 15 15 30	cm2-142
2	 (2 equiv)	 **21** **22**	10 60 40	cm2-150
3	 (1 equiv)		50 30 35	cm2-162

[a] 0.1-0.2 mmol scale, 5 mol % **2**, CH_2Cl_2, reflux, 18-26 h, ROCM product = 0.2M. [b] Calculated with respect to the ROCM product, unless not applicable.

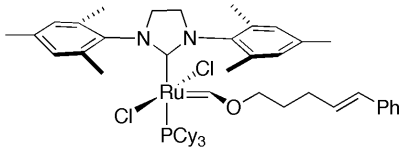
In contrast, approximately 80% of the opened cycloolefin moiety of the ROCM product derived from cycloheptene was recovered (Table 1.2.5, entry 3). Again, these results suggest that (a) the equilibrium mixture of cycloheptene favors the ring-opened form, whereas that of cyclopentene favors the ring-closed form; and (b) the presence of

acrylates (Type II alkenes) helps to trap the ring-opened form of cyclopentene to a greater extent than does the presence of Type I alkenes (Table 1.2.5, compare entries 1 and 2). The most important message to be taken from the results presented in Table 1.2.5, however, is that *every* step in these ROCM reactions is reversible, and thus neither of the two proposed mechanisms given in Scheme 1.2.1 is completely correct. Even so, these mechanisms still represent our best explanation for the results that we have obtained, and they can be viewed as approximate models to describe these ROCM reactions.

1.2.3. Competition experiments with 3,4-dihydro-2H-pyran

In order to distinguish between the two ROCM mechanisms illustrated in Scheme 1.2.1, the alkylidene that is responsible for initially opening the cycloolefin, either **17** or **18**, must be identified. We attempted to achieve this goal by conducting competition experiments between 3,4-dihydro-2H-pyran (DHP) and various cycloolefins. DHP reacts with ruthenium alkylidenes to form the metathesis-inactive, Fischer carbene complex **23** (Figure 1.2.3).[iii] Thus CM with DHP is irreversible, and it could conceivably be employed to trap the ring-opened form of a cycloolefin by incorporating it into the Fischer carbene complex. These experiments would need to be conducted in the presence of both **17** and **18** in order to ascertain whether each of these alkylidenes can open a given cycloolefin. Unfortunately, we have not yet been able to synthesize alkylidene **17**, and the rate of phosphine dissociation of alkylidene **18** is too slow to allow

Figure 1.2.3. Metathesis-inactive Fischer carbene complex formed from metathesis of 3,4-dihydro-2H-pyran and catalyst 2.



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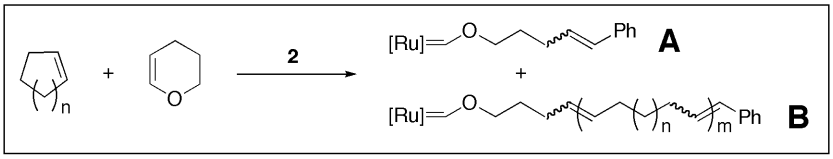
[iii] Fischer carbene complexes can be active for olefin metathesis,[21] but in all of our experiments, Fischer carbene formation was quantitative and irreversible.

it to enter into the catalytic cycle of a metathesis reaction to an appreciable extent.[4] Thus neither of the desired competition experiments could be carried out.

We were, however, able to carry out these competition experiments with catalyst **2**, as shown in Table 1.2.6. Cyclohexene was not incorporated into the Fischer carbene

Table 1.2.6. Trapping ruthenium alkylidene moieties with 3,4-dihydro-2H-pyran.[a,b]



entry	cycloolefin	δ_H carbene peak(s) (ppm)[c]	extent of oligomerization
1	none	13.64	------
2		13.64	none
3		13.61 13.64	none
4		13.61	partial
5		13.61	complete

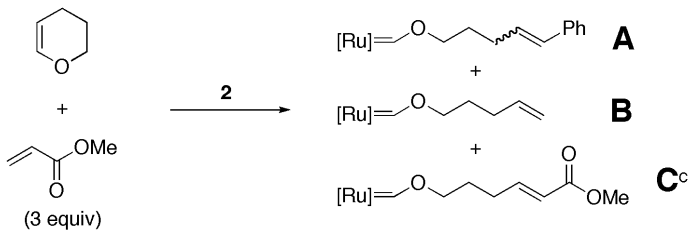
[a] 0.2 mmol scale, reaction performed in NMR tube, 1 equiv 3,4-dihydro-2H-pyran, 5 mol % **2**, CD_2Cl_2, 40 °C, 1 h, cycloolefin = 0.2M. [b] Notebook page: cm1-244. [c] Relative to CD_2Cl_2.

complex (entry 2). Cyclopentene formed two carbene products (entry 3): one that matched the control (entry 1) and one new carbene. No oligomerization of either cyclohexene or cyclopentene was detected. Cycloheptene and cyclooctene formed only the new carbene peak (entries 4-5), which we suggest corresponds to the general structure **B** (Table 1.2.6). Cycloheptene exhibited partial oligomerization during this reaction, and cyclooctene underwent quantitative oligomerization. Because the alkylidene responsible for opening the cycloolefins in these experiments was a benzylidene, these results do not offer conclusive information about the proposed mechanisms shown in Scheme 1.2.1.

However, these results do provide further support for the relative reactivity scale that we have proposed for these four cycloolefins: cyclooctene > cycloheptene > cyclopentene > cyclohexene.

A second competition experiment, this time between methyl acrylate and DHP, with catalyst **2**, provided some insight into the nature of the propagating ruthenium alkylidene in ROCM reactions that involve methyl acrylate. As illustrated in Scheme 1.2.2, this experiment resulted in the formation of multiple Fischer carbene products. Some of these carbenes exhibited methyl acrylate incorporation, and others did not. The most noteworthy observation, however, was that both the terminal alkene and the carbonyl moieties of methyl acrylate were incorporated into these Fischer carbene complexes. This result suggests that alkylidenes **17** and **18** are *both* present in these ROCM reactions, and, therefore, both of the mechanisms shown in Scheme 1.2.1 are operative to some extent.

Scheme 1.2.2. Interaction of methyl acrylate and 3,4-dihydro-2H-pyran with catalyst 2.[a,b]



[a] 0.8 mmol scale, 5 mol % **2**, CH_2Cl_2, reflux, 1 h, 3,4-dihydro-2H-pyran = 0.2M. [b] Notebook page: cm2-112. [c] ^{1}H NMR (300 MHz, C_6D_6): δ 14.04 (1H, s), 7.06 (1H, dt, *J* = 15.6, 6.9 Hz), 5.94 (1H, d, *J* = 15.9 Hz).

1.2.4. Three-component reactions involving cyclohexene

We briefly investigated the possibility of carrying out ROCM reactions with two different cross partners at the same time. The hope was that a different alkene would be added to each end of the opened cycloolefin, generating an unsymmetrical diene. Such

dienes would be more beneficial, relative to symmetric dienes, for the synthesis of diverse structures. Cyclohexene seemed to be the most promising cycloolefin for these reactions, because it could essentially only be opened in the presence of α,β-unsaturated carbonyl compounds like methyl acrylate. The assumption was that the acrylate would initiate the ring-opening event, adding the α,β-unsaturated carbonyl moiety to one side of the diene, and then the more electron-rich alkene, which would be used in excess, would add to the other side.

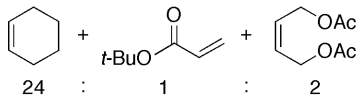
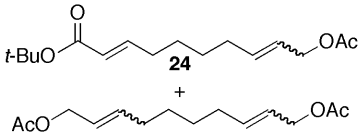
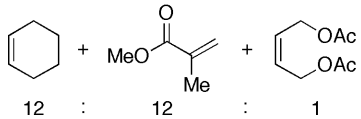
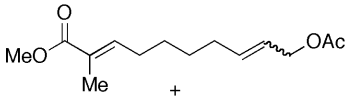
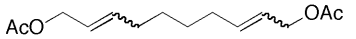
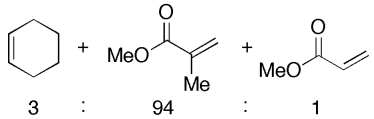
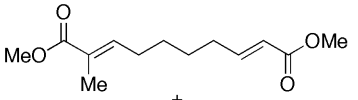
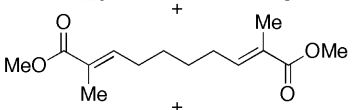
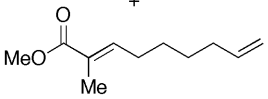
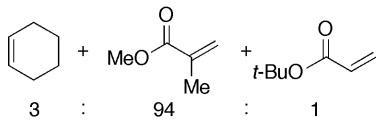
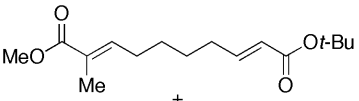
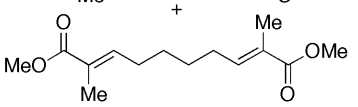
Table 1.2.7 lists the results of these three-component reactions. A large excess of cyclohexene was employed in order to favor ROCM with the cycloolefin over simple CM between the two cross partners.[iv] As shown in entry 1, both the electron-rich and the electron-deficient cross partners were able to promote the ring-opening event, leading to a mixture of products. We next employed an even less-reactive alkene, methyl methacrylate, as one of the cross partners, in hopes that it would not be able to participate in the ring-opening event. As shown in entries 2-4 of Table 1.2.7, all such reactions resulted in mixtures of products. In addition, the yields in these reactions were quite low, and thus the selective three-component ROCM of cycloolefins did not appear to be a viable reaction. These experiments did, however, further illustrate the reversible nature of these ROCM reactions, as nearly every possible ROCM product was formed to a similar extent in each of these three-component reactions.

1.2.5. Summary and conclusions

The ROCM of unsubstituted five- to eight-membered ring cycloolefins was evaluated in the presence of ruthenium catalyst **2** with a variety of cross partners. All of

[iv] Though not shown in Table 1.2.7, CM between the two cross partners was still observed during some of these reactions, despite the large excess of cyclohexene that was employed.

Table 1.2.7. Three-component ROCM reactions with cyclohexene.[a]

entry	reaction components	products	isolated yield (%)	notebook page
1	 24 : 1 : 2	 **24** +	< 20%	cm2-31
			5%	
2	 12 : 12 : 1	 +	5%	cm2-54
			5%	
3	 3 : 94 : 1	 +	10%[b]	cm2-87
		 +	10%	
			5%	
4	 3 : 94 : 1	 +	10%[b]	cm2-86
			5%	

[a] 0.4-0.6 mmol scale, 5 mol % **2**, neat, 50-80 °C. [b] Calculated with respect to cyclohexene.

these cycloolefins underwent ROCM in the presence of **2**, and the products in all cases were symmetric dienes in which the non-terminal alkene portion of the cross partner was incorporated onto each end. Cycloheptene and cyclooctene underwent ROCM efficiently in the presence of both electron-rich (e.g., *Z*-1,4-diacetoxy-2-butene) and electron-deficient (e.g., methyl acrylate) cross partners. Cyclopentene and cyclohexene, on the other hand, required the electron-deficient cross partners to achieve ROCM in relatively high yield. Cyclohexene exhibited much lower yields than did the other three cycloolefins. Three-component ROCM reactions involving cyclohexene and two different cross partners resulted in low yields and unselective product formation.

Our results indicate that the ROCM of unsubstituted, low-strain cycloolefins via catalyst **2** is a viable method for functionalized diene synthesis as long as (a) symmetrically-capped dienes (without terminal alkenes) are desirable, and (b) only α,β-unsaturated carbonyl compounds are employed as cross partners with five- and six-membered ring substrates. The first limitation presumably results from the high activity of catalyst **2**, which does not allow terminal alkenes to remain untouched during the ROCM reaction. The second limitation suggests that either (a) ester carbenes such as **17** are necessary to open these less-reactive ring systems, while the more reactive seven- and eight-membered ring cycloolefins can be opened by any type of alkylidene; or (b) CM with a Type II or a Type III alkene such as methyl acrylate, which is less reversible, is necessary to trap the ring-opened form of five- and six-membered ring cycloolefins, whereas ring-opened seven- and eight-membered ring cycloolefins can be trapped by CM with Type I, II, or III alkenes.

Our studies have provided some insight into the mechanism of these ROCM reactions. They have qualitatively revealed the relative rates at which these four cycloolefins open: cyclooctene > cycloheptene > cyclopentene > cyclohexene, which is consistent with the yields that we have observed in ROCM reactions. The experiments in which ROCM products were resubjected to metathesis conditions, the competition experiment with 3,4-dihydro-2H-pyran and methyl acrylate, and the three-component ROCM reactions of cyclohexene have all indicated that (a) every step is this reaction is reversible, and (b) every possible propagating ruthenium alkylidene forms to some extent during this reaction. These experiments did not, however, ascertain the identity of the propagating alkylidene that was responsible for the ring-opening event, which is a crucial

piece of information that is needed before our observations can be properly explained. Therefore the basis for our understanding of the inherently lower reactivity of cyclopentene and cyclohexene relative to that of cycloheptene and cyclooctene in these ROCM reactions remains empirical.

1.3. Substituted Cycloolefins

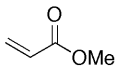
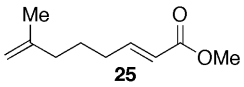
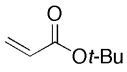
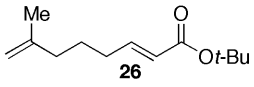
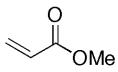
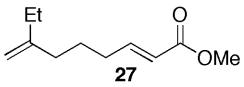
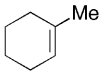
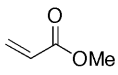
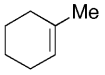
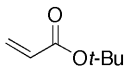
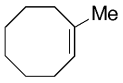
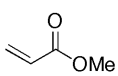
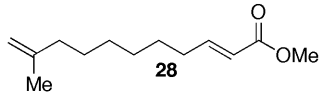
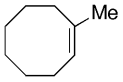
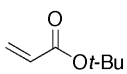
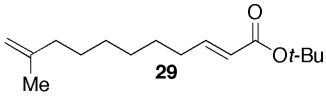
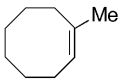
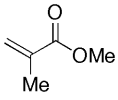
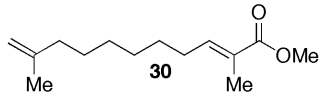
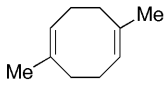
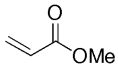
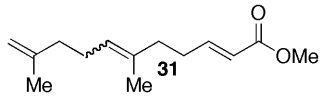
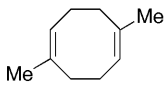
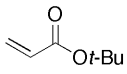
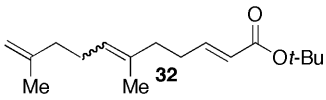
The formation of end-differentiated dienes, which possess different functional groups at each end, is highly desirable because subsequent selective reactions with one or both of the alkenes of these dienes could provide access to more complicated molecules. In fact, nearly all previously reported ROCM reactions, which employed catalyst **1**, resulted in the formation of such dienes, which all possessed a terminal alkene at one end (Scheme 1.1.6).[12,16-18] Conversely, only the formation of symmetric dienes has been observed during the ROCM of unsubstituted, low-strain cycloolefins[v] (see section 1.2),[9a,23] despite our attempts to accomplish three-component ROCM reactions. Presumably dienes that possess terminal alkenes initially formed in these reactions, but subsequent metathesis of these unhindered alkenes via highly active catalyst **2** prevented their isolation as products (Scheme 1.2.1, Path B). We postulated that a substituent on the cycloolefin, proximal to the alkene, might discourage the subsequent metathesis of the initially formed terminal alkene product, thus permitting the formation of unsymmetrical, end-differentiated dienes via ROCM of low-strain cycloolefins using catalyst **2**.

[v] We found one report of the formation of an end-differentiated diene via the ROCM of cyclopentene. However, the catalyst for this reaction was a ruthenium carbyne complex.[22]

1.3.1. Trisubstituted cycloolefins

We first investigated the ROCM of trisubstituted cycloolefins. These substrates were good candidates for the synthesis of end-differentiated dienes because our group had previously observed that the CM of α,β-unsaturated carbonyl compounds with geminally disubstituted alkenes was relatively slow. As illustrated in Table 1.3.1, the

Table 1.3.1. ROCM of trisubstituted cycloolefins with acrylates.[a,b]

entry	cycloolefin	acrylate	equiv acrylate	product[c]	isolated yield (%)	notebook page
1			0.3	 **25**	33	cm2-20
2			0.3	 **26**	43	cm2-19
3			0.3	 **27**	15	cm2-111
4			0.3	N. R.	------	cm1-206
5			0.3	N. R.	------	cm2-21
6			2	 **28**	81	cm1-280
7			2	 **29**	99	cm1-291
8[d]			47	 **30**	67	cm1-283
9[e]			0.3	 **31**	66[f]	cm2-12
10[e]			0.3	 **32**	70[g]	cm2-18

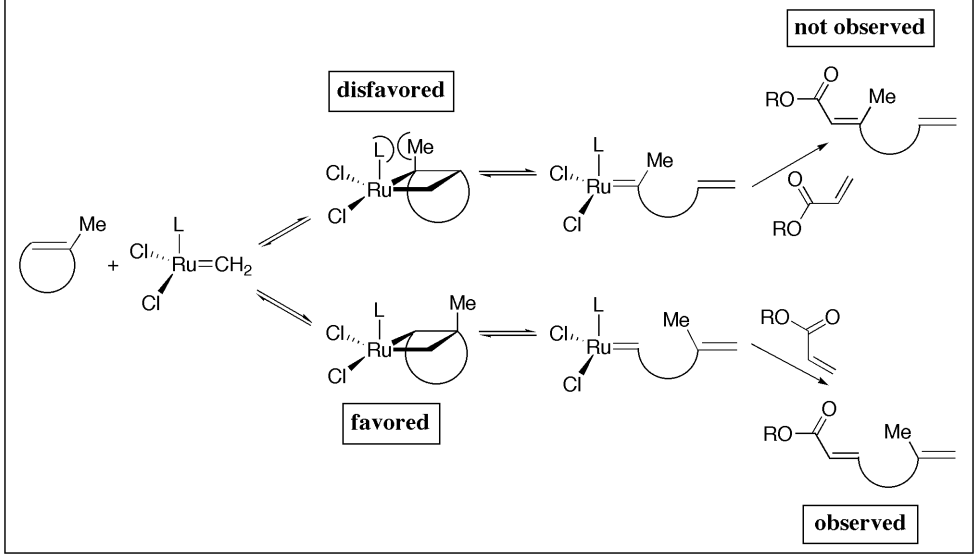
[a] 0.2-0.4 mmol scale, 5 mol % **2**, CH_2Cl_2, reflux, cycloolefin = 0.03-1.2M. [b] See ref. 24. [c] For alkenes alpha to carbonyl moieties, *E*:*Z* > 20:1 (^{1}H NMR). [d] Neat, 50 °C. [e] Starting material contains ca. 20% 1,6-dimethyl-cyclooctadiene contaminant. [f] 8% methyl 5-methylhexa-2,5-dienoate was isolated as well. [g] 12% *t*-butyl 5-methylhexa-2,5-dienoate was isolated as well.

ROCM of trisubstituted cycloolefins and various acrylates generated the desired end-differentiated products exclusively.[24] The yields were highly dependent upon ring size in these reactions: high yields could be obtained for eight-membered rings, low yields were obtained for five-membered rings, and six-membered rings did not open at all. This reactivity trend matched the one that we observed for the unsubstituted cycloolefins (see section 1.2). These trisubstituted cycloolefins exhibited significantly lower reactivity in ROCM than their unsubstituted analogs, especially the five- and six-membered ring cycloolefins. This reactivity loss was likely due to the increased steric demand for the binding of the alkene to the ruthenium catalyst. For a given trisubstituted cycloolefin, the yield decreased with increasing steric bulk of the alkene substituents. For example, changing an alkene substituent from a methyl group to an ethyl group lowered the yield from 33% to 15% (Table 1.3.1, entries 1 and 3, respectively).

The most notable observation, however, regarding the results presented in Table 1.3.1 was that all of these products formed with complete regioselectivity, placing the terminal alkene on the more-substituted side of the diene and the carbonyl moiety on the less-substituted side. The following rationale is our best explanation for this observed regioselectivity. Scheme 1.3.1 shows a possible mechanism for the ROCM of trisubstituted cycloolefins, in which the propagating ruthenium alkylidene is presumed to be a methylidene species. The more stable metallacyclobutane intermediate is generated when the bulky ruthenium center is distal to the more substituted side of the cycloolefin. This favored metallacycle leads to the observed product, in which geminal disubstitution shields the terminal alkene from further metathesis. Snapper *et al* have proposed a similar mechanism to rationalize the regioselective formation of products during the

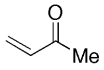
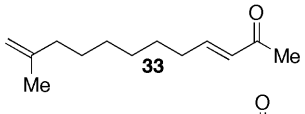
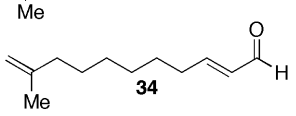
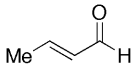
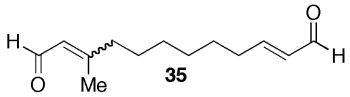
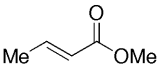
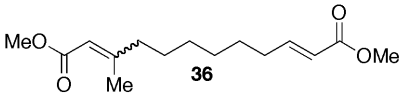
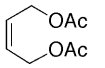
ROCM of unsymmetrical cyclobutenes.[1e,12b,17] Their evidence for this mechanism included an isolated ruthenium complex in which the ruthenium center was distal to the more-substituted end of a ring-opened cyclobutene unit.[25]

Scheme 1.3.1. Proposed mechanism for the ROCM of trisubstituted cycloolefins.



Investigation of the ROCM of 1-methylcyclooctene with non-acrylate cross partners led to some interesting results, which are listed in Table 1.3.2. We observed the same regioselectivity pattern as before when the cross partner possessed a terminal alkene (entries 1 and 2). However, the use of cross partners that contained disubstituted alkenes resulted in a complete loss of regioselectivity, as well as a significant decrease in yield (entries 3-5). It is possible, in these cases, that the extra substituent on the propagating ruthenium alkylidene crowded the resultant metallacycle intermediate enough to diminish the regioselective effects that were observed with the methylidenes. A more-crowded metallacycle would also be less energetically favorable, which may explain the low yields that were observed in these reactions. Our group has previously observed similar behavior with titanium alkylidenes (Scheme 1.3.2).[26] The reaction of a titanium methylidene complex with a norbornene derivative containing a 1-methyl

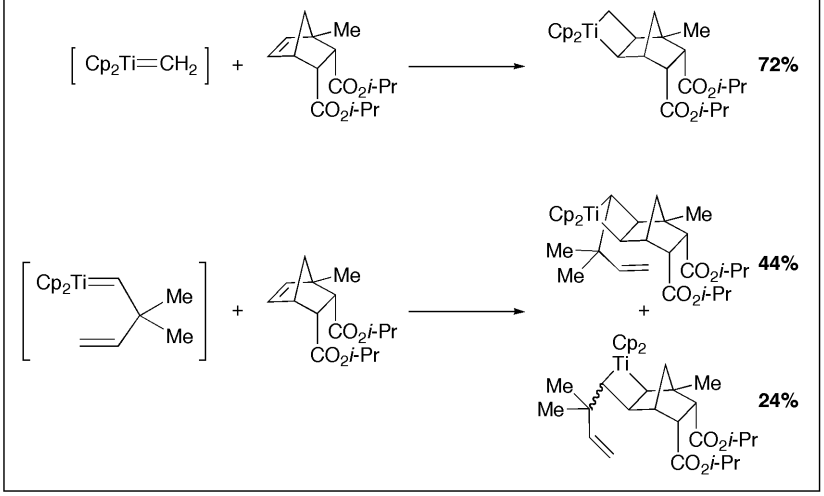
Table 1.3.2. ROCM of 1-methylcyclooctene with other cross partners.[a]

entry	cross partner	product[b]	isolated yield (%)	notebook page
1		 **33**	59	cm2-16
2		 **34**	6	cm2-122
3		 **35**	22[c]	cm1-282
4		 **36**	11	cm1-286
5		complex mixture	------	cm2-120

[a] 0.2 mmol scale, 1-2 equiv cross partner, 5 mol % **2**, CH_2Cl_2, reflux, cycloolefin = 0.02-0.2M. [b] For disubstituted alkenes, *E*:*Z* > 20:1 (^{1}H NMR). [c] For trisubstituted alkene, *E*:*Z* = 1:1 (^{1}H NMR).

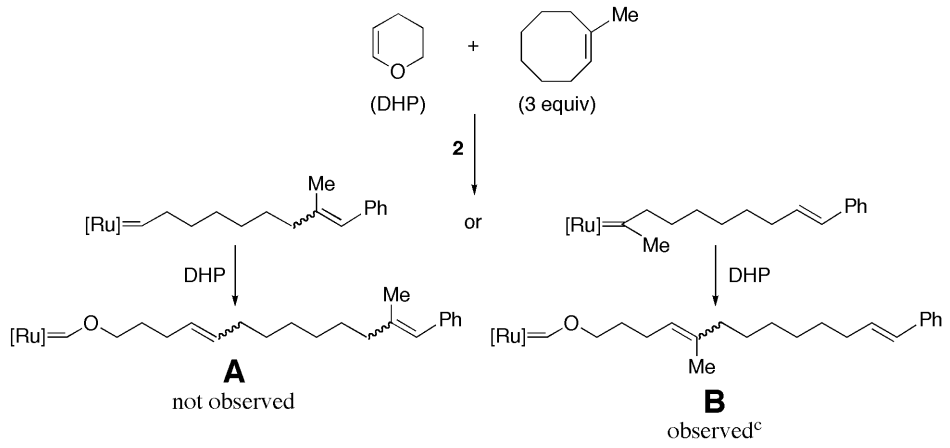
substituent produced a single metallacycle, in which the titanium center was distal to the 1-methyl substituent. However, an analogous reaction, conducted with a substituted titanium alkylidene, resulted in the formation of both possible titanacyclobutane regioisomers.

Scheme 1.3.2. Reactions of titanium alkylidenes with unsymmetrically substituted norbornenes resulted in diminished regioselectivity when a substituted titanium alkylidene was used.[26]



In an attempt to gain further insight into the mechanism of the ROCM of trisubstituted cycloolefins, we conducted a competition experiment with 1-methylcyclooctene, 3,4-dihydro-2H-pyran (DHP), and catalyst **2**, analogous to those described in section 1.2.3. Scheme 1.3.3 illustrates the two possible Fischer carbenes that

Scheme 1.3.3. Interaction of 3,4-dihydro-2H-pyran and 1-methylcyclooctene with catalyst 2.[a,b]

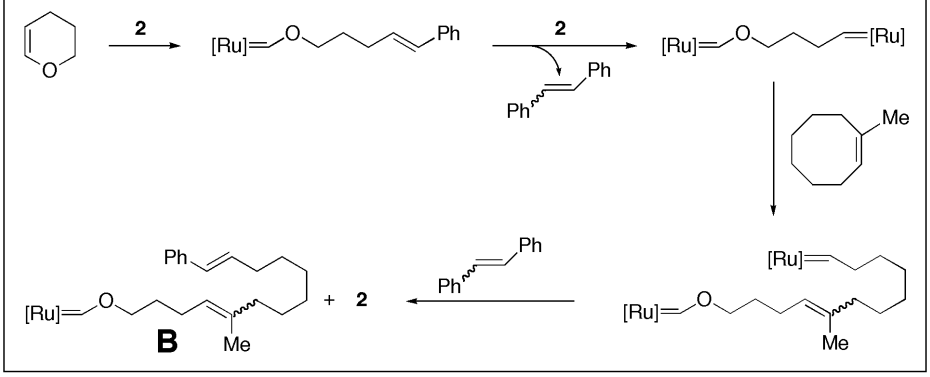


[a] 0.8 mmol scale, 5 mol % **2**, CH_2Cl_2, reflux, 1 h, 3,4-dihydro-2H-pyran = 0.2M. [b] Notebook page: cm2-134. [c] ^{1}H NMR (300 MHz, C_6D_6): δ 14.06 (1H, s), 6.45 (1H, d, *J* = 15.6 Hz), 6.26 (1H, dt, *J* = 15.6, 6.8 Hz), 5.38 (1H, t, *J* = 8.0 Hz). ^{31}P NMR (300 MHz, C_6D_6): δ 31.2.

could result from this experiment, assuming that 1-methylcyclooctene is opened before metathesis with DHP occurs. As shown in Scheme 1.3.3, the only carbene that was observed (via ^{1}H NMR) in these experiments was carbene **B**. This observation was quite surprising, because carbene **B** presumably results from an intermediate ruthenium alkylidene in which the methyl group is adjacent to the ruthenium center (Scheme 1.3.3). This alkylidene is the *opposite* of the favored alkylidene in the mechanism that we proposed for this ROCM reaction in Scheme 1.3.1. However, the formation of carbene **B** could also occur via the pathway shown in Scheme 1.3.4. We were unable to gain further insight into the nature of the reaction pathway that was responsible for the formation of

carbene **B**, and thus the results of this competition experiment neither favor nor disfavor our proposed mechanism.[vi]

Scheme 1.3.4. Alternate reaction pathway for the formation of Fischer carbene B.



1.3.2. Cycloolefins bearing allylic substituents

The regioselective formation of end-differentiated functionalized dienes from cycloolefins is a useful synthetic transformation, and thus the results of our ROCM reactions with the trisubstituted cycloolefins were exciting. However, these reactions were severely limited in scope. They required cross partners that possessed terminal alkenes, and, more importantly, they only resulted in high yields when eight-membered ring cycloolefins were employed. Of the various ring sizes of low-strain cycloolefins, eight-membered rings are the least readily available. Therefore, we endeavored to find a class of substituted cycloolefins that would exhibit efficient regioselective ROCM for five-, six-, and seven-membered ring systems.

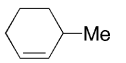
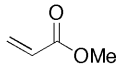
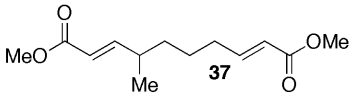
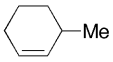
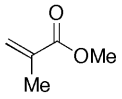
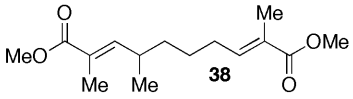
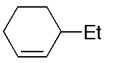
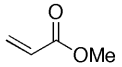
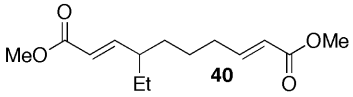
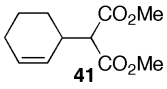
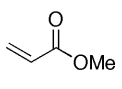
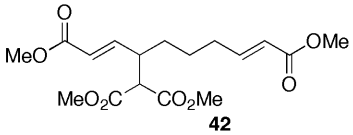
The obvious change in the substitution pattern on the cycloolefins was to shift the ring substituent one carbon unit farther from the alkene, to the allylic position. Allylic

[vi] Another important point is that these competition experiments involved a *benzylidene*. We have already noted that substituted alkylidene species lead to different (and less desirable) results in the ROCM of 1-methylcyclooctene (see Table 1.3.2). The truly relevant competition experiment would involve the use of methylidene **18**, rather than **2**. However, as described in section 1.2.3, this experiment could not be performed.

substitution is known to discourage the CM of terminal alkenes.[27] We thus reasoned that an allylic substituent on a cycloolefin would (a) be close enough to the ruthenium center in the metallacycle intermediate to achieve a regioselective ROCM reaction, (b) shield the adjacent terminal alkene from subsequent metathesis reactions, and (c) be distant enough from the alkene to allow the less-reactive cycloolefins to react efficiently. Thus we synthesized or purchased five-, six-, and seven-membered ring cycloolefins bearing various allylic substituents and investigated their efficiency as substrates for regioselective ROCM.

Six-membered ring cycloolefins bearing allylic substituents were unsuccessful with respect to both reaction yields and regioselectivity. Table 1.3.3 lists the results of the ROCM of these substrates with acrylates. The yields were significantly lower than

Table 1.3.3. ROCM of six-membered ring cycloolefins bearing allylic substituents.[a]

entry	cycloolefin	cross partner	product[b]	isolated yield (%)	notebook page
1			 **37**	17	cm2-92
2[c]			 **38**	15	cm2-59
3	 **39**		 **40**	15	cm2-133
4	 **41**		 **42**	< 6	cm2-95

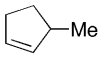
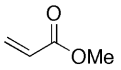
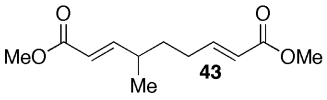
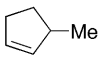
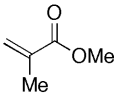
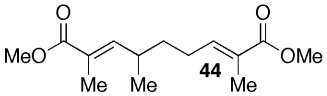
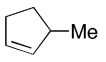
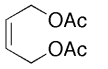
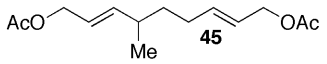
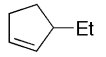
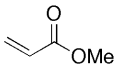
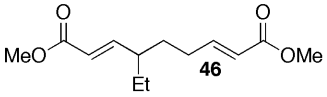
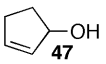
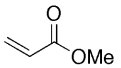
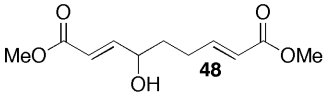
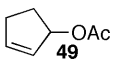
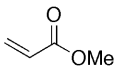
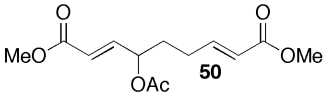
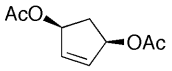
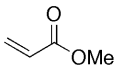
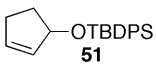
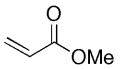
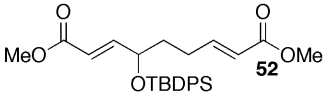
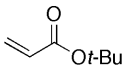
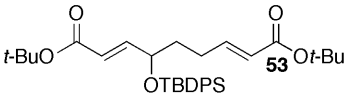
[a] 0.2 mmol scale, 2 equiv cross partner, 5 mol % **2**, CH_2Cl_2, reflux, cycloolefin = 0.2M.
[b] *E*:*Z* > 20:1 (^{1}H NMR). [c] Neat, 50 °C.

those obtained for unsubstituted cyclohexene, and all of the observed products were symmetrically-capped with the carbonyl moiety of the cross partner. Thus it appears that (a) cyclohexene cannot achieve efficient ROCM when it possesses even the smallest of

allylic substituents, and (b) allylic substitution does not allow terminal alkene moieties to be incorporated into the ROCM products of six-membered ring cycloolefins.

Five-membered ring cycloolefins possessing allylic substituents exhibited significantly higher yields than did their six-membered ring analogs. Therefore these substrates were investigated more thoroughly. Table 1.3.4 lists the results obtained during the initial studies. High yields could be obtained when unbranched alkyl

Table 1.3.4. ROCM of five-membered ring cycloolefins bearing allylic substituents.[a]

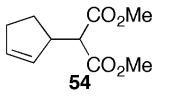
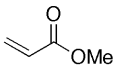
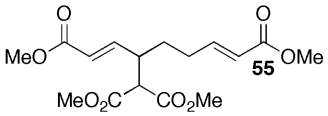
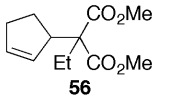
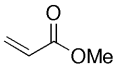
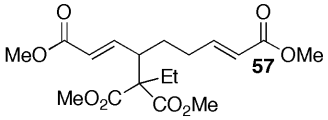
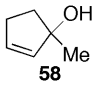
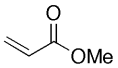
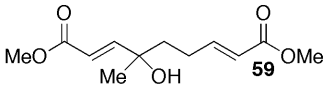
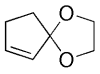
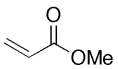
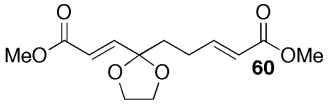
entry	cycloolefin	cross partner	product[b]	isolated yield (%)	notebook page
1			 **43**	82	cm2-38
2[c]			 **44**	31	cm1-145
3			 **45**	27[d]	cm2-46
4			 **46**	75	cm2-110
5	 **47**		 **48**	16	cm2-41
6	 **49**		 **50**	< 5	cm1-161
7			N. R.	------	cm1-113
8	 **51**		 **52**	29	cm2-42
9[e]	**51**		 **53**	< 27	cm1-173

[a] 0.2 mmol scale, 2 equiv cross partner, 5 mol % **2**, CH_2Cl_2, reflux, cycloolefin = 0.2M. [b] For alkenes alpha to carbonyl moieties, *E*:*Z* > 20:1 (^{1}H NMR). [c] Neat, 50 °C. [d] *E*:*Z* = 9:1 (^{1}H NMR). [e] 1 equiv cross partner.

substituents were used (entries 1, 4), but the yields fell when the allylic substituent contained an oxygen atom (entries 5-9). To our surprise, the sole product of these reactions, similar to that observed for the six-membered ring cycloolefins, was the bis-

carbonyl product, even when bulky protecting groups were placed on the allylic alcohol substituent (entries 8-9). As shown in Table 1.3.5, we investigated the use of even more bulky allylic substitution patterns on these substrates. Unfortunately the yields were low in all cases, and, more importantly, still no terminal alkenes were incorporated into the products.

Table 1.3.5. ROCM of five-membered ring cycloolefins bearing more bulky allylic substituents.[a]

entry	cycloolefin	cross partner	product[b]	isolated yield (%)	notebook page
1	 **54**		 **55**	19	cm2-43
2	 **56**		 **57**	15	cm1-239
3	 **58**		 **59**	24	cm1-163
4			 **60**	17	cm2-262

[a] 0.2 mmol scale, 2 equiv cross partner, 5 mol % **2**, CH_2Cl_2, reflux, cycloolefin = 0.2M.
[b] *E*:*Z* > 20:1 (^{1}H NMR).

The ROCM of seven-membered ring cycloolefins bearing allylic substituents resulted in a different product distribution than that observed with the five- and the six-membered ring substrates. Table 1.3.6 lists the initial results of the ROCM of these seven-membered ring substrates with methyl acrylate. Products containing terminal alkenes could be isolated from these reactions as long as sufficiently bulky allylic substituents were employed. These products exhibited the same regioselectivity pattern as that observed with the ROCM of trisubstituted cycloolefins, in which the terminal alkene resided on the more substituted end of the diene. In all cases, the diene capped with two carbonyl moieties was also formed. The amount of end-differentiated product

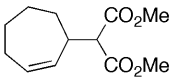
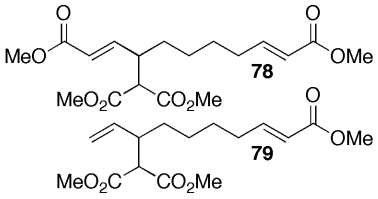
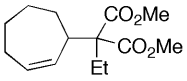
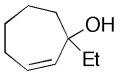
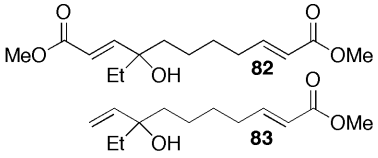
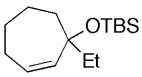
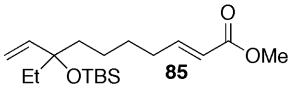
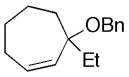
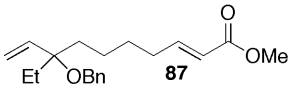
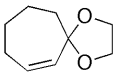
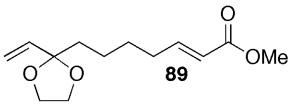
Table 1.3.6. ROCM of seven-membered ring cycloolefins bearing allylic substituents with methyl acrylate.[a]

entry	cycloolefin	product(s)[b]	isolated yield (%)	notebook page
1	**61** (Me)	**62**	39	cm2-77
2	**63** (OH)	**64**	12	cm1-185
3	**65** (OAc)	**66** **67**	12 8	cm1-189
4	**68** (Et)	**69** **70**	41 16	cm2-89
5	**71** (OTBS)	**72** **73**	23 42	cm1-210
6	**74** (OTBDPS)	**75** **76**	26 44	cm1-199

[a] 0.2 mmol scale, 2 equiv methyl acrylate, 5 mol % **2**, CH_2Cl_2, reflux, cycloolefin = 0.1-0.2M.
[b] *E*:*Z*> 20:1 (^{1}H NMR).

that was formed, relative to the amount of bis-carbonyl product formed, increased as the steric bulk of the allylic substituent increased. Table 1.3.7 lists the results of ROCM with cycloolefins possessing even more bulky allylic substitution patterns. Certain substrates resulted in the exclusive formation of the desired end-differentiated diene (entries 4-6). Unfortunately the yields were low in these cases, indicating that the steric bulk required of an allylic substituent for realization of completely regioselective ROCM was so large that it diminished the reactivity of the cycloolefin.

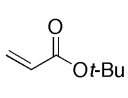
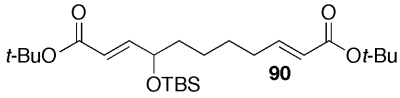
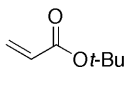
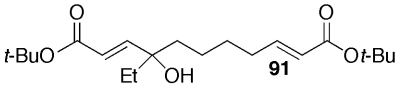
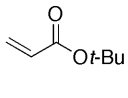
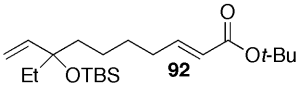
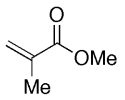
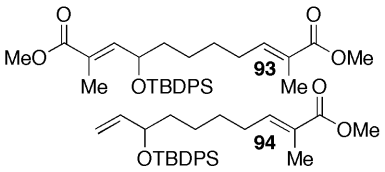
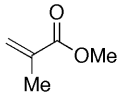
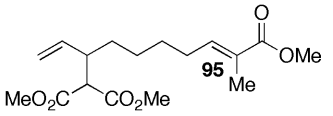
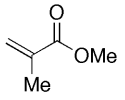
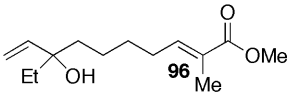
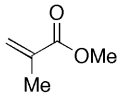
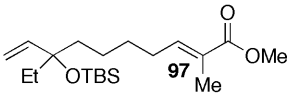
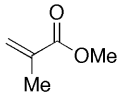
Table 1.3.7. ROCM of seven-membered ring cycloolefins bearing more bulky allylic substituents with methyl acrylate.[a]

entry	cycloolefin	product(s)[b]	isolated yield (%)	notebook page
1[c]	**77** 	 **78** **79**	21 35	cm2-238
2	**80** 	little or no reaction	------	cm1-251
3	**81** 	 **82** **83**	70 10	cm2-178
4	**84** 	 **85**	26	cm2-244
5	**86** 	 **87**	15	cm2-252
6	**88** 	 **89**	35	cm3-11

[a] 0.2 mmol scale, 2 equiv methyl acrylate, 5 mol % **2**, CH_2Cl_2, reflux, cycloolefin = 0.04-0.2M.
[b] *E*:*Z* > 20:1 (^{1}H NMR). [c] Also isolated 10% yield of a dimerized product.

We also explored the use of other acrylates as cross partners in the ROCM of these seven-membered ring cycloolefins bearing allylic substituents. Table 1.3.8 lists the results of these reactions. The use of *t*-butyl acrylate led to the exclusive formation of the bis-carbonyl products (entries 1-2) unless very bulky allylic substituents were employed (entry 3), in which case the result was similar to that obtained with the use of methyl acrylate (Table 1.3.7, entry 4). The use of methyl methacrylate, a more bulky cross partner, generally led to the exclusive formation of the end-differentiated product (Table 1.3.8, entries 5-7), but the yields were again low in these cases.

Table 1.3.8. ROCM of seven-membered ring cycloolefins bearing allylic substituents with other acrylates.[a]

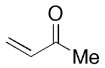
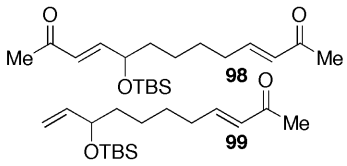
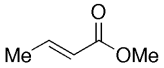
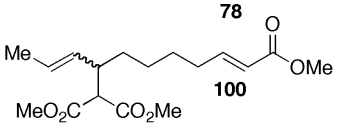
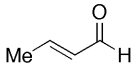
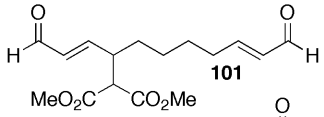
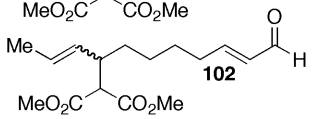
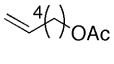
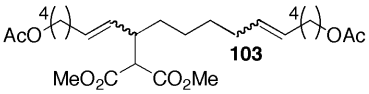
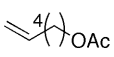
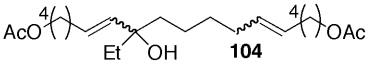
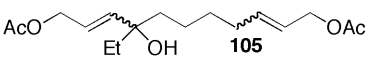
entry	cycloolefin	acrylate	product(s)[b]	isolated yield (%)	notebook page
1	**71**		 **90**	31	cm1-212
2	**81**		 **91**	61	cm2-183
3	**84**		 **92**	28	cm2-247
4[c]	**74**		 **93** **94**	18 61	cm2-166
5[c]	**77**		 **95**	30	cm2-165
6[c]	**81**		 **96**	40	cm2-179
7[c]	**84**		 **97**	14	cm2-245
8[c]	**86**		N. R.	------	cm2-251

[a] 0.2 mmol scale, 2 equiv acrylate, 5 mol % **2**, CH_2Cl_2, reflux, cycloolefin = 0.04-0.2M.
[b] *E*:*Z* > 20:1 (^{1}H NMR). [c] Neat, 50 °C.

Finally, we investigated the use of non-acrylate cross partners in the ROCM of these seven-membered ring cycloolefins. As shown in Table 1.3.9, these reactions generally resulted in the same product mixtures as previously observed. However, side product formation, usually of oligomeric species, was more prevalent in these reactions, which may account for the lower yields that were usually observed. We presume that products containing terminal alkenes were not isolated from the ROCM reactions involving 5-hexenyl acetate (entries 4-5) because this cross partner underwent

homodimerization, thus releasing all of the terminal alkenes as ethylene, prior to participating in the ROCM reaction.

Table 1.3.9. ROCM of seven-membered ring cycloolefins bearing allylic substituents with other cross partners.[a]

entry	cycloolefin	cross partner	product(s)[b]	isolated yield (%)	notebook page
1	**71**		 **98** **99**	49 19	cm1-219
2	**77**		**78**  **100**	< 25 18	cm2-144
3	**77**		 **101**  **102**	18 < 30	cm2-148
4	**77**		 **103**	20	cm2-163
5	**81**		 **104**	20	cm2-241
6	**81**		 **105**	59	cm2-240

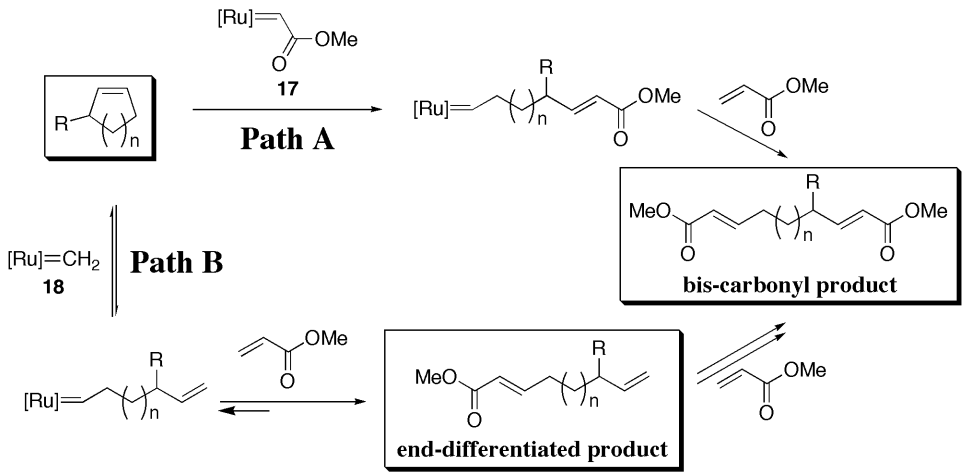
[a] 0.2 mmol scale, 2 equiv cross partner, 5 mol % **2**, CH_2Cl_2, reflux, cycloolefin = 0.2M. [b] For alkenes alpha to carbonyl moieties, *E*:*Z* > 20:1 (^{1}H NMR).

1.3.3. Mechanism

The product distribution for the ROCM of five- and six-membered ring cycloolefins bearing allylic substituents was inherently different from that of the seven-membered ring cycloolefins. The former always formed the bis-carbonyl product and never formed the end-differentiated product, while the latter could form either product, depending upon the bulk of the allylic substituent(s). We propose the model shown in

Scheme 1.3.5 to explain this observed difference in product distribution. The mechanisms illustrated in this model are analogous to those that we proposed for the ROCM of unsubstituted cycloolefins (see section 1.2.2). In both mechanisms, it is assumed that the ruthenium species attaches to the less-hindered side of the opened cycloolefin, as described in section 1.3.1. Two different explanations for the difference in reactivity of five- and six-membered ring cycloolefins versus the seven-membered ring substrates can be derived from the reaction pathways illustrated in Scheme 1.3.5.

Scheme 1.3.5. Possible mechanisms for the ROCM of cycloolefins bearing allylic substituents with methyl acrylate.



One explanation associates the product distribution pattern with the identity of the ruthenium alkylidene that is responsible for the initial ring-opening event, either ester carbene **17** or methylidene **18**. Ring-opening via **17** (Scheme 1.3.5, Path A) can only lead to the formation of the bis-carbonyl product, but ring-opening by **18** (Path B) can lead to the formation of either product. We have already proposed that five- and six-membered ring cycloolefins can only be efficiently opened by alkylidene **17**, whereas seven-membered ring cycloolefins can be opened by either **17** or **18** (see section 1.2.2). If this hypothesis is correct, then five- and six-membered ring cycloolefins would only be

able to form the bis-carbonyl product, but seven-membered ring cycloolefins could form either product, which is exactly what we observed in our ROCM studies.

The alternate explanation assumes that alkylidene **17** is too unstable to participate is these ROCM reactions.[20] Therefore all cycloolefins are opened by methylidene **18** (Scheme 1.3.5, Path B). In this situation, each cycloolefin would be expected to form both of the possible ROCM products, which is not what we observe. However, if the equilibrium mixture of the five- and six-membered ring cycloolefins more strongly favors the ring-closed form, relative to that of seven-membered ring cycloolefins, as discussed in section 1.2.2, then subsequent ring-closure of the end-differentiated product derived from five- and six-membered ring substrates may be too favorable to allow these products to be isolated. Thus these products can only be irreversibly trapped if they are bis-capped by the α,β-unsaturated carbonyl moieties. The end-differentiated products derived from seven-membered ring cycloolefins, on the other hand, will not undergo subsequent ring closure as readily, and thus they can be isolated as long as the allylic substituent is bulky enough to prevent subsequent CM with another equivalent of the acrylate.[vii] It should be noted that both of these explanations are merely proposals, and further studies are needed before conclusive statements can be made regarding the mechanisms of these ROCM reactions.

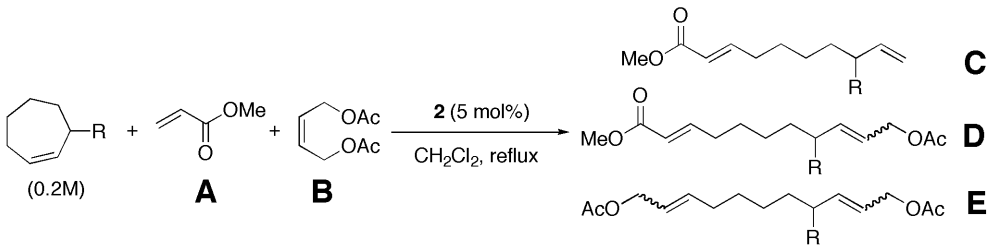
1.3.4. Three-component reactions

We briefly explored the efficacy of three-component ROCM reactions of cycloheptene rings bearing allylic substituents, similar to those described in section 1.2.4.

[vii] Product **76** was resubjected to metathesis with methyl acrylate (2 equiv) and 5 mol% **2**. Roughly one-third of **76** converted into **75** (notebook page: cm1-227). This result is consistent with the **76**:**75** ratio of ca. 2:1 that was observed in the original ROCM experiment (Table 1.3.6, entry 6).

The two cross partners employed in these reactions were methyl acrylate and *Z*-1,4-diacetoxy-*cis*-2-butene. We anticipated that the product selectivity in these reactions could be controlled by adjusting the relative stoichiometry between these two cross partners. Table 1.3.10 lists the results of these reactions. Three different products were observed. The reactions were regioselective because the carbonyl moiety always resided on the less-substituted side of the diene product. Unfortunately it was not possible to tune the reaction conditions such that a single ring-opened product could be obtained. In agreement with the results discussed in section 1.2, these results indicated that multiple pathways were operative in these ROCM reactions.

Table 1.3.10. Three-component ROCM reactions of seven-membered ring cycloolefins bearing allylic substituents.



entry	R	equiv **A**	equiv **B**	isolated yield (**C**)	isolated yield (**D**)	isolated yield (**E**)	notebook page
1	OTBDPS	2	2	20	40	20	cm1-243
2	OTBDPS	2	1.2	10	20	5	cm1-234
3[a]	OTBDPS	2	4	------	35	20	cm1-246
4[b]	OTBDPS	10	1.2	30	30	------	cm1-235
5	$CH(CO_2Me)_2$	2	2	------	30	15	cm1-232
6	$CH(CO_2Me)_2$	4	2	------	35	5	cm1-233
7	$CH(CO_2Me)_2$	4	1.2	20	40	------	cm1-240
8	$CH(CO_2Me)_2$	10	2	------	20	------	cm1-241

[a] 10 mol % **2**. [b] 8 mol % **2**.

1.3.5. Summary and conclusions

We have explored the ROCM, via catalyst **2**, of trisubstituted five-, six-, and eight-membered ring cycloolefins, as well as five-, six-, and seven-membered ring cycloolefins bearing various allylic substituents. Acrylates were the most efficient cross partners in all of these reactions. Two different diene products resulted from these reactions: a bis-carbonyl-capped diene and an end-differentiated diene. The end-differentiated dienes formed regioselectively: the carbonyl moiety resided on the less-hindered end, and the terminal alkene was located on the more-hindered end. Both the yield and the product selectivity were highly dependent upon the size of both the ring itself and its substituent(s).

While these ROCM reactions of substituted cycloolefins hold the potential to be of great use to synthetic chemists, the narrow substrate scope for efficient reactions is a severe limitation. At the conclusion of our studies, we find that only the trisubstituted eight-membered ring cycloolefins undergo ROCM in both high yield and high product selectivity.[24] All other classes of cycloolefins explored herein fall short in one or both of these two reaction properties. Certain substrates, namely the seven-membered ring cycloolefins bearing bulky allylic substituents and the smaller ring sizes of the trisubstituted cycloolefins, exhibit some promise with respect to product selectivity. Efficient ROCM of these substrates may become feasible as new metathesis catalysts, which are more tolerant of sterically bulky alkenes, are developed.

Finally, the inherent difference in both reactivity and product selectivity that we have observed for the ROCM of five- and six-membered ring cycloolefins versus seven- and eight-membered ring cycloolefins, with or without substitution, raises some

interesting questions regarding the mechanism of these reactions. Further studies in this area are needed, especially studies that will ascertain (a) the identity of the ruthenium alkylidene that is responsible for the initial ring-opening event, and (b) the extent to which ester carbene species such as **17** participate in these reactions. As understanding of the mechanism of these reactions increases, it may be possible to develop conditions that will improve the yields and the product selectivities of these potentially useful regioselective ROCM reactions.

1.4. Experimental Section

1.4.1. General experimental procedures

Ring-opening cross-metathesis. A solution of **2** (obtained from Materia) and dry dichloromethane was added via cannula to a flame-dried round-bottomed flask equipped with a reflux condenser and kept under an argon atmosphere. The cycloolefin and the cross partner were added via syringe. The brick-red solution was placed in a 45-50 °C oil bath (unless temperature otherwise noted) and allowed to stir, under an argon atmosphere, overnight. The mixture was then concentrated *in vacuo*, and the product was purified by silica gel chromatography.

1.4.2. Specific experimental procedures and characterization data

(2*E*,7*E*)-dimethyl nona-2,7-dienedioate (**3**).[23] Followed general procedure, with 18 μL (0.2 mmol) cyclopentene, 54 μL (0.6 mmol) methyl acrylate, 8 mg (0.009 mmol) **2**, and 1 mL CH_2Cl_2. Purified via silica gel chromatography (8:2 hexanes:ethyl acetate) to obtain 30 mg of **3** as an oil (71% yield).

(2*E*,8*E*)-dimethyl deca-2,8-dienedioate (**4**).[23] Followed general procedure, with 20 μL (0.2 mmol) cyclohexene, 54 μL (0.6 mmol) methyl acrylate, 8 mg (0.009 mmol) **2**, and 1 mL CH_2Cl_2. Purified via silica gel chromatography (8:2 hexanes:ethyl acetate) to obtain 20 mg of **4** as an oil (44% yield).

(2*E*,9*E*)-dimethyl undeca-2,9-dienedioate (**5**).[23] Followed general procedure, with 24 μL (0.21 mmol) cycloheptene, 36 μL (0.4 mmol) methyl acrylate, 8 mg (0.009 mmol) **2**, and 1 mL CH_2Cl_2. Purified via silica gel chromatography (8:2 hexanes:ethyl acetate) to obtain 38 mg of **5** as an oil (75% yield).

Dodeca-2,10-dienedioic acid dimethyl ester (**6**). Followed general procedure, with 26 μL (0.2 mmol) cyclooctene, 54 μL (0.6 mmol) methyl acrylate, 8 mg (0.009 mmol) **2**, and 2 mL CH_2Cl_2. Purified via silica gel chromatography (8:2 hexanes:ethyl acetate) to obtain 48 mg of **6** as an oil (95% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 6.95 (2H, dt, *J* = 15.6, 6.9 Hz), 5.80 (2H, dt, *J* = 15.9, 1.6 Hz), 3.72 (6H, s), 2.19 (4H, dtd, *J* = 7.2, 7.2, 1.5 Hz), 1.4 (8H, m). ^{13}C NMR (300 MHz, $CDCl_3$, ppm): δ 167.1, 149.6, 121.0, 51.6, 32.4, 29.1, 28.1. HRMS (DEI) calcd. for $C_{14}H_{22}O_4$ + H: 255.1596, found: 255.1592 (UC, Riverside).

Nona-2,7-dienedioic acid di-*tert*-butyl ester (**7**). Followed general procedure, with 18 μL (0.2 mmol) cyclopentene, 88 μL (0.6 mmol) *t*-butyl acrylate, 8 mg (0.009 mmol) **2**, and 1 mL CH_2Cl_2. Purified via silica gel chromatography (8:2 hexanes:ethyl acetate) to obtain

47 mg of **7** as an oil (80% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 6.8 (2H, dt), 5.7 (2H, dt), 2.2 (4H, dt), 1.6 (2H, m), 1.45 (18H, s).

Deca-2,8-dienedioic acid di-*tert*-butyl ester (**8**). Followed general procedure, with 20 μL (0.2 mmol) cyclohexene, 88 μL (0.6 mmol) *t*-butyl acrylate, 8 mg (0.009 mmol) **2**, and 1 mL CH_2Cl_2. Purified via silica gel chromatography (9:1 hexanes:ethyl acetate) to obtain 18 mg of **8** as an oil (40% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 6.8 (2H, dt), 5.7 (2H, d), 2.2 (4H, m), 1.45 (4H, m), 1.45 (18H, s).

2,8-Dimethyl-nona-2,7-dienedioic acid dimethyl ester (**9**). Followed general procedure, with 18 μL (0.2 mmol) cyclopentene, 1 mL (9.3 mmol) methyl methacrylate, and 8 mg (0.009 mmol) **2**. Purified via silica gel chromatography (8:2 hexanes:ethyl acetate) to obtain 18 mg of **9** as an oil (37% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 6.73 (2H, td, J = 7.4, 1.4 Hz), 3.73 (6H, s), 2.20 (4H, dt, J = 7.5, 7.5 Hz), 1.83 (6H, m), 1.61 (2H, m).

2,9-Dimethyl-deca-2,8-dienedioic acid dimethyl ester (**10**). Followed general procedure, with 20 μL (0.2 mmol) cyclohexene, 1 mL (9.3 mmol) methyl methacrylate, and 8 mg (0.009 mmol) **2**. Purified via silica gel chromatography (9:1 hexanes:ethyl acetate) to obtain 13 mg of **10** as an oil (26% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 6.75 (2H, t), 3.75 (6H, s), 2.2 (4H, m), 1.8 (6H, s), 1.5 (4H, m).

Nona-2,7-dienedial (**11**). Followed general procedure, with 70 μL (0.8 mmol) cyclopentene, 160 μL (1.94 mmol) crotonaldehyde, 37 mg (0.04 mmol) **2**, and 5.5 mL CH_2Cl_2. Purified via silica gel chromatography (7:3 hexanes:ethyl acetate) to obtain 46 mg of **11** as an oil (38% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 9.48 (2H, dd, *J* = 8.0, 0.8 Hz), 7.02 (carboxylic acid, 0.6H, dt), 6.82 (2H, dt, *J* = 15.6, 6.8 Hz), 6.12 (2H, dd, *J* = 15.3, 7.8 Hz), 5.83 (carboxylic acid, 0.6H, dt), 2.38 (4H, dt), 2.28 (carboxylic acid, 1.2H, dt), 1.73 (2.6H, m). ^{13}C NMR (300 MHz, $CDCl_3$, ppm): δ 193.8, 157.0, 133.4, 31.8, 25.8.

Acetic acid 15-acetoxy-pentadeca-5,10-dienyl ester (**12**). Followed general procedure, with 18 μL (0.2 mmol) cyclopentene, 100 μL (0.6 mmol) 5-hexenyl acetate, 8 mg (0.009 mmol) **2**, and 1 mL CH_2Cl_2. Purified via silica gel chromatography (8:2 hexanes:ethyl acetate) to obtain 9 mg of **12** (contaminated with minor impurities) as an oil (< 14% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 5.4 (4H, m), 4.1 (4H, t), 2.0 (8H, m), 2.0 (6H, s), 1.6 (10H, m).

Acetic acid 9-acetoxy-nona-2,7-dienyl ester (**13**). Followed general procedure, with 18 μL (0.2 mmol) cyclopentene, 94 μL (0.6 mmol) (*Z*)-but-2-ene-1,4-diyl diacetate, 8 mg (0.009 mmol) **2**, and 1 mL CH_2Cl_2. Purified via silica gel chromatography (8:2 hexanes:ethyl acetate) to obtain 19 mg of **13** as an oil (40% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 5.76 (2H, dt, *J* = 15.3, 6.8 Hz), 5.57 (2H, m), 4.61 (*Z*-isomer, 0.5H, d, *J* = 6.3 Hz), 4.51 (*E*-isomer, 3.5H, dd, *J* = 6.3, 0.9 Hz), 2.1 (4H, m), 2.07 (6H, s), 1.50 (2H,

quint, 7.4 Hz). ^{13}CNMR (300 MHz, $CDCl_3$, ppm): δ 170.9, 136.0, 124.3, 65.4, 31.9, 28.3, 21.3.

Acetic acid 10-acetoxy-deca-2,8-dienyl ester (**14**). Followed general procedure, with 1 mL (9.9 mmol) cyclohexene, 32 μL (0.2 mmol) (*Z*)-but-2-ene-1,4-diyl diacetate, and 8 mg (0.009 mmol) **2**. Purified via silica gel chromatography (8:2 hexanes:ethyl acetate) to obtain 6 mg of **14** as an oil (12% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 5.75 (2H, dt), 5.55 (2H, dt), 4.5 (4H, d), 2.05 (4H, m), 2.05 (6H, s), 1.4 (4H, m).

Acetic acid 11-acetoxy-undeca-2,9-dienyl ester (**15**). Followed general procedure, with 24 μL (0.21 mmol) cycloheptene, 94 μL (0.6 mmol) (*Z*)-but-2-ene-1,4-diyl diacetate, 8 mg (0.009 mmol) **2**, and 1 mL CH_2Cl_2. Purified via silica gel chromatography (8:2 hexanes:ethyl acetate) to obtain 46 mg of **15** as an oil (82% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 5.75 (2H, dt), 5.55 (2H, dt), 4.6 (*Z*-isomer, 0.6H, d), 4.5 (*E*-isomer, 3.4H, d), 2.05 (6H, dt), 2.05 (6H, s), 1.35 (6H, m).

Acetic acid 12-acetoxy-dodeca-2,10-dienyl ester (**16**). Followed general procedure, with 26 μL (0.2 mmol) cyclooctene, 94 μL (0.6 mmol) (*Z*)-but-2-ene-1,4-diyl diacetate, 8 mg (0.009 mmol) **2**, and 1 mL CH_2Cl_2. Purified via silica gel chromatography (8:2 hexanes:ethyl acetate) to obtain 41 mg of **16** as an oil (73% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 5.76 (2H, dt, J = 15.3, 6.8 Hz), 5.5 (2H, m), 4.61 (*Z*-isomer, 0.4H, d, J = 6.6 Hz), 4.50 (*E*-isomer, 3.6H, d, J = 5.4 Hz), 2.05 (6H, s), 2.04 (4H, m), 1.3 (8H, m).

^{13}C NMR (300 MHz, $CDCl_3$, ppm): δ 170.9, 136.7 (*E*-isomer), 135.4 (*Z*-isomer), 123.8 (*E*-isomer), 123.4 (*Z*-isomer), 65.5 (*E*-isomer), 60.6 (*Z*-isomer), 32.5, 29.2, 29.0, 21.3.

Nona-2,7-dienedioic acid *tert*-butyl ester methyl ester (**20**). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 6.95 (1H, dt, *J* = 15.3, 7.0 Hz), 6.82 (1H, dt, *J* = 15.3, 6.8 Hz), 5.84 (1H, dt, *J* = 15.9, 1.5 Hz), 5.75 (1H, dt, *J* = 16.2, 1.3 Hz), 3.74 (3H, s), 2.23 (4H, m), 1.64 (2H, m), 1.49 (9H, s).

Acetic acid 10-acetoxy-dec-5-enyl ester (**21**). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 5.40 (2H, m), 4.06 (4H, t, *J* = 6.6 Hz), 2.06 (6H, s), 2.03 (4H, m), 1.63 (4H, m), 1.42 (4H, m).

7-Acetoxy-hept-2-enoic acid methyl ester (**22**). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 6.94 (1H, dt, *J* = 15.9, 6.8 Hz), 5.83 (1H, dt, *J* = 15.6, 1.5 Hz), 4.06 (2H, t, *J* = 6.6 Hz), 3.72 (3H, s), 2.24 (2H, dtd, *J* = 7.1, 7.1, 1.5 Hz), 2.05 (3H, s), 1.65 (2H, m), 1.55 (2H, m). ^{13}C NMR (300 MHz, $CDCl_3$, ppm): δ 171.2, 167.1, 148.8, 121.5, 64.3, 51.7, 32.0, 28.3, 24.7, 21.3.

10-Acetoxy-deca-2,8-dienoic acid *tert*-butyl ester (**24**). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 6.85 (1H, dt), 5.75 (2H, m), 5.55 (1H, dt), 4.5 (2H, d), 2.15 (4H, dt), 2.05 (3H, s), 1.45 (9H, s), 1.4 (4H, m).

7-Methyl-octa-2,7-dienoic acid methyl ester (**25**). Followed general procedure, with 134 μL (1.23 mmol) 1-methylcyclopentene, 36 μL (0.4 mmol) methyl acrylate, 17 mg (0.02

mmol) **2**, and 1 mL CH_2Cl_2. Purified via silica gel chromatography (19:1 hexanes:ethyl acetate) to obtain 22.2 mg of **25** as an oil (33% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 6.98 (1H, dt, *J* = 15.6, 6.9 Hz), 5.83 (1H, dt, *J* = 15.6, 1.5 Hz), 4.73 (1H, m), 4.68 (1H, m), 3.73 (3H, s), 2.21 (2H, dtd, *J* = 7.3, 7.3, 1.6 Hz), 2.04 (2H, t, *J* = 7.7 Hz), 1.71 (3H, s), 1.6 (2H, m). ^{13}CNMR (300 MHz, $CDCl_3$, ppm): δ 167.0, 149.3, 145.0, 121.0, 110.3, 51.5, 37.1, 31.7, 25.9, 22.4. HRMS (DCI) calcd. for $C_{10}H_{16}O_2$ + H: 169.1229, found: 169.1231 (UC, Riverside).

7-Methyl-octa-2,7-dienoic acid *tert*-butyl ester (**26**). Followed general procedure, with 134 μL (1.23 mmol) 1-methylcyclopentene, 60 μL (0.41 mmol) *t*-butyl acrylate, 17 mg (0.02 mmol) **2**, and 1 mL CH_2Cl_2. Purified via silica gel chromatography (19:1 hexanes:ethyl acetate) to obtain 37 mg of **26** as an oil (43% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 6.86 (1H, dt, *J* = 15.6, 7.0 Hz), 5.75 (1H, dt, *J* = 15.6, 1.4 Hz), 4.72 (1H, m), 4.68 (1H, m), 2.17 (2H, dtd, *J* = 7.3, 7.3, 1.5 Hz), 2.04 (2H, t, *J* = 7.5 Hz), 1.71 (3H, s), 1.6 (2H, m), 1.49 (9H, s). ^{13}C NMR (300 MHz, $CDCl_3$, ppm): δ 166.0, 147.6, 145.1, 123.0, 110.2, 80.0, 37.2, 31.6, 28.2, 26.0, 22.4.

7-Ethyl-octa-2,7-dienoic acid methyl ester (**27**). Followed general procedure, with 140 μL (1.2 mmol) 1-ethylcyclopentene, 36 μL (0.4 mmol) methyl acrylate, 17 mg (0.02 mmol) **2**, and 2 mL CH_2Cl_2. Purified via silica gel chromatography (8:2 hexanes:ethyl acetate) to obtain 11 mg of **27** as an oil (15% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 6.98 (1H, dt, *J* = 15.9, 6.8 Hz), 5.83 (1H, dt, *J* = 15.3, 1.7 Hz), 4.73 (1H, m), 4.70 (1H, m), 3.73 (3H, s), 2.21 (2H, dt, *J* = 7.4, 7.4 Hz), 2.05 (4H, m), 1.6 (2H, m), 1.03 (3H, t, *J*

= 7.4 Hz). ^{13}C NMR (300 MHz, $CDCl_3$, ppm): δ 167.0, 150.5, 149.3, 120.9, 108.0, 51.5, 35.6, 31.8, 28.7, 26.1, 12.4.

10-Methyl-undeca-2,10-dienoic acid methyl ester (**28**). Followed general procedure, with 30 μL (0.2 mmol) 1-methylcyclooctene, 36 μL (0.4 mmol) methyl acrylate, 8 mg (0.009 mmol) **2**, and 5 mL CH_2Cl_2. Purified via silica gel chromatography (9:1 hexanes:ethyl acetate) to obtain 34 mg of **28** as a golden yellow oil (81% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 6.96 (1H, dt, *J* = 15.6, 6.9 Hz), 5.81 (1H, dt, *J* = 15.9, 1.5 Hz), 4.67 (1H, m), 4.64 (1H, m), 3.71 (3H, s), 2.19 (2H, dtd, *J* = 7.2, 7.2, 1.5 Hz), 1.98 (2H, t, *J* = 7.5 Hz), 1.69 (3H, s), 1.4 (8H, m). ^{13}C NMR (300 MHz, $CDCl_3$, ppm): δ 167.0, 150.0, 145.9, 120.7, 109.6, 51.4, 37.8, 32.2, 29.1, 28.0, 27.5, 22.4. HRMS (DCI) calcd. for $C_{13}H_{22}O_2$ + H: 211.1698, found: 211.1693 (UC, Riverside).

10-Methyl-undeca-2,10-dienoic acid *tert*-butyl ester (**29**). Followed general procedure, with 30 μL (0.2 mmol) 1-methylcyclooctene, 60 μL (0.41 mmol) *t*-butyl acrylate, 8 mg (0.009 mmol) **2**, and 5 mL CH_2Cl_2. Purified via silica gel chromatography (9:1 hexanes:ethyl acetate) to obtain 50 mg of **29** as an oil (99% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 6.84 (1H, dt, *J* = 15.6, 7.2 Hz), 5.71 (1H, dt, *J* = 15.6, 1.7 Hz), 4.67 (1H, m), 4.64 (1H, m), 2.15 (2H, dt, *J* = 6.8, 6.8 Hz), 1.98 (2H, t, *J* = 7.7 Hz), 1.69 (3H, s), 1.47 (9H, s), 1.4 (8H, m). ^{13}C NMR (300 MHz, $CDCl_3$, ppm): δ 166.0, 148.0, 146.0, 122.8, 109.6, 79.9, 37.8, 32.1, 29.09, 29.08, 28.2, 28.1, 27.5, 22.4. HRMS (EI) calcd. for $C_{16}H_{28}O_2$: 252.2089, found: 252.2094 (UCLA).

2,10-Dimethyl-undeca-2,10-dienoic acid methyl ester (**30**). Followed general procedure, with 30 μL (0.2 mmol) 1-methylcyclooctene, 1 mL (9.3 mmol) methyl methacrylate, and 8 mg (0.009 mmol) **2**. Purified via silica gel chromatography (9:1 hexanes:ethyl acetate) to obtain 30 mg of **30** as an orange oil (67% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 6.76 (1H, td, *J* = 7.6, 1.3 Hz), 4.68 (1H, br), 4.65 (1H, br), 3.73 (3H, s), 2.17 (2H, dt, *J* = 7.0, 7.0 Hz), 2.00 (2H, t, *J* = 7.4 Hz), 1.83 (3H, s), 1.71 (3H, s), 1.4 (8H, m). ^{13}C NMR (300 MHz, $CDCl_3$, ppm): δ 168.6, 146.0, 142.6, 127.3, 109.5, 51.7, 37.8, 29.3, 29.1, 28.7, 28.6, 27.5, 22.4, 12.5. HRMS (DEI) calcd. for $C_{14}H_{24}O_2$ + H: 225.1855, found: 225.1859 (UC, Riverside).

6,10-Dimethyl-undeca-2,6,10-trienoic acid methyl ester (**31**). Followed general procedure, with 96 μL (0.61 mmol) 1,5-dimethylcyclooctadiene, 18 μL (0.2 mmol) methyl acrylate, 8 mg (0.009 mmol) **2**, and 20 mL CH_2Cl_2. Purified via silica gel chromatography (19:1 hexanes:ethyl acetate) to obtain 29 mg of **31** as an oil (66% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 6.96 (1H, dt, *J* = 15.6, 6.8 Hz), 5.83 (1H, dt, *J* = 15.6, 1.5 Hz), 5.17 (1H, t, *J* = 6.9 Hz), 4.70 (1H, m), 4.67 (1H, m), 3.72 (3H, s), 2.2 (8H, m), 1.72 (3H, s), 1.69 (3H, m). ^{13}C NMR (300 MHz, $CDCl_3$, ppm): δ 166.9, 149.0, 145.5, 133.5, 125.8, 120.9, 109.9, 51.4, 37.9, 30.7, 30.4, 26.1, 23.3, 22.6. HRMS (PCI) calcd. for $C_{14}H_{22}O_2$ + H: 223.1698, found: 223.1698 (UCLA).

6,10-Dimethyl-undeca-2,6,10-trienoic acid *tert*-butyl ester (**32**). Followed general procedure, with 96 μL (0.61 mmol) 1,5-dimethylcyclooctadiene, 30 μL (0.2 mmol) *t*-butyl acrylate, 8 mg (0.009 mmol) **2**, and 20 mL CH_2Cl_2. Purified via silica gel

chromatography (19:1 hexanes:ethyl acetate) to obtain 37 mg of **32** as an oil (70% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 6.85 (1H, dt, *J* = 15.9, 6.6 Hz), 5.75 (1H, dt, *J* = 15.3, 1.5 Hz), 5.17 (1H, t, *J* = 6.8 Hz), 4.71 (1H, m), 4.67 (1H, m), 2.1 (8H, m), 1.72 (3H, s), 1.69 (3H, d, *J* = 0.9 Hz), 1.48 (9H, s). ^{13}C NMR (300 MHz, $CDCl_3$, ppm): δ 165.8, 147.3, 145.5, 133.7, 125.7, 123.0, 109.9, 80.0, 38.0, 30.6, 30.5, 28.2, 26.1, 23.3, 22.6. HRMS (EI) calcd. for $C_{17}H_{29}O_2$: 264.2089, found: 264.2084 (UCLA).

(*E*)-11-methyldodeca-3,11-dien-2-one (**33**). Followed general procedure, with 30 μL (0.2 mmol) 1-methylcyclooctene, 18 μL (0.22 mmol) methyl vinyl ketone, 8 mg (0.009 mmol) **2**, and 10 mL CH_2Cl_2. Purified via silica gel chromatography (8:2 hexanes:ethyl acetate) to obtain 23 mg of **33** as a yellow-orange oil (59% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 6.80 (1H, dt, *J* = 15.6, 6.9 Hz), 6.06 (1H, d, *J* = 16.2 Hz), 4.68 (1H, m), 4.65 (1H, m), 2.24 (3H, s), 2.2 (2H, m), 2.00 (2H, t, *J* = 7.4 Hz), 1.70 (3H, s), 1.4 (8H, m). ^{13}C NMR (300 MHz, $CDCl_3$, ppm): δ 198.5, 148.4, 145.9, 131.2, 109.6, 37.8, 32.5, 29.11, 29.05, 28.1, 27.5, 26.9, 22.4. HRMS (EI) calcd. for $C_{13}H_{22}O$: 194.1671, found: 194.1670 (UCLA).

(*E*)-10-methylundeca-2,10-dienal (**34**). Followed general procedure, with 30 μL (0.2 mmol) 1-methylcyclooctene, 16 μL (0.22 mmol) acrolein (90%), 8 mg (0.009 mmol) **2**, and 5 mL CH_2Cl_2. Purified via silica gel chromatography (8:2 hexanes:ethyl acetate) to obtain 2 mg of **34** as an oil (6% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 9.5 (1H, d), 6.85 (1H, dt), 6.15 (1H, dd), 4.7 (1H, m), 4.65 (1H, m), 2.35 (2H, dt), 2.0 (2H, t), 1.75 (3H, s), 1.4 (8H, m).

(10*E*)-3-methyldodeca-2,10-dienedial (**35**). Followed general procedure, with 30 μL (0.2 mmol) 1-methylcyclooctene, 34 μL (0.41 mmol) crotonaldehyde, 8 mg (0.009 mmol) **2**, and 5 mL CH_2Cl_2. Purified via silica gel chromatography (7:3 hexanes:ethyl acetate) to obtain 9 mg of **35** as an oil (22% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 10.00 (0.5H, dd, *J* = 7.7, 1.7 Hz), 9.95 (0.5H, dd, *J* = 8.3, 1.7 Hz), 9.51 (1H, dd, *J* = 7.7, 1.7 Hz), 6.85 (1H, dt, *J* = 15.9, 7.3 Hz), 6.13 (1H, ddd, *J* = 15.6, 8.0, 1.4 Hz), 5.90 (0.5H, m), 5.87 (0.5H, m), 2.59 (1H, t, *J* = 7.4 Hz), 2.35 (2H, dt, *J* = 7.2, 7.2 Hz), 2.23 (1H, t, *J* = 7.5 Hz), 2.18 (1.5H, s), 1.99 (1.5H, s), 1.4 (8H, m). ^{13}C NMR (300 MHz, $CDCl_3$, ppm): δ 193.9, 191.1, 190.5, 163.9, 158.5, 132.9, 128.3, 127.2, 40.5, 32.7, 32.5, 29.2, 29.0, 28.7, 27.7, 27.0, 25.1, 17.6. HRMS (DEI) calcd. for $C_{13}H_{20}O_2$ + H: 209.1542, found: 209.1535 (UC, Riverside).

(10*E*)-dimethyl 3-methyldodeca-2,10-dienedioate (**36**). Followed general procedure, with 30 μL (0.2 mmol) 1-methylcyclooctene, 44 μL (0.41 mmol) methyl crotonate, 8 mg (0.009 mmol) **2**, and 5 mL CH_2Cl_2. Purified via silica gel chromatography (9:1 hexanes:ethyl acetate) to obtain 6 mg of **36** as an oil (11% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 6.95 (1H, m), 5.83 (1H, d), 5.65 (1H, m), 3.75 (3H, s), 3.65 (3H, m), 2.4 (4H, m), 2.15 (1.5H, s), 1.85 (1.5H, s), 1.4 (8H, m).

(2*E*,8*E*)-dimethyl 4-methyldeca-2,8-dienedioate (**37**). Followed general procedure, with 22 μL (0.21 mmol) 3-methylcyclohexene, 38 μL (0.42 mmol) methyl acrylate, 8 mg (0.009 mmol) **2**, and 1 mL CH_2Cl_2. Purified via silica gel chromatography (8:2 hexanes:ethyl acetate) to obtain 8.5 mg of **37** as an white solid (17% yield). ^{1}H NMR

(300 MHz, $CDCl_3$, ppm): δ 6.93 (1H, dt, *J* = 15.9, 7.0 Hz), 6.84 (1H, dd, *J*= 15.6, 8.1 Hz), 5.81 (1H, dt, *J* = 15.6, 1.6 Hz), 5.78 (1H, dd, *J* = 15.6, 1.2 Hz), 3.731 (3H, s), 3.727 (3H, s), 2.31 (1H, m), 2.19 (2H, dtd, *J* = 7.0, 7.0, 1.4 Hz), 1.4 (4H, m), 1.05 (3H, d, *J* = 6.6 Hz). ^{13}C NMR (300 MHz, $CDCl_3$, ppm): δ 167.0, 154.1, 148.9, 121.1, 119.5, 51.5, 36.5, 35.4, 32.2, 25.7, 19.5.

(2*E*,8*E*)-dimethyl 2,4,9-trimethyldeca-2,8-dienedioate (**38**). Followed general procedure, with 22 μL (0.21 mmol) 3-methylcyclohexene, 1 mL (9.3 mmol) methyl methacrylate, and 8 mg (0.009 mmol) **2**. Purified via silica gel chromatography (9:1 hexanes:ethyl acetate) to obtain 8 mg of **38** as an oil (15% yield). ^1H NMR (300 MHz, $CDCl_3$, ppm): δ 6.73 (1H, t), 6.5 (1H, d), 3.75 (6H, s), 2.5 (1H, m), 2.15 (2H, dt), 1.82 (3H, s), 1.81 (3H, s), 1.4 (4H, m), 1.0 (3H, d).

3-Ethylcyclohex-1-ene (**39**).[28] To a flame-dried, round-bottomed flask, under an argon atmosphere, added 3-bromocyclohexene (distilled from K_2CO_3, 1 mL, 8.7 mmol) and THF (2 mL). At room temperature, slowly added a 0.8M THF solution of ethylmagnesium bromide (14 mL, 11.2 mmol) dropwise, via addition funnel, over 15 minutes. Reaction immediately began to heat up upon Grignard addition. Let stir at room temperature for about 2 hours, then slowly added an ice-cold aqueous solution of dilute H_2SO_4. Extracted 4 times with 15 mL ether, then washed with 60 mL aqueous NH_4Cl solution, 60 mL H_2O, and 60 mL brine. Dried with Mg_2SO_4. Purified via silica gel chromatography (19:1 hexanes:ether) to obtain 194 mg of **39** as a clear, slightly

yellow oil (20% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 5.6 (2H, m), 1.1-2.2 (9H, m), 0.95 (3H, t).

(2*E*,8*E*)-dimethyl 4-ethyldeca-2,8-dienedioate (**40**). Followed general procedure, with 24 μL (0.2 mmol) **39**, 36 μL (0.4 mmol) methyl acrylate, 8 mg (0.009 mmol) **2**, and 1 mL CH_2Cl_2. Purified via silica gel chromatography (9:1 hexanes:ethyl acetate) to obtain 7.6 mg of **40** as a yellow solid (15% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 6.93 (1H, dt, *J* = 15.3, 7.1 Hz), 6.72 (1H, dd, *J* = 15.6, 9.3 Hz), 5.81 (1H, dt, *J* = 15.9, 1.5 Hz), 5.79 (1H, d, *J* = 15.6 Hz), 3.74 (3H, s), 3.73 (3H, s), 2.2 (3H, m), 1.4 (6H, m), 0.86 (3H, t, *J* = 7.4 Hz).

Dimethyl 2-(cyclohex-2-enyl)malonate (**41**). *Step 1*: To a flame-dried, round-bottomed flask, under an argon atmosphere, added 2-cyclohexenone (3 mL, 31 mmol), methanol (155 mL), and CH_2Cl_2 (155 mL). Placed in an ice bath, added cerium(III) chloride heptahydrate (14.3 g, 38 mmol) and let stir for 5 minutes. Added $NaBH_4$ (1.5 g, 40 mmol) in portions. Bubbling was observed upon initial $NaBH_4$ addition. Let stir at 0 °C for 1 hour. Added 155 mL aqueous $NaHCO_3$ solution, then concentrated via rotovap at 40 °C (to remove all methanol from the reaction). Extracted 3 times with 250 mL ether and dried with Na_2SO_4. Purified via Kugelrohr distillation to obtain cyclohex-2-enol, which was used directly in the next reaction without calculating the yield. *Step 2*: To a flame-dried, round-bottomed flask, under an argon atmosphere, added 2-cyclohexenol (obtained above, ca. 30 mmol), acetic anhydride (8.5 mL, 90 mmol), triethylamine (12.5 mL, 90 mmol), dimethylaminopyridine (550 mg, 4.5 mmol), and CH_2Cl_2 (17 mL). Let

stir at room temperature overnight. Transferred to a separatory funnel, added 50 mL 10% aqueous HCl solution, extracted twice with 50 mL CH_2Cl_2, washed with 75 mL 5% aqueous NaOH solution, and dried with Na_2SO_4. Purified via Kugelrohr distillation to obtain 6.4 g of cyclohex-2-enyl acetate plus solvents (> 90% yield from step 1). *Step 3*:[29] To a flame-dried, round-bottomed flask, under an argon atmosphere, added 95% sodium hydride (780 mg, 31 mmol) and THF (95 mL). Let stir for 5 minutes. Added dimethyl malonate (3.5 mL, 31 mmol) in portions. Let stir at room temperature for one hour. To a second flame-dried, round-bottomed flask, under an argon atmosphere, added tetrakis-(triphenylphosphine)palladium(0) (860 mg, 0.74 mmol) and THF (180 mL). Let stir for 5 minutes. Added cyclohex-2-enyl acetate (ca. 2 g, 15 mmol) and THF (25 mL) via cannula. Let stir for 15 minutes, then added (via cannula) the sodium dimethyl malonate solution prepared above. Let stir at room temperature for approximately 2.5 days. Added 300 mL H_2O, let stir for 5 minutes, extracted 3 times with 200 mL ether, and dried with $MgSO_4$. Purified via silica gel chromatography (8:2 hexanes:ethyl acetate) to obtain 1.3 g of **41** as a yellow oil (40% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 5.78 (1H, m), 5.53 (1H, dd), 3.78 (6H, s), 3.3 (1H, d), 2.9 (1H, br), 2.0 (2H, br), 1.78 (2H, m), 1.58 (1H, m), 1.4 (1H, m). ^{13}C NMR (300 MHz, $CDCl_3$, ppm): δ 168.7, 129.6, 127.2, 56.9, 52.4, 35.4, 26.7, 25.0, 20.9.

(*E*)-trimethyl 2-((*E*)-3-methoxy-3-oxoprop-1-enyl)hept-6-ene-1,1,7-tricarboxylate (**42**). Followed general procedure, with 28 μL (0.2 mmol) **41**, 36 μL (0.4 mmol) methyl acrylate, 8 mg (0.009 mmol) **2**, and 1 mL CH_2Cl_2. Purified via silica gel chromatography (7:3 hexanes:ethyl acetate) to obtain 4 mg of **42**, contaminated with solvents, as an oil (<

6% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 6.9 (1H, dt), 6.75 (1H, dd), 5.85 (1H, d), 5.8 (1H, d), 3.7 (12H, m), 3.41 (1H, d), 2.93 (1H, br), 2.2 (2H, t), 1.4 (4H, m).

(2*E*,7*E*)-dimethyl 4-methylnona-2,7-dienedioate (**43**). Followed general procedure, with 22 μL (0.2 mmol) 3-methylcyclopentene, 36 μL (0.4 mmol) methyl acrylate, 8 mg (0.009 mmol) **2**, and 1 mL CH_2Cl_2. Purified via silica gel chromatography (8:2 hexanes:ethyl acetate) to obtain 37 mg of **43** as a yellow oil (82% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 6.92 (1H, dt, *J* = 15.6, 6.9 Hz), 6.82 (1H, dd, *J* = 15.8, 7.8 Hz), 5.81 (1H, dt, *J* = 15.6, 3.6 Hz), 5.79 (1H, dd, *J* = 15.6, 1.2 Hz), 3.73 (3H, s), 3.72 (3H, s), 2.33 (1H, m), 2.19 (2H, m), 1.54 (2H, dt, *J* = 7.4, 7.4 Hz), 1.07 (3H, d, *J* = 6.9 Hz). ^{13}C NMR (300 MHz, $CDCl_3$, ppm): δ 166.9, 166.8, 153.4, 148.4, 121.2, 119.9, 51.52, 51.47, 36.0, 34.1, 29.8, 19.5. HRMS (DCI) calcd. for $C_{12}H_{18}O_4$ + H: 227.1283, found: 227.1280 (UC, Riverside).

(2*E*,7*E*)-dimethyl 2,6-dimethylnona-2,7-dienedioate (**44**). Followed general procedure, with 22 μL (0.2 mmol) 3-methylcyclopentene, 1 mL (9.3 mmol) methyl methacrylate, and 7 mg (0.008 mmol) **2**. Purified via silica gel chromatography (8:2 hexanes:ethyl acetate) to obtain 16 mg of **44** as an oil (31% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 6.71 (1H, tq, *J* = 7.4, 1.4 Hz), 6.53 (1H, dq, *J* = 10.2, 1.2 Hz), 3.75 (3H, s), 3.74 (3H, s), 2.52 (1H, m), 2.12 (2H, dt, *J* = 7.5, 7.5 Hz), 1.83 (3H, m), 1.80 (3H, m), 1.5 (2H, m), 1.02 (3H, d, *J* = 6.6 Hz). ^{13}C NMR (300 MHz, $CDCl_3$, ppm): δ 168.4, 147.1, 141.8, 127.7, 126.7, 51.79, 51.76, 35.6, 33.0, 29.8, 26.7, 20.1, 12.5.

4-Methylnona-2,7-diene-1,9-diyl diacetate (**45**). Followed general procedure, with 22 μL (0.2 mmol) 3-methylcyclopentene, 64 μL (0.41 mmol) (*Z*)-but-2-ene-1,4-diyl diacetate, 8 mg (0.009 mmol) **2**, and 1 mL CH_2Cl_2. Purified via silica gel chromatography (8:2 hexanes:ethyl acetate) to obtain 13 mg of **45** as an oil (27% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 5.6 (4H, m), 4.6 (*Z*-isomer, 0.4H, d), 4.5 (*E*-isomer, 3.6H, dd), 2.1 (3H, m), 2.05 (6H, s), 1.4 (2H, m), 1.0 (3H, d). ^{13}C NMR (300 MHz, $CDCl_3$, ppm): δ 170.7, 141.3, 136.1, 123.8, 122.4, 65.3, 36.0, 35.6, 30.0, 21.1, 20.2.

(2*E*,7*E*)-dimethyl 4-ethylnona-2,7-dienedioate (**46**). Followed general procedure, with 24 μL (0.21 mmol) 3-ethylcyclopentene, 36 μL (0.4 mmol) methyl acrylate, 8 mg (0.009 mmol) **2**, and 1 mL CH_2Cl_2. Purified via silica gel chromatography (8:2 hexanes:ethyl acetate) to obtain 38 mg of **46** as an oil (75% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 6.90 (1H, dt, J = 15.6, 6.9 Hz), 6.68 (1H, dd, J = 15.6, 9.6 Hz), 5.79 (2H, d, J = 15.6 Hz), 3.72 (3H, s), 3.71 (3H, s), 2.1 (3H, m), 1.5 (4H, m), 0.84 (3H, t, J = 7.4 Hz). ^{13}C NMR (300 MHz, $CDCl_3$, ppm): δ 166.8, 166.7, 152.3, 148.6, 121.5, 121.1, 51.5, 51.4, 43.7, 32.3, 29.9, 27.3, 11.6. HRMS (DEI) calcd. for $C_{13}H_{20}O_4$ + H: 241.144, found: 241.1448 (UC, Riverside).

Cyclopent-2-enol (**47**). To a flame-dried, round-bottomed flask, under an argon atmosphere, added 2-cyclopentenone (15 mL, 179 mmol) and MeOH (425 mL). Placed in an ice bath, then added cerium(III) chloride heptahydrate (34 g, 89 mmol). Added $NaBH_4$ (7g, 180 mmol) in portions. Observed intense bubbling upon initial $NaBH_4$ addition. Let stir at 0 °C for 30 minutes, then added 425 mL brine and concentrated via

rotovap for 30 minutes. Extracted twice with 450 mL ether and dried with Mg_2SO_4. Obtained 13.2 g of **47** as a slightly yellow oil, contaminated only by residual solvents (ca. 88% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 5.95 (1H, m), 5.8 (1H, m), 4.8 (1H, m), 2.5 (1H, m), 2.2 (4H, m), 1.65 (1H, m). ^{13}C NMR (300 MHz, $CDCl_3$, ppm): δ 134.8, 133.1, 77.3, 33.2, 31.0.

(2*E*,7*E*)-dimethyl 4-hydroxynona-2,7-dienedioate (**48**). Followed general procedure, with 16 μL (0.21 mmol) **47**, 36 μL (0.4 mmol) methyl acrylate, 8 mg (0.009 mmol) **2**, and 1 mL CH_2Cl_2. Purified via silica gel chromatography (7:3 hexanes:ethyl acetate) to obtain 9 mg of **48** as a dark yellow oil (16% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 6.96 (1H, dt, *J* = 15.6, 6.7 Hz), 6.93 (1H, dd, *J* = 15.6, 4.5 Hz), 6.06 (1H, dd, *J* = 15.8, 1.7 Hz), 5.86 (1H, dt, *J* = 15.6, 1.4 Hz), 4.35 (1H, br), 3.75 (3H, s), 3.73 (3H, s), 2.35 (2H, dtd, *J* = 7.3, 7.3, 1.3 Hz), 1.7 (2H, m). ^{13}C NMR (300 MHz, $CDCl_3$, ppm): δ 166.8, 149.5, 148.0, 121.6, 120.2, 70.1, 51.8, 51.6, 34.6, 27.9). HRMS (DCI) calcd. for $C_{11}H_{16}O_5$ + H: 229.1076, found: 229.1082 (UC, Riverside).

Cyclopent-2-enyl acetate (**49**). Followed procedure given for **41** (Step 2), with 2 mL (18 mmol) **47**, 2 mL (21 mmol) acetic anhydride, 3 mL (22 mmol) triethylamine, 88 mg (0.72 mmol) dimethylaminopyridine, and 18 mL CH_2Cl_2. Purified via Kugelrohr distillation to obtain 2.4 g of **49** as a clear, almost colorless, oil (ca. 99% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 6.1 (1H, m), 5.82 (1H, m), 5.68 (1H, m), 2.5 (1H, m), 2.3 (2H, m), 2.05 (3H, s), 1.8 (1H, m).

(2*E*,7*E*)-dimethyl 4-acetoxynona-2,7-dienedioate (**50**). Followed general procedure, with 22 μL (0.21 mmol) **49**, 36 μL (0.4 mmol) methyl acrylate, 8 mg (0.009 mmol) **2**, and 1 mL CH_2Cl_2. Purified via silica gel chromatography (8:2 hexanes:ethyl acetate) to obtain a very small amount of **50** as an oil (< 5% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 6.92 (1H, dt, *J* = 15.6, 6.9 Hz), 6.83 (1H, dd, *J* = 15.6, 5.4 Hz), 5.96 (1H, dd, *J* = 15.9, 1.5 Hz), 5.84 (1H, dt, *J* = 15.6, 1.7 Hz), 5.43 (1H, dtd, *J* = 6.0, 6.0, 1.7 Hz), 3.75 (3H, s), 3.73 (3H. s), 2.27 (3H, m), 2.12 (3H, s), 1.85 (2H, m).

Tert-butyl(cyclopent-2-enyloxy)diphenylsilane (**51**). To a flame-dried, round-bottomed flask, under an argon atmosphere, added **47** (0.5 mL, 6 mmol), imidazole (1 g, 15 mmol), and DMF (1 mL). Added *t*-butyldiphenylsilyl chloride (2 mL, 7.7 mmol). Let stir at room temperature for 24 hours. Added 5 mL 10% aqueous HCl solution, extracted 3 times with CH_2Cl_2, and dried with Na_2SO_4. Purified via silica gel chromatography (9:1 hexanes:ethyl acetate) to obtain ca. 1.2 g of **51** as an oil (ca. 60% yield). Further purified via Kugelrohr distillation. ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 7.7 (4H, d), 7.4 (6H, m), 5.85 (1H, m), 5.65 (1H, m), 4.9 (1H, m), 2.45 (1H, m), 2.1 (2H, m), 1.78 (1H, m), 1.05 (9H, s).

(2*E*,7*E*)-dimethyl 4-(*tert*-butyldiphenylsilyloxy)nona-2,7-dienedioate (**52**). Followed general procedure, with 66 mg (0.2 mmol) **51**, 36 μL (0.4 mmol) methyl acrylate, 8 mg (0.009 mmol) **2**, and 1 mL CH_2Cl_2. Purified via silica gel chromatography (8:2 hexanes:ethyl acetate) to obtain 27 mg of **52** as an oil (29% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 7.65 (2H, d, *J* = 8.1 Hz), 7.59 (2H, d, *J* = 7.8 Hz), 7.4 (6H, m), 6.84 (1H,

dd, *J* = 15.6, 5.1 Hz), 6.78 (1H, dt, *J* = 15.6, 6.9 Hz), 5.97 (1H, d, *J* = 15.6 Hz), 5.68 (1H, d, *J* = 15.8 Hz), 4.43 (1H, dt, *J* = 5.0, 5.0 Hz), 3.74 (3H, s), 3.71 (3H, s), 2.20 (1H, m), 2.08 (1H, m), 1.55 (2H, m), 1.09 (9H, s). ^{13}C NMR (300 MHz, $CDCl_3$, ppm): δ 166.7, 166.6, 149.3, 148.4, 135.62, 135.59, 133.4, 132.9, 129.86, 129.75, 127.63, 127.56, 120.98, 120.39, 71.4, 51.6, 51.4, 34.7, 27.1, 26.6, 19.4. HRMS (DCI) calcd. for $C_{27}H_{34}O_5Si$ + H: 467.2254, found: 467.2261 (UC, Riverside).

(2*E*,7*E*)-di-*tert*-butyl 4-(*tert*-butyldiphenylsilyloxy)nona-2,7-dienedioate (**53**). Followed general procedure, with 85 mg (0.26 mmol) **51**, 30 μL (0.2 mmol) *t*-butyl acrylate, 8 mg (0.009 mmol) **2**, and 1 mL CH_2Cl_2. Purified via silica gel chromatography (9:1 hexanes:ethyl acetate) to obtain 15 mg of **53** (contaminated with minor impurities) as an oil (< 27% yield).

Dimethyl 2-(cyclopent-2-enyl)malonate (**54**). Followed procedure given for **41** (Step 3), with 1 mL (9.5 mmol) **49**, 550 mg (ca. 20 mmol) sodium hydride (95%), 2 mL (17.5 mmol) dimethyl malonate, 549 mg (0.48 mmol) tetrakis-(triphenylphosphine)-palladium(0), 140 mL THF, and a reaction time of 8 hours. Purified via silica gel chromatography (8:2 hexanes:ethyl acetate) to obtain 1.13 g of **54** as an oil (60% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 5.85 (1H, m), 5.65 (1H, m), 3.79 (6H, s), 3.36 (1H, br), 3.28 (1H, d), 2.35 (2H, m), 2.15 (1H, m), 1.6 (1H, m). ^{13}C NMR (300 MHz, $CDCl_3$, ppm): δ 133.3, 131.5, 57.0, 52.74, 52.72, 45.7, 32.1, 28.2.

(*E*)-trimethyl 2-((*E*)-3-methoxy-3-oxoprop-1-enyl)hex-5-ene-1,1,6-tricarboxylate (**55**). Followed general procedure, with 32 μL (0.21 mmol) **54**, 36 μL (0.4 mmol) methyl acrylate, 8 mg (0.009 mmol) **2**, and 1 mL CH_2Cl_2. Purified via silica gel chromatography (7:3 hexanes:ethyl acetate) to obtain 14 mg of **55** as a dark oil (19% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 6.87 (1H, dt, *J* = 15.6, 6.9 Hz), 6.75 (1H, dd, *J* = 15.6, 9.9 Hz), 5.89 (1H, d, *J* = 15.6 Hz), 5.81 (1H, dt, *J* = 15.6, 1.5 Hz), 3.748 (3H, s), 3.730 (3H, s), 3.721 (3H, s), 3.700 (3H, s), 3.46 (1H, d, *J* = 8.4 Hz), 2.96 (1H, dtd, *J* = 8.4, 8.4, 3.3 Hz), 2.2 (2H, m), 1.6 (2H, m). ^{13}C NMR (300 MHz, $CDCl_3$, ppm): δ 167.7, 167.6, 166.6, 166.0, 147.3, 146.5, 124.1, 121.7, 55.7, 52.8, 52.7, 51.7, 51.5, 41.7, 30.1, 29.6. HRMS (PCI) calcd. for $C_{16}H_{22}O_8$ + H: 343.1393, found: 343.1393 (UCLA).

Dimethyl 2-(cyclopent-2-enyl)-2-ethylmalonate (**56**). To a flame-dried, round-bottomed flask, under an argon atmosphere, added 95% sodium hydride (149 mg, 5.9 mmol) and THF (16 mL). Let stir for 5 minutes, then added **54** (0.5 mL, 3.3 mmol). No bubbling was observed upon addition of **54**. Let stir for several hours at room temperature, then placed in an 80 °C oil bath and fit with a reflux condenser. Added a solution of 1-bromoethane (0.5 mL, 6.7 mmol) and THF (16 mL). Let stir under reflux for 12 hours, then removed from heat, let cool to room temperature, and slowly added 40 mL H_2O. Transferred to a separatory funnel and extracted 3 times with 40 mL ether. Dried with $MgSO_4$. Purified via silica gel chromatography (8:2 hexanes:ethyl acetate) to obtain 671 mg of **56** as an orange-yellow oil (90% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 5.8 (2H, m), 3.71 (3H, s), 3.68 (3H, s), 3.4 (1H, br), 2.25 (2H, m), 1.9 (3H, m), 1.7 (1H, m),

0.88 (3H, t). ^{13}C NMR (300 MHz, $CDCl_3$, ppm): δ 171.7, 171.5, 131.9, 131.3, 61.6, 52.1, 51.9, 49.0, 31.8, 26.5, 25.2, 9.3.

(*E*)-trimethyl 5-((*E*)-3-methoxy-3-oxoprop-1-enyl)oct-1-ene-1,6,6-tricarboxylate (**57**). Followed general procedure, with 38 μL (0.2 mmol) **56**, 36 μL (0.4 mmol) methyl acrylate, 10 mg (0.01 mmol) **2**, and 1 mL CH_2Cl_2. Purified via silica gel chromatography (7:3 hexanes:ethyl acetate) to obtain 11 mg of **57** as an oil (15% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 6.89 (1H, dt, *J* = 15.6, 6.9 Hz), 6.70 (1H, dd, *J* = 15.6, 10.5 Hz), 5.86 (1H, d, *J* = 15.6 Hz), 5.82 (1H, d, *J* = 15.6 Hz), 3.75 (3H, s), 3.74 (6H, s), 3.72 (3H, s), 2.78 (1H, td, *J* = 10.9, 1.8 Hz), 2.0 (4H, m), 1.3 (2H, m), 0.83 (3H, t, 7.5 Hz).

1-Methylcyclopent-2-enol (**58**). To a flame-dried, round-bottomed flask, under an argon atmosphere, added THF (8 mL). Placed in a dry ice/acetone bath. Added a 1.4M ether solution of methyllithium (1.4 mL, 2 mmol) and let stir. Via cannula, added a (cooled to –78 °C first) solution of 2-cyclopentenone (168 μL, 2 mmol) and THF (10 mL). Let stir at –78 °C for 1.5 hours. Removed from cold bath, added 12 mL H_2O, and stirred at room temperature for 10 minutes. Extracted 3 times with 20 mL CH_2Cl_2, washed with 40 mL brine, and dried with Na_2SO_4. Purified via silica gel chromatography (100% ether) to obtain 73 mg of **58** as a light yellow oil (37% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 5.8 (1H, m), 5.68 (1H, m), 2.48 (1H, m), 2.28 (1H, m), 1.9 (3H, m), 1.4 (3H, s).

(2*E*,7*E*)-dimethyl 4-hydroxy-4-methylnona-2,7-dienedioate (**59**). Followed general procedure, with 17 mg (0.17 mmol) **58**, 30 μL (0.33 mmol) methyl acrylate, 8 mg (0.009

mmol) **2**, and 1 mL CH_2Cl_2. Purified via silica gel chromatography (6:4 hexanes:ethyl acetate) to obtain 10 mg of **59** as an oil (24% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 6.95 (1H, m), 6.93 (1H, d, *J* = 15.6 Hz), 6.06 (1H, d, *J* = 15.6 Hz), 5.82 (1H, d, *J* = 15.6 Hz), 3.75 (3H, s), 3.72 (3H, s), 2.3 (2H, m), 1.73 (2H, m), 1.65 (1H, br), 1.38 (3H, s).

(*E*)-methyl 5-(2-((*E*)-3-methoxy-3-oxoprop-1-enyl)-1,3-dioxolan-2-yl)pent-2-enoate (**60**). Followed general procedure, with 24 μL (0.2 mmol) 2-cyclopenten-1-one ethylene ketal, 36 μL (0.4 mmol) methyl acrylate, 8 mg (0.009 mmol) **2**, and 1 mL CH_2Cl_2. Purified via silica gel chromatography (7:3 hexanes:ethyl acetate) to obtain 9 mg of **60** as an oil (17% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 6.95 (1H, dt), 6.75 (1H, d), 6.1 (1H, d), 5.8 (1H, d), 3.9 (4H, m), 3.8 (3H, s), 3.75 (3H, s), 2.35 (2H, dt), 1.9 (2H, dd).

(*Z*)-3-methylcyclohept-1-ene (**61**). *Step 1*: To a flame-dried, round-bottomed flask, under an argon atmosphere, added cycloheptene (10 mL, 86 mmol), *N*-bromosuccinimide (10.2 g, 57 mmol), benzoyl peroxide (208 mg, 0.86 mmol), and CCl_4 (60 mL). Let stir at room temperature for a couple of minutes, then placed in an 80 °C oil bath and let stir under reflux for 3 hours. Removed from heat, let cool to room temperature, filtered away the white solid (the succinimide side product), and washed 3 times with 5 mL CCl_4. Concentrated *in vacuo* and purified via Kugelrohr distillation over $MgSO_4$ to obtain 9.9 g of bromocyclohept-2-ene as a clear, slightly yellow oil (99% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 5.86 (2H, m), 4.96 (1H, t), 1.4-2.3 (8H, m). ^{13}C NMR (300 MHz, $CDCl_3$, ppm): δ 135.5, 132.1, 53.9, 36.3, 28.4, 26.7, 26.5. *Step 2*: To a flame-dried, round-bottomed flask, under an argon atmosphere, added bromocyclohept-2-ene (1 mL,

7.4 mmol), and ether (2 mL). Placed in a dry ice/acetone bath, kept roughly at –20 °C, let stir for 5 minutes, and then slowly added a 3.0M ether solution of methylmagnesium bromide (3 mL, 9 mmol) dropwise, over 10-15 minutes. Let stir for 30 minutes at –20 °C, then let warm to room temperature and let stir another 2 hours. Added 6 mL of ice cold dilute aqueous H_2SO_4 solution, extracted 4 times with 10 mL ether, washed with 40 mL aqueous NH_4Cl solution, 40 mL H_2O, and 40 mL brine, and dried with $MgSO_4$. Purified via silica gel chromatography (19:1 hexanes:ether) to obtain 249 mg of **61** as a yellow oil (31% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 5.6 (2H, m), 1.2-2.4 (9H, m), 1.02 (3H, d). ^{13}C NMR (300 MHz, $CDCl_3$, ppm): δ 139.3, 130.5, 36.0, 34.6, 30.7, 29.0, 27.1, 23.3.

(2*E*,9*E*)-dimethyl 4-methylundeca-2,9-dienedioate (**62**). Followed general procedure, with 24 μL (0.21 mmol) **61**, 36 μL (0.4 mmol) methyl acrylate, 8 mg (0.009 mmol) **2**, and 1 mL CH_2Cl_2. Purified via silica gel chromatography (8:2 hexanes:ethyl acetate) to obtain 21 mg of **62** as an oil (39% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 6.94 (1H, dt, *J* = 15.3, 7.1 Hz), 6.84 (1H, dd, *J* = 15.8, 8.0 Hz), 5.80 (1H, dt, *J* = 15.3, 1.5 Hz), 5.76 (1H, d, *J* = 16.1 Hz), 3.720 (3H, s), 3.716 (3H, s), 2.28 (1H, m), 2.18 (2H, dtd, *J* = 7.2, 7.2, 1.4 Hz), 1.4 (6H, m), 1.04 (3H, d, *J* = 7.2 Hz). ^{13}CNMR (300 MHz, $CDCl_3$, ppm): δ 167.1, 154.5, 149.2, 120.9, 119.2, 51.5, 51.4, 36.5, 35.8, 32.1, 28.1, 26.8, 19.5. HRMS (DCI) calcd. for $C_{14}H_{22}O_4$ + H: 255.1596, found: 255.1603 (UC, Riverside).

(*Z*)-cyclohept-2-enol (**63**). Followed procedure given for **41** (Step 1), with 3.5 mL (31 mmol) 2-cycloheptenone, 14.3 g (38 mmol) cerium(III) chloride heptahydrate, 1.5 g (40

mmol) $NaBH_4$, MeOH (155 mL) and CH_2Cl_2 (155 mL). Concentrated after workup to obtain 3.3 g of **63** as a yellow oil (95% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 5.63 (2H, m), 4.3 (1H, d), 3.3 (1H, br), 2.07 (1H, m), 1.8 (3H, m), 1.5 (3H, m), 1.21 (1H, m). ^{13}C NMR (300 MHz, $CDCl_3$, ppm): δ 138, 130, 72, 37, 29, 27, 26.5.

(2*E*,9*E*)-dimethyl 4-hydroxyundeca-2,9-dienedioate (**64**). Followed general procedure, with 26 mg (0.23 mmol) **63**, 42 μL (0.47 mmol) methyl acrylate, 8 mg (0.009 mmol) **2**, and 2 mL CH_2Cl_2. Purified via silica gel chromatography (7:3 hexanes:ethyl acetate) to obtain 7 mg of **64** as an oil (12% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 6.95 (2H, m), 6.04 (1H, dd, J = 15.5, 1.4 Hz), 5.82 (1H, dt, J = 15.6, 1.4 Hz), 4.35 (1H, br), 3.75 (3H, s), 3.73 (3H, s), 1.2-2.7 (8H, m).

(*Z*)-cyclohept-2-enyl acetate (**65**). Followed procedure given for **41** (Step 2) with 1.5 mL (16 mmol) **63**, 3 mL (32 mmol) acetic anhydride, 4.5 mL (32 mmol) triethylamine, 205 mg (1.7 mmol) dimethylaminopyridine, and 14 mL CH_2Cl_2. Purified via Kugelrohr distillation to obtain 3.13 g of **65** as a an oil (ca. 99% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 5.82 (1H, m), 5.64 (1H, m), 5.4 (1H, m), 1.2-2.3 (11H, m).

(2*E*,9*E*)-dimethyl 4-acetoxyundeca-2,9-dienedioate (**66**). Followed general procedure, with 34 mg (0.22 mmol) **65**, 40 μL (0.44 mmol) methyl acrylate, 6 mg (0.007 mmol) **2**, and 1 mL CH_2Cl_2. Purified via silica gel chromatography (8:2 hexanes:ethyl acetate) to obtain 7 mg of **66** as an oil (12% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 6.93 (1H, dt, J = 15.6, 6.9 Hz), 6.83 (1H, dd, J = 15.8, 5.6 Hz), 5.94 (1H, dd, J = 15.8, 1.4 Hz), 5.82

(1H, d, *J* = 15.6 Hz), 5.39 (1H, dt, *J* = 6.0, 6.0 Hz), 3.75 (3H, s), 3.73 (3H, s), 2.21 (2H, dt, *J* = 6.6, 6.6 Hz), 2.10 (3H, s), 1.5 (6H, m). ^{13}C NMR (300 MHz, $CDCl_3$, ppm): δ 169.9, 166.9, 166.2, 148.8, 145.3, 121.2, 121.1, 72.2, 51.8, 51.5, 33.6, 32.0, 27.7, 24.5, 21.1. HRMS (PCI) calcd. for $C_{15}H_{22}O_6$ + H: 299.1495, found: 299.1495 (UCLA).

(*E*)-methyl 8-acetoxydeca-2,9-dienoate (**67**). Same reaction as for **66**. Obtained 4 mg of **67** as an oil (8% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 6.95 (1H, dt, *J* = 15.6, 7.0 Hz), 5.82 (1H, d, *J* = 15.6 Hz), 5.77 (1H, m), 5.23 (3H, m), 3.73 (3H, s), 2.21 (2H, dt, *J* = 6.3, 6.3 Hz), 2.07 (3H, s), 1.4 (6H, m). ^{13}C NMR (300 MHz, $CDCl_3$, ppm): δ 170.2, 166.9, 149.1, 136.2, 121.0, 116.7, 74.6, 51.5, 33.9, 32.1, 27.8, 24.8, 21.4.

(*Z*)-3-ethylcyclohept-1-ene (**68**). Followed procedure given for **39**, with 1 mL (7.4 mmol) bromocyclohept-2-ene (described for **61**, Step 1), 12 mL (9.6 mmol) ethylmagnesium bromide (0.80 M in THF), and 2 mL THF. Purified via silica gel chromatography (19:1 hexanes:ether) to obtain 441 mg of **68** as an almost colorless oil (48% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 5.76 (1H, m), 5.56 (1H, m), 1.2-2.2 (11H, m), 0.9 (3H, t). ^{13}C NMR (300 MHz, $CDCl_3$, ppm): δ 138, 131, 42, 34, 31, 30, 29, 27, 12.

(2*E*,9*E*)-dimethyl 4-ethylundeca-2,9-dienedioate (**69**). Followed general procedure, with 28 μL (0.21 mmol) **68**, 38 μL (0.42 mmol) methyl acrylate, 8 mg (0.009 mmol) **2**, and 1 mL CH_2Cl_2. Purified via silica gel chromatography (9:1 hexanes:ethyl acetate) to obtain 23 mg of **69** as an oil (41% yield). ^{1}HNMR (300 MHz, $CDCl_3$, ppm): δ 6.94 (1H, dt, *J* =

15.3, 7.1 Hz), 6.71 (1H, dd, *J* = 15.3, 9.3 Hz), 5.80 (1H, dt, *J* = 15.9, 1.5 Hz), 5.77 (1H, d, *J* = 15.9 Hz), 3.73 (3H, s), 3.72 (3H, s), 2.18 (2H, dt, *J* = 7.2, 7.2 Hz), 2.04 (1H, m), 1.4 (8H, m), 0.84 (3H, t, *J* = 7.4 Hz). ^{13}CNMR (300 MHz, $CDCl_3$, ppm): δ 166.9, 153.3, 149.3, 120.8, 51.4, 44.3, 33.9, 32.1, 28.1, 27.3, 26.8, 11.7. HRMS (DCI) calcd. for $C_{15}H_{24}O_4$ + H: 269.1753, found: 269.1751 (UC, Riverside).

(*E*)-methyl 8-ethyldeca-2,9-dienoate (**70**). Same reaction as for **69**. Obtained 7 mg of **70** as an oil (16% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 6.97 (1H, dt, *J* = 15.6, 6.9 Hz), 5.81 (1H, dt, *J* = 15.9, 1.5 Hz), 5.50 (1H, ddd, *J* = 16.9, 10.3, 8.6 Hz), 4.95 (2H, m), 3.73 (3H, s), 2.19 (2H, dtd, *J* = 7.2, 7.2, 1.7 Hz), 1.9 (1H, m), 1.3 (8H, m), 0.85 (3H, t, *J* = 7.2 Hz).

(*Z*)-*tert*-butyl(cyclohept-2-enyloxy)dimethylsilane (**71**). Followed procedure given for **51**, with 0.2 mL (2 mmol) **63**, 760 mg (5 mmol) *t*-butyldimethylsilyl chloride, 400 mg (5.9 mmol) imidazole, and 0.5 mL DMF. Purified via silica gel chromatography (100% hexanes) to obtain 393 mg of **71** as an oil (87% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 5.68 (2H, m), 4.35 (1H, d), 1.2-2.2 (8H, m), 0.9 (9H, s), 0.05 (6H, s).

(2*E*,9*E*)-dimethyl 4-(*tert*-butyldimethylsilyloxy)undeca-2,9-dienedioate (**72**). Followed general procedure, with 46 μL (0.2 mmol) **71**, 36 μL (0.4 mmol) methyl acrylate, 9 mg (0.01 mmol) **2**, and 1 mL CH_2Cl_2. Purified via silica gel chromatography (9:1 hexanes:ethyl acetate) to obtain ca. 15 mg of **72** as an oil (23% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 6.93 (2H, m), 5.97 (1H, dd, *J* = 15.5, 0.9 Hz), 5.81 (1H, d, *J* =

15.6 Hz), 4.29 (1H, dt, *J* = 5.7, 5.7 Hz), 3.74 (3H, s), 3.72 (3H, s), 2.19 (2H, dt, *J* = 6.9, 6.9 Hz), 1.4 (6H, m), 0.90 (9H, s), 0.047 (3H, s), 0.027 (3H, s). ^{13}C NMR (300 MHz, $CDCl_3$, ppm): δ 166.5, 150.6, 148.7, 120.5, 118.9, 70.9, 51.2, 51.0, 36.6, 31.7, 27.6, 25.4, 23.9, 17.8, –4.9, –5.2. HRMS (PCI) calcd. for $C_{19}H_{34}O_5Si$ + H: 371.2254, found: 371.2254 (UCLA).

(*E*)-methyl 8-(*tert*-butyldimethylsilyloxy)deca-2,9-dienoate (**73**). Same reaction as for **72**. Obtained ca. 25 mg of **73** as an oil (42% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 6.96 (1H, dt, *J* = 15.3, 7.2 Hz), 5.81 (1H, d, *J* = 15.9 Hz), 5.76 (1H, m), 5.12 (1H, d, *J* = 17.4 Hz), 5.01 (1H, d, *J* = 10.2 Hz), 4.07 (1H, dt, *J* = 5.7, 5.7 Hz), 3.72 (3H, s), 2.20 (2H, dt, *J* = 6.6, 6.6 Hz), 1.4 (6H, m), 0.89 (9H, s), 0.045, (3H, s), 0.029 (3H, s). ^{13}C NMR (300 MHz, $CDCl_3$, ppm): δ 167.0, 149.5, 141.5, 120.8, 113.6, 73.6, 51.4, 37.8, 32.3, 28.1, 25.9, 24.8, 18.3, –4.2, –4.7. HRMS (PCI) calcd. for $C_{17}H_{32}O_3Si$ + H: 313.2199, found: 313.2183 (UCLA).

(*Z*)-*tert*-butyl(cyclohept-2-enyloxy)diphenylsilane (**74**). Followed procedure given for **51**, with 0.2 mL (2 mmol) **63**, 1.3 mL (5 mmol) *t*-butyldiphenylsilyl chloride, 440 mg (6.5 mmol) imidazole, 2 small scoops of dimethylaminopyridine, and 0.5 mL DMF. Purified via silica gel chromatography (8:2 hexanes:ethyl acetate) to obtain ca. 700 mg of **74** as an oil (ca. 99% yield).

(2*E*,9*E*)-dimethyl 4-(*tert*-butyldiphenylsilyloxy)undeca-2,9-dienedioate (**75**). Followed general procedure, with 84 mg (0.24 mmol) **74**, 44 μL (0.49 mmol) methyl acrylate, 8 mg

(0.009 mmol) **2**, and 1 mL CH_2Cl_2. Purified via silica gel chromatography (9:1 hexanes:ethyl acetate) to obtain ca. 30 mg of **75** as an oil (26% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 7.63 (4H, m), 7.40 (6H, m), 6.87 (2H, m), 5.95 (1H, dd, *J* = 15.6, 1.5 Hz), 5.74 (1H, dt, *J* = 15.9, 1.4 Hz), 4.36 (1H, dtd, *J* = 6.0, 6.0, 1.7 Hz), 3.734 (3H, s), 3.727 (3H, s), 2.05 (2H, dt, *J* = 5.7, 5.7 Hz), 1.4 (2H, m), 1.25 (4H, m), 1.08 (9H, s). ^{13}C NMR (300 MHz, $CDCl_3$, ppm): δ 166.8, 150.1, 149.2, 135.7, 133.7, 133.2, 129.7, 129.7, 127.5, 127.5, 120.8, 119.8, 72.1, 51.6, 51.4, 36.4, 32.0, 27.8, 27.1, 23.5, 19.4. HRMS (PCI) calcd. for $C_{29}H_{38}O_5Si$ + H: 495.2567, found: 495.2567 (UCLA).

(*E*)-methyl 8-(*tert*-butyldiphenylsilyloxy)deca-2,9-dienoate (**76**). Same reaction as for **75**. Obtained ca. 45 mg of **76** as an oil (44% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 7.66 (4H, m), 7.38 (6H, m), 6.90 (1H, dt, *J* = 15.6, 7.0 Hz), 5.78 (1H, m), 5.75 (1H, d, *J* = 16.2 Hz), 4.98 (2H, m), 4.14 (1H, dt, *J* = 5.4, 5.4 Hz), 3.73 (3H, s), 2.07 (2H, dt, *J* = 6.3, 6.3), 1.43 (2H, m), 1.25 (4H, m), 1.07 (9H, s). ^{13}C NMR (300 MHz, $CDCl_3$, ppm): δ 1667.0, 149.5, 140.6, 135.8, 135.8, 134.3, 134.0, 129.5, 129.3, 127.4, 127.2, 120.7, 114.3, 74.3, 51.4, 37.2, 32.1, 27.9, 27.1, 24.0, 19.4.

(*Z*)-dimethyl 2-(cyclohept-2-enyl)malonate (**77**). Followed procedure given for **41** (Step 3), with 0.5 mL (3.9 mmol) **65**, 600 mg (ca. 15 mmol) sodium hydride (60%), 1.5 mL (13 mmol) dimethyl malonate, 255 mg (0.22 mmol) tetrakis-(triphenylphosphine)-palladium(0), 70 mL THF, and a reaction time of 17 hours. Purified via silica gel chromatography (8:2 hexanes:ethyl acetate) to obtain 556 mg of **77** as an oil (63% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 5.83 (1H, m), 5.59 (1H, dd, *J* = 11.1, 4.5 Hz), 3.74

(3H, s), 3.73 (3H, s), 3.47 (1H, d, *J* = 8.7 Hz), 3.06 (1H, br), 2.16 (2H, dt, *J* = 6.0, 6.0 Hz), 1.95 (1H, m), 1.64 (4H, m), 1.34 (2H, m).

(*E*)-trimethyl 2-((*E*)-3-methoxy-3-oxoprop-1-enyl)oct-7-ene-1,1,8-tricarboxylate (**78**). Followed general procedure, with 38 μL (0.2 mmol) **77**, 36 μL (0.4 mmol) methyl acrylate, 8 mg (0.009 mmol) **2**, and 1 mL CH_2Cl_2. Purified via silica gel chromatography (7:3 hexanes:ethyl acetate) to obtain 15 mg of **78** as an oil (21% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 6.91 (1H, dt, *J* = 15.9, 6.9 Hz), 6.75 (1H, dd, *J* = 15.9, 9.6 Hz), 5.86 (1H, d, *J* = 15.6 Hz), 5.79 (1H, d, *J* = 15.6 Hz), 3.735 (3H, s), 3.718 (3H, s), 3.711 (3H, s), 3.685 (3H, s), 3.44 (1H, d, *J* = 8.4 Hz), 2.93 (1H, dtd, *J* = 8.7, 8.7, 3.6 Hz), 2.17 (2H, dt, *J* = 7.5, 7.5 Hz), 1.4 (6H, m). ^{13}C NMR (300 MHz, $CDCl_3$, ppm): δ 168.0, 167.8, 166.9, 166.2, 148.9, 147.4, 123.4, 121.0, 55.9, 52.7, 52.6, 51.7, 51.5, 42.1, 32.0, 31.6, 27.7, 26.6. HRMS (PCI) calcd. for $C_{18}H_{26}O_8$ + H: 371.1706, found: 371.1706 (UCLA).

(*E*)-trimethyl 2-vinyloct-7-ene-1,1,8-tricarboxylate (**79**). Same reaction as for **78**. Obtained 22 mg of **79** as an oil (35% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 6.93 (1H, dt, *J* = 15.6, 7.2 Hz), 5.79 (1H, dt, *J* = 15.9, 1.8 Hz), 5.60 (1H, ddd, *J* = 17.4, 9.6, 9.3 Hz), 5.08 (1H, d, *J* = 17.1 Hz), 5.07 (1H, d, *J* = 9.9 Hz), 3.725 (3H, s), 3.713 (3H, s), 3.678 (3H, s), 3.37 (1H, d, *J* = 9.0 Hz), 2.73 (1H, dtd, *J* = 9.3, 9.3, 3.0), 2.18 (2H, dt, *J* = 6.9, 6.9 Hz), 1.37 (6H, m). ^{13}C NMR (300 MHz, $CDCl_3$, ppm): δ 168.5, 168.3, 167.0, 149.2, 137.6, 120.8, 117.7, 56.9, 52.5, 52.3, 51.4, 44.1, 32.0, 32.0, 27.7, 26.5. HRMS (DEI) calcd. for $C_{16}H_{24}O_6$ + H: 313.1651, found: 313.1647 (UC, Riverside).

(*Z*)-dimethyl 2-(cyclohept-2-enyl)-2-ethylmalonate (**80**). Followed procedure given for **56**, with 0.5 mL (2.7 mmol) **77**, 170 mg (6.7 mmol) sodium hydride (95%), 0.5 mL (6.7 mmol) 1-bromoethane, and 26 mL THF. Purified via silica gel chromatography (8:2 hexanes:ethyl acetate) to obtain 367 mg of **80** as a light yellow oil (53% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 5.8 (1H, m), 5.75 (1H, m), 3.73 (6H, s), 2.95 (1H, m), 2.15 (2H, dt), 2.0 (1H, m), 1.95 (2H, q), 1.7 (3H, m), 1.2 (2H, m), 0.85 (3H, t).

(*Z*)-1-ethylcyclohept-2-enol (**81**). To a flame-dried, round-bottomed flask under an argon atmosphere, added a 0.8M THF solution of ethylmagnesium bromide (18 mL, 14.4 mmol). Slowly added a solution of 2-cyclohepten-1-one (1 mL, 7.2 mmol) and ether (7 mL) dropwise, over 15 minutes. Let stir at room temperature for 7 hours. Slowly added 6 mL aqueous NH_4Cl solution, added 15 mL H_2O, extracted 3 times with 25 mL ether, and dried with $MgSO_4$. Purified via silica gel chromatography (85:15 hexanes:ethyl acetate) to obtain ca. 700 mg of **81** as an oil (69% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 5.72 (1H, dt, *J* = 11.4, 5.9 Hz), 5.59 (1H, d, *J* = 6.0 Hz), 2.15 (3H, m), 1.7 (10H, m), 0.94 (3H, t, *J* = 7.4 Hz). ^{13}C NMR (300 MHz, $CDCl_3$, ppm): δ 138.9, 130.3, 76.3, 38.2, 34.1, 27.9, 27.8, 24.3, 8.1.

(2*E*,9*E*)-dimethyl 4-ethyl-4-hydroxyundeca-2,9-dienedioate (**82**). Followed general procedure, with 28 μL (0.2 mmol) **81**, 36 μL (0.4 mmol) methyl acrylate, 8 mg (0.009 mmol) **2**, and 1 mL CH_2Cl_2. Purified via silica gel chromatography (7:3 hexanes:ethyl acetate) to obtain ca. 40 mg of **82** as an oil (70% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 6.93 (1H, dt, *J* = 15.3, 7.1 Hz), 6.87 (1H, d, *J* = 15.9 Hz), 6.03 (1H, d, *J* = 16.5

Hz), 5.80 (1H, d, *J* = 14.9 Hz), 3.74 (3H, s), 3.71 (3H, s), 2.19 (2H, dt, 7.0, 7.0 Hz), 1.5 (9H, m), 0.87 (3H, t, *J* = 7.7 Hz). ^{13}C NMR (300 MHz, $CDCl_3$, ppm): δ 167.14, 167.07, 153.4, 149.3, 121.1, 119.6, 75.7, 51.8, 51.6, 40.3, 33.6, 32.4, 28.6, 23.3, 8.0.

(*E*)-methyl 8-ethyl-8-hydroxydeca-2,9-dienoate (**83**). Same reaction as for **82**. Obtained ca. 5 mg of **83** as an oil (10% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 6.96 (1H, dt, *J* = 15.3, 7.1 Hz), 5.80 (2H, m), 5.20 (1H, dd, *J* = 17.3, 1.4 Hz), 5.12 (1H, dd, *J* = 11.1, 1.2 Hz), 3.73 (3H, s), 2.21 (2H, dt, 7.0, 7.0 Hz), 1.5 (9H, m), 0.87 (3H, t, *J* = 7.4 Hz). ^{13}C NMR (300 MHz, $CDCl_3$, ppm): δ 167.2, 149.6, 143.7, 121.0, 112.8, 75.8, 51.7, 40.3, 33.6, 32.5, 28.8, 23.4, 8.0.

(*Z*)-*tert*-butyl(1-ethylcyclohept-2-enyloxy)dimethylsilane (**84**). To flame-dried, round-bottomed flask under an argon atmosphere, added 95% sodium hydride (200 mg, 7.9 mmol) and THF (5 mL). Let stir for 5 minutes. Added a solution of **81** (370 mg, 2.64 mmol) and THF (9 mL) via cannula transfer. Let stir for 5 minutes, placed in an 85 °C oil bath, let stir for 30 minutes, cooled to room temperature, added *t*-butyldimethylsilyl chloride (600 mg, 4.0 mmol), and replaced in 85 °C oil bath. Let stir under reflux for 10 hours, then removed from heat, added 30 mL H_2O, extracted 3 times with 25 mL ether, and dried with Na_2SO_4. Purified twice via silica gel chromatography (100% hexanes) to obtain 451 mg of **84** as a clear oil (67% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 5.6 (2H, m), 2.1 (2H, m), 1.7 (8H, m), 0.9 (3H, m), 0.89 (9H, s), 0.10 (3H, s), 0.08 (3H, s). ^{13}C NMR (300 MHz, $CDCl_3$, ppm): δ 140.6, 128.6, 79.2, 38.8, 34.8, 28.1, 27.9, 26.2, 24.4, 18.7, 8.4, –1.7, –1.8.

(*E*)-methyl 8-(*tert*-butyldimethylsilyloxy)-8-ethyldeca-2,9-dienoate (**85**). Followed general procedure, with 56 μL (0.2 mmol) **84**, 36 μL (0.4 mmol) methyl acrylate, 8 mg (0.009 mmol) **2**, and 1 mL CH_2Cl_2. Purified via silica gel chromatography (9:1 hexanes:ethyl acetate) to obtain ca. 17 mg of **85** as an oil (26% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 6.97 (1H, dt, *J* = 15.9, 6.9 Hz), 5.80 (2H, m), 5.15 (1H, dd, *J* = 17.3, 2.0 Hz), 5.05 (1H, dd, *J* = 10.4, 1.7 Hz), 3.73 (3H, s), 2.21 (2H, dtd, 7.3, 7.3, 1.4 Hz), 1.4 (8H, m), 0.90 (9H, s), 0.84 (3H, t, *J* = 7.5 Hz), 0.084 (3H, s), 0.075 (3H, s).

(*Z*)-3-(benzyloxy)-3-ethylcyclohept-1-ene (**86**). Followed procedure given for **84**, with 77 mg (0.55 mmol) **81**, 98 μL (0.82 mmol) benzyl bromide, 30 mg (1.2 mmol) sodium hydride (95%), 4 mL THF, and a reaction time of 4 hours. Purified via silica gel chromatography (100% hexanes to 9:1 hexanes:ethyl acetate) to obtain 112 mg of **86** as a yellow oil (88% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 7.3 (5H, m), 5.88 (1H, dt), 5.64 (1H, d), 4.45 (2H, m), 1.5-2.3 (10H, m), 0.95 (3H, t).

(*E*)-methyl 8-(benzyloxy)-8-ethyldeca-2,9-dienoate (**87**). Followed general procedure, with 53 mg (0.23 mmol) **86**, 42 μL (0.47 mmol) methyl acrylate, 8 mg (0.009 mmol) **2**, and 5 mL CH_2Cl_2. Purified via silica gel chromatography (9:1 hexanes:ethyl acetate) to obtain 11 mg of **87** as an oil (15% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 7.34 (5H, m), 6.96 (1H, dt), 5.78 (2H, m), 5.24 (2H, m), 4.32 (2H, s), 3.72 (3H, s), 2.2 (2H, dt), 1.2-1.7 (8H, m), 0.87 (3H, t, *J* = 7.5 Hz).

(*Z*)-1,4-dioxaspiro[4.6]undec-6-ene (**88**). *Step 1:* To a flame-dried, round-bottomed flask, under an argon atmosphere, added cycloheptanone (0.7 mL, 5.9 mmol), anhydrous ethylene glycol (3 mL, 54 mmol), *p*-toluenesulfonic acid, monohydrate (70 mg, 0.37 mmol), and anhydrous toluene (30 mL). Placed in a 130 °C oil bath and allowed to reflux, with azeotropic removal of water via a Dean Stark trap, for 5.5 hours. Cooled to room temperature, washed 2 times with 30 mL aqueous $NaHCO_3$ solution and 2 times with 30 mL H_2O, then dried with Na_2SO_4. Purified via silica gel chromatography (9:1 hexanes:ethyl acetate) to obtain 888 mg of 1,4-dioxaspiro[4.6]undecane as a clear oil (96% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 3.92 (4H, s), 1.8 (4H, m), 1.55 (8H, m). ^{13}C NMR (300 MHz, $CDCl_3$, ppm): δ 113.3, 64.2, 38.8, 29.7, 22.8. *Step 2*: To a flame-dried, round-bottomed flask, under an argon atmosphere, added 1,4-dioxaspiro[4.6]undecane (0.5 mL, 3.5 mmol) and THF (18 mL). Added 90% pyridinium hydrobromide perbromide (1.4 g, 3.9 mmol) all at once and let stir at room temperature. Solution immediately turned from red to yellow. Added several extra scoops of the brominating reagent and let stir at room temperature for 30 minutes. Added 20 mL aqueous $NaHCO_3$ solution, extracted 3 times with 30 mL ethyl acetate; then washed with 75 mL H_20, 75 mL aqueous $CuSO_4$ solution, 75 mL H_2O, and 75 mL brine. Dried with Na_2SO_4. Purified via silica gel chromatography (9:1 hexanes:ethyl acetate) to obtain ca. 820 mg of 6-bromo-1,4-dioxaspiro[4.6]undecane as a yellow oil (99% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 4.21 (1H, dd), 4.0 (4H, m), 1.4-2.3 (10H, m). ^{13}C NMR (300 MHz, $CDCl_3$, ppm): δ 111.1, 65.7, 65.3, 60.9, 35.2, 33.0, 26.4, 25.0, 20.7. *Step 3:* To a flame-dried, round-bottomed flask, under an argon atmosphere, added potassium *t*-butoxide (1.2 g, 10.2 mmol) and DMSO (5.5 mL). Placed in a 40 °C oil bath and let stir

for 30 minutes. Added 6-bromo-1,4-dioxaspiro[4.6]undecane (1 mL, 6.4 mmol) via syringe and raised heat to 50 °C. Solution immediately changed from off-white to orange. Let stir at 50 °C for 6 hours, then removed from heat, added 15 mL H_2O, extracted 8 times with ether, and dried with $MgSO_4$. Purified via silica gel chromatography (8:2 hexanes:ethyl acetate) to obtain 477 mg of **88** as a slightly yellow oil (48% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 5.88 (1H, dt, *J* = 12.0, 5.9 Hz), 5.64 (1H, d, *J* = 11.7 Hz), 3.95 (4H, m), 2.2 (2H, dt), 1.7 (6H, m). ^{13}C NMR (300 MHz, $CDCl_3$, ppm): δ 133.8, 133.7, 109.7, 64.5, 36.2, 27.9, 27.0, 23.9.

(*E*)-methyl 7-(2-vinyl-1,3-dioxolan-2-yl)hept-2-enoate (**89**). Followed general procedure, with 28 μL (0.2 mmol) **88**, 36 μL (0.4 mmol) methyl acrylate, 8 mg (0.009 mmol) **2**, and 5 mL CH_2Cl_2. Purified via silica gel chromatography (9:1 hexanes:ethyl acetate) to obtain 17 mg of **89** as a yellow oil (35% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 6.96 (1H, dt, *J* = 15.9, 7.1 Hz), 5.81 (1H, d, *J* = 15.3, 1.5 Hz), 5.71 (1H, dd, *J* = 17.7, 10.5 Hz), 5.35 (1H, dd, *J* = 12.3, 2.0 Hz), 5.17 (1H, dd, *J* = 10.5, 1.8 Hz), 3.9 (4H, m), 3.73 (3H, s), 2.2 (2H, dt), 1.6 (6H, m). ^{13}C NMR (300 MHz, $CDCl_3$, ppm): δ 167.2, 149.6, 137.6, 121.0, 115.7, 109.0, 64.7, 51.7, 38.1, 32.5, 28.4, 23.3.

(2*E*,9*E*)-di-*tert*-butyl 4-(*tert*-butyldimethylsilyloxy)undeca-2,9-dienedioate (**90**). Followed general procedure, with 46 μL (0.2 mmol) **71**, 60 μL (0.41 mmol) *t*-butyl acrylate, 8 mg (0.009 mmol) **2**, and 1 mL CH_2Cl_2. Purified via silica gel chromatography (9:1 hexanes:ethyl acetate) to obtain ca. 30 mg of **90** as an oil (31% yield). ^{1}H NMR (300

MHz, $CDCl_3$, ppm): δ 6.8 (2H, m), 5.85 (1H, d), 5.7 (1H, d), 4.25 (1H, m), 2.2 (2H, m), 1.5 (6H, m), 1.45 (18H, s), 0.95 (9H, s), 0.05 (6H, m).

(2*E*,9*E*)-di-*tert*-butyl 4-ethyl-4-hydroxyundeca-2,9-dienedioate (**91**). Followed general procedure, with 28 μL (0.2 mmol) **81**, 60 μL (0.41 mmol) *t*-butyl acrylate, 8 mg (0.009 mmol) **2**, and 1 mL CH_2Cl_2. Purified via silica gel chromatography (8:2 hexanes:ethyl acetate) to obtain 45 mg of **91** as a yellow oil (61% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 6.82 (1H, dt), 6.77 (1H, d), 5.94 (1H, d), 5.72 (1H, d), 2.15 (2H, dt), 1.5 (6H, m), 1.5 (9H, s), 1.45 (9H, s), 0.85 (3H, t).

(*E*)-*tert*-butyl 8-(*tert*-butyldimethylsilyloxy)-8-ethyldeca-2,9-dienoate (**92**). Followed general procedure, with 56 μL (0.2 mmol) **84**, 58 μL (0.4 mmol) *t*-butyl acrylate, 8 mg (0.009 mmol) **2**, and 5 mL CH_2Cl_2. Purified via silica gel chromatography (9:1 hexanes:ethyl acetate) to obtain 20 mg of **92** as an orange oil (28% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 6.85 (1H, dt), 5.76 (2H, m), 5.14 (1H, dd), 5.05 (1H, dd), 2.17 (2H, dt), 1.4 (17H, m), 0.89 (9H, s), 0.83 (3H, t), 0.08 (6H, s).

(2*E*,9*E*)-dimethyl 4-(*t*-butyldiphenylsilyloxy)-2,10-dimethylundeca-2,9-dienedioate (**93**). Followed general procedure, with 73 mg (0.21 mmol) **74**, 1 mL (9.3 mmol) methyl methacrylate, and 8 mg (0.009 mmol) **2**. Purified via silica gel chromatography (9:1 hexanes:ethyl acetate) to obtain 18 mg of **93** as an oil (18% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 7.65 (4H, m), 7.35 (6H, m), 6.70 (1H, td), 6.64 (1H, dd), 4.40 (1H, m),

3.75 (3H, s), 3.70 (3H, s), 2.1 (2H, dt), 1.8 (3H, s), 0.8-1.8 (6H, m), 1.4 (3H, s), 1.05 (9H, s).

(*E*)-methyl 8-(*tert*-butyldiphenylsilyloxy)-2-methyldeca-2,9-dienoate (**94**). Same reaction as for **93**. Obtained ca. 50 mg of **94** as an oil (61% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 7.7 (4H, m), 7.4 (6H, m), 6.7 (1H, t), 5.8 (1H, m), 5.01 (1H, d), 4.98 (1H, d), 4.14 (1H, dt), 3.75 (3H, s), 2.05 (2H, dt), 1.8 (3H, s), 1.3 (6H, m), 1.05 (9H, s).

(*E*)-trimethyl 2-vinylnon-7-ene-1,1,8-tricarboxylate (**95**). Followed general procedure, with 38 μL (0.2 mmol) **77**, 1 mL (9.3 mmol) methyl methacrylate, and 8 mg (0.009 mmol) **2**. Purified via silica gel chromatography (7:3 hexanes:ethyl acetate) to obtain ca. 20 mg of **95** as an oil (30% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 6.73 (1H, t), 5.62 (1H, m), 5.08 (2H, m), 3.7 (9H, m), 3.4 (1H, d), 2.77 (1H, m), 2.15 (2H, dt), 1.8 (3H, s), 1.35 (6H, m).

(*E*)-methyl 8-ethyl-8-hydroxy-2-methyldeca-2,9-dienoate (**96**). Followed general procedure, with 28 μL (0.2 mmol) **81**, 1 mL (9.3 mmol) methyl methacrylate, and 8 mg (0.009 mmol) **2**. Purified via silica gel chromatography (7:3 hexanes:ethyl acetate) to obtain 19 mg of **96** as a dark brown oil (40% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 6.75 (1H, t), 5.8 (1H, dd), 5.2 (1H, dd), 5.13 (1H, dd), 3.75 (3H, s), 2.2 (2H, dt), 1.8 (3H, s), 1.5 (8H, m), 0.85 (3H, t).

(*E*)-methyl 8-(*tert*-butyldimethylsilyloxy)-8-ethyl-2-methyldeca-2,9-dienoate (**97**). Followed general procedure, with 56 μL (0.2 mmol) **84**, 1 mL (9.3 mmol) methyl methacrylate, and 8 mg (0.009 mmol) **2**. Purified via silica gel chromatography (9:1 hexanes:ethyl acetate) to obtain 10 mg of **97** as a clear oil (14% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 6.78 (1H, t), 5.78 (1H, dd), 5.25 (1H, dd), 5.05 (1H, dd), 3.74 (3H, s), 2.2 (2H, dt), 1.8 (3H, s), 1.4 (8H, m), 0.89 (9H, s), 0.83 (3H, t), 0.075 (3H, s), 0.066 (3H, s).

(3*E*,10*E*)-5-(*tert*-butyldimethylsilyloxy)trideca-3,10-diene-2,12-dione (**98**). Followed general procedure, with 46 μL (0.2 mmol) **71**, 34 μL (0.41 mmol) methyl vinyl ketone, 9 mg (0.01 mmol) **2**, and 1 mL CH_2Cl_2. Purified via silica gel chromatography (9:1 hexanes:ethyl acetate) to obtain 33 mg of **98** as a dark oil (49% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 6.78 (1H, dt, *J* = 15.9, 6.9 Hz), 6.71 (1H, dd, *J* = 15.9, 5.1 Hz), 6.20 (1H, dd, *J* = 15.8, 1.4 Hz), 6.06 (1H, dt, *J* = 15.9, 1.4 Hz), 4.3 (1H, m), 2.26 (3H, s), 2.24 (3H, s), 2.2 (2H, m), 1.4 (6H, m), 0.90 (9H, s), 0.05 (3H, s), 0.02 (3H, s). ^{13}C NMR (300 MHz, $CDCl_3$, ppm): δ 198.5, 198.4, 149.5, 147.9, 131.3, 128.9, 71.5, 37.1, 32.4, 28.1, 27.5, 27.0, 25.9, 24.5, 18.3, –4.4, –4.8.

(*E*)-9-(*tert*-butyldimethylsilyloxy)undeca-3,10-dien-2-one (**99**). Same reaction as for **98**. Obtained 11 mg of **99** as an oil (19%). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 6.79 (1H, dt, *J* = 16.2, 6.8 Hz), 6.06 (1H, dt, *J* = 15.9, 1.6 Hz), 5.78 (1H, ddd, *J* = 17.1, 10.3, 6.1 Hz), 5.13 (1H, dt, *J* = 17.1, 1.6 Hz), 5.02 (1H, d, *J* = 10.2 Hz), 4.17 (1H, m), 2.24 (3H, s), 2.23 (2H, m), 1.4 (6H, m), 0.89 (9H, s), 0.04 (3H, s), 0.03 (3H, s). ^{13}C NMR (300 MHz,

$CDCl_3$, ppm): δ 198.6, 148.3, 141.5, 131.3, 113.6, 73.6, 37.8, 32.5, 28.2, 26.9, 25.9, 24.8, 18.3, –4.2, –4.7.

(7*E*)-trimethyl 2-(prop-1-enyl)oct-7-ene-1,1,8-tricarboxylate (**100**). Followed general procedure, with 38 μL (0.2 mmol) **77**, 42 μL (0.4 mmol) methyl crotonate, 8 mg (0.009 mmol) **2**, and 1 mL CH_2Cl_2. Purified via silica gel chromatography (7:3 hexanes:ethyl acetate) to obtain 12 mg of **100** as an oil (18% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 6.94 (1H, dt, *J* = 15.9, 6.8 Hz), 5.81 (1H, d, *J* = 15.9 Hz), 5.51 (1H, dq, *J* = 15.6, 6.4 Hz), 5.20 (1H, ddd, *J* = 15.2, 9.5, 1.4 Hz), 3.73 (6H, s), 3.68 (3H, s), 3.33 (1H, d, *J* = 9.0 Hz), 2.70 (1H, m), 2.20 (2H, dt), 1.65 (3H, dd, *J* = 6.6, 1.5 Hz), 1.4 (6H, m). ^{13}C NMR (300 MHz, $CDCl_3$, ppm): δ 168.9, 168.7, 167.2, 149.6, 130.4, 128.6, 121.0, 57.5, 52.6, 52.5, 51.6, 43.4, 32.6, 32.3, 27.9, 26.8, 18.2.

Dimethyl 2-((2*E*,9*E*)-1,11-dioxoundeca-2,9-dien-4-yl)malonate (**101**). Followed general procedure, with 38 μL (0.2 mmol) **77**, 34 μL (0.41 mmol) crotonaldehyde, 8 mg (0.009 mmol) **2**, and 1 mL CH_2Cl_2. Purified via silica gel chromatography (6:4 hexanes:ethyl acetate) to obtain 11 mg of **101** as a yellow oil (18% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 9.52 (1H, d, *J* = 7.8 Hz), 9.50 (1H, d, *J* = 7.8 Hz), 6.80 (2H, m), 6.15 (2H, m), 3.76 (3H, s), 3.73 (3H, s), 3.54 (1H, d, *J* = 7.8 Hz), 3.15 (1H, m), 2.34 (2H, dt, *J* = 6.9 Hz), 1.4 (6H, m). ^{13}C NMR (300 MHz, $CDCl_3$, ppm): δ 194.0, 193.5, 168.0, 167.9, 157.9, 156.2, 134.7, 133.3, 55.7, 53.1, 52.9, 42.6, 32.6, 31.8, 27.7, 27.0.

Dimethyl 2-((9*E*)-11-oxoundeca-2,9-dien-4-yl)malonate (**102**). Same reaction as for **101**. Obtained 19 mg of **102** (contaminated with minor impurities) as a yellow oil (< 30% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 9.50 (1H, d, *J* = 7.8 Hz), 6.83 (1H, dt, *J* = 15.9, 6.6 Hz), 6.10 (1H, dd, *J* = 15.9, 8.1 Hz), 5.54 (1H, m), 5.20 (1H, m), 3.73 (3H, s), 3.68 (3H, s), 3.33 (1H, d, *J* = 8.7 Hz), 2.70 (1H, m), 2.33 (2H, dt, *J* = 7.0 Hz), 1.65 (3H, d, *J* = 6.0 Hz), 1.4 (6H, m).

Dimethyl 2-(1,17-diacetoxyheptadeca-5,12-dien-7-yl)malonate (**103**). Followed general procedure, with 38 μL (0.2 mmol) **77**, 66 μL (0.4 mmol) 5-hexenyl acetate, 8 mg (0.009 mmol) **2**, and 1 mL CH_2Cl_2. Purified via silica gel chromatography (7:3 hexanes:ethyl acetate) to obtain 19 mg of **103** as an oil (20% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 5.37 (4H, m), 4.06 (4H, m), 3.73 (3H, s), 3.68 (3H, s), 3.33 (1H, d, *J* = 9.3 Hz), 2.70 (1H, m), 2.05 (6H, s), 2.0 (6H, m), 1.4 (14H, m).

7-Ethyl-7-hydroxyheptadeca-5,12-diene-1,17-diyl diacetate (**104**). Followed general procedure, with 26 μL (0.2 mmol) **81**, 68 μL (0.41 mmol) 5-hexenyl acetate, 8 mg (0.009 mmol) **2**, and 1 mL CH_2Cl_2. Purified via silica gel chromatography (7:3 hexanes:ethyl acetate) to obtain 16 mg of **104** as an oil (20% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 5.45 (4H, m), 4.06 (4H, m), 2.05 (6H, s), 2.05 (6H, m), 1.45 (16H, m), 0.85 (3H, t, 7.5 Hz). ^{13}C NMR (300 MHz, $CDCl_3$, ppm): δ 171.3, 136.3, 131.0, 129.8, 128.0, 75.3, 64.7, 64.6, 40.8, 33.7, 32.8, 32.4, 32.2, 30.3, 28.3, 26.12, 26.06, 23.4, 21.3, 8.2.

4-Ethyl-4-hydroxyundeca-2,9-diene-1,11-diyl diacetate (**105**). Followed general procedure, with 26 μL (0.2 mmol) **81**, 64 μL (0.41 mmol) (*Z*)-but-2-ene-1,4-diyl diacetate, 8 mg (0.009 mmol) **2**, and 1 mL CH_2Cl_2. Purified via silica gel chromatography (7:3 hexanes:ethyl acetate) to obtain 37 mg of **105** as an oil (59% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 5.65 (4H, m), 4.58 (2H, d, *J* = 4.5 Hz), 4.49 (2H, d, *J* = 6.0 Hz), 2.07 (3H, s), 2.06 (3H, s), 2.05 (2H, m), 1.4 (8H, m), 0.85 (3H, t, *J* = 7.4 Hz). ^{13}C NMR (300 MHz, $CDCl_3$, ppm): δ 170.9, 140.3, 136.4, 124.0, 122.6, 75.1, 65.5, 64.8, 40.4, 33.6, 32.4, 29.5, 23.2, 21.33, 21.30, 8.1.

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Chapter 2.

Cross-Metathesis of Vinyl Boronates

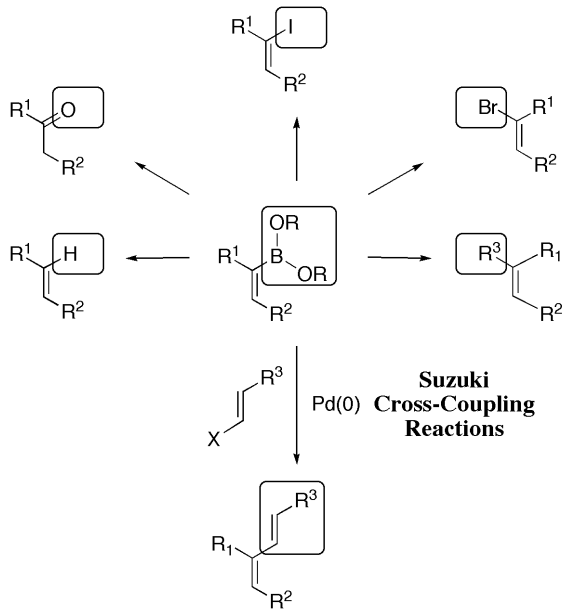
Abstract

The cross-metathesis (CM) of various vinyl boronates, catalyzed by a ruthenium alkylidene complex possessing an *N*-heterocyclic carbene ligand, was investigated. The CM of vinyl boronates lacking α-substitution occurred readily with almost all Type I alkenes, as well as with certain Type II and Type III alkenes. The resultant functionalized vinyl boronate products were isolated in moderate-to-high yields and were formed in moderate-to-high *E*-stereoselectivity. The *E*-vinyl boronate products were subsequently converted into either *Z*-vinyl bromides or *E*-vinyl iodides, demonstrating a two-step procedure to stereoselectively transform terminal alkenes into either *E*- or *Z*-vinyl halides. The CM/bromination reaction sequence could be performed efficiently as a one-pot reaction. Vinyl boronates bearing α-substituents underwent CM in certain cases. When the α-substituent was a methyl group, the CM reaction proceeded with moderate yield and high *Z*-stereoselectivity, as long as unhindered, Type I alkenes were employed as cross partners. When the α-substituent was larger than a methyl group, both the yields and the *Z*-stereoselectivities dropped significantly. These latter reactions also appeared to be highly substrate specific, based on their observed reactivity patterns. Vinyl boronates lacking α-substitution were designated as Type II alkenes, while those bearing an α-substituent were classified as either Type III or Type IV alkenes.

2.1. Background

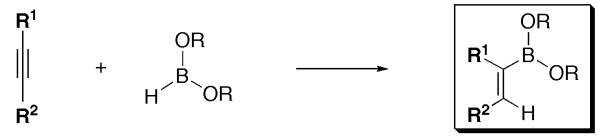
Vinyl boronic acids and esters serve as versatile synthetic intermediates for organic chemists.[1] As illustrated in Scheme 2.1.1, the boronate moiety of these compounds can be converted into numerous other functional groups, such as hydrogen,[1d] an aldehyde or a ketone,[1d,2] a halide,[3] or an alkyl group.[4] Most notably, 1-alkenylboron compounds are excellent components in Suzuki cross-coupling reactions, which have become ubiquitous in organic synthesis.[5]

Scheme 2.1.1. Vinyl boronates: versatile synthetic intermediates.



Alkyne hydroboration, illustrated in Scheme 2.1.2, is usually employed to prepare these vinyl boron reagents. This hydroboration protocol can deliver high yields of the vinyl boronate products under mild reaction conditions, but efficient and selective

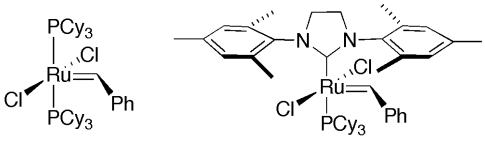
Scheme 2.1.2. Vinyl boronate synthesis via alkyne hydroboration.



reactions are often limited to those of terminal alkynes (Scheme 2.1.2, R^1 = H).[1c,6] In addition, β,β-disubstituted vinyl boronates cannot be synthesized using this procedure.[i] An even greater disadvantage of alkyne hydroboration is that the alkynes that are needed to carry out this reaction often require several steps to prepare.[8]

As previously described in Chapter 1, olefin cross-metathesis (CM) has become a viable synthetic strategy for the generation of highly functionalized alkenes, due primarily to the development of ruthenium catalysts such as **1** and **2** (Figure 2.1.1).

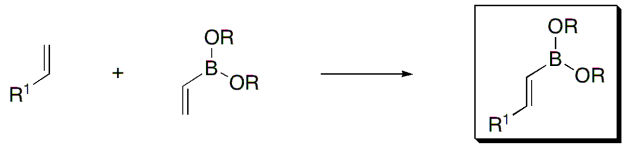
Figure 2.1.1. Most common ruthenium-based olefin metathesis catalysts (Cy = cyclohexyl).



1 **2**

Therefore, CM offers an attractive alternative to alkyne hydroboration for vinyl boronate synthesis, as illustrated in Scheme 2.1.3. This synthetic strategy is advantageous as compared to alkyne hydroboration because alkenes are more easily prepared than are alkynes. In addition, the number of commercially available alkenes far exceeds that of terminal alkynes. To further illustrate the benefits of a vinyl boronate CM

Scheme 2.1.3. Vinyl boronate synthesis via cross-metathesis (CM).

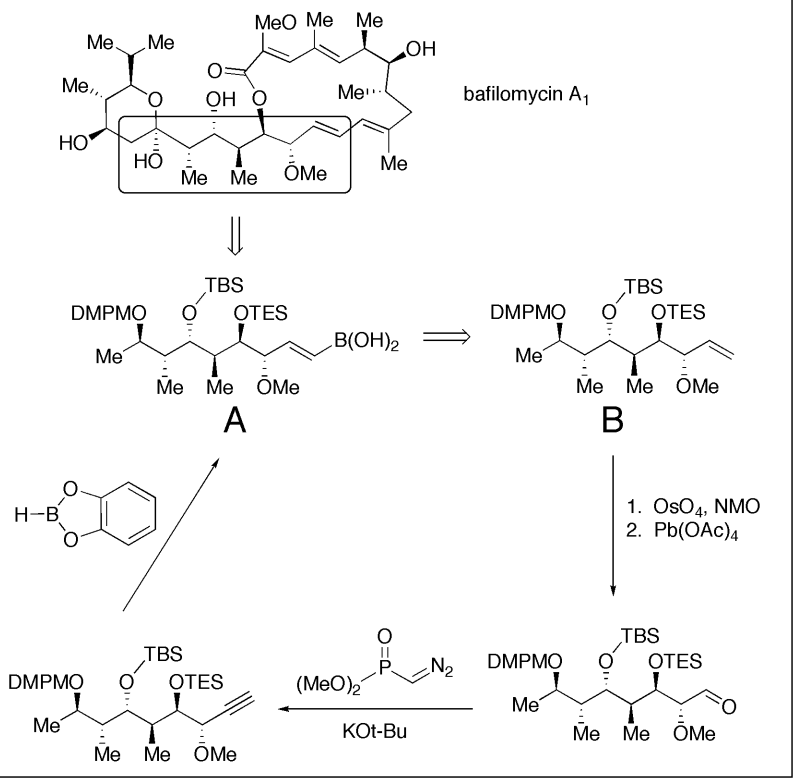


reaction, Scheme 2.1.4 shows a segment of the total synthesis of bafilomycin A_1.[9] In this synthesis, a vinyl boronate **A** was needed to synthesize one of the conjugated diene portions of this molecule. Vinyl boronate **A**, in turn, had to be generated from alkene **B**. As shown in Scheme 2.1.4, four steps were required to transform **B** into **A**. In addition, several synthetic strategies had to be explored in order to find reactions that would not

[i] β,β-disubstituted vinyl boronates can be synthesized using a two-step haloboration/cross-coupling procedure.[7]

epimerize the allylic methoxy group of **B**. If vinyl boronate CM had instead been employed in this synthesis, the transformation from **B** to **A** would have been accomplished in a single step under very mild reaction conditions.

Scheme 2.1.4. Segment of the total synthesis of bafilomycin A_1: Generation of vinyl boronate A from an alkene B requires four steps.[9]



When I began work in this area of research, our group had already discovered that vinyl boronate CM could be accomplished with catalyst **1** when aliphatic terminal alkenes were employed as cross partners,[10] and Danishefsky had successfully applied this methodology to the synthesis of Suzuki macrocyclization precursors.[11] The scope of this reaction, however, had not been explored. In addition, the use of catalyst **2** in vinyl boronate CM had not been exploited. As catalyst **2** is able to undergo CM with many more alkenes than is catalyst **1**, we anticipated that a wide variety of functionalized vinyl boronates could be synthesized from alkenes via CM using catalyst **2**. Thus the purpose

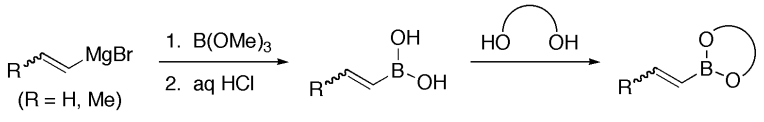
of our research during this project was to explore the scope of vinyl boronate CM, especially with the use of catalyst **2**.

2.2. Vinyl Boronates Lacking α-Substitution

2.2.1. Boronate cross partners

The first issue that had to be addressed in this project was the identity of the boronate cross partner in these reactions. Two general choices were available: boronic acids and boronic esters. In the latter case, only cyclic boronic esters were considered, due to their significantly higher stability relative to acyclic boronic esters. All of these boronates were synthesized from the corresponding Grignard reagent according to the general procedure illustrated in Scheme 2.2.1.[12] The products were either isolated as

Scheme 2.2.1. General procedure for the synthesis of boronate cross partners.

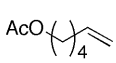
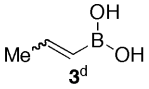
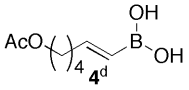
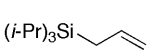
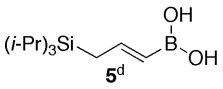
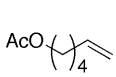
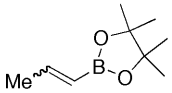
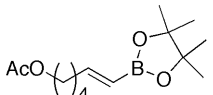
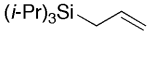
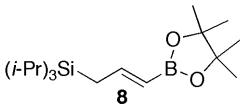
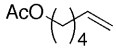
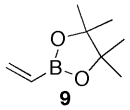
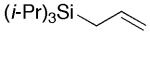
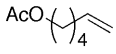
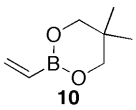
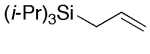
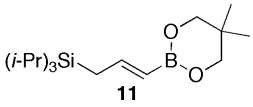


boronic acids or directly condensed with a diol, such as pinacol or neopentyl glycol, and then isolated as boronic esters. Both vinyl- and 1-propenylmagnesium bromide (Scheme 2.2.1, R = H, Me, respectively) were employed as Grignard reagents. We were unable to isolate vinylboronic acid (R = H), due to its rapid polymerization upon concentration.[13] 1-Propenylboronic acid (R = Me) was also prone to polymerization, but it was more stable than its vinyl analog.[14] We were able to isolate 1-propenylboronic acid as a white, air-stable solid in 10-20% yield via recrystallization from benzene. This substrate existed primarily as a cyclic trimer, as evidenced by GC/MS analysis, and it contained a mixture of stereoisomers, whose *E*:*Z* ratio varied widely from batch to batch. Both vinyl- and 1-

propenylboronic acid could be directly converted into various boronate esters, which were all purified via silica gel chromatography.

As shown in Table 2.2.1,[15] 1-propenylboronic acid (**3**) was able to participate in these CM reactions (entries 1-2), and, in fact, **3** exhibited the highest *E*-selectivity of any of the boronates that were tested. Unfortunately the CM reactions involving **3** resulted in

Table 2.2.1. Comparison of CM with different boronates.[a,b]

entry	cross partner	boronate	product	isolated yield (%)	*E*:*Z*[c]	notebook page
1		 **3**[d]	 **4**[d]	34	> 20:1	cm3-44
2		**3**	 **5**[d]	58	> 20:1	cm3-55
3		 **6**	 **7**	65	> 20:1	cm3-50
4		**6**	 **8**	99	10:1	cm3-191
5		 **9**	**7**	59	> 20:1	cm3-28
6		**9**	**8**	86	12:1	cm3-36
7		 **10**	N. R.	------	------	cm4-69
8		**10**	 **11**	90	20:1	cm4-68

[a] 0.2 mmol scale, 1 equiv boronate, 5 mol% **2**, CH_2Cl_2, reflux, cross partner = 0.1-0.2M. [b] See ref. 15. [c] Determined for the isolated material by ^1H NMR. [d] Isolated as a mixture of monomer (as shown above) and cyclic trimer.

low isolated yields, due in part to the high polarity and the monomeric/trimeric mixtures of the resultant cross products. Thus **3** was not a practical reagent for these reactions. The CM reactions involving the boronic esters resulted in much higher yields (Table 2.2.1, entries 3-8). Both pinacol (**6**, **9**) and neopentyl (**10**) boronic esters were

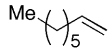
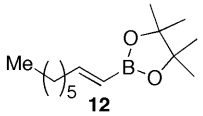
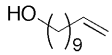
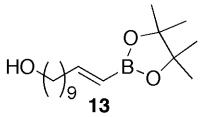
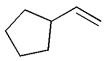
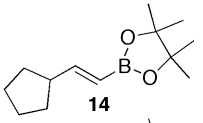
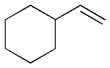
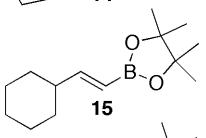
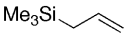
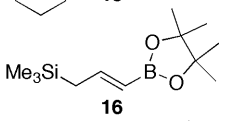
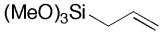
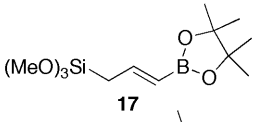
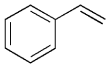
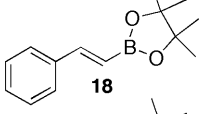
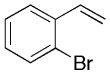
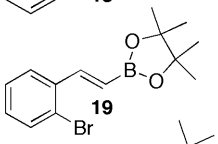
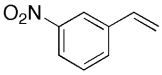
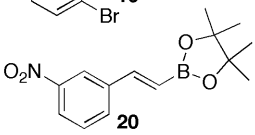
investigated, and the former exhibited the larger substrate scope (compare entries 5-6 and 7-8). Thus pinacol boronic esters became the reagent of choice for these CM reactions. Both vinyl (**9**) and 1-propenyl (**6**) pinacol boronate were suitable reagents, as they each led to similar yields and *E*-selectivities (compare entries 3-4 and 5-6). Because boronate **6** was generally isolated in higher yield (ca. 80%) than **9** (ca. 60%), it was employed as the cross partner in the bulk of the subsequent studies.

2.2.2. Substrate scope

Table 2.2.2 lists the results of the CM of boronate **6** with various cross partners.[15] These cross partners were primarily Type I alkenes, as discussed in Chapter 1. In these reactions, little or no homodimerization of **6** was observed, whereas the Type I cross partners homodimerized readily. Therefore, excess boronate **6** was often employed in order to diminish the amount of cross partner homodimer that formed (for ease of purification). The product yield itself (based on the limiting reagent) did not change significantly when the relative stoichiometry between boronate **6** and the cross partner was varied. As shown in Table 2.2.2, the yields in these CM reactions were good in all cases except for that of allyltrimethoxysilane (entry 6), although CM reactions with both the methyl (entry 5) and the *iso*-propyl (Table 2.2.1, entry 4) analogs of this cross partner proceeded in high yield. It is also noteworthy that styrenes with bulky *ortho*-substituents, which are Type II alkenes, participated readily in this reaction (Table 2.2.2, entry 8). These CM reactions exhibited moderate-to-high *E*-selectivity. The highest levels of *E*-

selectivity were generally achieved by using either alkenes possessing secondary or tertiary allylic substitution (entries 3-4) or styrenes (entries 7-9) as the cross partner.[ii]

Table 2.2.2. CM with 1-propenyl pinacol boronate (6).[a,b]

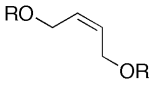
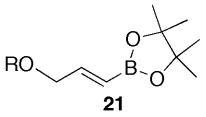
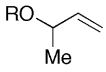
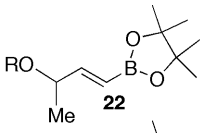
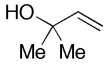
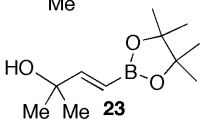
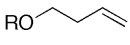
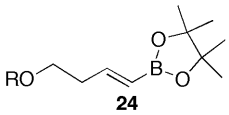
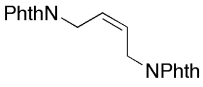
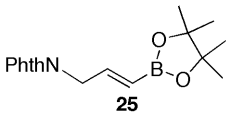
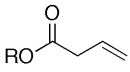
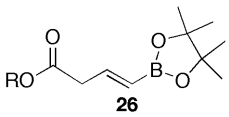
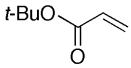
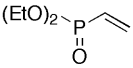
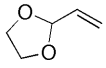
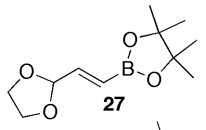
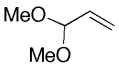
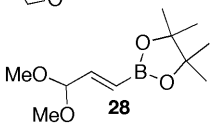
entry	cross partner	equiv **6**	product	isolated yield (%)	*E*:*Z* [c]	notebook page
1		2	 **12**	83	9:1	cm3-196
2		2	 **13**	71	14:1	cm3-197
3		2	 **14**	80	20:1	cm3-199
4		1	 **15**	85	> 20:1	cm3-72
5		1	 **16**	89	8:1	cm3-190
6		1	 **17**	26	> 20:1	cm3-106
7		1	 **18**	96	> 20:1	cm3-160
8		1	 **19**	83	> 20:1	cm3-161
9		1	 **20**	68	> 20:1	cm3-174

[a] 0.2-0.4 mmol scale, 5 mol% **2**, CH_2Cl_2, reflux, cross partner = 0.1-0.2M. [b] See ref. 15.
[c] Determined for the isolated material by ^1H NMR.

Table 2.2.3 lists the results of CM reactions of boronate **6** with cross partners possessing allylic or homoallylic heteroatoms.[15] In these cases, the success of the CM

[ii] In most cases, the reported *E*:*Z* ratios reflect the actual *E*:*Z*-selectivity of the CM reaction. However, in some cases the two stereoisomers were at least partially separable by silica gel chromatography. In these cases, the relative amount of *E*-isomer present in the isolated product mixture, which is the value given in all of the tables herein, was enriched somewhat.

Table 2.2.3. CM with 1-propenyl pinacol boronate (6): cross partners with allylic/homoallylic heteroatoms.[a,b]

entry	R	cross partner	equiv **6**	product	isolated yield (%)[c]	*E*:*Z*[d]	notebook page
1	Tr (a)		1		N. D.	------	cm3-156
2	TBS (b)		1		N. D.	------	cm3-152
3	Bn (c)		1		N. D.	------	cm3-150
4	Ac (d)		1		29	> 20:1	cm3-62
5	Bz (e)		1		50	13:1	cm3-166
6	Bz (e)		2.5	 **21**	59	8:1	cm3-167
7	H (a)		2	 **22**	N. R.	------	cm3-131
8	Bz (b)		2		36	> 20:1	cm3-215
9			2	 **23**	64	> 20:1	cm3-223
10	H (a)		1	 **24**	< 13	> 20:1	cm3-146
11	Bz (b)		2		66	6:1	cm3-182
12			2.5	 **25**	65	> 20:1	cm3-175
13	H (a)		1	 **26**	N. D.	------	cm3-163
14	Me (b)		1		33	7:1	cm3-205
15			3	------	N. R.	------	cm3-98
16			1	------	N. R.[e]	------	cm3-139
17			2	 **27**	< 20	> 20:1	cm3-162
18			2	 **28**	< 20	N. D.	cm3-204

[a] 0.2-0.4 mmol scale, 5 mol% **2**, CH_2Cl_2, reflux, cross partner = 0.1-0.2M. [b] See ref. 15. [c] For yields designated as N. D., the isolated product contained a complex mixture of unidentified compounds. [d] Determined for the isolated material by ^1H NMR. [e] The methyl group of **6** crossed onto ca. 30% of the cross partner.

reaction was much more substrate dependent. We found that the use of cross partners possessing free alcohols resulted in little or no CM (entries 7 and 10), unless these alcohols were tertiary (entry 9). Substrates possessing alcohols or amines could, however, participate in the CM reaction if suitable protecting groups were used (entries

4-6, 8, 11-12). It is interesting to note, by comparing entries 1-5 of Table 2.2.3, that the choice of protecting group had an enormous impact on the success of these CM reactions. Finally, these CM reactions resulted in little or no reaction with cross partners containing functionalities such as carboxylic acids (entry 13), esters (entry 14), acrylates (entry 15), vinyl phosphonates (entry 16), or protected acrolein moieties (entries 17-18). For the most part, the cross partners listed in Table 2.2.3 that led to ≥ 50% yield of the desired product are Type I alkenes, and those resulting in < 50% yield are either Type II or Type III alkenes.

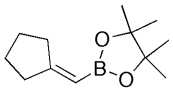
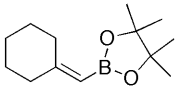
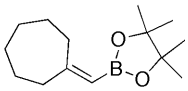
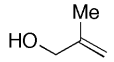
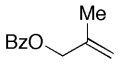
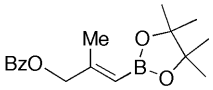
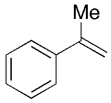
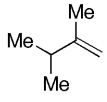
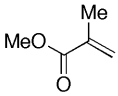
A general observation that was made regarding the results presented in Tables 2.2.1-2.2.3 was that the isolated yield of the product decreased with increasing polarity. The relatively non-polar products, namely **8**, **12**, **14**-**16**, **18**-**19**, were isolated in ≥ 80% yield, whereas the more polar products, namely **7**, **13**, **17**, **20**, and every product shown in Table 2.2.3, were isolated in ≤ 70% yield. A possible explanation for this trend is that some of the product decomposed, presumably via hydrolysis to the boronic acid, during purification by silica gel chromatography. To test this hypothesis, the crude reaction mixtures of some of these CM reactions were investigated by ^{1}H NMR (CD_2Cl_2 solvent). We found that, for these more polar cross partners, the percent conversion to product was often significantly higher than the isolated yield. For example, in the CM reaction of 2-methylbut-3-en-2-ol with two equivalents of boronate **6**, 88% of the 2-methylbut-3-en-2-ol converted into boronate product **23**, and the remainder of the material underwent homodimerization.[iii] This 88% conversion was markedly higher than the 64% isolated yield that we obtained for **23** (Table 2.2.3, entry 9). Thus it appears that, indeed, some of

[iii] Notebook page: cm3-239.

the vinyl boronate product was lost upon purification, especially for the more polar boronates.

We also investigated the CM of pinacol boronates **6** and/or **9** with geminally-disubstituted alkenes, which are generally designated as Type III alkenes. The products of these reactions are β,β-disubstituted vinyl boronates, which cannot be directly synthesized via alkyne hydroboration. Table 2.2.4 lists the results of these experiments.[15] High yields were obtained when the two geminal substituents of the cross partner were tied back in a small, five- or six-membered ring system (entries 1-2). However, when

Table 2.2.4. CM with pinacol boronates (6 or 9): geminally-disubstituted cross partners.[a,b]

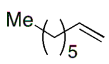
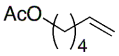
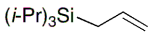
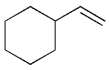
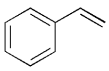
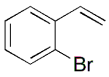
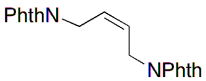
entry	cross partner	boronate	product	isolated yield (%)	*E*:*Z* [c]	notebook page
1		**6**	 **29**	87	------	cm3-169
2		**6**	 **30**	96	------	cm3-168
3	 **31**	**9**	 **32**	23	------	cm4-203
4		**6**	N. R.	------	------	cm3-78
5		**6**	 **33**	45	1:1	cm3-227
6		**9**	complex mixture	------	------	cm4-90
7[d]		**6**	N. R.	------	------	cm3-141
8[d]		**6**	N. R.	------	------	cm3-140

[a] 0.2-0.4 mmol scale, 1 equiv **6** or **9**, 5 mol% **2**, CH_2Cl_2, reflux, cross partner = 0.2M. [b] See ref. 15. [c] Determined for the isolated material by ^1H NMR. [d] Neat, 50 °C.

these geminal substituents were not tied back (entries 4-8), or when they were part of a larger ring system (entry 3), the yields were much lower, and the desired CM reaction did not proceed at all in many cases. Presumably tying back the geminal substituents in a small ring system decreases the steric bulk around the alkene, rendering it more reactive toward CM. It is also important to note that, for the unsymmetrical cross partners, these reactions did not exhibit any appreciable stereoselectivity (entry 5).

The original vinyl boronate CM reaction reported by our group employed the less-reactive catalyst **1**,[10] and thus we were interested to see how many of the CM reactions that we had carried out with catalyst **2** could also be accomplished with this, much less expensive, catalyst. Table 2.2.5 shows the results of these comparison studies between

Table 2.2.5. CM with 1-propenyl pinacol boronate (6): comparison between catalyst 1 and catalyst 2.[a]

				Catalyst 1		Catalyst 2	
entry	cross partner	equiv **6**	product	isolated yield (*E*:*Z*)[b]	notebook page	isolated yield (*E*:*Z*)[b]	notebook page
1		2	**12**	56% (9:1)	cm4-14	83% (9:1)	cm3-196
2		2	**7**	76% (11:1)	cm4-15	66% (13:1)	cm3-221
3		1	**8**	85% (> 20:1)	cm4-18	99% (10:1)	cm3-191
4		1	**15**	89% (> 20:1)	cm4-20	85% (> 20:1)	cm3-72
5		1	**18**	76% (> 20:1)	cm4-22	96% (> 20:1)	cm3-160
6		1	**19**	< 29%[c] (> 20:1)	cm4-23	83% (> 20:1)	cm3-161
7		2.5	**25**	< 21%[c] (N. D.)	cm4-19	65% (> 20:1)	cm3-175
8		1	**30**	4% (------)	cm4-21	96% (------)	cm3-168

[a] 0.1-0.4 mmol scale, 5 mol% **1** or **2**, CH_2Cl_2, reflux, cross partner = 0.2M. [b] Determined for the isolated material by ^1H NMR. [c] Conversion (^1H NMR), not isolated yield.

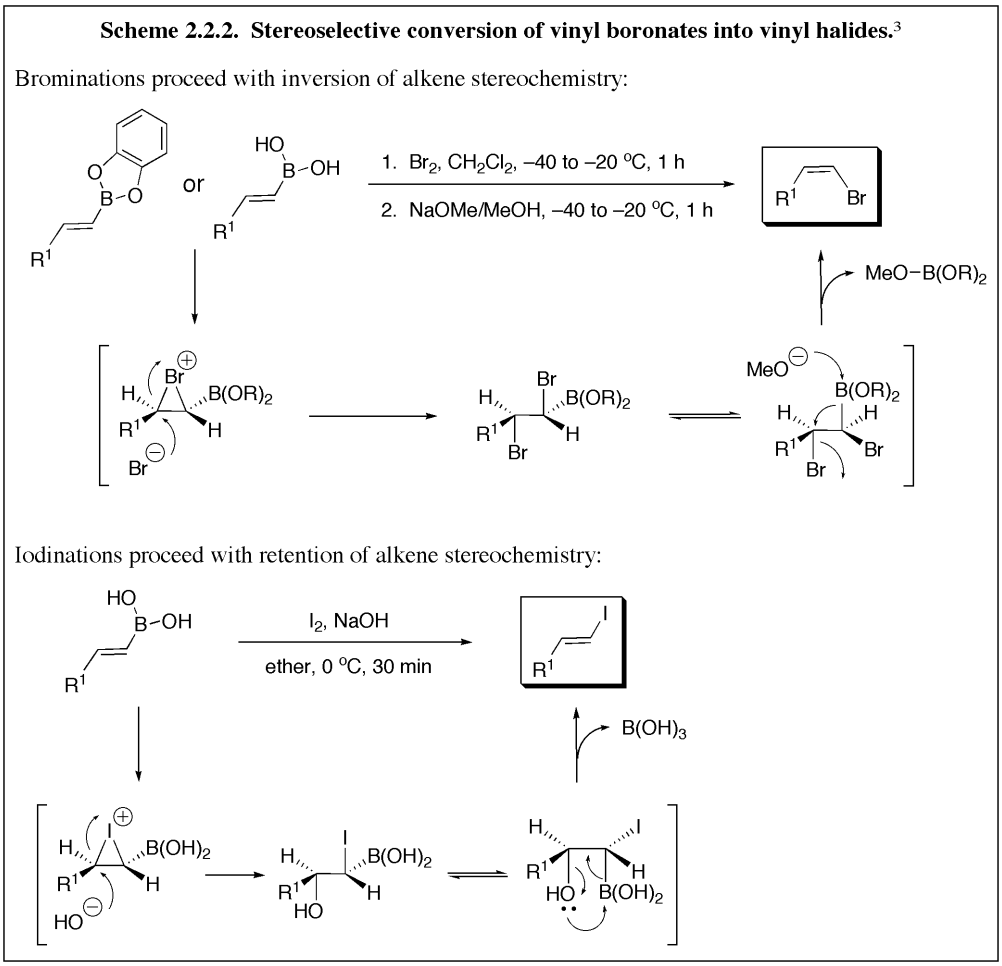
catalysts **1** and **2**. In many of these reactions, the two catalysts were comparable. In one case catalyst **1** exhibited superior *E*-selectivity relative to **2** (entry 3), but this observation was not general. The advantage of using catalyst **2** became evident, however, when cross partners possessing sterically demanding substituents were used (entries 6-8). In these cases, CM via catalyst **1** resulted in significantly lower yields than did CM via **2**.

2.2.3. Subsequent conversion of vinyl boronate products into vinyl halides

As we were exploring the scope of vinyl boronate CM, we also became interested in investigating the potential applications of the functionalized vinyl boronate products of these reactions. Two reactions that caught our attention involved the stereoselective conversion of vinyl boronates into vinyl halides, which were initially reported by Brown and co-workers (Scheme 2.2.2).[3] In these reactions, the brominations proceeded with inversion of the alkene stereochemistry,[3b] whereas the iodinations proceeded with stereochemical retention.[3a]

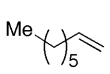
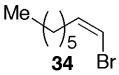
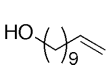
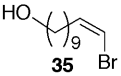
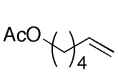
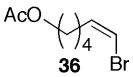
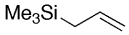
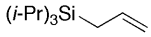
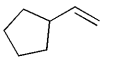
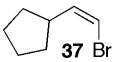
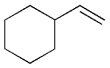
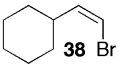
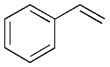
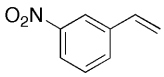
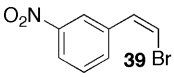
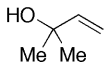
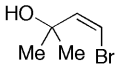
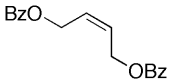
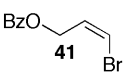
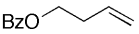
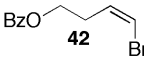
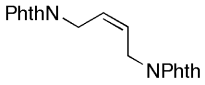
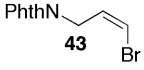
Vinyl halides, like vinyl boronates, are valuable components in Suzuki cross-coupling reactions. In addition, they have been designated as one of the most important building blocks of transition metal-catalyzed syntheses in general.[16] The inability to directly synthesize vinyl halides using CM has been a long-standing problem in our group. However, now that a wide variety of vinyl boronates could be prepared efficiently via CM, Brown's halogenation procedures presented the possibility of developing a two-step CM/halogenation procedure, through which a terminal alkene would be stereoselectively converted into either an *E*- or a *Z*-vinyl halide, a transformation that had not previously been feasible in organic synthesis.

Scheme 2.2.2. Stereoselective conversion of vinyl boronates into vinyl halides.[3]



The bromination conditions reported by Brown (Br_2, CH_2Cl_2; NaOMe, MeOH)[3b] proved to be compatible with our pinacol boronate cross products. In fact, these brominations could be performed *in situ* with the CM reaction, resulting in a one-pot reaction to convert alkenes into vinyl bromides. The results of these one-pot reactions are listed in Table 2.2.6.[15] In agreement with Brown's observations,[3b] the alkene stereochemistry of the vinyl boronate intermediate was always inverted upon bromination, resulting in the formation of predominantly *Z*-vinyl bromides. As illustrated in Table 2.2.6, the *Z*:*E* ratio of the vinyl bromide products, in general, matched the *E*:*Z* ratio of the vinyl boronate products of the corresponding CM reaction.

Table 2.2.6. One-pot CM/bromination with boronates 6 and/or 9.[a,b]

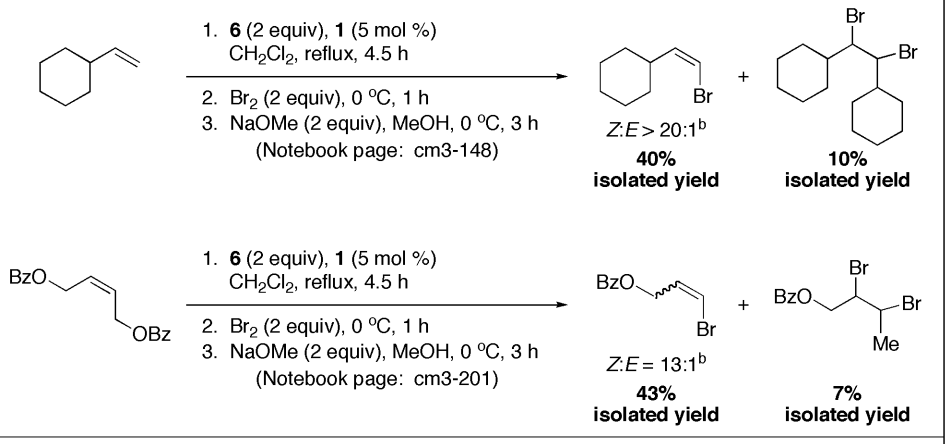
entry	cross partner	boronate	product	isolated yield (%)	*Z*:*E* [c]	boronate *E*:*Z* [d]	notebook page
1		**6** (2 equiv)	 **34**	73	9:1	9:1	cm3-123 cm3-225
2		**6** (2 equiv)	 **35**	85	> 20:1	14:1	cm3-145
3		**6** (2 equiv)	 **36**	64	13:1	13:1	cm3-122
4		**6** (1 equiv)	complex mixture	------	------	------	cm3-103
5		**9** (1.2 equiv)	complex mixture	------	------	------	cm3-192
6		**9** (2 equiv)	 **37**	54	> 20:1	20:1	cm3-188
7		**6** (2 equiv)	 **38**	40	> 20:1	> 20:1	cm3-148
8		**6** (2 equiv)	complex mixture	------	------	------	cm3-129
9 10		**6** (1.2 equiv) **9** (1.2 equiv)	 **39**	87 93	> 20:1 > 20:1	> 20:1	cm3-289 cm3-187
11		**6** (2 equiv)	 **40**	42	> 20:1	> 20:1	cm3-258
12		**9** (2.5 equiv)	 **41**	48	11:1	8:1	cm3-220
13 14		**6** (2 equiv) **9** (2 equiv)	 **42**	73 68	9:1 10:1	6:1	cm3-290 cm3-189
15 16		**6** (2.5 equiv) **9** (2.5 equiv)	 **43**	61 85	8:1 8:1	> 20:1	cm3-291 cm3-195
17		**9** (1.2 equiv)	complex mixture	------	------	------	cm3-186

[a] 0.2-1.8 mmol scale. Step 1: 5 mol% **2**, CH_2Cl_2, reflux, cross partner = 0.1-0.2M. Step 2: Br_2 (2 equiv), 0 °C. Step 3: NaOMe (2 equiv), MeOH, 0 °C. [b] See ref. 15. [c] Determined for the isolated product by ^{1}H NMR. [d] For isolated product of the corresponding CM reaction, taken from Tables 2.2.1-2.2.5.

The yields varied widely in these CM/bromination reactions. A few substrates, such as allylsilanes (Table 2.2.6, entries 4-5), unsubstituted styrene (entry 8), and geminally-disubstituted alkenes (entry 17) were not successful in these reactions, but all of the other substrates investigated were at least somewhat successful. The unsuccessful substrates all possessed substituents that would stabilize the carbocation that could result from bromine addition to the double bond. It is likely that the bromination of these

substrates failed because this stabilized carbocation was long-lived enough to undergo various side reactions. For example, bromide addition to the silyl group of carbocationic allylsilane-derived intermediates (entries 4-5) would generate allyl bromide species. Surprisingly, in some cases the isolated yields of these vinyl halide products were greater than the isolated yields of the corresponding vinyl boronate cross product (entries 2, 9-10, 13, and 16), which indicated that *in situ* bromination may provide a way to curb the losses that we encountered with some of the more polar vinyl boronate cross products during purification. It should be noted that excess boronate (**6** or **9**) was utilized in these one-pot bromination/CM reactions in order to minimize the formation of cross partner homodimers, which subsequently formed dibrominated side products (Scheme 2.2.3). In addition, it was sometimes advantageous to employ boronate **9** rather than **6**, as the methyl group of **6** often became incorporated onto the cross partner alkene, generating additional side products (Scheme 2.2.3).

Scheme 2.2.3. Examples of side product formation that was sometimes observed during the one-pot vinyl boronate CM/bromination reactions.[a]

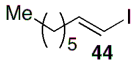
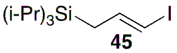
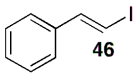
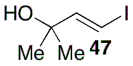


[a] 0.4-1.0 mmol scale, cross partner = 0.1M. [b] Determined for the isolated product by ^{1}H NMR.

The reaction of iodine with a vinyl boronate is more sensitive to steric bulk on the boron atom than is that of bromine. Brown observed that iodination of boronate catechol

esters was unsuccessful and thus had to hydrolyze these substrates to the corresponding boronic acids prior to iodination. Bromination, on the other hand, readily occurred for both the boronic acids and their catechol esters (Scheme 2.2.2).[3] In addition, pinacol boronate esters have been reported to resist reaction with iodine.[17] We observed little or no iodination of our vinyl boronate cross products under Brown's conditions (I_2, NaOH, ether, 0 °C), but high yields of the iodination products were obtained when we employed a more polar solvent (THF) and conducted the reactions at room temperature. The results of these reactions are listed in Table 2.2.7.[15] As Brown had observed,[3a] all of these reactions resulted in the retention of the stereochemistry of the vinyl boronate, forming the *E*-vinyl iodides. Several substrates that had been unsuccessful in the bromination reactions were highly successful in this iodination reaction (e.g., entries 2 and 3). The yields were high for all substrates except those possessing functionalities that were incompatible with the basic conditions required for this iodination procedure (entry 5).

Table 2.2.7. Iodination of vinyl pinacol boronate cross products.[a,b]

entry	boronate	*E*:*Z* [b]	product	isolated yield (%)	*E*:*Z* [c]	notebook page
1	**12**	9:1	 **44**	87	11:1	cm3-276
2	**8**	8:1	 **45**	99	8:1	cm3-286
3	**18**	> 20:1	 **46**	99	> 20:1	cm3-272
4	**23**	> 20:1	 **47**	82	> 20:1	cm3-270
5	**25**	N. D.	complex mixture	------	------	cm3-277

[a] 0.2-0.4 mmol scale, I_2 (2.5 equiv), NaOH (3 equiv), THF, rt, boronate = 0.2M.
[b] See ref. 15. [c] Determined for the isolated material by ^{1}H NMR.

We were unfortunately unable to obtain high yields of the vinyl iodide product using one-pot CM/iodination procedures. For example, one-pot versions of the reactions

shown in entries 1 and 3 of Table 2.2.7 resulted in isolated product yields of 39% and 62%, respectively.[iv] It is possible that the sensitivity of these iodination reactions to solvent polarity contributed to the inefficiency of these attempted one-pot CM/iodination reactions, which had to be carried out in either CH_2Cl_2 or a CH_2Cl_2/THF mixed solvent system in order to allow efficient performance of the CM reaction.

2.2.4. Summary and conclusions

We have generated a wide variety of functionalized vinyl boronates with moderate-to-high *E*-stereoselectivity using CM via catalyst **2**. Both vinyl and 1-propenyl pinacol boronate (**9** and **6**, respectively) served as efficient cross partners in this reaction. Since both of these substrates can be readily synthesized from commercially available reagents, this CM reaction provided a facile method for converting alkenes into *E*-vinyl boronates. The products of these CM reactions were stereoselectively transformed into either *Z*-vinyl bromides or *E*-vinyl iodides, with the bromination procedure being achievable in one-pot with the CM reaction. This CM reaction had only a few limitations with respect to its substrate scope, namely the poor reactivity of highly electron-deficient alkenes or sterically hindered alkenes. Most other alkenes participated readily in this reaction, although the more polar boronate products did undergo a small amount of decomposition upon purification via silica gel chromatography. Therefore, the components of Suzuki and numerous other metal-catalyzed coupling reactions can now be stereoselectively constructed out of alkenes, under very mild reaction conditions, using the chemistry that we have developed during this project.

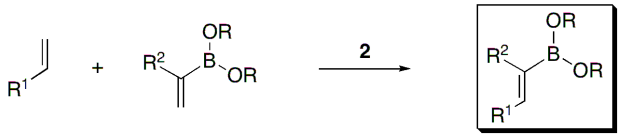
[iv] Notebook pages: cm3-240 and cm3-253, respectively.

We conclude that vinyl boronates such as **6** and **9** behave as Type II alkenes in the presence of both catalyst **1** and **2**. For catalyst **2**, these substrates most likely lie on the less-reactive side of the Type II grouping. This assignment is based on three observations that we have made during our studies. First, **6** and **9** undergo little or no homodimerization. Second, these two boronates, in general, only undergo efficient CM with Type I alkenes. Third, **6** and **9** do not react at all with many Type II (e.g., acrylates) and Type III (e.g., vinyl phosphonates, many geminally-disubstituted alkenes) cross partners. It is interesting that vinyl boronates are able to act as Type II alkenes in the presence of both catalysts **1** and **2**. This behavior is notably different from that of acrylates, which are also highly electron-deficient alkenes. The latter act as reactive Type II alkenes in the presence of catalyst **2**, but they act as Type IV (i.e., completely unreactive) alkenes in the presence of **1**.

2.3. α-Substituted Vinyl Boronates

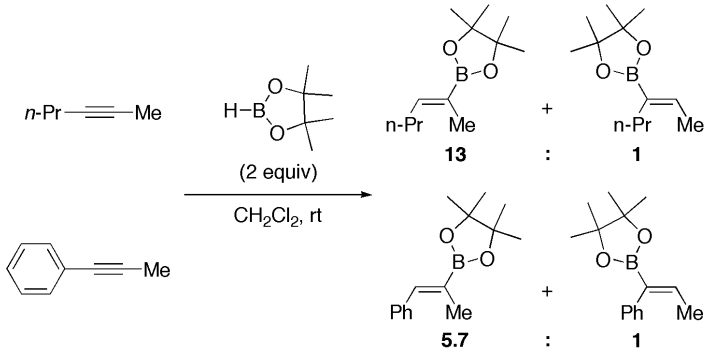
Having demonstrated the efficiency of CM in the generation of functionalized *E*-disubstituted vinyl boronates, we attempted to extend this methodology to the synthesis of α,α',β-trisubstituted vinyl boronates. This task could conceivably be accomplished through the CM of α-substituted vinyl boronates, according to the general reaction illustrated in Scheme 2.3.1. This CM reaction would mark an even more significant contribution to organic synthesis than did the vinyl boronate CM reactions described in section 2.2, because α,α',β-trisubstituted vinyl boronates are much more difficult to

Scheme 2.3.1. CM of α-substituted vinyl boronates.



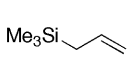
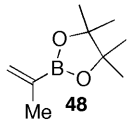
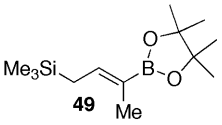
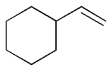
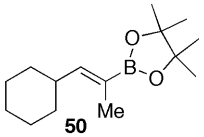
synthesize selectively using alkyne hydroboration. As shown in Scheme 2.3.2, these hydroboration reactions often exhibit low levels of regioselectivity.[18] Desirable results can only be obtained when the two substituents of the internal alkyne differ significantly with respect to steric bulk, and even then these results are still dependent upon reaction conditions such as the solvent, the temperature, and the boron source.[19] These regioselectivity issues would not be present in the CM reaction shown in Scheme 2.3.1, and thus we explored the CM of α-substituted vinyl boronates in hopes of developing a more selective route for the synthesis of α,α',β-trisubstituted vinyl boronates.

Scheme 2.3.2. Hydroboration reactions of internal alkynes often exhibit low regioselectivity.[18b]



The initial results that we obtained in these CM reactions were quite promising (Table 2.3.1). In these reactions, the CM of boronate **48**, which possessed an α-methyl substituent, resulted in moderate yields of the desired α,α',β-trisubstituted vinyl boronates. Most importantly, however, these reactions were highly *Z*-selective. At this point in the project, Timothy W. Funk further investigated the substrate scope of CM reactions involving α-methyl vinyl boronate **48**,[20] while I focused on the CM reactions of vinyl boronates possessing larger α-substituents.

Table 2.3.1. CM with 2-propenyl pinacol boronate (48).[a]

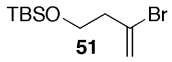
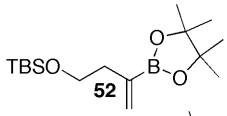
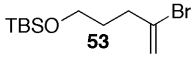
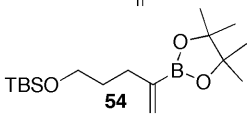
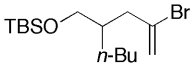
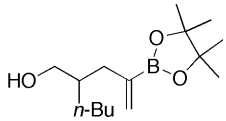
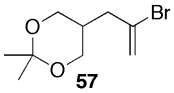
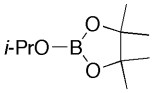
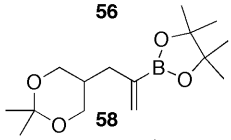
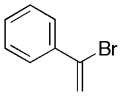
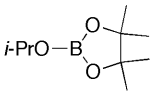
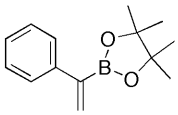
entry	cross partner	boronate	product	isolated yield (%)	*Z*:*E* [b]	notebook page
1		 **48**	 **49**	73	> 20:1	cm3-105
2		**48**	 **50**	59	> 20:1	cm4-62

[a] 0.2 mmol scale, 1 equiv boronate, 5 mol% **2**, CH_2Cl_2, reflux, cross partner = 0.2M.
[b] Determined for the isolated material by ^1H NMR.

2.3.1. Synthesis of α-substituted vinyl boronates

The most challenging aspect of this project turned out to be the synthesis of the various α-substituted vinyl boronates. As before, we employed pinacol boronic esters in these studies, due to their relatively high stability. Initially we attempted to generate these α-substituted vinyl boronates through the reaction of the corresponding vinyl lithium species, which was generated *in situ* via treatment of a vinyl bromide with *t*-butyllithium,[21] with various boron sources. As shown by the results listed in Table 2.3.2, this synthetic strategy proved to be highly inefficient. The yields were low in all cases except for that of conjugated vinyl bromides (entry 5). In most cases, unreacted starting material was recovered, which indicated incomplete lithium/halogen exchange. We also isolated the corresponding monosubstituted alkenes from the product mixtures, which was indicative of successful vinyl lithium formation but unsuccessful boron addition. The sum of the isolated products never accounted for the bulk of the material. Therefore we concluded that a large amount of the starting material and/or the products decomposed over the course of these reactions.

Table 2.3.2. Synthesis of α-substituted pinacol vinyl boronates from vinyl bromides.[a]

entry	vinyl bromide	boron source	boronate product	isolated yield (%)[b]	notebook page
1	 **51**	$B(OMe)_3$	 **52**	19	cm4-43
2	 **53**	$B(O\textit{i}\text{-}Pr)_3$	 **54**	20	cm4-54
3	 **55**	$B(OMe)_3$	 **56**	23	cm4-76
4	 **57**		 **58**	20	cm4-87
5			 **59**	99	cm4-171

[a] 2-8 mmol scale, 1.5-2.5 equiv boron source, *t*-BuLi (1.5-2.5 equiv), ether or THF, –78 °C, bromide = 0.1-0.2M. [b] Calculated after treatment with pinacol/molecular sieves (ether, rt), except for entries 4 and 5.

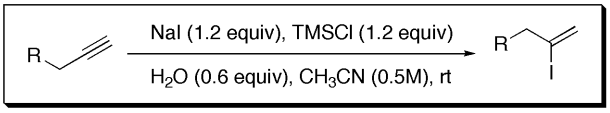
As an alternative to lithium/halogen exchange, we attempted to convert vinyl bromide **53** into boronate **54** using a palladium-catalyzed cross-coupling reaction with bis(pinacolato)diboron.[22] This reaction resulted in a 68% isolated yield of the desired product **54**.[v] Unfortunately the product of this coupling reaction was completely unreactive toward CM, even with the use of cross partners for which batches of **54** synthesized by other means had been successful. Upon closer examination, it appeared that the vinyl boronate synthesized using this coupling reaction contained a small amount of an aromatic impurity, which presumably arose from either the triphenylphosphine or the potassium phenoxide that had been employed in the coupling reaction. Unfortunately the identity of this impurity was never confirmed, and all attempts to remove it proved futile. Thus this synthetic route had to be abandoned.

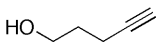
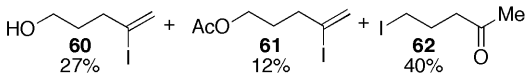
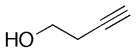
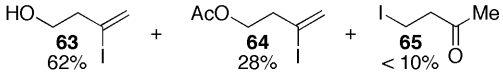
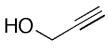
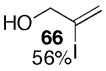
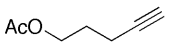
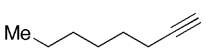
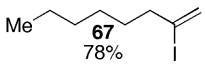
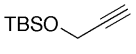
[v] Notebook page: cm4-102.

A more promising synthetic route to these α-substituted vinyl boronates involved formation of the corresponding vinyl lithium species from vinyl iodides, rather than from vinyl bromides. Vinyl iodides are much more reactive toward lithium/halogen exchange than are vinyl bromides, as the former react readily with *n*-butyllithium,[23] while the latter require the use of *t*-butyllithium.[21a] In addition, vinyl lithium species derived from the corresponding vinyl iodides had already been reported to undergo addition to boron sources.[23]

We employed the procedure illustrated at the top of Table 2.3.3 for the synthesis of the necessary vinyl iodides. In this procedure, HI, which is generated *in situ*, regioselectively adds across the triple bond of a terminal alkyne.[24] As shown in entries 1 and 2 of Table 2.3.3, we initially encountered significant issues with side reactions. The formation of acetate side products **61** and **64** could easily be explained as resulting from

Table 2.3.3. Synthesis of vinyl iodides from terminal alkynes.[a,b]

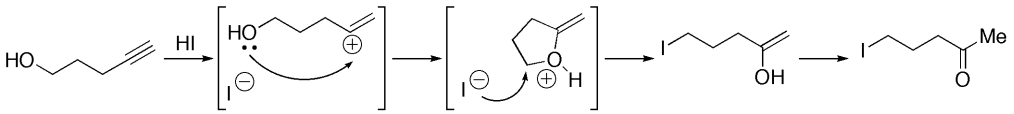


entry	terminal alkyne	product(s) and isolated yield(s)	notebook page
1		 **60** 27% + **61** 12% + **62** 40%	cm4-116
2		 **63** 62% + **64** 28% + **65** < 10%	cm4-146
3		 **66** 56%	cm4-150
4		**60** 81%[c]	cm4-163
5		 **67** 78%	cm4-158
6		complex mixture	cm4-198

[a] 11-86 mmol scale. [b] See ref. 24. [c] Yield calculated after deprotection ($NaOH/H_2O$, rt).

the reaction of the alcohol functionalities with the acetonitrile solvent, followed by hydrolysis. The appearance of methyl ketone side products **62** and **65**, however, was more surprising. It was especially interesting that the extent of ketone formation was dependent upon the size of the carbon chain that linked the alcohol to the alkyne. The ketone was the major product for the 3-carbon linker (entry 1); it was a minor product for the 2-carbon linker (entry 2); and it did not form at all in the case of the 1-carbon linker (entry 3). Further examination of the mechanism of this reaction led us to propose the reaction sequence shown in Scheme 2.3.3 to explain the formation of these methyl ketone

Scheme 2.3.3. Mechanism for formation of methyl ketone side products during synthesis of vinyl iodides from terminal alkynes.

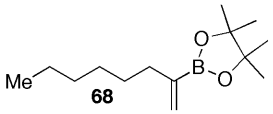
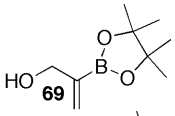
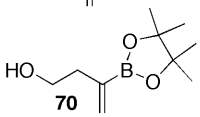


side products. In this reaction, the pendant alcohol, rather than the iodide anion, attacks the carbocation that results from HI addition across the alkyne. For the alcohol linked by a 3-carbon unit (shown in Scheme 2.3.3), the resultant cyclic intermediate would be a five-membered ring, whereas the corresponding intermediate derived from alcohols linked by 2- and 1-carbon units would possess much less energetically favorable four- and three-membered rings, respectively. Thus this mechanism matches the trend that we observed with respect to methyl ketone formation in entries 1-3 of Table 2.3.3. In an effort to suppress these side reactions, the alcohol functionality of 4-pentyn-1-ol was protected as an acetate group. The iodination of this alkyne led to the isolation of the desired product (**60**) in 81% yield, with no observable methyl ketone formation (entry 4). This result further supported the proposed reaction shown in Scheme 2.3.3. Thus we were able to, in general, synthesize various α-substituted vinyl iodides from terminal

alkynes in high yield. It should be noted that *t*-butyldimethylsilyl (TBS) protecting groups were not compatible with this chemistry (entry 6).

As shown in Table 2.3.4, these vinyl iodides were successfully converted into the corresponding α-substituted vinyl boronates.[23] The use of unfunctionalized substrates resulted in high yields (entry 1). The use of vinyl iodides possessing free alcohols resulted in low yields (entries 2-4). However, considering the reactivity of free alcohols under these highly basic conditions, it is noteworthy that the reactions shown in entries 2 and 3 still provided access to the desired products.

Table 2.3.4. Synthesis of α-substituted vinyl boronates from vinyl iodides.[a,b]

entry	vinyl iodide	base	boronate product	isolated yield (%)	notebook page
1	**67**	*n*-BuLi (1.3 equiv)	 **68**	75	cm4-145
2	**66**	*t*-BuLi (3.5 equiv)	 **69**	10	cm4-133
3	**63**	*n*-BuLi (2.2 equiv)	 **70**	43	cm4-164
4	**60**	*n*-BuLi (2.5 equiv)	complex mixture	------	cm4-177

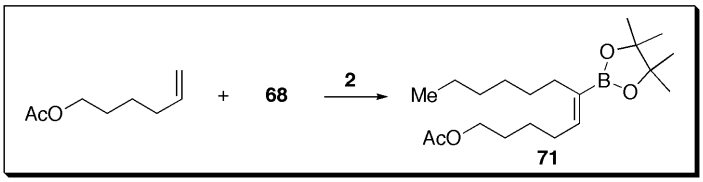
[a] 12-24 mmol scale, 2-isopropyloxy-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (1.5-2.7 equiv), ether, –78 °C, iodide = 0.1-0.4M. [b] See ref. 23.

2.3.2. Cross-metathesis of α-substituted vinyl boronates

As boronate **68** was synthesized in the highest yield compared to the other α-substituted vinyl boronates investigated, it was used to evaluate the substrate scope of this CM reaction. Unfortunately this substrate scope proved to be quite narrow. The only cross partner that exhibited efficient CM with boronate **68** was 5-hexenyl acetate. For

reasons that we do not understand, the use of other cross partners[vi] resulted in low yields of the desired products, as well as in the formation of numerous side products. Table 2.3.5 shows our attempts to optimize the CM reaction of 5-hexenyl acetate with boronate **68**, including the use of **68** as the reaction solvent (entry 2), a higher reaction temperature (entry 3), and a higher catalyst loading (entry 4). None of these reaction conditions led to improved results from those obtained under the standard CM conditions (entry 1). Thus, even at its very best, this CM reaction resulted in a 54% yield, with a *Z*:*E* ratio of 4:1 (entry 4).[20]

Table 2.3.5. CM of 5-hexenyl acetate with boronate 68.[a,b]



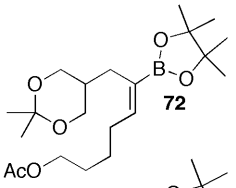
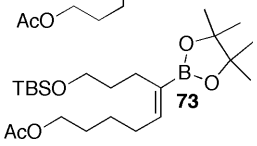
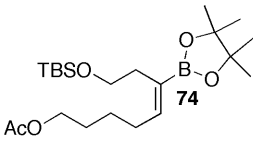
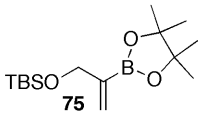
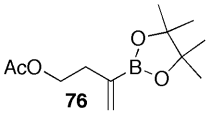
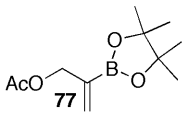
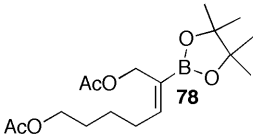
entry	equiv **68**	mol % **2**	solvent, temperature	isolated yield (%)	*Z*:*E* [c]	notebook page
1	2	5	CH_2Cl_2, reflux	40	2.7:1	cm4-148
2	10.5	5	neat, 45 °C	20	2.3:1	cm4-167
3	2	5	C_6H_6, 60 °C	40	2.2:1	cm4-152
4	2	20	CH_2Cl_2, reflux	54	4:1	cm4-185

[a] 0.4 mmol scale, cross partner = 0.2-0.4M. [b] See ref. 20. [c] Determined for the isolated material by ^{1}H NMR.

Table 2.3.6 lists the results of the CM of 5-hexenyl acetate with the other α-substituted vinyl boronates.[20] The yields varied widely in these reactions and were moderate at best, with no CM reaction occurring at all for substrates whose α-substituent possessed a free alcohol (entries 7-9) or for α-phenyl substrates (entry 10). The *Z*-selectivity in these reactions was only moderate as well, although the *E*- and *Z*-isomers

[vi] Specifically, 1-octene (notebook page: cm4-157), allyltriisopropylsilane (cm4-149), and (*Z*)-but-2-ene-1,4-diyl dibenzoate (cm4-156) were also investigated.

Table 2.3.6. CM of 5-hexenyl acetate with other α-substituted pinacol vinyl boronates.[a,b]

entry	α-substituted vinyl boronate	equiv boronate	product	isolated yield (%)	*Z*:*E* [c]	notebook page
1	**58**	2	 **72**	41	3:1	cm4-91
2	**54**	1.2	 **73**	35	4.3:1	cm4-65
3	**52**	1.3	 **74**	17	4.5:1	cm4-64
4	 **75**	2	complex mixture	------	------	cm4-202
5	 **76**	2	N.R.	------	------	cm4-188
6	 **77**	2	 **78**	41	1.1:1	cm4-192
7[d]	**56**	0.1	N. R.	------	------	cm4-82
8	**70**	2	N. R.	------	------	cm4-172
9	**69**	2	complex mixture	------	------	cm4-160
10	**59**	2	N. R.	------	------	cm4-179

[a] 0.2-0.7 mmol scale, 5 mol% **2**, CH_2Cl_2, reflux, 5-hexenyl acetate = 0.2M. [b] See ref. 20.
[c] Determined for the isolated material by ^1H NMR. [d] Neat, 50 °C.

could usually be separated by column chromatography, allowing the isolation of each stereoisomer. It had become clear that adding an α-substituent to a vinyl boronate rendered the substrate much less reactive toward CM. Even the α-methyl substituent of boronate **48** led to a significant loss of metathesis reactivity. Tim Funk's further studies involving the CM of **48** revealed that, although this substrate did exhibit significantly higher *Z*-selectivity as compared to the other α-substituted vinyl boronates, it never led to yields higher than those observed in our initial studies (Table 2.3.1). In addition, the

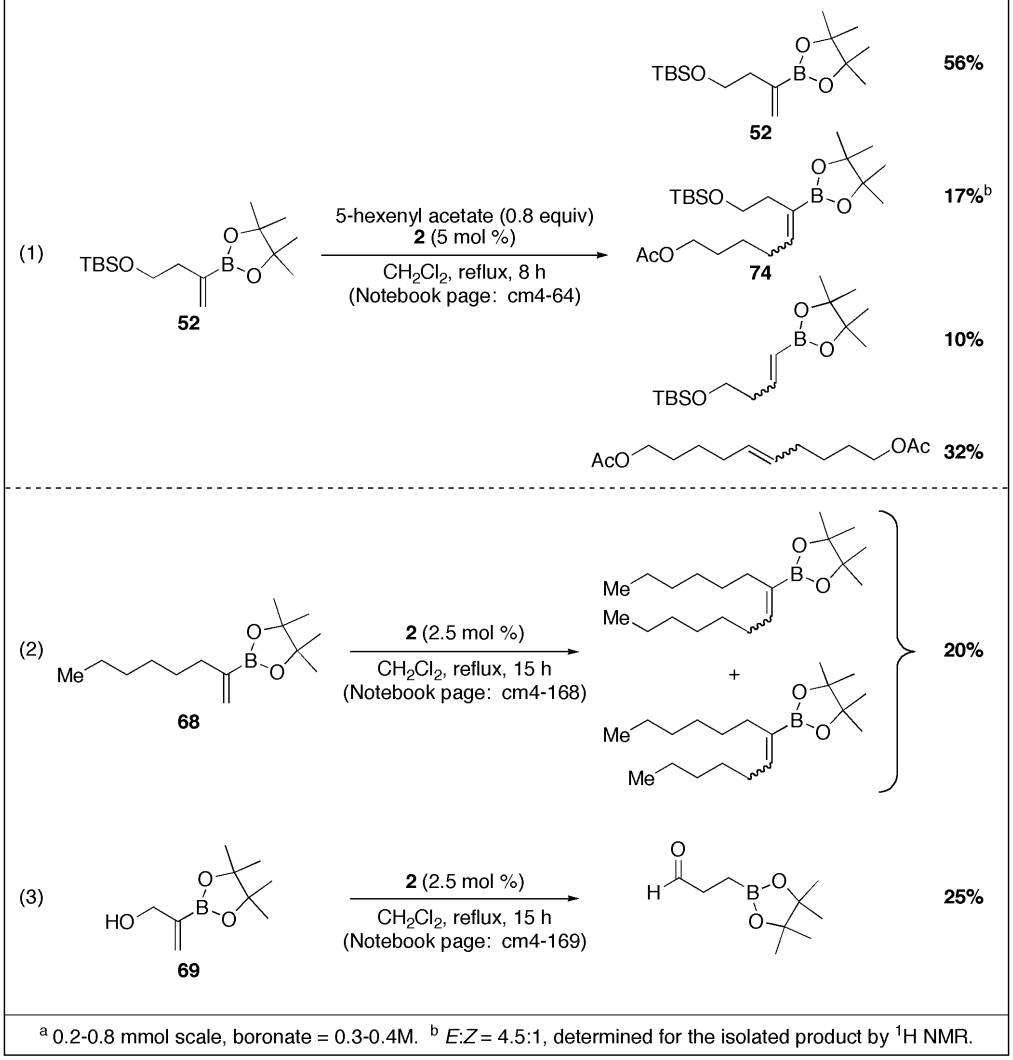
substrate scope of CM with boronate **48** was limited to unhindered, unfunctionalized, Type I alkenes.[20]

Examination of the results listed in Table 2.3.6 revealed that the success of these CM reactions was extremely dependent upon the steric bulk surrounding the alkene of the α-substituted vinyl boronate starting materials. For example, when the α-substituent was an alkyl chain with a bulky silyloxy group at the end, decreasing the number of methylene units in the chain from three to two reduced the CM yield by about half (compare entries 2 and 3). Furthermore, when this alkyl chain was reduced to only a single methylene unit, no efficient CM was observed (entry 4). CM yields also varied widely when the protecting groups were changed. For example, in entry 6 of Table 2.3.6, the CM product was isolated in 41% yield when the α-substituent of the starting material contained an acetate group, but no efficient CM was observed when this acetate was replaced with a *t*-butyldimethylsilyloxy (TBS) group (entry 4). We can offer no explanation for these results other than to reiterate that these CM reactions involving α-substituted vinyl boronates are extremely sensitive to sterics.

Finally, it should be mentioned that some unusual side products were formed during many of these CM reactions. These side products resulted from the migration of the α-substituent on the vinyl boronate to the β-position. An example to illustrate this observation is shown in reaction 1 of Scheme 2.3.4, in which this isomerized product was isolated in 10% yield for boronate **52**. We also performed some control experiments, in which α-substituted boronates **68** and **69** underwent reaction with catalyst **2** in the absence of a cross partner. As shown in reactions 2 and 3 of Scheme 2.3.4, up to 25% of the material isomerized under these reaction conditions. Tim Funk observed similar

behavior to a small extent with boronate **48**.[20] In these cases involving boronate **48**, the isomerized product was boronate **6**, which subsequently reacted with the cross partner to form a disubstituted vinyl boronate, as described in section 2.2. We can, at present, offer no explanation for the formation of these side products other than to speculate that some of catalyst **2** formed a ruthenium hydride species upon decomposition, which subsequently inserted into the carbon-boron bond and promoted the observed rearrangement.

Scheme 2.3.4. Rearrangements observed for α-substituted vinyl pinacol boronates in the presence of catalyst 2.[a]



[a] 0.2-0.8 mmol scale, boronate = 0.3-0.4M. [b] *E*:*Z* = 4.5:1, determined for the isolated product by ^{1}H NMR.

2.3.3. Summary and conclusions

We have investigated the use of CM of α-substituted vinyl boronates to generate α,α',β-trisubstituted vinyl boronates. These α-substituted vinyl boronate starting materials were efficiently synthesized in two steps from terminal alkynes. When the α-substituent of these boronates was a methyl group, the CM products could be isolated in moderate yields (ca. 60%) and possessed almost entirely *Z*-stereochemistry, as long as sterically unhindered cross partners were used. CM products could also be obtained from vinyl boronates possessing α-substituents that were larger than a methyl group. However, in these cases the yields and stereoselectivity dropped significantly (54% yield, *Z*:*E* = 4:1 at best), and the success of a given CM reaction was highly substrate dependent. In addition, side reactions often rendered these CM reactions even less efficient.

Most of the α,α',β-trisubstituted vinyl boronates that we have synthesized would be difficult or impossible to generate regioselectively using conventional hydroboration procedures, and thus this CM procedure could be extremely useful to organic chemists. However, because α-substituted vinyl boronates all behave as either Type III or Type IV alkenes in the presence of catalyst **2**, both the yields and the stereoselectivities in their CM reactions are too low to allow the potential utility of this methodology to be realized. We believe that the development of a new metathesis catalyst, one that is more tolerant of sterically hindered alkenes, will overcome this difficulty and thus allow CM to become a viable synthetic route to α,α',β-trisubstituted vinyl boronates.

2.4. Experimental Section

2.4.1. General experimental procedures

Vinyl boronate cross-metathesis. A solution of **1** or **2** (obtained from Materia) and dry dichloromethane was added via cannula to a flame-dried, round-bottomed flask equipped with a reflux condenser and kept under an argon atmosphere. The vinyl boronate starting material and the cross partner were added via syringe. The brick-red solution was placed in a 45-50 °C oil bath (unless temperature otherwise noted) and allowed to stir, under an argon atmosphere, overnight. The mixture was then concentrated *in vacuo*, and the product was purified by silica gel chromatography. The carbon adjacent to the boron atom was not visible by ^{13}C NMR spectroscopy for any of the vinyl boronates reported herein. This phenomenon is presumably due to the large boron quadrupole, which induces broadening of the ^{13}C peak corresponding to this adjacent carbon atom.[25]

One-pot cross-metathesis/bromination. After completion of the cross-metathesis reaction (carried out as described above), the reaction vessel was placed in an ice bath, and bromine was added dropwise via syringe. The reaction was allowed to stir at 0 °C for 30 minutes, and then a solution of sodium methoxide in anhydrous methanol was added via syringe. The solution was allowed to stir at 0 °C for 30 minutes, and then 6 mL aqueous sodium thiosulfate solution was added. The aqueous layer was extracted 3 times with 10 mL dichloromethane and then dried with $MgSO_4$. The mixture was then concentrated *in vacuo*, and the product was purified by silica gel chromatography.

Iodination of vinyl pinacol boronates. The boronate and reagent-grade THF were added via syringe to a round-bottomed flask equipped with an addition funnel and kept under an argon atmosphere. A solution of aqueous sodium hydroxide was added via syringe and the solution was stirred vigorously at room temperature for about 10 minutes. A THF solution of iodine was then added dropwise (via addition funnel) to the reaction, waiting for the red-orange color of the reaction to turn to yellow before adding more iodine solution. Total addition time was approximately 20 minutes. As the iodine addition progressed, the red-orange color disappeared more slowly, and toward the end of the addition (ca. 15 minutes), it did not go away at all. Reaction progress was monitored by TLC, and the reaction times were, on average, about 4 hours. At the end of the reaction, 4 mL aqueous sodium thiosulfate solution was added. The aqueous layer was extracted 3 times with 5 mL of ether and then dried with $MgSO_4$. The mixture was concentrated *in vacuo*, and the product was purified by silica gel chromatography.

2.4.2. Specific experimental procedures and characterization data

(*E*)-prop-1-enylboronic acid (**3**). To a flame-dried, round-bottomed flask, under an argon atmosphere, added trimethyl borate (3.5 mL, 31 mmol) and THF (10 mL). Placed in a dry ice/acetone bath and added a 0.5M THF solution of 1-propenyl magnesium bromide (100 mL, 50 mmol) dropwise, over about 20 minutes. Let stir at –78 °C for 1 hour, then placed in an ice bath and slowly added 70 mL of 30% aqueous HCl solution. Let stir for 30 minutes at 0 °C, warmed to room temperature, extracted 3 times with 150 mL ether, dried with Na_2SO_4, and concentrated *in vacuo* to obtain a slimy, yellow solid. Purified via recrystallization from benzene to obtain 884 mg of **3** as a white solid (33% yield).

Product existed as a mixture of **3** and its cyclic trimer, and *E*:*Z* varied widely from batch to batch. ^{1}H NMR (300 MHz, CD_3CN, ppm): (cyclic trimer) δ 6.49 (3H, dq, *J* = 17.7, 6.0 Hz), 5.37 (3H, dq, *J* = 17.6, 1.7 Hz), 1.80 (9H, dd, *J* = 6.6, 1.8 Hz). ^{13}C NMR (300 MHz, CD_3CN, ppm): (cyclic trimer) δ 147.8, 22.1. HRMS (EI) calcd. for $C_9H_{15}B_3O_3$: 204.1300, found: 204.1301.

(*E*)-6-acetoxyhex-1-enylboronic acid (**4**). Followed general procedure, with 19 mg (0.22 mmol) **3**, 36 μL (0.22 mmol) 5-hexenyl acetate, 8 mg (0.009 mmol) **2**, and 2 mL CH_2Cl_2. Purified via silica gel chromatography (7:3 to 5:5 hexanes:ethyl acetate) to obtain 14 mg of **4** as a clear oil (34% yield). Product existed as a mixture of **4** and its cyclic trimer. ^{1}H NMR (300 MHz, CD_2Cl_2, ppm): δ 6.95 (0.8H, dt, *J* = 17.7, 6.3 Hz), 6.51 (0.2H, dt, *J* = 18.3, 6.3 Hz), 5.56 (0.8, d, *J* = 17.4 Hz), 5.44 (0.2H, d, *J* = 17.7 Hz), 4.08 (2H, t), 2.28 (2H, dt), 2.05 (3H, s), 1.6 (4H, m).

(*E*)-3-(triisopropylsilyl)prop-1-enylboronic acid (**5**). Followed general procedure, with 17 mg (0.2 mmol) **3**, 48 μL (0.2 mmol) allyltriisopropylsilane, 8 mg (0.009 mmol) **2**, and 2 mL CH_2Cl_2. Purified via silica gel chromatography (7:3 hexanes:ethyl acetate) to obtain 28 mg of **5** as a yellow oil (58% yield). Product existed as a mixture of **5** and its cyclic trimer. ^{1}H NMR (300 MHz, $CDCl_3$, ppm): (cyclic trimer) δ 7.10 (3H, dt, *J* = 17.1, 8.5 Hz), 5.43 (3H, d, *J* = 17.1 Hz), 1.90 (6H, d, *J* = 7.8 Hz), 1.082 (54H, s), 1.075 (9H, s). ^{13}C NMR (300 MHz, $CDCl_3$, ppm): (cyclic trimer) δ 156.1, 21.5, 19.0, 11.4. HRMS (CI) calcd. for $C_{36}H_{75}B_3O_3Si_3$ + H: 673.5382, found: 673.5382.

4,4,5,5-Tetramethyl-2-(prop-1-enyl)-1,3,2-dioxaborolane (**6**). *Step 1*: To a flame-dried, round-bottomed flask, under an argon atmosphere, added trimethyl borate (4.5 mL, 40 mmol), and ether (10 mL). Placed in a dry ice/acetone bath and let stir. Slowly added a 0.5M THF solution of propenyl magnesium bromide (100 mL, 50 mmol) dropwise. Let stir at –78 °C for 1 hour. Placed in an ice bath and slowly added 30% aqueous HCl solution (70 mL). Let stir at 0 °C for 1 hour, then warmed to room temperature, extracted 3 times with 100 mL ether, dried with Na_2SO_4, and removed most (but not all) of the solvent *in vacuo* to obtain a concentrated solution of **3**. *Step 2*: Immediately following step 1, cannula-transferred the above solution of **3**, plus 15 mL ether, into a flame-dried, round-bottomed flask, under an argon atmosphere, containing 4 g of activated (via flame-drying under vacuum) 4 Å powdered molecular sieves and 20 mL ether. Added pinacol (7 g, 59 mmol) and let stir at room temperature overnight. Filtered through Celite, washing Celite with lots of ether, concentrated *in vacuo* (> 150 torr), and purified via silica gel chromatography (39:1 pentane:ether) to obtain 5.3 g of **6** as a yellow oil (79% yield). *E*:*Z* varied widely from batch to batch. ^{1}H NMR (300 MHz, $CDCl_3$, ppm): (***E*-isomer**): δ 6.65 (1H, dq, *J* = 17.9, 6.5 Hz), 5.46 (1H, dq, *J* = 18.2, 1.7 Hz), 1.85 (3H, dd, *J* = 6.6, 1.8 Hz), 1.27 (12H, s). (***Z*-isomer**): δ 6.5 (1H, m), 5.35 (1H, dq, *J* = 13.8, 1.5 Hz), 1.98 (3H, dd, *J* = 7.1, 1.7 Hz), 1.28 (12H, s). ^{13}C NMR (300 MHz, $CDCl_3$, ppm): (***E*-isomer**): δ 149.8, 83.2, 25.1, 22.1. (***Z*-isomer**): δ 149.8, 83.0, 25.2, 18.9. HRMS (EI) calcd. for $C_9H_{17}BO_2$: 168.1322, found: 168.1321.

(*E*)-6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)hex-5-enyl acetate (**7**). Followed general procedure, with 38 μL (0.2 mmol) **6**, 34 μL (0.2 mmol) 5-hexenyl acetate, 8 mg

(0.009 mmol) **2**, and 2 mL CH_2Cl_2. Purified via silica gel chromatography (9:1 hexanes:ethyl acetate) to obtain 35 mg of **7** as a yellow oil (65% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 6.60 (1H, dt, *J* = 17.7, 6.4 Hz), 5.43 (1H, dt, *J* = 18.0, 1.5 Hz), 4.04 (2H, t, *J* = 6.5 Hz), 2.17 (2H, ddt, *J* = 6.7, 6.7, 1.7 Hz), 2.03 (3H, s), 1.65 (2H, m), 1.50 (2H, m), 1.25 (12H, s). ^{13}C NMR (300 MHz, $CDCl_3$, ppm): δ 171.4, 153.9, 83.2, 64.5, 35.4, 28.3, 25.0, 24.7, 21.2. HRMS (EI) calcd. for $C_{14}H_{25}BO_4$: 268.1846, found: 268.1854.

(*E*)-triisopropyl(3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)allyl)silane (**8**). Followed general procedure, with 38 μL (0.2 mmol) **6**, 48 μL (0.2 mmol) allyltriisopropylsilane, 8 mg (0.009 mmol) **2**, and 1 mL CH_2Cl_2. Purified via silica gel chromatography (19:1 hexanes:ethyl acetate) to obtain 67 mg of **8** as a yellow-orange oil (99% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 6.76 (1H, dt, *J* = 17.7, 8.3 Hz), 5.33 (1H, dt, *J* = 17.4, 1.1 Hz), 1.81 (2H, dd, *J* = 8.3, 1.1 Hz), 1.25 (12H, s), 1.06 (18H, s), 1.05 (3H, s). ^{13}C NMR (300 MHz, $CDCl_3$, ppm): δ 153.3, 82.9, 25.0, 21.2, 19.0, 11.3. HRMS (EI) calcd. for $C_{18}H_{37}BO_2Si$: 324.2656, found: 324.2660.

4,4,5,5-Tetramethyl-2-vinyl-1,3,2-dioxaborolane (**9**). Followed procedure given for **6**, with: *Step 1*: 11.5 mL (103 mmol) trimethyl borate, 100 mL (100 mmol) vinyl magnesium bromide (1.0M in THF), 20 mL ether, and 100 mL 30% aqueous HCl solution. Took great care not to let the crude vinylboronic acid solution become too concentrated (which would lead to decomposition). *Step 2*: 10 g 4 Å powdered molecular sieves, 24 g (203 mmol) pinacol, and 100 mL ether. Purified via silica gel

chromatography (3:1 pentane:ether, keeping rotovap vacuum above 150 torr) to obtain 9.53 g of **9** as a yellow oil (62% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 6.0 (3H, m), 1.29 (12H, s). ^{13}C NMR (300 MHz, $CDCl_3$, ppm): δ 137.1, 83.5, 25.1. HRMS (EI) calcd. for $C_8H_{15}BO_2$: 154.1165, found: 154.1165.

5,5-Dimethyl-2-vinyl-1,3,2-dioxaborinane (**10**). Followed same procedure as for **6**, with: *Step 1*: 3 mL (26.8 mmol) trimethyl borate, 28 mL (28 mmol) vinyl magnesium bromide (1.0M in THF), 4 mL THF, and 30 mL 20% aqueous HCl solution. Took great care not to let the crude vinylboronic acid solution become too concentrated (which would lead to decomposition). *Step 2*: 2.8 g 4 Å powdered molecular sieves, 5.6 g (53.8 mmol) neopentyl glycol, and 50 mL ether. Purified via silica gel chromatography (1:1 pentane:ether, keeping rotovap vacuum above 150 torr) to obtain 2.20 g of **10** as a yellow oil (59% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 5.90 (3H, m), 3.63 (4H, s), 1.0 (6H, s). ^{13}C NMR (300 MHz, $CDCl_3$, ppm): δ 134.7, 72.3, 32.0, 22.0.

(*E*)-(3-(5,5-dimethyl-1,3,2-dioxaborinan-2-yl)allyl)triisopropylsilane (**11**). Followed general procedure, with 32 μL (0.2 mmol) **10**, 48 μL (0.2 mmol) allyltriisopropylsilane, 8 mg (0.009 mmol) **2**, and 1 mL CH_2Cl_2. Purified via silica gel chromatography (8:2 hexanes:ethyl acetate) to obtain 56 mg of **11** as an orange oil (90% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 6.7 (1H, dt), 5.25 (1H, dt, J = 17.7 Hz), 3.6 (4H, s), 1.8 (2H, d), 1.05 (21H, s), 0.9 (6H, s).

(*E*)-4,4,5,5-tetramethyl-2-(oct-1-enyl)-1,3,2-dioxaborolane (**12**). Followed general procedure, with 148 μL (0.8 mmol) **6**, 62 μL (0.4 mmol) 1-octene, 17 mg (0.02 mmol) **2**, and 2 mL CH_2Cl_2. Purified via silica gel chromatography (19:1 hexanes:ethyl acetate) to obtain 79 mg of **12** as a yellow-orange oil (83% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 6.64 (1H, dt, *J* = 18.3, 6.5 Hz), 5.43 (1H, *J* = 18.3, 1.7 Hz), 2.16 (2H, dtd, *J* = 7.0, 7.0, 1.8 Hz), 1.4 (8H, m), 1.28 (12H, s), 0.89 (3H, t, *J* = 6.9 Hz). ^{13}C NMR (300 MHz, $CDCl_3$, ppm): δ 155.1, 83.2, 36.1, 31.9, 29.1, 28.4, 25.0, 22.8, 14.3. HRMS (EI) calcd. for $C_{14}H_{27}BO_2$: 238.2104, found: 238.2109.

(*E*)-11-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)undec-10-en-1-ol (**13**). Followed general procedure, with 148 μL (0.8 mmol) **6**, 80 μL (0.4 mmol) 10-undecen-1-ol, 17 mg (0.02 mmol) **2**, and 2 mL CH_2Cl_2. Purified via silica gel chromatography (7:3 hexanes:ethyl acetate) to obtain 84 mg of **13** as a yellow oil (71% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 6.64 (1H, dt, *J* = 17.7, 6.5 Hz), 5.43 (1H, dt, *J* = 17.7, 1.4 Hz), 3.64 (2H, t, *J* = 6.6 Hz), 2.13 (2H, dtd, *J* = 7.1, 7.1, 1.4 Hz), 1.6 (3H, m), 1.3 (12H, m), 1.27 (12H, s). ^{13}C NMR (300 MHz, $CDCl_3$, ppm): δ 155.0, 83.2, 63.3, 36.0, 33.0, 29.7, 29.6, 29.4, 28.4, 25.9, 25.0.

(*E*)-2-(2-cyclopentylvinyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (**14**). Followed general procedure, with 148 μL (0.8 mmol) **6**, 56 μL (0.41 mmol) vinylcyclopentane, 17 mg (0.02 mmol) **2**, and 2 mL CH_2Cl_2. Purified via silica gel chromatography (19:1 hexanes:ethyl acetate) to obtain 72 mg of **14** as a yellow-orange oil (80% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 6.62 (1H, dd, *J* = 17.9, 7.4 Hz), 5.37 (1H, dd, *J* = 17.7, 1.2

Hz), 2.5 (1H, m), 1.7 (6H, m), 1.4 (1H, m), 1.28 (12H, s), 1.1 (1H, m). ^{13}C NMR (300 MHz, $CDCl_3$, ppm): δ 159.2, 83.2, 46.4, 32.6, 25.5, 25.0. HRMS (CI) calcd. for $C_{13}H_{23}BO_2$: 222.1791, found: 222.1799.

(*E*)-2-(2-cyclohexylvinyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (**15**). Followed general procedure, with 38 μL (0.2 mmol) **6**, 28 μL (0.2 mmol) vinylcyclohexane, 8 mg (0.009 mmol) **2**, and 2 mL CH_2Cl_2. Purified via silica gel chromatography (9:1 hexanes:ethyl acetate) to obtain 40 mg of **15** as an orange oil (85% yield). ^{1}H NMR (300 MHz, $CDCl_3$ ppm): δ 6.58 (1H, dd, *J* = 18.2, 6.2 Hz), 5.38 (1H, dd, *J* = 18.3, 1.5 Hz), 2.0 (1H, m), 1.6 (5H, m), 1.27 (12H, s), 1.2 (5H, m). ^{13}C NMR (300 MHz, $CDCl_3$, ppm): δ 160.1, 83.2, 43.5, 32.1, 26.4, 26.2, 25.0. HRMS (EI) calcd. for $C_{14}H_{25}BO_2$: 236.1948, found: 236.1956.

(*E*)-trimethyl(3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)allyl)silane (**16**). Followed general procedure, with 38 μL (0.2 mmol) **6**, 32 μL (0.2 mmol) allyltrimethylsilane, 8 mg (0.009 mmol) **2**, and 1 mL CH_2Cl_2. Purified via silica gel chromatography (19:1 hexanes:ethyl acetate) to obtain 43 mg of **16** as a yellow oil (89% yield). ^{1}H NMR (300 MHz, $CDCl_3$ ppm): δ 6.67 (1H, dt, *J* = 17.4, 8.3 Hz), 5.24 (1H, dt, *J* = 18.0, 1.4 Hz), 1.70 (2H, dd, *J* = 8.3, 1.1 Hz), 1.27 (12H, s), 0.029 (9H, s). ^{13}C NMR (300 MHz, $CDCl_3$, ppm): δ 152.3, 82.9, 28.5, 25.0, –1.6.

(*E*)-2-(3-methoxyprop-1-enyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (**17**). Followed general procedure, with 38 μL (0.2 mmol) **6**, 34 μL (0.2 mmol) allyltrimethoxysilane, 8

mg (0.009 mmol) **2**, and 1 mL CH_2Cl_2. Purified via silica gel chromatography (8:2 hexanes:ethyl acetate) to obtain 15 mg of **17** as a yellow oil (26% yield). ^{1}H NMR (300 MHz, $CDCl_3$ ppm): δ 6.66 (1H, dt, *J* = 17.7, 7.9 Hz), 5.44 (1H, dt, *J* = 17.7, 1.4 Hz), 3.6 (9H, s), 1.8 (2H, d), 1.25 (12H, s). ^{13}C NMR (300 MHz, $CDCl_3$, ppm): δ 148.4, 83.1, 51.0, 25.0, 20.4.

(*E*)-4,4,5,5-tetramethyl-2-styryl-1,3,2-dioxaborolane (**18**). Followed general procedure, with 38 μL (0.2 mmol) **6**, 24 μL (0.21 mmol) styrene, 8 mg (0.009 mmol) **2**, and 1 mL CH_2Cl_2. Purified via silica gel chromatography (9:1 hexanes:ethyl acetate) to obtain 44 mg of **18** as a reddish oil (96% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 7.50 (2H, dd, *J* = 7.8, 1.5 Hz), 7.41 (1H, d, *J* = 19.2 Hz), 7.3 (3H, m), 6.18 (1H, d, *J* = 18.6 Hz), 1.33 (12H, s). ^{13}C NMR (300 MHz, $CDCl_3$, ppm): δ 149.7, 137.7, 129.1, 128.8, 127.3, 83.6, 25.0. HRMS (EI) calcd. for $C_{14}H_{19}BO_2$: 230.1478, found: 230.1473.

(*E*)-2-(2-bromostyryl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (**19**). Followed general procedure, with 38 μL (0.2 mmol) **6**, 26 μL (0.21 mmol) 2-bromostyrene, 8 mg (0.009 mmol) **2**, and 1 mL CH_2Cl_2. Purified via silica gel chromatography (9:1 hexanes:ethyl acetate) to obtain 51 mg of **19** as a very dark oil (83% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 7.72 (1H, d, *J* = 18.3 Hz), 7.62 (1H, dd, *J* = 8.0, 1.7 Hz), 7.56 (1H, dd, *J* = 7.8, 1.2 Hz), 7.30 (1H, ddd, *J* = 6.9, 6.9, 0.6 Hz), 7.15 (1H, ddd, *J* = 7.5, 7.5, 1.8 Hz), 6.13 (1H, d, *J* = 18.3 Hz), 1.33 (12H, s). ^{13}C NMR (300 MHz, $CDCl_3$, ppm): δ 147.7, 137.6, 133.3, 130.1, 127.7, 127.5, 124.5, 83.7, 25.0. HRMS (EI) calcd. for $C_{14}H_{18}BBrO_2$: 308.0583, found: 308.0589.

(*E*)-4,4,5,5-tetramethyl-2-(3-nitrostyryl)-1,3,2-dioxaborolane (**20**). Followed general procedure, with 38 μL (0.2 mmol) **6**, 28 μL (0.2 mmol) 3-nitrostyrene, 8 mg (0.009 mmol) **2**, and 1 mL CH_2Cl_2. Purified via silica gel chromatography (8:2 hexanes:ethyl acetate) to obtain 37 mg of **20** as a bright yellow solid (68% yield). ^{1}H NMR (300 MHz, CD_2Cl_2, ppm): δ 8.32 (1H, s), 8.12 (1H, d, *J* = 8.3 Hz), 7.81 (1H, d, *J* = 7.5 Hz), 7.53 (1H, dd, *J* = 7.8, 7.8 Hz), 7.39 (1H, d, *J* = 18.6 Hz), 6.29 (1H, d, *J* = 18.3 Hz), 1.29 (12H, s). ^{13}C NMR (300 MHz, CD_2Cl_2, ppm): δ 149.2, 146.9, 139.8, 133.3, 130.2, 123.7, 122.0, 84.2, 25.2. HRMS (EI) calcd. for $C_{14}H_{18}BNO_4$: 275.1329, found: 275.1330.

(*E*)-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)allyl acetate (**21d**). Followed general procedure, with 38 μL (0.2 mmol) **6**, 32 μL (0.2 mmol) (*Z*)-but-2-ene-1,4-diyl diacetate, 8 mg (0.009 mmol) **2**, and 2 mL CH_2Cl_2. Purified via silica gel chromatography (8:2 hexanes:ethyl acetate) to obtain 13 mg of **21d** as a clear oil (29% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 6.61 (1H, dt, *J* = 17.7, 4.7 Hz), 5.68 (1H, dt, *J* = 18.0, 1.9 Hz), 4.66 (2H, dd, *J* = 4.7, 2.0 Hz), 2.1 (3H, s), 1.28 (12H, s).

(*E*)-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)allyl benzoate (**21e**). Followed general procedure, with 38 μL (0.2 mmol) **6**, 60 mg (0.2 mmol) (*Z*)-but-2-ene-1,4-diyl dibenzoate, 8 mg (0.009 mmol) **2**, and 1 mL CH_2Cl_2. Purified via silica gel chromatography (8:2 hexanes:ethyl acetate) to obtain 29 mg of **21e** as a brown oil (50% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 8.08 (2H, d, *J* = 7.2 Hz), 7.57 (1H, t, *J* = 7.4 Hz), 7.44 (2H, dd, *J* = 7.5, 7.5 Hz), 6.74 (1H, dt, *J* = 18.3, 4.4 Hz), 5.79 (1H, dt, *J* = 18.3, 2.0 Hz), 4.92 (2H, dd, *J* = 4.4, 1.7 Hz), 1.28 (12H, s). ^{13}C NMR (300 MHz, $CDCl_3$,

ppm): δ 166.3, 146.2, 133.2, 130.2, 129.9, 128.6, 83.7, 65.9, 25.0. HRMS (EI) calcd. for $C_{16}H_{21}BO_4$: 288.1533, found: 288.1534.

(*E*)-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)but-3-en-2-yl benzoate (**22b**). Followed general procedure, with 148 μL (0.8 mmol) **6**, 68 μL (0.4 mmol) but-3-en-2-yl benzoate, 17 mg (0.02 mmol) **2**, and 2 mL CH_2Cl_2. Purified via silica gel chromatography (9:1 hexanes:ethyl acetate) to obtain 43 mg of **22b** as a dark brown oil (36% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 8.05 (2H, d), 7.55 (1H, m), 7.4 (2H, m), 6.68 (1H, dd, *J* = 18.2, 4.4 Hz), 5.71 (1H, d, *J* = 18.3 Hz), 5.67 (1H, m), 1.45 (3H, d), 1.25 (12H, s).

(*E*)-2-methyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)but-3-en-2-ol (**23**). Followed general procedure, with 148 μL (0.8 mmol) **6**, 42 μL (0.4 mmol) 2-methyl-3-buten-2-ol, 17 mg (0.02 mmol) **2**, and 2 mL CH_2Cl_2. Purified via silica gel chromatography (7:3 hexanes:ethyl acetate) to obtain 54 mg of **23** as a brown oil (64% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 6.72 (1H, d, *J* = 18.0 Hz), 5.61 (1H, d, *J* = 18.3 Hz), 1.58 (1H, br), 1.32 (6H, s), 1.29 (12H, s). ^{13}C NMR (300 MHz, $CDCl_3$, ppm): δ 160.0, 83.5, 72.0, 29.3, 25.0. HRMS (EI) calcd. for $C_{11}H_{21}BO_3 - CH_3$: 197.1349, found: 197.1348.

(*E*)-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)but-3-en-1-ol (**24a**). Followed general procedure, with 38 μL (0.2 mmol) **6**, 18 μL (0.21 mmol) 3-buten-1-ol, 8 mg (0.009 mmol) **2**, and 1 mL CH_2Cl_2. Purified via silica gel chromatography (6:4

hexanes:ethyl acetate) to obtain 5 mg of **24a** plus some impurities as an oil (< 13% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 6.61 (1H, dt, *J* = 18.3, 6.6 Hz), 5.57 (1H, dt, *J* = 18.0, 1.4 Hz), 3.75 (2H, t), 2.45 (2H, dt), 1.55 (1H, br), 1.25 (12H, s).

(*E*)-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)but-3-enyl benzoate (**24b**). Followed general procedure, with 74 μL (0.4 mmol) **6**, 34 μL (0.2 mmol) but-3-enyl benzoate, 8 mg (0.009 mmol) **2**, and 1 mL CH_2Cl_2. Purified via silica gel chromatography (9:1 hexanes:ethyl acetate) to obtain ca. 40 mg of **24b** as a yellow oil (66% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 8.04 (2H, dd, *J* = 8.4, 1.5 Hz), 7.56 (1H, tt, *J* = 7.4, 1.8 Hz), 7.44 (2H, dd, *J* = 8.1, 6.6 Hz), 6.67 (1H, dt, *J* = 17.4, 6.3 Hz), 5.61 (1H, dt, *J* = 18.3, 1.5 Hz), 4.41 (2H, t, *J* = 6.9 Hz), 2.65 (2H, ddd, *J* = 6.6, 6.6, 1.2 Hz), 1.28 (12H, s). ^{13}C NMR (300 MHz, $CDCl_3$, ppm): δ 166.8, 149.2, 133.1, 130.5, 129.8, 128.5, 83.4, 63.7, 35.2, 25.0. HRMS (EI) calcd. for $C_{17}H_{23}BO_4$: 302.1689, found: 302.1683.

(*E*)-2-(3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)allyl)isoindoline-1,3-dione (**25**). Followed general procedure, with 46 μL (0.25 mmol) **6**, 35 mg (0.1 mmol) (*Z*)-2,2'-(but-2-ene-1,4-diyl)diisoindoline-1,3-dione, 8 mg (0.009 mmol) **2**, and 1 mL CH_2Cl_2. Purified via silica gel chromatography (7:3 hexanes:ethyl acetate) to obtain 41 mg of **25** as a yellow oil (65% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 7.85 (2H, dd, *J* = 5.7, 3.3 Hz), 7.72 (2H, dd, *J* = 5.6, 2.9 Hz), 6.59 (1H, dt, *J* = 18.0, 4.4 Hz), 5.48 (1H, dt, *J* = 18.3, 1.7 Hz), 4.39 (2H, dd, *J* = 4.5, 1.5 Hz), 1.23 (12H, s). ^{13}C NMR (300 MHz, $CDCl_3$, ppm): δ 167.8, 145.3, 134.1, 132.1, 123.4, 83.6, 41.2, 25.0. HRMS (EI) calcd. for $C_{17}H_{20}BNO_4$: 313.1485, found: 313.1476.

(*E*)-methyl 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)but-3-enoate (**26b**). Followed general procedure, with 38 μL (0.2 mmol) **6**, 22 μL (0.2 mmol) methyl-3-butenoate, 8 mg (0.009 mmol) **2**, and 1 mL CH_2Cl_2. Purified via silica gel chromatography (8:2 hexanes:ethyl acetate) to obtain 15 mg of **26b** as a yellow oil (33% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 6.67 (1H, dt, *J* = 17.7, 6.8 Hz), 5.57 (1H, dt, *J* = 17.7, 1.6 Hz), 3.7 (3H, s), 3.2 (2H, dd), 1.25 (12H, s).

(*E*)-2-(2-(1,3-dioxolan-2-yl)vinyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (**27**). Followed general procedure, with 74 μL (0.4 mmol) **6**, 20 μL (0.2 mmol) 2-vinyl-1,3-dioxolane, 8 mg (0.009 mmol) **2**, and 1 mL CH_2Cl_2. Purified via silica gel chromatography (8:2 hexanes:ethyl acetate) to obtain 9 mg of **27** plus impurities as a light oil (< 20% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 6.49 (1H, dd, *J* = 18.0, 5.4 Hz), 5.86 (1H, d, *J* = 18.0 Hz), 5.3 (1H, m), 3.95 (4H, m), 1.3 (12H, s).

(*E*)-2-(3,3-dimethoxyprop-1-enyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (**28**). Followed general procedure, with 74 μL (0.4 mmol) **6**, 24 μL (0.2 mmol) acrolein dimethyl acetal, 8 mg (0.009 mmol) **2**, and 1 mL CH_2Cl_2. Purified via silica gel chromatography (8:2 hexanes:ethyl acetate) to obtain ca. 9 mg of **28** plus impurities as a brown oil (< 20% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 6.48 (1H, dd, *J* = 18.5, 4.7 Hz), 5.80 (1H, dd, *J* = 18.5, 1.4 Hz), 4.78 (1H, dd, *J* = 4.4, 1.4 Hz), 3.35 (6H, s), 1.25 (12H, s).

2-(Cyclopentylidenemethyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (**29**). Followed general procedure, with 38 μL (0.2 mmol) **6**, 22 μL (0.21 mmol) methylene cyclopentane, 8 mg (0.009 mmol) **2**, and 1 mL CH_2Cl_2. Purified via silica gel chromatography (9:1 hexanes:ethyl acetate) to obtain 36 mg of **29** as a white solid (87% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 5.28 (1H, quint, J = 2.2 Hz), 2.53 (2H, t, J = 7.5 Hz), 2.37 (2H, t, J = 6.8 Hz), 1.65 (4H, m), 1.26 (12H, s). ^{13}C NMR (300 MHz, $CDCl_3$, ppm): δ 172.2, 112.5, 82.7, 37.2, 33.5, 27.0, 26.1, 25.1. HRMS (EI) calcd. for $C_{12}H_{21}BO_2$: 208.1635, found: 208.1627.

2-(Cyclohexylidenemethyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (**30**). Followed general procedure, with 38 μL (0.2 mmol) **6**, 24 μL (0.2 mmol) methylene cyclohexane, 8 mg (0.009 mmol) **2**, and 1 mL CH_2Cl_2. Purified via silica gel chromatography (9:1 hexanes:ethyl acetate) to obtain 43 mg of **30** as a clear oil (96% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 5.02 (1H, s), 2.52 (2H, t, J = 6.3 Hz), 2.20 (2H, t, J = 5.6 Hz), 1.57 (6H, m), 1.26 (12H, s). ^{13}C NMR (300 MHz, $CDCl_3$, ppm): δ 167.2, 82.7, 40.3, 33.4, 28.9, 28.7, 26.6, 25.0. HRMS (EI) calcd. for $C_{13}H_{23}BO_2$: 222.1791, found: 222.1790.

Methylenecycloheptane (**31**). To a flame-dried, round-bottomed flask, under an argon atmosphere, added triphenylmethyl phosphonium bromide (5.8 g, 16.2 mmol) and ether (100 mL). Let stir at room temperature. Added a 1.6M hexanes solution of *n*-butyllithium (8.5 mL, 13.6 mmol) dropwise. Solution immediately turned bright yellow. Let stir at room temperature for 1 hour, then placed in an ice bath. At 0 ºC, slowly, over

40 minutes, added a solution of cycloheptanone (1.5 mL, 12.7 mmol) and ether (9 mL). Let stir at 0 ºC for 3.5 hours. By the end, the reaction had turned completely white, and a lot of white precipitate was visible. Still at 0 ºC, added 50 mL H_2O, removed ice bath, extracted 2 times with 50 mL ether, and dried with Na_2SO_4. The crude product could be visualized on TLC place using an I_2 stain. Purified via silica gel chromatography (9:1 pentane:ether) to obtain 385 mg of **31** as an oil (28% yield). (To removed excess solvent, the purified product was placed on a rotovap at 100 torr for about 2 hours.) ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 4.7 (2H, m), 2.3 (4H, m), 1.55 (8H, m). ^{13}C NMR (300 MHz, $CDCl_3$, ppm): δ 152.5, 110.5, 36.4, 29.7, 28.6.

2-(Cycloheptylidenemethyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (**32**). Followed general procedure, with 68 μL (0.4 mmol) **9**, 48 μL (0.4 mmol) **31**, 17 mg (0.02 mmol) **2**, and 2 mL CH_2Cl_2. Purified via silica gel chromatography (9:1 hexanes:ethyl acetate) to obtain 22 mg of **32** as an orange oil (23% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 5.12 (1H, s), 2.6 (2H, t), 2.4 (2H, t), 1.55 (8H, m), 1.25 (12H, s).

(*E*)-2-methyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)allyl benzoate (**33**). Followed general procedure, with 38 μL (0.2 mmol) **6**, 34 μL (0.2 mmol) 2-methylallyl benzoate, 8 mg (0.009 mmol) **2**, and 1 mL CH_2Cl_2. Purified via silica gel chromatography (9:1 hexanes:ethyl acetate) to obtain 27 mg of **33** as a brown oil (45% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 8.1 (2H, m), 7.6 (1H, m), 7.45 (2H, m), 5.48 (0.6H, m), 5.43 (0.4H, m), 5.19 (0.8H, s), 4.78 (1.2H, m), 2.05 (1.8H, s), 2.0 (1.2H, s), 1.3 (12H, m).

1-Bromooct-1-ene (**34**). Followed general procedure, with 150 μL (0.8 mmol) **6**, 62 μL (0.4 mmol) 1-octene, 17 mg (0.02 mmol) **2**, and 4 mL CH_2Cl_2; followed by 82 μL (1.6 mmol) bromine and 4 mL (1.6 mmol) NaOMe (0.4M in MeOH). Purified via silica gel chromatography (100% hexanes) to obtain 56 mg of **34** as a clear oil (73% yield). ^{1}H NMR (300 MHz, C_6D_6, ppm): (***Z*-isomer**): δ 5.85 (1H, dt, *J* = 7.2, 1.4 Hz), 5.66 (1H, dt, *J* = 6.9, 6.9 Hz), 2.09 (2H, dtd, *J* = 7.1, 7.1, 1.4 Hz), 1.2 (8H, m), 0.57 (3H, t, *J* = 6.9 Hz). (***E*-isomer**): δ 5.97 (1H, dt, *J* = 13.5, 7.4 Hz), 5.70 (1H, dt, *J* = 13.8, 1.5 Hz), 2.09 (2H, dtd, *J* = 7.1, 7.1, 1.4 Hz), 1.2 (8H, m), 0.57 (3H, t, *J* = 6.9 Hz). ^{13}C NMR (300 MHz, $CDCl_3$, ppm): (***Z*-isomer**): δ 135.2, 107.7, 31.9, 30.0, 29.1, 28.4, 22.9, 14.1. HRMS calcd. for $C_8H_{15}Br$: 190.0357, found: 190.0360.

(*Z*)-11-bromoundec-10-en-1-ol (**35**). Followed general procedure, with 150 μL (0.8 mmol) **6**, 80 μL (0.4 mmol) 10-undecen-1-ol, 17 mg (0.02 mmol) **2**, and 4 mL CH_2Cl_2; followed by 82 μL (1.6 mmol) bromine and 4 mL (1.6 mmol) NaOMe (0.4M in MeOH). Purified via silica gel chromatography (7:3 hexanes:ethyl acetate) to obtain 85 mg of **35** as a brown oil (85% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 6.14 (1H, d, *J* = 6.7 Hz), 6.08 (1H, dt, *J* = 6.6, 6.6 Hz), 3.6 (2H, t), 2.2 (2H, dt), 1.4 (14H, m). ^{13}C NMR (300 MHz, $CDCl_3$, ppm): δ 135.2, 107.8, 63.3, 33.0, 29.9, 29.7, 29.6, 29.5, 29.3, 28.3, 25.9.

6-Bromohex-5-enyl acetate (**36**). Followed general procedure, with 150 μL (0.8 mmol) **6**, 66 μL (0.4 mmol) 5-hexenyl acetate, 17 mg (0.02 mmol) **2**, and 4 mL CH_2Cl_2; followed by 82 μL (1.6 mmol) bromine and 4 mL (1.6 mmol) NaOMe (0.4M in MeOH). Purified via silica gel chromatography (9:1 hexanes:ethyl acetate) to obtain 69 mg of **36**

as a brown oil (64% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): (***Z*-isomer**): δ 6.18 (1H, d, *J* = 7.5 Hz), 6.09 (1H, dt, *J* = 6.8, 6.8 Hz), 4.08 (2H, t, *J* = 6.6 Hz), 2.24 (2H, dt, *J* = 7.3, 7.3 Hz), 2.05 (3H, s), 1.7 (2H, m), 1.5 (2H, m). ^{13}C NMR (300 MHz, $CDCl_3$, ppm): (***Z*-isomer**): δ 171.4, 134.5, 108.5, 64.4, 29.5, 28.3, 24.8, 21.2. (***E*-isomer**): δ 137.7, 105.0, 64.3, 32.7, 28.1, 25.2. HRMS (EI) calcd. for $C_8H_{13}BrO_2$: 220.0099, found: 220.0104.

(*Z*)-(2-bromovinyl)cyclopentane (**37**). Followed general procedure, with 136 μL (0.8 mmol) **9**, 54 μL (0.4 mmol) vinylcyclopentane, 17 mg (0.02 mmol) **2**, and 2.5 mL CH_2Cl_2; followed by 82 μL (1.6 mmol) bromine and 2.5 mL (1.6 mmol) NaOMe (0.6M in MeOH). Purified via silica gel chromatography (100% hexanes) to obtain 38 mg of **37** as a white solid (54% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 6.04 (2H, m), 2.9 (1H, m), 0.9-2.0 (8H, m).

(*Z*)-(2-bromovinyl)cyclohexane (**38**). Followed general procedure, with 150 μL (0.8 mmol) **6**, 54 μL (0.4 mmol) vinylcyclohexane, 17 mg (0.02 mmol) **2**, and 4 mL CH_2Cl_2; followed by 82 μL (1.6 mmol) bromine and 4 mL (1.6 mmol) NaOMe (0.4M in MeOH). Purified via silica gel chromatography (100% hexanes) to obtain 30 mg of **38** as a clear oil (40% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 6.05 (1H, dd, *J* = 6.9, 0.9 Hz), 5.93 (1H, dd, *J* = 8.6, 6.9 Hz), 2.5 (1H, m), 0.9-2.2 (10H, m).

(*Z*)-1-(2-bromovinyl)-3-nitrobenzene (**39**). Followed general procedure, with 82 μL (0.48 mmol) **9**, 56 μL (0.4 mmol) 3-nitrostyrene, 17 mg (0.02 mmol) **2**, and 2.5 mL

CH_2Cl_2; followed by 48 μL (0.93 mmol) bromine and 2.5 mL (0.93 mmol) NaOMe (0.4M in MeOH). Purified via silica gel chromatography (9:1 hexanes:ethyl acetate) to obtain 85 mg of **39** as a yellow oil/solid (93% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 8.56 (1H, dd, *J* = 2.0, 2.0 Hz), 8.20 (1H, dd, *J* = 8.3, 1.7 Hz), 8.00 (1H, d, *J* = 7.5 Hz), 7.57 (1H, dd, *J* = 8.0, 8.0 Hz), 7.15 (1H, d, *J* = 8.1 Hz), 6.65 (1H, d, *J* = 8.1 Hz). ^{13}C NMR (300 MHz, $CDCl_3$, ppm): δ 148.4, 136.7, 134.9, 130.5, 129.4, 123.9, 123.2, 110.0. HRMS (EI) calcd. for $C_8H_6BrNO_2$: 226.9582, found: 226.9580.

(*Z*)-4-bromo-2-methylbut-3-en-2-ol (**40**). Followed general procedure, with 148 μL (0.8 mmol) **6**, 42 μL (0.4 mmol) 2-methyl-3-buten-2-ol, 17 mg (0.02 mmol) **2**, and 2 mL CH_2Cl_2; followed by 82 μL (1.6 mmol) bromine and 2.7 mL (1.6 mmol) NaOMe (0.6M in MeOH). Purified via silica gel chromatography (8:2 hexanes:ethyl acetate) to obtain 28 mg of **40** as a brown oil (42% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 6.38 (1H, d, *J* = 7.8 Hz), 6.16 (1H, d, *J* = 8.4 Hz), 2.25 (1H, br), 1.48 (6H, s).

(*Z*)-3-bromoallyl benzoate (**41**). Followed general procedure, with 86 μL (0.5 mmol) **9**, 62 mg (0.21 mmol) (*Z*)-but-2-ene-1,4-diyl dibenzoate, 17 mg (0.02 mmol) **2**, and 2 mL CH_2Cl_2; followed by 50 μL (0.97 mmol) bromine and 1.6 mL (0.96 mmol) NaOMe (0.6M in MeOH). Purified via silica gel chromatography (39:1 pentane:ether) to obtain 49 mg of **41** as a clear oil (48% yield). ^{1}H NMR (300 MHz, C_6D_6, ppm): δ 8.07 (2H, m), 7.05 (3H, m), 5.88 (1H, dt, *J* = 7.5, 6.0 Hz), 5.76 (1H, dt, *J* = 7.2, 1.6 Hz), 4.79 (2H, dd, *J* = 6.2, 1.4 Hz). ^{13}C NMR (300 MHz, $CDCl_3$, ppm): δ 166.5, 133.4, 130.0, 129.9, 129.7, 128.6, 111.4, 63.0.

(*Z*)-4-bromobut-3-enyl benzoate (**42**). Followed general procedure, with 150 μL (0.8 mmol) **6**, 68 μL (0.4 mmol) but-3-enyl benzoate, 17 mg (0.02 mmol) **2**, and 2 mL CH_2Cl_2; followed by 82 μL (1.6 mmol) bromine and 2.7 mL (1.6 mmol) NaOMe (0.6M in MeOH). Purified via silica gel chromatography (19:1 hexanes:ethyl acetate) to obtain 75 mg of **42** as a yellow-brown oil (73% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 8.06 (2H, d, *J* = 6.6 Hz), 7.58 (1H, t, *J* = 7.5 Hz), 7.45 (2H, dd, *J* = 7.7, 7.7 Hz), 6.34 (1H, dt, *J* = 7.2, 1.2 Hz), 6.24 (1H, dt, *J* = 6.9, 6.9 Hz), 4.41 (2H, t, *J* = 6.5 Hz), 2.71 (2H, dtd, *J* = 6.7, 6.7, 1.4 Hz). ^{13}C NMR (300 MHz, $CDCl_3$, ppm): δ 166.7, 133.2, 130.6, 130.3, 129.8, 128.9, 110.7, 63.1, 29.8. HRMS (CI) calcd. for $C_{11}H_{11}BrO_2$ + H: 255.0021, found: 255.0009.

(*Z*)-2-(3-bromoallyl)isoindoline-1,3-dione (**43**). Followed general procedure, with 400 μL (2.3 mmol) **9**, 320 mg (0.92 mmol) (*Z*)-2,2'-(but-2-ene-1,4-diyl)diisoindoline-1,3-dione, 80 mg (0.094 mmol) **2**, and 11.5 mL CH_2Cl_2; followed by 236 μL (4.6 mmol) bromine and 8 mL (4.8 mmol) NaOMe (0.6M in MeOH). Purified via silica gel chromatography (8:2 pentane:ether) to obtain 414 mg of **43** as a white/yellow solid (85% yield). Further purified via recrystallization from hexanes to obtain 58 mg of **43** as white, needle-like crystals (12% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 7.87 (2H, dd, *J* = 5.3, 3.2 Hz), 7.74 (2H, dd, *J* = 5.6, 3.2 Hz), 6.39 (1H, dt, *J* = 7.2, 1.7 Hz), 6.24 (1H, dt, *J* = 6.9, 6.2 Hz), 4.48 (2H, dd, *J* = 6.2, 1.4 Hz). ^{13}C NMR (300 MHz, $CDCl_3$, ppm): δ 167.9, 134.3, 132.2, 129.1, 123.6, 111.1, 37.6. HRMS (CI) calcd. for $C_{11}H_8BrNO_2$ + H: 265.9817, found: 265.9825.

(*E*)-1-iodooct-1-ene (**44**). Followed general procedure, with 200 μL (0.405 mmol) **12**, 500 mg (1.97 mmol) iodine, 800 μL (2.4 mmol) NaOH (3M in H_2O), 6 mL THF, and a reaction time of 3 hours. Purified via silica gel chromatography (100% hexanes) to obtain 84 mg of **44** as a yellow oil/solid (87% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 6.52 (1H, dt, *J* = 14.1, 7.1 Hz), 5.98 (1H, dt, *J* = 14.1, 1.4 Hz), 2.06 (2H, dtd, *J* = 7.2, 7.2, 1.2 Hz), 1.4 (8H, m), 0.90 (3H, t, *J* = 6.6 Hz). ^{13}C NMR (300 MHz, $CDCl_3$, ppm): δ 146.9, 74.5, 36.4, 31.9, 28.9, 28.6, 22.9, 14.4. HRMS (CI) calcd. for $C_8H_{15}I$: 238.0218, found: 238.0224.

(3-Iodoallyl)triisopropylsilane (**45**). Followed general procedure, with 150 μL (0.388 mmol) **8**, 250 mg (0.98 mmol) iodine, 390 μL (1.2 mmol) NaOH (3M in H_2O), 6 mL THF, and a reaction time of 4 hours. Purified via silica gel chromatography (100% hexanes) to obtain ca. 125 mg of **45** as a yellow oil (99% yield). ^{1}H NMR (300 MHz, C_6D_6, ppm): (***E*-isomer**): δ 6.52 (1H, dt, *J* = 14.4, 8.6 Hz), 5.76 (1H, dt, *J* = 14.4, 1.3 Hz), 1.67 (2H, dd, *J* = 8.6, 1.4 Hz), 1.07 (18H, s), 1.06 (3H, s). (***Z*-isomer**): δ 6.25 (1H, dt, *J* = 7.7, 7.7 Hz), 6.01 (1H, dt, *J* = 7.2, 1.4 Hz), 1.75 (2H, dd, *J* = 8.0, 1.4 Hz), 1.10 (21H, s). ^{13}C NMR (300 MHz, $CDCl_3$, ppm): (***E*-isomer**): δ 143.9, 70.7, 20.4, 18.9, 11.2. (***Z*-isomer**): δ 139.1, 80.5, 30.0, 19.0, 11.6. HRMS (EI) calcd. for $C_{12}H_{25}SiI$: 324.0770, found: 324.0775.

(*E*)-(2-iodovinyl)benzene (**46**). Followed general procedure, with 120 μL (0.4 mmol) **18**, 250 mg (0.98 mmol) iodine, 400 μL (1.2 mmol) NaOH (3M in H_2O), 6 mL THF, and a reaction time of 11 hours. Purified via silica gel chromatography (100% hexanes) to

obtain ca. 90 mg of **46** as a bright yellow oil (99% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 7.45 (1H, d, *J* = 14.7 Hz), 7.3 (5H, m), 6.84 (1H, d, *J* = 15.0 Hz). ^{13}C NMR (300 MHz, $CDCl_3$, ppm): δ 145.0, 137.7, 128.8, 128.5, 126.1, 76.9. HRMS (CI) calcd. for C_8H_7I: 229.9592, found: 229.9592.

(*E*)-4-iodo-2-methylbut-3-en-2-ol (**47**). Followed general procedure, with 130 μL (0.38 mmol) **23**, 240 mg (0.95 mmol) iodine, 380 μL (1.14 mmol) NaOH (3M in H_2O), 6 mL THF, and a reaction time of 13 hours. Purified via silica gel chromatography (8:2 hexanes:ethyl acetate) to obtain 66 mg of **47** as a yellow oil (82% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 6.68 (1H, d, *J* = 14.1 Hz), 6.34 (1H, d, *J* = 14.7 Hz), 1.71 (1H, br), 1.31 (6H, s). ^{13}C NMR (300 MHz, $CDCl_3$, ppm): δ 153.1, 75.0, 74.0, 29.5. HRMS (CI) calcd. for C_5H_9IO: 211.9698, found: 211.9696.

4,4,5,5-Tetramethyl-2-(prop-1-en-2-yl)-1,3,2-dioxaborolane (**48**). Followed same procedure as for **6**, with: *Step 1*: 4.5 mL (40 mmol) trimethyl borate, 100 mL (50 mmol) isopropenylmagnesium bromide (0.5M in THF), 10 mL ether, and 70 mL 30% aqueous HCl solution. Took great care not to let the crude isopropenyl boronic acid solution become too concentrated (which would lead to decomposition). *Step 2*: 4 g 4 Å powdered molecular sieves, 9.5 g (80 mmol) pinacol, and 50 mL ether. Purified via silica gel chromatography (19:1 pentane:ether, keeping rotovap vacuum above 150 torr) to obtain 4.8 g of **48** as a slightly yellow oil (71% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 5.76 (1H, br), 5.64 (1H, br), 1.8 (3H, m), 1.25 (12H, s). ^{13}C NMR (300 MHz, $CDCl_3$, ppm): δ 130.2, 83.6, 25.0, 21.4.

(*Z*)-trimethyl(3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)but-2-enyl)silane (**49**). Followed general procedure, with 38 μL (0.2 mmol) **48**, 32 μL (0.2 mmol) allyltrimethylsilane, 8 mg (0.009 mmol) **2**, and 1 mL CH_2Cl_2. Purified via silica gel chromatography (19:1 hexanes:ethyl acetate) to obtain 37 mg of **49** as a yellow oil (73% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 6.44 (1H, td, *J* = 8.9, 1.4 Hz), 1.66 (2H, d, *J* = 9.0 Hz), 1.63 (3H, m), 1.25 (12H, s), 0.01 (9H, s). ^{13}C NMR (300 MHz, $CDCl_3$, ppm): δ 143.7, 83.0, 25.0, 21.6, 13.9, –1.2.

(*Z*)-2-(1-cyclohexylprop-1-en-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (**50**). Followed general procedure, with 38 μL (0.2 mmol) **48**, 28 μL (0.2 mmol) vinylcyclohexane, 8 mg (0.009 mmol) **2**, and 1 mL CH_2Cl_2. Purified via silica gel chromatography (19:1 hexanes:ethyl acetate) to obtain 30 mg of **50** as an orange oil (59% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 6.13 (1H, dd, *J* = 8.9, 1.7 Hz), 2.38 (1H, m), 1.7 (4H, m), 1.69 (3H, d, *J* = 1.8 Hz), 1.27 (12H, s), 1.2 (6H, m). ^{13}C NMR (300 MHz, $CDCl_3$, ppm): δ 152.0, 83.2, 37.7, 32.4, 26.3, 26.2. 25.0, 14.1.

(3-Bromobut-3-enyloxy)(*tert*-butyl)dimethylsilane (**51**). To a flame-dried, round-bottomed flask, under an argon atmosphere, added 3-bromo-3-buten-1-ol (purchased from Fluka, 5 mL, 50 mmol), triethylamine (14 mL, 100 mmol), dimethylaminopyridine (240 mg, 2.0 mmol), and CH_2Cl_2 (65 mL). Placed in an ice bath and let stir. Added, via cannula, a solution of *t*-butyldimethylsilyl chloride (11 g, 73 mmol) and CH_2Cl_2 (15 mL). Let slowly warm to room temperature and allowed to stir overnight. Transferred to separatory funnel, added 70 mL 10% aqueous HCl solution, extracted 2 times with 80 mL

CH_2Cl_2, and dried with Na_2SO_4. Purified via silica gel chromatography (9:1 hexanes:ethyl acetate) to obtain 9.9 g of **51** as a light yellow oil (74% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 5.65 (1H, m), 5.45 (1H, m), 3.8 (2H, t), 2.6 (2H, t), 0.92 (9H, s), 0.08 (6H, s). ^{13}C NMR (300 MHz, $CDCl_3$, ppm): δ 130.9, 118.6, 61.1, 45.0, 26.2, 18.6, –5.0.

Tert-butyldimethyl(3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)but-3-enyloxy)silane (**52**). *Step 1*: To a flame-dried, round-bottomed flask, under an argon atmosphere, added **51** (2 mL, 8.14 mmol) and ether (20 mL). Placed in a dry ice/acetone bath and let stir. Added a 1.7M pentane solution of *t*-butyllithium (10 mL, 17.0 mmol) dropwise, over about 10 minutes. Placed in an ice bath and let stir for 20 minutes. Returned to dry ice/acetone bath and added a solution of trimethyl borate (2.5 mL, 22.3 mmol) and ether (5 mL) dropwise, over about 10 minutes. Transferred to ice bath and let stir for 1 hour. Added 30 mL H_2O and let stir for 30 minutes. Transferred to separatory funnel, extracted 3 times with 30 mL ether, dried with $MgSO_4$, and removed the bulk of the solvent *in vacuo*. *Step 2*: Cannula-transferred the above crude reaction mixture, along with 10 mL ether, to a flame-dried, round-bottomed flask, under an argon atmosphere, which contained 800 mg of activated (via flame-drying under vacuum) 4 Å powdered molecular sieves. Added pinacol (3 g, 25.4 mmol) and let stir at room temperature overnight. Filtered through Celite, rinsing with ether. Purified via silica gel chromatography (19:1 hexanes:ethyl acetate) to obtain 475 mg of **52** as a clear oil (19% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 5.84 (1H, d, J = 3.6 Hz), 5.68 (1H, br), 3.67 (2H, t, J = 7.2 Hz), 2.38 (2H, t, J = 7.2 Hz), 1.27 (12H, s), 0.90 (9H, s), 0.055 (6H, s). ^{13}C NMR (300 MHz,

$CDCl_3$, ppm): δ 131.7, 83.6, 63.3, 39.3, 26.2, 25.0, 18.6, –5.0. HRMS (EI) calcd. for $C_{16}H_{33}BO_3Si$ – H: 311.2208, found: 311.2221.

(4-Bromopent-4-enyloxy)(*tert*-butyl)dimethylsilane (**53**).[26] *Step 1*: To a flame-dried, round-bottomed flask, under an argon atmosphere, added *t*-butyl acetate (16 mL, 119 mmol) and THF (60 mL). Placed in a dry ice/acetone bath and let stir. Added a 1.8M heptane/THF/ethylbenzene solution of lithium diisopropylamide (100 mL, 180 mmol) dropwise, over about 20 minutes. Placed in an ice bath and let stir for 30 minutes, then returned to dry ice/acetone bath. Added a solution of 2,3-dibromopropene (distilled from CaH_2, 10 mL, 102 mmol) and THF (40 mL) dropwise, over about 15 minutes. Let stir at –78 °C for 2 hours, then removed dry ice/acetone bath and let warm to room temperature. Transferred to a separatory funnel, added 150 mL H_2O, extracted 3 times with 150 mL ether, washed with 200 mL brine, and dried with Na_2SO_4. Purified via Kugelrohr distillation to obtain 21.2 g of *tert*-butyl 4-bromopent-4-enoate as a yellow oil (88% yield). *Step 2*: To a flame-dried, round-bottomed flask, under an argon atmosphere, added *tert*-butyl 4-bromopent-4-enoate (obtained above) and ether (100 mL). Added a 1.0M ether solution of lithium aluminum hydride (100 mL, 100 mmol) dropwise, over about 20 minutes. Solution refluxed upon initial lithium aluminum hydride addition, but it had reached room temperature by the end of the addition. Let stir at room temperature for 1 hour. Slowly added 30 mL H_2O, 30 mL 5% aqueous NaOH solution, and 30 mL H_2O again. Lots of white solid formed. Filtered through Celite, extracted 2 times with 50 mL ether, and concentrated to obtain 4-bromopent-4-en-1-ol as a yellow oil that turned orange-red overnight. *Step 3*: To a flame-dried, round-bottomed flask, under an

argon atmosphere, added crude 4-bromopent-4-en-1-ol (obtained above), triethylamine (30 mL, 215 mmol), dimethylaminopyridine (700 mg, 5.7 mmol), and CH_2Cl_2 (300 mL). Placed in an ice bath and let stir. Added *t*-butyldimethylsilyl chloride (20 g, 133 mmol). Let slowly warm to room temperature and allowed to stir overnight. Transferred to a separatory funnel, added 250 mL 1% aqueous HCl solution, extracted 2 times with 200 mL CH_2Cl_2, and dried with Na_2SO_4. Purified via silica gel chromatography (39:1 hexanes:ethyl acetate) to obtain 13.81 g of **53** as a yellow oil (48% yield from step 1). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 5.6 (1H, m), 5.4 (1H, m), 3.63 (2H, t), 2.55 (2H, t), 1.78 (2H, m), 0.9 (9H, s), 0.02 (6H, s). ^{13}C NMR (300 MHz, $CDCl_3$, ppm): δ 134.6, 116.9, 61.7, 38.1, 31.2, 26.1, 18.5, –5.1.

Tert-butyldimethyl(4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pent-4-enyloxy)silane (**54**). Followed procedure given for **52**, with: *Step 1*: 1 mL (3.9 mmol) **53**, 3.5 mL (6.0 mmol) *t*-butyllithium (1.7M in pentane), 2.5 mL (10.8 mmol) triisopropyl borate, and 13 mL ether. *Step 2*: 400 mg 4 Å powdered molecular sieves, 920 mg (7.8 mmol) pinacol, and 10 mL ether. Purified via silica gel chromatography (9:1 hexanes:ethyl acetate) to obtain 249 mg of **54** as a clear oil (20% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 5.78 (1H, d, J = 3.6 Hz), 5.62 (1H, br), 3.61 (2H, t, J = 6.8 Hz), 2.18 (2H, t, J = 7.5 Hz), 1.65 (3H, m), 1.27 (12H, s), 0.90 (9H, s), 0.052 (6H, s). ^{13}C NMR (300 MHz, $CDCl_3$, ppm): δ 129.4, 83.5, 63.2, 32.6, 31.8, 26.2, 25.0, 18.6, –5.0. HRMS (EI) calcd. for $C_{17}H_{35}BO_3Si$ + H: 327.2527, found: 327.2535.

(2-(2-Bromoallyl)hexyloxy)(*tert*-butyl)dimethylsilane (**55**). To a flame-dried, round-bottomed flask, under an argon atmosphere, added diisopropylamine (6 mL, 42.8 mmol) and THF (10 mL). Placed in a dry ice/acetone bath and let stir. Added a 1.6M hexanes solution of *n*-butyllithium (23 mL, 36.8 mmol) dropwise, over 10 minutes. Transferred to an ice bath and let stir for 1 hour. Returned to dry ice/acetone bath, added a solution of ethyl caproate (4 mL, 24.2 mmol) and THF (10 mL), and returned to the ice bath. Let stir at 0 °C for 30 minutes, then returned to dry ice/acetone bath. Added a solution of 2,3-dibromopropene (distilled from CaH_2, 3 mL, 30.7 mmol), hexamethyl phosphoamide (distilled from CaH_2, 3 mL, 17.2 mmol), and THF (5 mL) dropwise, over about 10 minutes. Let stir at –78 °C for 3 hours, then moved to ice bath and let stir for about 15 minutes. Transferred to a separatory funnel, added 100 mL H_2O, extracted 3 times with 80 mL ether, washed with 100 mL brine, and dried with Na_2SO_4. Purified via Kugelrohr distillation to obtain 4.6 g of ethyl 2-(2-bromoallyl)hexanoate as a yellow oil (72%). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 5.6 (1H, m), 5.42 (1H, m), 4.15 (2H, q), 2.75 (2H, m), 2.5 (1H, m), 1.55 (2H, m), 1.3 (4H, m), 1.3 (3H, t), 0.85 (3H, t). ^{13}C NMR (300 MHz, $CDCl_3$, ppm): δ 175.2, 131.7, 118.8, 60.6, 44.1, 44.0, 31.5, 29.3, 22.7, 14.5, 14.1. *Step 2*: Followed procedure given for **53** (Step 2), with 5.6 g (ca. 17 mmol) ethyl 2-(2-bromoallyl)hexanoate, 19 mL (19 mmol) lithium aluminum hydride (1.0M in ether), and 5 mL ether. Purified via silica gel chromatography (7:3 hexanes:ethyl acetate) to obtain 3 g of 2-(2-bromoallyl)hexan-1-ol as a yellow oil (80% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 5.61 (1H, m), 5.43 (1H, m), 3.6 (2H, m), 2.55 (1H, dd), 2.4 (1H, dd), 1.9 (1H, m), 1.35 (6H, m), 0.9 (3H, t). ^{13}C NMR (300 MHz, $CDCl_3$, ppm): δ 133.7, 118.4, 64.4, 43.5, 38.9, 30.0, 29.2, 23.1, 14.3. *Step 3*: Followed procedure given for **53** (step 3), with

3.1 g (14 mmol) 2-(2-bromoallyl)hexan-1-ol, 5 mL (36 mmol) triethylamine, 100 mg (0.82 mmol) dimethylaminopyridine, 4.2 g (28 mmol) *t*-butyldimethylsilyl chloride, and 40 mL CH_2Cl_2. Purified via silica gel chromatography (39:1 hexanes:ethyl acetate) to obtain 4.3 g of **55** as a clear oil (92% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 5.6 (1H, m), 5.42 (1H, m), 3.55 (2H, m), 2.58 (1H, dd), 2.23 (1H, dd), 1.82 (1H, br), 1.3 (6H, m), 0.9 (12H, m), 0.02 (6H, s). ^{13}C NMR (300 MHz, $CDCl_3$, ppm): δ 134.2, 118.0, 63.9, 43.7, 38.7, 30.0, 29.3, 26.1, 23.2, 18.5, 14.3, –5.2, –5.3.

2-(2-(4,4,5,5-Tetramethyl-1,3,2-dioxaborolan-2-yl)allyl)hexan-1-ol (**56**). Followed procedure given for **52**, with: *Step 1*: 1 mL (3.3 mmol) **55**, 3 mL (5.1 mmol) *t*-butyllithium (1.7M in pentane), 1 mL (8.8 mmol) trimethyl borate, and 12 mL THF. *Step 2*: 330 mg 4 Å powdered molecular sieves, 780 mg (6.6 mmol) pinacol, and 10 mL ether. Purified via silica gel chromatography (9:1 to 8:2 hexanes:ethyl acetate) to obtain ca. 200 mg of **56** as an oil (23% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 5.7 (1H, m), 5.4 (1H, m), 3.59 (2H, d), 2.2 (2H, d), 1.7 (1H, br), 1.35 (6H, m), 0.9 (15H, m).

5-(2-Bromoallyl)-2,2-dimethyl-1,3-dioxane (**57**). *Step 1*: To a flame-dried, round-bottomed flask, under an argon atmosphere, added 60% sodium hydride (1.1 g, 27.5 mmol) and THF (20 mL). Let stir for 5 minutes, then added dimethyl malonate (3 mL, 26.2 mmol) dropwise. Let stir for 30 minutes at room temperature, then added a solution of 2,3-dibromopropene (2 mL, 16.4 mmol) and THF (2 mL) dropwise. Let stir at room temperature for 4 hours, then added 20 mL H_2O, extracted 3 times with 20 mL ether, washed with 30 mL brine, and dried with Na_2SO_4. Purified via silica gel chromatography

(8:2 hexanes:ethyl acetate) to obtain 3.16 g of dimethyl 2-(2-bromoallyl)malonate as a clear oil (77%). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 5.65 (1H, m), 5.43 (1H, m), 3.82 (1H, t), 3.78 (6H, s), 3.1 (2H, d). ^{13}C NMR (300 MHz, $CDCl_3$, ppm): δ 168.6, 129.3, 120.0, 53.0, 50.7, 40.8. *Step 2*: Followed procedure given for **53** (step 2), with 3.14 g (12.5 mmol) dimethyl 2-(2-bromoallyl)malonate, 27 mL (27 mmol) lithium aluminum hydride (1.0M in ether), and 35 mL ether. Purified via silica gel chromatography (1:1 to 2:8 hexanes:ethyl acetate) to obtain 1.43 g of 2-(2-bromoallyl)propane-1,3-diol as a clear oil (59% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 5.65 (1H, m), 5.45 (1H, m), 3.8 (2H, m), 3.7 (2H, m), 2.5 (4H, m), 2.18 (1H, m). ^{13}C NMR (300 MHz, $CDCl_3$, ppm): δ 132.4, 118.9, 64.7, 40.2, 40.0. *Step 3*: To a flame-dried, round-bottomed flask, under an argon atmosphere, added 2-(2-bromoallyl)propane-1,3-diol (2.8 g, 14.4 mmol), acetone (10 mL, 136 mmol), *p*-toluenesulfonic acid-monohydrate (140 mg, 0.74), and benzene (70 mL). Placed in a 95 °C oil bath and let stir under reflux, with azeotropic removal of water via Dean Stark trap, for 3.5 hours. Removed from heat, let cool to room temperature, added 70 mL aqueous $NaHCO_3$ solution, extracted 2 times with ether, washed with 50 mL brine, and dried with Na_2SO_4. Purified via silica gel chromatography (8:2 hexanes:ethyl acetate) to obtain 2.14 g of **57** as a clear oil (63% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 5.65 (1H, m), 5.45 (1H, m), 3.99 (2H, dd), 3.6 (2H, dd), 2.5 (2H, d), 2.08 (1H, m), 1.4 (6H, d). ^{13}C NMR (300 MHz, $CDCl_3$, ppm): δ 131.6, 118.9, 98.2, 63.5, 41.3, 32.5, 24.3, 24.2.

2-(3-(2,2-Dimethyl-1,3-dioxan-5-yl)prop-1-en-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (**58**). To a flame-dried, round-bottomed flask, under an argon atmosphere,

added a solution of **57** (530 mg, 2.25 mmol) and ether (20 mL). Placed in a dry ice/acetone bath and let stir. Added, all at once, a 1.7M pentane solution of *t*-butyllithium (3.5 mL, 6.0 mmol). Let stir at –78 °C for 1 hour, then added 2-isopropoxy-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (0.5 mL, 3.4 mmol) via syringe and let stir at –78 °C for 30 minutes. Removed dry ice/acetone bath and let slowly warm to room temperature. Added 20 mL H_2O, extracted 3 times with 25 mL ether, and dried with Na_2SO_4. Purified via silica gel chromatography (9:1 hexanes:ethyl acetate) to obtain 125 mg of **58** as a clear oil (20% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 5.82 (1H, m), 5.6 (1H, m), 3.81 (2H, dd), 3.55 (2H, m), 2.2 (3H, m), 1.41 (3H, s), 1.39 (3H, s), 1.25 (12H, s).

4,4,5,5-Tetramethyl-2-(1-phenylvinyl)-1,3,2-dioxaborolane (**59**). Followed procedure given for **58**, with 1 mL (6.9 mmol) α-bromostyrene, 10 mL (17 mmol) *t*-butyllithium (1.7M in pentane, added dropwise over 5 minutes), 3 mL (14.7 mmol) 2-isopropoxy-4,4,5,5-tetramethyl-1,3,2-dioxaborolane, and 60 mL ether. Purified via silica gel chromatography (19:1 hexanes:ether) to obtain 1.6 g of **59** as a yellow solid (99% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 7.51 (2H, m), 7.32 (3H, m), 6.09 (2H, m), 1.36 (12H, s).

4-Iodopent-4-en-1-ol (**60**). To flamed-dried, round-bottomed flask, under an argon atmosphere, added sodium iodide (3.2 g, 21.3 mmol) and acetonitrile (18 mL). Let stir until NaI had all dissolved (a couple minutes). Added trimethylsilyl chloride (2.8 mL, 22.1 mmol), followed by H_20 (195 μL, 10.8 mmol). Let stir at room temperature for 10

minutes. Added 4-pentyn-1-ol (1 mL, 10.8 mmol) and let stir at room temperature for 1.5 hours. Solution heated somewhat over the course of the reaction. Added 25 mL H_2O, added 25 mL aqueous sodium thiosulfate solution, extracted 3 times with 50 mL ether, and dried with $MgSO_4$. Purified via silica gel chromatography (7:3 hexanes:ethyl acetate) to obtain 626 mg of **60** as a red oil (27% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 6.03 (1H, m), 5.7 (1H, m), 3.6 (2H, t), 2.48 (2H, t), 2.1 (1H, br), 1.75 (2H, m). ^{13}C NMR (300 MHz, $CDCl_3$, ppm): δ 126.1, 111.6, 61.2, 41.8, 32.1.

4-Iodopent-4-enyl acetate (**61**). Same reaction as for **60**. Obtained 316 mg of **61** as a yellow oil (12% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 6.03 (1H, m), 5.7 (1H, m), 4.05 (2H, t), 2.48 (2H, t), 2.02 (3H, s), 1.82 (2H, t). ^{13}C NMR (300 MHz, $CDCl_3$, ppm): δ 171.2, 126.5, 110.6, 62.9, 42.0, 28.2, 21.1.

5-Iodopentan-2-one (**62**). Same reaction as for **60**. Obtained 912 mg of **62** as a red oil (40% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 3.2 (2H, t), 2.59 (2H, t), 2.18 (3H, s), 2.02 (2H, m). ^{13}C NMR (300 MHz, $CDCl_3$, ppm): δ 207.3, 43.9, 30.3, 27.2, 6.6.

3-Iodobut-3-en-1-ol (**63**). Followed procedure given for **60**, with 4 mL (53 mmol) 3-butyn-1-ol, 15.9 g (106 mmol) sodium iodide, 13.5 mL (106 mmol) trimethylsilyl chloride, 955 μL (53 mmol) H_2O, and 100 mL anhydrous acetonitrile. Purified via silica gel chromatography (8:2 hexanes:ethyl acetate) to obtain 6.5 g of **63** as a red oil (62% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 6.2 (1H, m), 5.82 (1H, m), 3.75 (2H, t), 2.6 (2H, t), 1.7 (1H, br).

3-Iodobut-3-enyl acetate (**64**). Same reaction as for **63**. Obtained 3.5 g of **64** as a red oil (28% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 6.15 (1H, m), 5.8 (1H, m), 4.2 (2H, t), 2.72 (2H, t), 2.05 (3H, s).

4-Iodobutan-2-one (**65**). Same reaction as for **63**. Obtained 1.1 g of **65** (contaminated with impurities) as a dark red oil/solid (< 10% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 3.3 (2H, t), 2.9 (2H, t), 2.4 (3H, s).

2-Iodoprop-2-en-1-ol (**66**). Followed procedure given for **60**, with 3.5 mL (59.3 mmol) propargyl alcohol, 17.8 g (119 mmol) sodium iodide, 15 mL (118 mmol) trimethylsilyl chloride, 1070 μL (59.4 mmol) H_2O, and 100 mL anhydrous acetonitrile. Purified via silica gel chromatography (7:3 hexanes:ethyl acetate) to obtain 6.1 g of **66** as a yellow oil (56% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 6.41 (1H, m), 5.9 (1H, m), 4.2 (2H, s), 2.2 (1H, br). ^{13}C NMR (300 MHz, $CDCl_3$, ppm): δ 124.7, 110.7, 71.2.

2-Iodooct-1-ene (**67**). Followed procedure given for **60**, with 10 mL (67.7 mmol) 1-octyne, 12 g (80.1 mmol) sodium iodide, 10 mL (78.8 mmol) trimethylsilyl chloride, 730 μL (40.5 mmol) H_2O, and 135 mL anhydrous acetonitrile. Purified via silica gel chromatography (100% hexanes) to obtain 12.5 g of **67** as a red oil (78% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 6.02 (1H, m), 5.68 (1H, m), 2.4 (2H, t), 1.4 (8H, m), 0.9 (3H, t). ^{13}C NMR (300 MHz, $CDCl_3$, ppm): δ 125.3, 113.1, 45.5, 31.7, 29.3, 28.0, 22.8, 14.3.

4,4,5,5-Tetramethyl-2-(oct-1-en-2-yl)-1,3,2-dioxaborolane (**68**). To a flame-dried, round-bottomed flask, under an argon atmosphere, added **67** (5.6 g, 23.5 mmol) and ether (200 mL). Placed in a dry ice/acetone bath and let stir. Added a 1.6M hexanes solution of *n*-butyllithium (19 mL, 30.4 mmol) dropwise, over about 10 minutes. Let stir at –78 °C for 30 minutes, then added 2-isopropoxy-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (6.8 mL, 46.9 mmol) dropwise over about 5 minutes. Let stir at –78 °C for 30 minutes, then removed dry ice/acetone bath and let warm slowly to room temperature. Added 100 mL H_2O, extracted 3 times with 100 mL ether, washed with 100 mL brine, and dried with $MgSO_4$. Purified via silica gel chromatography (19:1 hexanes:ethyl acetate) to obtain 5.2 g of **68**:2-butyl-4,4,5,5-tetramethyl-1,3,2-dioxaborolane = 3.3:1.0 as a clear oil (75% yield). Further purified **68** using silica gel chromatography again (29:1 pentane:ether). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 5.76 (1H, d, J = 3.6 Hz), 5.59 (1H, m), 2.14 (2H, t, J = 7.5 Hz), 1.3 (8H, m), 1.27 (12 H, s), 0.88 (3H, t, J = 6.8 Hz). ^{13}C NMR (300 MHz, $CDCl_3$, ppm): δ 128.9, 83.5, 35.6, 32.0, 29.4, 29.2, 25.04, 25.01, 24.95, 22.8, 14.3. HRMS (EI) calcd. for $C_{14}H_{27}BO_2$: 238.2104, found: 238.2106.

2-(4,4,5,5-Tetramethyl-1,3,2-dioxaborolan-2-yl)prop-2-en-1-ol (**69**). Followed procedure given for **68**, with 3.23 g (17.6 mmol) **66**, 36 mL (61.2 mmol) *t*-butyllithium (1.7M in pentane), 3.8 mL (18.6 mmol) 2-isopropoxy-4,4,5,5-tetramethyl-1,3,2-dioxaborolane, and 10 mL ether. Purified via silica gel chromatography (6:4 hexanes:ethyl acetate) to obtain 329 mg of **69** as a yellow oil (10% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 5.89 (1H, m), 5.84 (1H, br), 4.24 (2H, t, J = 1.4 Hz), 1.98 (1H, br), 1.28 (12H, s). ^{13}C NMR (300 MHz, $CDCl_3$, ppm): δ 129.1, 83.9, 66.1, 25.0.

3-(4,4,5,5-Tetramethyl-1,3,2-dioxaborolan-2-yl)but-3-en-1-ol (**70**). Followed procedure given for **68**, with 7 g (35 mmol) **63**, 48 mL (77 mmol) *n*-butyllithium (1.6M in hexanes), 12.5 mL (61 mmol) 2-isopropoxy-4,4,5,5-tetramethyl-1,3,2-dioxaborolane, and 100 mL ether. Purified via silica gel chromatography (1:1 pentane:ether) to obtain 5.55 g of **70**:4,4,5,5-tetramethyl-2-(3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)but-3-enyloxy)-1,3,2-dioxaborolane:4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-ol = 5.3:2.4:1 as a clear oil. Added this mixture to 100 mL MeOH and let stir at room temperature for 3 hours. Purified again via silica gel chromatography (7:3 hexanes:ethyl acetate) to obtain 3 g of **70** as a clear oil (43% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 5.91 (1H, d, *J* = 3.6 Hz), 5.72 (1H, br), 3.68 (2H, t, *J* = 6.2 Hz), 2.44 (2H, t, *J* = 6.0 Hz), 2.01 (1H, s), 1.28 (12H, s). ^{13}C NMR (300 MHz, $CDCl_3$, ppm): δ 132.5, 84.0, 62.7, 39.5, 24.9. HRMS (EI) calcd. for $C_{10}H_{19}BO_3 - CH_3$: 183.1187, found: 183.1192.

(*Z*)-6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)dodec-5-enyl acetate (**71**). Followed general procedure, with 212 μL (0.8 mmol) **68**, 64 μL (0.4 mmol) 5-hexenyl acetate, 17 mg (0.02 mmol) **2**, and 2 mL CH_2Cl_2. Purified via silica gel chromatography (8:2 hexanes:ethyl acetate) to obtain 56 mg of **71** as a brown oil (40% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 6.24 (1H, t, *J* = 7.1 Hz), 4.06 (2H, t, *J* = 6.5 Hz), 2.1 (4H, m), 2.04 (3H, s), 1.7 (3H, m), 1.5 (2H, m), 1.3 (7H, m), 1.25 (12H, s), 0.88 (3H, t, *J* = 6.6 Hz). ^{13}C NMR (300 MHz, $CDCl_3$, ppm): δ 171.4, 145.0, 83.2, 64.7, 32.1, 30.3, 29.5, 28.8, 28.6, 28.2, 25.7, 24.9, 22.9, 21.2, 14.3. HRMS (EI) calcd. for $C_{20}H_{37}BO_4$ + H: 353.2863, found: 353.2864.

(*Z*)-7-(2,2-dimethyl-1,3-dioxan-5-yl)-6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)hept-5-enyl acetate (**72**). Followed general procedure, with 110 mg (0.39 mmol) **58**, 32 μL (0.2 mmol) 5-hexenyl acetate, 8 mg (0.009 mmol) **2**, and 1 mL CH_2Cl_2. Purified via silica gel chromatography (8:2 hexanes:ethyl acetate) to obtain 32 mg of **72** as an oil (41% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 6.36 (1H, t), 4.05 (2H, t), 3.8 (2H, dd), 3.6 (2H, m), 2.05 (3H, s), 1.45 (3H, s), 1.4 (3H, s), 1.25 (12H, s), 1.2-2.2 (9H, m).

(*Z*)-9-(*tert*-butyldimethylsilyloxy)-6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)non-5-enyl acetate (**73**). Followed general procedure, with 95 μL (0.26 mmol) **54**, 34 μL (0.21 mmol) 5-hexenyl acetate, 8 mg (0.009 mmol) **2**, and 1 mL CH_2Cl_2. Purified via silica gel chromatography (9:1 hexanes:ethyl acetate) to obtain 32 mg of **73** as an oil (35% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 6.36 (1H, t, *J* = 6.9 Hz), 4.06 (2H, t, *J* = 6.8 Hz), 3.57 (2H, t, *J* = 7.8 Hz), 2.39 (2H, t, *J* = 7.5 Hz), 2.20 (2H, dt, *J* = 7.4, 7.4 Hz), 2.05 (3H, s), 1.65 (2H, m), 1.5 (2H, m), 1.26 (12H, s), 0.90 (9H, s), 0.065 (6H, s). ^{13}C NMR (300 MHz, $CDCl_3$, ppm): δ 171.4, 147.6, 83.3, 64.6, 63.3, 32.8, 28.7, 28.5, 26.3, 25.8, 25.0, 21.2, 18.7, –5.0. HRMS (FAB) calcd. for $C_{23}H_{45}BO_5Si$ + H: 441.3208, found: 441.3207.

(*Z*)-8-(*tert*-butyldimethylsilyloxy)-6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)oct-5-enyl acetate (**74**). Followed general procedure, with 95 μL (0.27 mmol) **52**, 34 μL (0.21 mmol) 5-hexenyl acetate, 8 mg (0.009 mmol) **2**, and 1 mL CH_2Cl_2. Purified via silica gel chromatography (9:1 hexanes:ethyl acetate) to obtain 16 mg of **74** as an oil (17% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 6.27 (1H, t, *J* = 7.1 Hz), 4.06 (2H, t, *J* = 6.6 Hz), 3.59 (2H, t, *J* = 6.6 Hz), 2.08 (4H, m), 2.05 (3H, s), 1.6 (4H, m), 1.25 (12H, s), 0.90 (9H,

s), 0.051 (6H, s). ^{13}C NMR (300 MHz, $CDCl_3$, ppm): δ 171.4, 145.6, 83.2, 64.6, 63.3, 33.6, 28.7, 28.2, 26.2, 25.7, 25.1, 25.0, 21.2, 18.5, -5.0. HRMS (FAB) calcd. for $C_{22}H_{43}BO_5Si$ + H: 427.3051, found: 427.3063.

Tert-butyldimethyl(2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)allyloxy)silane (**75**). Followed procedure given for **68**, with 1 mL (4.7 mmol) *tert*-butyl(2-iodoallyloxy)-dimethylsilane, 3.5 mL (5.6 mmol) *n*-butyllithium (1.6M in hexanes), 1.3 mL (6.4 mmol) 2-isopropoxy-4,4,5,5-tetramethyl-1,3,2-dioxaborolane, and 50 mL ether. Purified via silica gel chromatography (19:1 hexanes:ethyl acetate) to obtain 317 mg of **75** as a light yellow oil (23% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 5.97 (1H, m), 5.88 (1H, m), 4.29 (2H, t, J = 2.3 Hz), 1.27 (12H, s), 0.93 (9H, s), 0.075 (6H, s). HRMS (FAB) calcd. for $C_{15}H_{31}BO_3Si$ + H: 299.2214, found: 299.2220.

3-(4,4,5,5-Tetramethyl-1,3,2-dioxaborolan-2-yl)but-3-enyl acetate (**76**). To a flame-dried, round-bottomed flask, under an argon atmosphere, added **70** (1.9 g, 9.6 mmol), triethylamine (2.5 mL, 18 mmol), dimethylaminopyridine (94 mg, 0.77 mmol), and CH_2Cl_2 (14 mL). Placed in an ice bath and let stir. Added acetic anhydride (2 mL, 21 mmol), then removed ice bath. Let stir at room temperature for 3.5 hours. Added 15 mL aqueous NH_4Cl solution, extracted 2 times with 20 mL CH_2Cl_2, and dried with Na_2SO_4. Purified via silica gel chromatography (8:2 hexanes:ethyl acetate) to obtain 1.08 g of **76** as a clear yellow oil (47% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 5.88 (1H, d, J = 3.3 Hz), 5.70 (1H, br), 4.16 (2H, t, J = 6.9 Hz), 2.47 (2H, t, J = 6.9 Hz), 2.03 (3H, s), 1.27

(12H, s). ^{13}C NMR (300 MHz, $CDCl_3$, ppm): δ 171.3, 132.1, 83.8, 64.1, 34.9, 25.0, 21.2. HRMS (EI) calcd. for $C_{12}H_{21}BO_4$ + H: 241.1611, found: 241.1611.

2-(4,4,5,5-Tetramethyl-1,3,2-dioxaborolan-2-yl)allyl acetate (**77**). Followed procedure given for **76**, with 1.6 g (10 mmol) **69**, 2 mL (21 mmol) acetic anhydride, 3 mL (22 mmol) triethylamine, 100 mg (0.8 mmol) dimethylaminopyridine, and 15 mL CH_2Cl_2. Purified via silica gel chromatography (8:2 hexanes:ethyl acetate) to obtain 805 mg of **77** as a clear oil (36% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 5.91 (1H, m), 5.81 (1H, br), 4.67 (2H, s), 2.06 (3H, s), 1.24 (12H, s). ^{13}C NMR (300 MHz, $CDCl_3$, ppm): δ 170.8, 130.0, 83.8, 66.1, 24.9, 21.1. HRMS (FAB) calcd. for $C_{11}H_{19}BO_4$ + H: 227.1455, found: 227.1446.

2-(4,4,5,5-Tetramethyl-1,3,2-dioxaborolan-2-yl)hept-2-ene-1,7-diyl diacetate (**78**). Followed general procedure, with 180 μL (0.8 mmol) **77**, 64 μL (0.4 mmol) 5-hexenyl acetate, 17 mg (0.02 mmol) **2**, and 2 mL CH_2Cl_2. Purified via silica gel chromatography (8:2 hexanes:ethyl acetate) to obtain 56 mg of **78** as an oil (41% yield). (***Z*-isomer**): ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 6.50 (1H, t, J = 7.2 Hz), 4.69 (2H, s), 4.05 (2H, t, J = 6.6 Hz), 2.24 (2H, dt, J = 7.3, 7.3 Hz), 2.04 (3H, s), 2.03 (3H, s), 1.65 (2H, m), 1.5 (2H, m), 1.26 (12H, s). ^{13}C NMR (300 MHz, $CDCl_3$, ppm): δ 171.3, 171.2, 150.8, 83.7, 64.4, 61.2, 28.8, 28.5, 25.5, 24.9, 21.25, 21.16. HRMS (FAB) calcd. for $C_{17}H_{29}BO_6$ + H: 341.2135, found: 341.2122. (***E*-isomer**): ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 6.28 (1H, t, J = 7.5 Hz), 4.61 (2H, s), 4.07 (2H, t, J = 6.5 Hz), 2.41 (2H, dt, J = 7.3, 7.3 Hz), 2.04 (6H, s), 1.6 (2H, m), 1.45 (2H, m), 1.27 (12H, s). ^{13}C NMR (300 MHz, $CDCl_3$,

ppm): δ 171.4, 171.0, 149.8, 83.5, 68.6, 64.6, 30.6, 28.2, 25.9, 25.0, 21.3, 21.2. HRMS (FAB) calcd. for $C_{17}H_{29}BO_6$ + H: 341.2135, found: 341.2141.

2.5. References

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Chapter 3.

Rhenium-Catalyzed 1,3-Isomerization of Allylic Alcohols

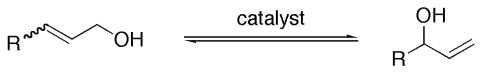
Abstract

We have developed two different reaction strategies to efficiently promote the selective 1,3-isomerization of allylic alcohols using rhenium-oxo catalyst $O_3ReOSiPh_3$. The first strategy involved choosing starting materials that possessed 1-aryl substituents. The 1,3-regioisomers of these substrates were thermodynamically favored because they contained conjugated alkenes. This reaction strategy enabled the selective synthesis of conjugated allylic alcohols containing di- or trisubstituted alkenes. These reactions proceeded with high *E*-stereoselectivity, regardless of the initial alkene geometry. The second reaction strategy involved the selective silylation of the 1,3-regioisomer, which was promoted by N,O-bis(trimethylsilyl)acetamide. This procedure led to the selective synthesis of both conjugated and non-conjugated primary allylic alcohols containing trisubstituted *E*-alkenes. Both of these procedures featured low catalyst loadings and short reaction times. Chirality was transferred with high levels of stereoselectivity during the 1,3-isomerization of enantioenriched secondary allylic alcohols that possessed 1-aryl substituents. The absolute stereochemistry of these nonracemic products correlated to the alkene geometry of the starting material. Isomerization reactions involving electron-deficient substrates proceeded more slowly, but they exhibited superior product selectivity and chirality transfer, than did the reactions involving more electron-rich substrates. All of our observations support the contention that a reaction mechanism involving a chair-like transition state, which exhibits a partially cationic allyl moiety and a partially anionic perrhenate moiety, operates as the primary reaction pathway.

3.1. Background

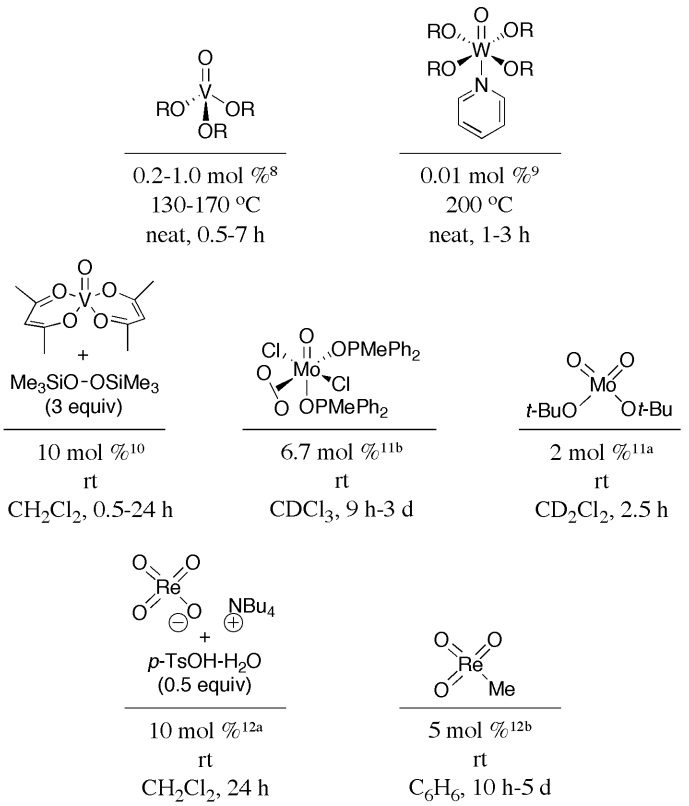
Allylic alcohols and their derivatives serve as useful precursors for numerous synthetic transformations, including Claisen[1] and Cope[2] rearrangements, directed epoxidations[3] and cyclopropanations,[4] carbonyl formation,[5] and palladium-catalyzed electrophilic substitutions.[6] The 1,3-isomerization of allylic alcohols, illustrated in Scheme 3.1.1, is a reaction that allows the two regioisomers of an allylic alcohol to be interchanged. Such a reaction is quite useful in organic synthesis because oftentimes one regioisomer of the allylic alcohol will be more difficult to prepare than the other.

Scheme 3.1.1. 1,3-Isomerization of allylic alcohols.



Various transition metal oxo complexes catalyze this isomerization reaction.[7] These different catalyst systems are summarized in Figure 3.1.1. Early systems involved vanadium[8] and tungsten[9] complexes. These systems required the use of reaction temperatures above 120 ºC in order for efficient catalysis to occur. Later catalyst systems employed alternative vanadium complexes,[10] as well as molybdenum[10,11] and rhenium complexes.[12] Isomerization reactions catalyzed by these later complexes proceeded at ambient temperature, but they generally exhibited long reaction times (Figure 3.1.1). In 1997 Osborn and co-workers reported that the rhenium(VII) complex of the form $O_3ReOSiPh_3$ (**1**)[13] catalyzed the 1,3-isomerization of allylic alcohols at 0 °C.[14] Using 2 mol % of **1**, reaction times on the order of 5 minutes were observed for these isomerization reactions, making **1** the most active catalyst yet known for this transformation.

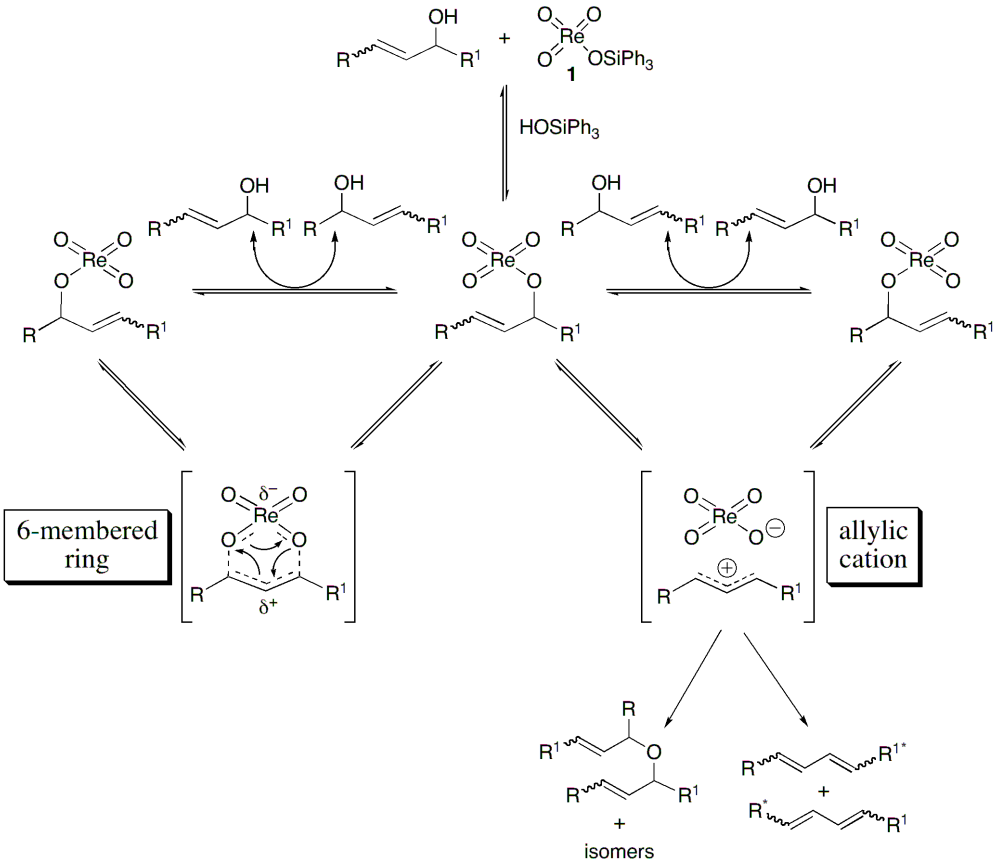
Figure 3.1.1. Various catalyst systems known to promote the 1,3-isomerization of allylic alcohols.



Two potential mechanisms have been proposed for this 1,3-isomerization reaction. Each mechanism is illustrated, with the use of catalyst **1**, in Scheme 3.1.2. The mechanism that is shown on the left side involves a [3,3]-sigmatropic rearrangement, which proceeds through a chair-like transition state. This mechanism has been proposed for a number of the known catalysts for this reaction,[7,8,10,11] including catalyst **1.**[14] Theoretical studies support the proposal that this mechanism is operative in isomerization reactions involving catalyst **1**.[15] These studies also indicate that the six-membered ring transition state contains an anionic perrhenate moiety and a cationic allyl moiety (Scheme 3.1.2), which suggests that the superior catalytic activity of **1** arises from the stabilizing effect of its additional spectator oxo ligands. In addition, rhenium(III) oxo complexes do not promote this isomerization reaction, even after one week at 70 °C.[16] This observation

provides further evidence that a highly electron deficient transition metal complex is needed to efficiently catalyze this reaction.

Scheme 3.1.2. Two possible mechanisms for the 1,3-isomerization of allylic alcohols, shown with the use of catalyst 1.

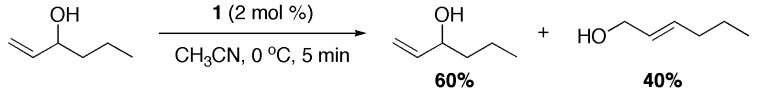


The alternative mechanism that has been proposed for this reaction is shown on the right side of Scheme 3.1.2. In this mechanism, the catalyst promotes the complete dissociation of the alcohol moiety, forming an allylic cation as the reaction intermediate. This cation is then attacked by the perrhenate anion at the other terminus, generating the 1,3-regioisomer. Similar to the first proposed mechanism, highly oxidized transition metal complexes would be expected to exhibit superior catalytic activity in this process, because, in this case, the intermediate species contains a fully anionic perrhenate moiety. As shown in Scheme 3.1.2, this alternative mechanism could readily lead to the formation

of side products, via condensation and dehydration reactions, and it has been proposed as the operative mechanism in cases where the formation of such products was significant.[7,12a]

Despite its extremely high catalytic activity, rhenium catalyst **1** still exhibited a significant limitation with respect to synthetic utility. As shown in Scheme 3.1.2, regardless of which mechanism is operative, every step in this reaction is reversible. Thus the product exists as an equilibrium mixture of regioisomers, whose relative amounts are determined solely by their corresponding thermodynamic stabilities. As shown in the reaction given in Scheme 3.1.3, which is taken from Osborne's initial report of catalyst **1**,[14] the product ratio of regioisomers was often close to 1:1, which seriously limited the utility of this reaction.[i] The high catalytic activity of **1** still created the potential for this isomerization reaction to be of use to the synthetic chemist, but only if its product selectivity could be improved. Therefore, in this project we endeavored to develop strategies by which this isomerization reaction, catalyzed by complex **1**, could be selective for formation of a single regioisomer of a given allylic alcohol, while maintaining the short reactions times, the low catalyst loadings, and the mild reaction conditions that Osborn initially reported.[14]

Scheme 3.1.3. 1,3-Isomerization of allylic alcohols catalyzed by 1 results in the formation of a thermodynamic mixture of regioisomers.[14]

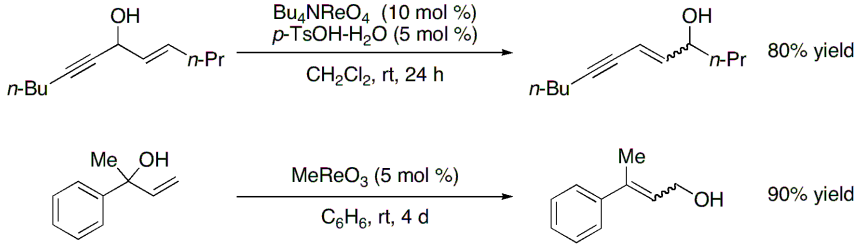


[i] In these studies, the yield of the 1,3-isomer did not increase from the amount shown in Scheme 3.1.3, even with longer reaction times or a higher catalyst loading. It reflects the thermodynamic equilibrium ratio of these two regioisomers.

3.2. Formation of Conjugated Allylic Alcohols

Our first approach to promoting a selective 1,3-isomerization reaction, catalyzed by complex **1**, involved utilizing allylic alcohols that possessed a 1-aryl substituent as the starting material. The 1,3-isomer of these substrates contains a conjugated alkene. We anticipated that the reaction equilibrium would favor the formation of this conjugated regioisomer over that of the non-conjugated starting material. Thus this approach would capitalize on the thermodynamics of the system to obtain high product yields. Previous work involving other metal oxo catalyst systems had indicated that, indeed, the conjugated regioisomer would predominate at equilibrium when these types of substrates were employed (Scheme 3.2.1).[11b,12a,b]

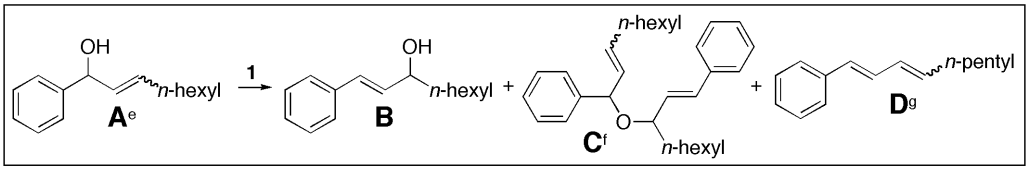
Scheme 3.2.1. Previous 1,3-allylic alcohol isomerization reactions in which the conjugated regioisomer formed as the major product.[12a,b]



3.2.1. Formation of products with disubstituted alkenes

Initial experiments employed 1-phenylnon-2-en-1-ol as a model substrate. Numerous conditions were investigated for the reaction of this substrate with **1** (2 mol %), which are summarized in Table 3.2.1. We initially employed the reaction conditions that were reported by Osborn to be the most effective (CH_2Cl_2, rt).[17] The use of these conditions resulted in extensive dehydration and condensation reactions, leading to numerous side products. As shown in entry 1 of Table 3.2.1, under these conditions,

Table 3.2.1. 1,3-isomerization of 1-phenylnon-2-en-1-ol (A): effect of reaction solvent, temperature, and time on product selectivity.[a,b,c,d]



entry	solvent	temp.	time	**A** (%)	**B** (%)	**C** (%)	**D** (%)	notebook page
1	CH_2Cl_2	rt	2 min	0	15	55	30	cm4-256
2	CH_2Cl_2	rt	2 h	0	0	0	100	cm4-241
3	CH_2Cl_2	0 °C	10 min	0	18	71	11	cm5-8
4	CH_2Cl_2	–20 °C	30 min	8	25	67	0	cm4-262
5	CH_2Cl_2	–50 °C	40 min	4	57	39	0	cm5-41
6	CH_2Cl_2	–78 °C	2 h	86	14	0	0	cm5-41
7	CH_3CN	rt	35 min	0	19	73	8	cm4-250
8	C_6H_6	rt	35 min	0	51	49	0	cm4-253
9	toluene	rt	35 min	0	51	49	0	cm4-252
10	toluene	0 °C	10 min	0	59	41	0	cm5-10
11	toluene	–20 °C	1 h	0	75	25	0	cm4-280
12	toluene	–50 °C	40 min	28	72	0	0	cm5-41
13	toluene	–78 °C	2 h	65	35	0	0	cm5-41
14	toluene/H_2O[h]	rt	20 min	44	34	22	0	cm4-259
15	THF	rt	35 min	0	38	38	24	cm4-249
16	THF	0 °C	10 min	0	75	22	3	cm5-9
17	**THF**	**–50 °C**	**40 min**	**0**	**100**	**0**	**0**	**cm5-41**
18	THF	–78 °C	2 h	73	27	0	0	cm5-41
19	ether	rt	35 min	0	37	51	12	cm4-247
20	ether	0 °C	10 min	0	75	25	0	cm4-283
21	ether	–20 °C	15 min	0	86	14	0	cm4-284
22	**ether**	**–50 °C**	**40 min**	**0**	**100**	**0**	**0**	**cm5-41**
23	ether	–78 °C	2 h	31	69	0	0	cm5-41

[a] 0.2 mmol scale, 2 mol % **1**, 0.2M. [b] Reactions were quenched with either NEt_3, $N(n\text{-}Pr)_3$, or a silica gel plug. [c] *E*:*Z* was determined by ^1H NMR and was > 20:1 for all alkenes not drawn as nonspecific. [d] Relative amounts of **A**-**D** determined by ^1H NMR. [e] *E*:*Z* = 11:1. [f] Plus various isomers. [g] *E*:*Z* = ca. 2:1. [h] 3.4 equiv H_2O relative to **A**.

all of the 1-phenylnon-2-en-1-ol (**A**) had already disappeared after only 2 minutes, but only a 15% conversion to the desired 1,3-isomer (**B**) was observed. The remainder of the material had converted into side products **C** and **D**. After about 2 hours, all of the material had been converted into dehydration product **D** (entry 2). Lowering the reaction temperature enabled us to partially suppress these side reactions (entries 3-5), and they were completely prevented when the reaction was performed at –78 °C (entry 6).

Unfortunately, at this low temperature the desired 1,3-isomerization also slowed significantly, with only a 14% conversion after 2 hours.

Further investigation revealed that this reaction was highly solvent dependent. For example, CH_2Cl_2 favored the formation of the dehydration product (Table 3.2.1, entry 2), while acetonitrile favored allylic ether (**C**) formation (entry 7). Even at room temperature, both benzene and toluene completely suppressed dehydration. Only the allylic ethers and the desired 1,3-isomer were formed (entries 8-9). While benzene and toluene exhibited similar product selectivities, toluene was more desirable because it permitted the use of lower reaction temperatures. As with CH_2Cl_2, the use of toluene at lower temperatures suppressed the allylic ether formation. It also slowed the desired 1,3-isomerization reaction (entries 10-13), albeit to a lesser extent than with the use of CH_2Cl_2. We briefly investigated the use of a small amount of water in this reaction to discourage the unwanted condensation reactions, but the water suppressed *all* reaction pathways to a similar extent (entry 14).

THF and ether proved to be the most effective solvents for this isomerization. Both of these solvents allowed the desired reaction to proceed readily at the low temperatures ($\leq -50°C$) required to completely suppress side product formation (Table 3.2.1, entries 15-23) and thus allowed the quantitative 1,3-isomerization of 1-phenylnon-2-en-1-ol to be complete in approximately half an hour at –50°C (entries 17 and 22). THF and ether led to essentially the same result in these reactions, however, 1,3-isomerization was significantly slower in THF than it was in ether at –78 °C (compare entries 18 and 23).

We hypothesized that the formation of the observed side products in these reactions involving 1-phenylnon-2-en-1-ol resulted from the reaction pathway that is shown on the right side of Scheme 3.1.2, which involves the formation of an allylic cation, whereas the desired 1,3-isomerization reaction proceeded primarily through the concerted mechanism shown on the left. The reaction pathway that invokes an allylic cation involves an increase in molecularity and should therefore exhibit a more positive $\Delta S^{\ddagger}$ value relative to the concerted mechanism, which involves no change in molecularity and requires the formation of a highly ordered transition state. Indeed, Osborn reported a $\Delta S^{\ddagger}$ value of –18.3 ± 2.2 e.u. for the 1,3-isomerization reaction (promoted by **1**) of *E*-2-hexen-1-ol and attributed this negative entropy value to the existence of a cyclic transition state.[14] If our mechanistic analysis is correct, then the side product formation should be easier to suppress, relative to the isomerization reaction, with the use of low reaction temperatures. This trend is exactly what we observed (Table 3.2.1, entries 17 and 22). Side product formation was completely suppressed at –50 °C, while the 1,3-isomerization proceeded readily.

Our observation that the product selectivity in these reactions was highly solvent dependent is also consistent with the hypothesis that side product formation arises from a competing reaction pathway that involves the formation of an ion pair. Solvents with higher dielectric constants should better stabilize this ionic intermediate. Indeed, acetonitrile, which has a significantly higher dielectric constant than the other solvents investigated, exhibited allylic ether formation to the largest extent under similar reaction conditions (Table 3.2.1, entry 7).[ii] Our observation that THF and ether were the optimal

[ii] Acetonitrile has a dielectric constant of 35.94. CH_2Cl_2 has the next highest dielectric constant, which is 8.93.[18] Beyond acetonitrile, however, none of the solvents investigated fit this trend.

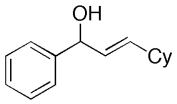
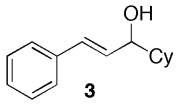
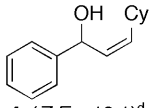
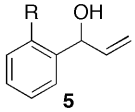
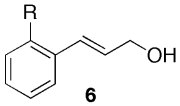
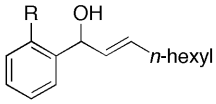
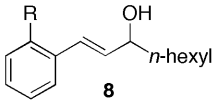
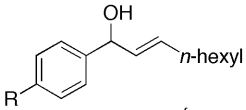
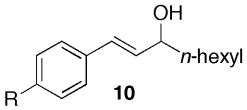
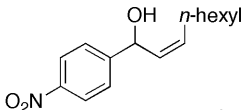
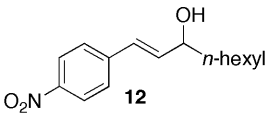
reaction solvents was interesting, because Osborn reported that this isomerization reaction was relatively slow in coordinating solvents like THF and ether,[17] presumably because these solvents competed with the alcohols for coordination to catalyst **1**. However, Osborn's observations were made at much higher temperatures (25 ºC) than the low reaction temperatures (≤ –50 ºC) at which we began to observe a significant difference among solvents with respect to the isomerization rate (see Table 3.2.1).[iii]

Table 3.2.2 lists the optimized 1,3 isomerization reactions of benzylic allylic alcohols possessing various substitution patterns.[19] This isomerization reaction proceeded efficiently for substrates possessing both mono- (entries 3-5) and disubstituted (entries 1-2 and 6-13) alkenes, as well as for substrates with both electron-donating (entries 5, 8-9, and 11-12) and electron-withdrawing (entries 4, 7, 10, and 13) substituents on their phenyl group. The yields were nearly quantitative in all cases except for those involving the methoxy-substituted substrates, which exhibited moderate yields (entries 5, 8-9, and 11-12).

It was especially noteworthy that these reactions were highly *E*-selective, regardless of the alkene geometry of the starting material. The product possessed almost exclusively *E*-stereochemistry when the starting material contained either predominantly *E*-stereochemistry (Table 3.2.2, entries 1 and 6-12) or predominantly *Z*-stereochemistry (entries 2 and 13). This high *E*-selectivity can be rationalized by examining the possible

[iii] The primary advantage of THF and ether as solvents arose because they were able to maintain efficient isomerization at temperatures ≤ –50 °C. It is possible that the lower viscosity of these solvents at such temperatures, relative to CH_2Cl_2 and toluene, was responsible for their efficiency. This hypothesis would explain the observation that ether, which has the lowest freezing point, was the optimal solvent at –78 °C (Table 3.2.1, compare entries 6, 13, 18, and 23).

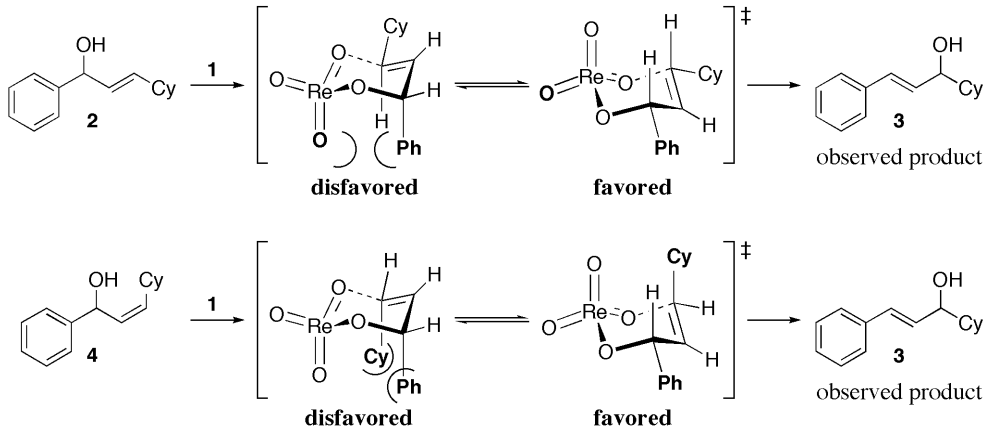
Table 3.2.2. 1,3-Isomerization of allylic alcohols to form conjugated, disubstituted *E*-alkenes.[a,b]

entry	R	substrate	solvent	temp. (°C)	time (h)	product[c]	isolated yield (%)	notebook page
1		 **2** (*E*:*Z* = 12:1)[d]	ether	–50	0.5	 **3**	96	cm5-74
2		 **4** (*Z*:*E* = 12:1)[d]	ether	–50	0.5	**3**	93	cm5-94
3	H (a)	 **5**	ether	0	0.5	 **6**	98	cm5-172
4	NO_2 (b)		CH_2Cl_2	rt	0.5		98	cm5-160
5	OMe (c)		ether	–50	0.5		65	cm5-156
6	H (a)	 **7** (*E*:*Z* = ca. 10:1)[f]	ether	–50	0.5	 **8**	99	cm5-69
7	NO_2 (b)		ether	rt	0.5		99	cm5-90
8	OMe (c)		ether	–50	0.5		69[g]	cm5-155
9[e]	OMe (c)		ether	–78	2		68	cm5-220
10[h]	CF_3 (a)	 **9** (*E*:*Z* > 20:1)[f]	ether	–50	1	 **10**	98	cm6-115
11	OMe (b)		ether	–50	0.5		68	cm5-208
12[e]	OMe (b)		ether	–78	2		79	cm5-221
13		 **11** (*Z*:*E* > 20:1)[f]	ether	0	0.5	 **12**	94	cm6-127

[a] 0.2-0.4 mmol scale, 2 mol % **1**, 0.2M. [b] See ref. 19. [c] *E*:*Z* > 20:1 (^{1}H NMR). [d] Determined by GC. [e] 4 mol % **1**. [f] Determined by ^{1}H NMR. [g] 3% of **7c** recovered. [h] 3 mol % **1**.

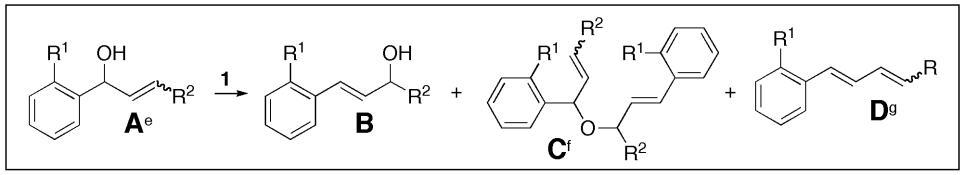
chair-like transition states that would arise from the reaction of the *E*- and the *Z*-isomers of a given allylic alcohol. As shown for substrates **2** and **4** in Scheme 3.2.2, in both cases the transition state that would lead to the *Z*-product exhibits a destabilizing diaxial steric interaction. For **2**, this interaction is between the phenyl group and a rhenium oxo ligand,[15] and for **4** it is between the phenyl and the cyclohexyl groups. Therefore in each case the more favorable transition state leads to the formation of the *E*-product, alcohol **3**, which is consistent with our observations (Table 3.2.2, entries 1-2).

Scheme 3.2.2. Stereochemical rationale for observed *E*-selectivity, which is independent of the alkene geometry of the starting material.



We have also observed that the reactivity of an allylic alcohol depends strongly upon its electronic properties. Table 3.2.3 gives some examples to illustrate this observation. Of the substrates bearing disubstituted alkene components, nitro-substituted alcohol **7b** was the least reactive. It exhibited quantitative 1,3-isomerization at room temperature, without side product formation (entry 1), and it showed low reactivity at

Table 3.2.3. Effect of sterics and electronics on reactivity: electronics have a larger impact.[a,b,c,d]



entry	substrate A	R^1	R^2	temp.	time	A (%)	B (%)	C (%)	D (%)	notebook page
1	**7b**	NO_2	*n*-hexyl	rt	30 min	0	100	0	0	cm5-82
2	**7b**	NO_2	*n*-hexyl	–50 °C	35 min	43	57	0	0	cm5-73
3	**7a**	H	*n*-hexyl	rt	35 min	0	37	51	12	cm4-247
4	**7a**	H	*n*-hexyl	–50 °C	40 min	0	100	0	0	cm5-41
5	**7c**	OMe	*n*-hexyl	rt	35 min	0	15	59	26	cm5-22
6	**7c**	OMe	*n*-hexyl	–50 °C	35 min	10	74	16	0	cm5-33
7	**5a**	H	H	rt	30 min	0	95	5	------	cm5-102
8	**5a**	H	H	–50 °C	35 min	100	0	0	------	cm5-71
9	**5b**	NO_2	H	rt	30 min	11	89	0	------	cm5-140
10	**5c**	OMe	H	rt	30 min	0	35	65	------	cm5-109

[a] 0.2 mmol scale, 2 mol % **1**, ether, 0.2M. [b] Reactions were quenched with either NEt_3, $N(n\text{-}Pr)_3$, or a silica gel plug. [c] *E*:*Z* was determined by ^1H NMR, and was > 20:1 for all alkenes not drawn as nonspecific. [d] Relative amounts of **A**-**D** determined by ^1H NMR. [e] *E*:*Z* = ca. 10:1. [f] Plus various isomers. [g] *E*:*Z* = ca. 2:1.

–50 °C (entry 2). The analogous substrate possessing an unsubstituted phenyl group (**7a**) was much more reactive. It exhibited significant side product formation at room temperature (entry 3), and it underwent quantitative 1,3-isomerization at –50 °C (entry 4). Finally, the methoxy-substituted analog (**7c**) showed the highest reactivity. It formed a larger amount of side products (**C** and **D**) than **7a** at room temperature (entry 5), and these side reactions were not completely suppressed at –50 °C (entry 6). These results demonstrate that electron-deficient substrates are less reactive with catalyst **1**. This observation is consistent with both of the mechanisms presented in Scheme 3.1.2, because the transition state for each pathway contains a positively charged allyl moiety, which should be less stabilized for electron-deficient substrates.

It was interesting that the reaction involving substrate **7c** still showed unreacted **7c** after 35 minutes at –50 °C, even though significant side product formation had occurred by this point (Table 3.2.3, entry 6). We suspected that the *ortho*-methoxy substituent of **7c** might have coordinated to the rhenium moiety during this reaction, hindering the desired isomerization but still permitting condensation reactions. To test this hypothesis, we investigated the reaction of the *para*-analog of **7c**, substrate **9b**, with catalyst **1**. The results, after isolation of the product, of these studies are included in Table 3.2.2. At –50 °C, both **7c** and **9b** exhibited essentially identical product yields (compare entries 8 and 11). However, a small amount of unreacted starting material was isolated from the reaction of **7c**, while none was observed with the **9b** reaction. In addition, *para*-substrate **9b** exhibited an 11% higher product yield than did *ortho*-substrate **7c** when the reaction was performed at –78 °C (entries 9 and 12). These results indicated that the position of the methoxy substituent may have had a small effect on the

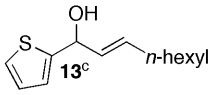
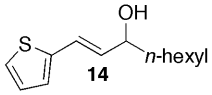
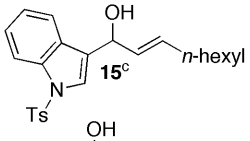
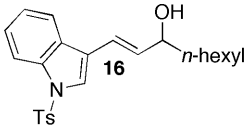
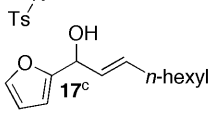
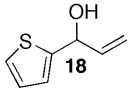
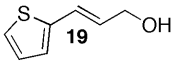
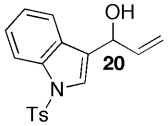
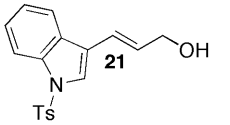
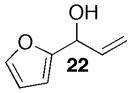
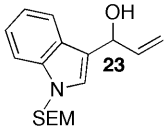
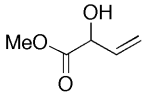
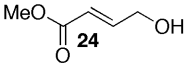
relative reactivity of **7c** and **9b**, but they did not fully account for the consistently lower isolated yields obtained for the reactions of *all* substrates possessing methoxy-substituted phenyl substituents (Table 3.2.2, entries 5, 8-9, and 11-12).[iv]

The results shown in Table 3.2.3 also indicate that a substrate's electronic properties affect its reactivity to a much larger extent than do its steric properties. While the reaction of catalyst **1** with substrate **7a**, which possessed a disubstituted alkene component, resulted in quantitative 1,3-isomerization at –50 °C (entry 4), the analogous substrate possessing a monosubstituted alkene component, alcohol **5a**, essentially did not react at all with catalyst **1** at –50 °C (entry 8). Based upon its steric properties, the less-hindered alkene of substrate **5a** should have rendered **5a** *more* reactive with **1**, relative to **7a**. Since we observed the opposite scenario, we concluded that the electron-deficiency of the allyl system of **5a**, relative to that of **7a**, overrode its more favorable steric properties in this reaction. Nitro- and methoxy-substituted substrates **5b** and **5c**, respectively, exhibited similar trends relative to their disubstituted alkene analogs **7b** and **7c** (compare entries 1 and 9, and entries 5 and 10). In fact, substrate **5b** was so unreactive that CH_2Cl_2, which normally led to extensive side reactions when used as the solvent (see Table 3.2.1), had to be employed as the reaction solvent in order to obtain optimal yields (Table 3.2.2, entry 4).

We also investigated the 1,3-isomerization of allylic alcohols containing other (non-phenyl) 1-substituents that would lead to the formation of conjugated products. The results of these studies are listed in Table 3.2.4. With the exception of thiophenyl

[iv] A possible explanation for this observation is that the electron-rich methoxy-substituted substrates were more acid-sensitive than the other substrates. Thus they were simply less stable to silica gel chromatography, and the lower isolated yields arose because a small amount of the product decomposed via dehydration reactions upon purification.

Table 3.2.4. 1,3-Isomerization of allylic alcohols to form conjugated, disubstituted *E*-alkenes: non-phenyl substituted alcohols.[a]

entry	substrate	solvent	temp. (°C)	time (min)	product[c]	isolated yield (%)	notebook page
1[b]	 **13**[c]	ether	–50	15	 **14**	92	cm5-242
2	 **15**[c]	ether	–50	30	 **16**	66	cm6-130
3	 **17**[c]	ether	–50	30	complex mixture	------	cm6-143
4	 **18**	THF	–50	30	 **19**	70	cm6-73
5[d]	 **20**	THF	–50	10	 **21**	56	cm6-7
6	 **22**	THF	–20	30	complex mixture	------	cm6-137
7	 **23**	CH_2Cl_2	rt	30	N. R.	------	cm5-293
8		CH_2Cl_2	rt	210	 **24**	N.R.	cm4-269
9		toluene	60	270		18%[e]	cm4-273
10	**24**[c]	CH_2Cl_2	rt	1165	N. R.	------	cm4-288
11		toluene	60	1030		------	cm4-290

[a] 0.2-0.4 mmol scale, 2 mol % **1**, 0.2M. [b] See ref. 19. [c] *E*:*Z* > 20:1 (^{1}H NMR). [d] 1.5 mol % **1**. [e] Approximate conversion value (^{1}H NMR).

substrate **13** (entry 1), all of the reactions of substrates possessing heterocyclic 1-substituents (entries 2-7) led to less desirable results than those previously obtained for the various phenyl-substituted substrates (see Table 3.2.2). In the reactions shown in entries 1-6 of Table 3.2.4, all of the starting material was consumed, but various side products formed, some of which appeared to be polymeric in form. The extent of the side product formation increased, for substrates containing both disubstituted (entries 1-3) and monosubstituted (entries 4-6) alkene components, according to the trend thiophenyl <

tosyl-protected indolyl < furyl, with the furyl substrates leading primarily to the formation of side products. This trend was consistent with the electronic trends that we had already observed (see Table 3.2.3) in this reaction, in which side product formation increased upon raising the electron density of the allyl system.

It was interesting that the interaction substrate **23**, which possessed a 2-(trimethylsilyl)ethoxymethyl chloride (SEM)-protected indolyl substituent, with catalyst **1** resulted in no reaction at all, rather than in side product formation (Table 3.2.4, entry 7). Substrate **23** did, however, form a deep red solution upon exposure to **1**.[v] We suspect that association with **1** readily promoted the dehydration of **23**, forming the corresponding perrhenate salt. The reason for the absence of subsequent reactions involving this salt, however, was unclear.

The reactions of the electron-deficient substrates shown in Table 3.2.4 (entries 8-11) were also consistent with our hypothesis regarding the effect of a substrate's electronics on its reactivity with catalyst **1**. Methyl 2-hydroxybut-3-enoate, whose allyl moiety is highly electron-deficient, was quite unreactive toward **1**, even at high reaction temperatures (entries 8-9). We assumed that thermodynamics would drive this reaction to selectively form the conjugated regioisomer, alcohol **24**. However, to ensure that the thermodynamic equilibrium did not simply lie in the opposite direction, we investigated the reaction of alcohol **24** with catalyst **1** as well. Alcohol **24** exhibited no reaction at all in these studies (entries 10-11). Thus we concluded that the allyl systems of both methyl 2-hydroxybut-3-enoate and alcohol **24** were electron-deficient enough that they raised the energy of the required transition state for this reaction such that efficient isomerization

[v] Substrate **23** was yellow in color.

could not be achieved. We do note that it is also possible that coordination of the ester moieties of these two substrates to catalyst **1** could also be responsible for their observed lack of reactivity.

3.2.2. Formation of substrates with trisubstituted alkenes

We were also interested in extending the scope of this allylic alcohol isomerization reaction to tertiary allylic alcohols possessing 1-aryl substituents. The 1,3-isomerization of these substrates would lead to the formation of trisubstituted alkenes. We employed 2-phenylbut-3-en-2-ol as a model substrate in these studies. Table 3.2.5 summarizes the numerous conditions that were explored for the reaction of this substrate with catalyst **1**, which were all monitored by GC.[vi]

As illustrated in Table 3.2.5, the reaction of 2-phenylbut-3-en-2-ol (**A**) with catalyst **1** resulted in the formation of side products analogous to those observed with the secondary alcohols in section 3.2.1 unless the proper reaction conditions were employed. For the reactions performed in ether at either room temperature or 0 °C, both the conversion to the 1,3-isomer (**B**) and the *E*-selectivity of this isomerization reaction were low, and the product isomer continuously converted into various side products over time (Table 3.2.5, entries 1-6).[vii] Already two differences between 2-phenylbut-3-en-2-ol and its secondary analog **5a** were clear. First, 2-phenylbut-3-en-2-ol is more reactive than **5a**, as **5a** exhibited essentially no side product formation at 0 °C (compare Table 3.2.5, entry

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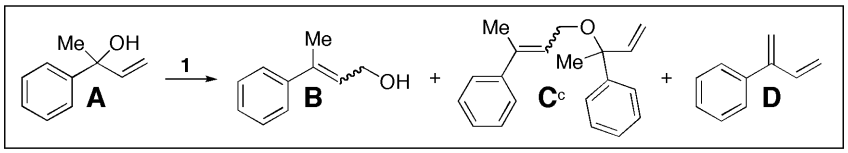
[vi] There appeared to be some systematic error made upon analysis of the reactions reported in Table 3.2.5 (for example, see entries 17, 20, and 24, which add up to > 100% conversion). This error possibly arose from decomposition of some of the material on the GC. Thus the conversion values reported for these reactions should be viewed primarily in a relative, rather than in an absolute, sense. The *E*:*Z* ratios, on the other hand, should be accurate.

[vii] It was surprising that a small amount of unreacted 2-phenylbut-3-en-2-ol was still visible by GC at these higher temperatures, even after long reaction times. It is possible that some 2-phenylbut-3-en-2-ol formed during GC analysis. Unfortunately the ^{1}H NMR spectra of these reactions were too complex to provide information about the amount of unreacted 2-phenylbut-3-en-2-ol remaining in these product mixtures.

Table 3.2.5. 1,3-isomerization of 2-phenylbut-3-en-2-ol: effect of various reaction conditions on product selectivity and on *E*-selectivity.[a,b]



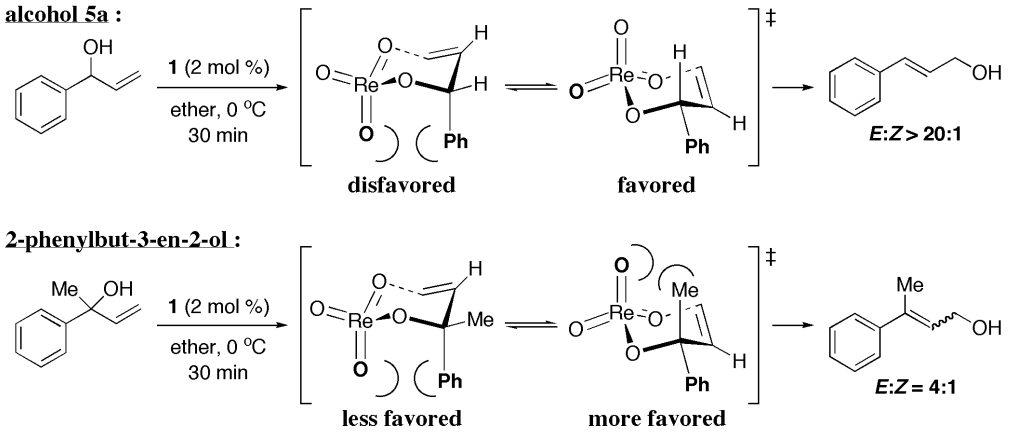
entry	solvent	mol % **1**	temp.	time	**A** (%)[d]	**B** (%)[d]	*E*:*Z* of **B**[d]	**C** + **D** (%)[e]	notebook page
1	ether	2	rt	30 min	6	55	3:1	39	cm5-36
2	ether	2	rt	2 h	5	45	3:1	50	cm5-36
3	ether	2	rt	18 h	3	32	3:1	65	cm5-36
4	ether	2	0 °C	30 min	11	66	4:1	23	cm5-36
5	ether	2	0 °C	2 h	6	67	3:1	27	cm5-36
6	ether	2	0 °C	18 h	5	56	3:1	39	cm5-36
7	ether	2	–20 °C	30 min	56	32	19:1	12	cm5-36
8	ether	2	–20 °C	2 h	15	73	15:1	12	cm5-36
9	ether	2	–20 °C	18 h	6	73	6:1	21	cm5-36
10	ether	2	–40 °C	1.5 h	68	17	> 99:1	15	cm5-37
11	ether	2	–40 °C	7 h	31	62	33:1	7	cm5-37
12	ether	2	–40 °C	18 h	11	80	31:1	9	cm5-37
13	ether	2	–40 °C	40 h	7	78	28:1	15	cm5-36
14[f]	ether	2	–50 °C	38.5 h	27	72	41:1	1	cm5-35
15	ether	4	–40 °C	1.5 h	51	40	27:1	9	cm5-37
16	ether	4	–40 °C	7 h	11	81	28:1	8	cm5-37
17	**ether**	**4**	**–40 °C**	**18 h**	**7**	**98**	**24:1**	**< 5**	**cm5-37**
18	ether	6	–40 °C	1.5 h	42	48	23:1	10	cm5-37
19	ether	6	–40 °C	7 h	7	81	25:1	12	cm5-37
20	ether	6	–40 °C	18 h	7	105	17:1	< 5	cm5-37
21	CH_2Cl_2	4	–40 °C	10 h	24	32	5:1	44	cm5-40
22	toluene	4	–40 °C	10 h	29	50	20:1	21	cm5-40
23	THF	4	–40 °C	10 h	19	80	36:1	1	cm5-40
24	**ether**	**4**	**–40 °C**	**10 h**	**12**	**95**	**31:1**	**< 5**	**cm5-40**

[a] 0.2 mmol scale, 0.2M. [b] Reactions were quenched with NEt_3. [c] Plus various isomers. [d] Determined by GC, relative to a tridecane standard. [e] Assumed based on mass balance, **C** and **D** were observed by GC but not quantified. [f] % conversion and *E*:*Z* determined by ^{1}H NMR.

4 to Table 3.2.2, entry 3). Second, the 1,3-isomerization of 2-phenylbut-3-en-2-ol is much less *E*-selective than that of **5a**, which proceeded with *E*:*Z* > 20:1, regardless of the reaction conditions. Neither of these reactivity trends was surprising. First, the allyl system derived from a tertiary allylic alcohol like 2-phenylbut-3-en-2-ol is more electron-rich than that derived from a secondary allylic alcohol like **5a**, and thus 2-phenylbut-3-en-2-ol should be more reactive with catalyst **1**. Second, as illustrated in Scheme 3.2.3,

the difference between the transition states leading to the *E*- and the *Z*-product is much more pronounced for **5a** than it is for 2-phenylbut-3-en-2-ol. For the former, the rhenium oxo ligand must experience a diaxial interaction with either a phenyl group (A-value = 2.7 kcal/mol) or a hydrogen atom (A-value = 0), whereas for the latter, this interaction must be with either a phenyl group or a methyl group (A-value = 1.74).[20]

Scheme 3.2.3. Stereochemical rationale for the greater *E*-selectivity observed for alcohol 5a, relative to that observed for 2-phenylbut-3-en-2-ol.



As we had observed with the isomerization reactions of the secondary alcohol substrates in section 3.2.1, lowering the temperature of the reactions involving 2-phenylbut-3-en-2-ol allowed the product formation to be favored over the side reactions (Table 3.2.5, entries 7-14). At –20 °C, a decent, though incomplete, conversion to product (**B**) was observed after about 2 hours (entry 8). Unfortunately the *E*:*Z* ratio of this product, while initially high, dropped significantly over time at –20 °C (compare entries 7-9). It thus appeared that the kinetic product of this reaction possessed entirely *E*-stereochemistry but that the thermodynamic *E*:*Z* product ratio was approximately 3:1 (see entries 1-3). At –40 °C, the *E*:*Z* product ratio was higher than it was at –20 °C, and it appeared to be relatively stable over time (entries 10-13). However, the isomerization

reaction was much slower and leveled off at about 80% conversion. At –50 °C, the *E*:*Z* product ratio remained high, even after almost 40 hours, but the isomerization was extremely slow (entry 14). Based upon these results, we determined that –40 °C was the optimal reaction temperature for the *E*-selective 1,3-isomerization of 2-phenylbut-3-en-2-ol. Upon increasing the catalyst loading of **1** in this reaction, we were able to increase the amount of product formed without significantly diminishing the *E*-selectivity (entries 15-20). We determined the optimal catalyst loading to be 4 mol % (entry 17).

Finally, we briefly explored the use of other reaction solvents for the 1,3-isomerization of 2-phenylbut-3-en-2-ol, using the optimized reaction conditions of 4 mol % **1** and –40 °C (Table 3.2.5, entries 21-24). The solvent trend matched that described in section 3.2.1, in which the product selectivity according to solvent was ether > THF > toluene > CH_2Cl_2. Thus we determined the optimal conditions for the *E*-selective 1,3-isomerization of 2-phenylbut-3-en-2-ol to be 4 mol % **1**, ether, –40 °C, and 10-18 hours (entries 17 and 24).

3.2.3. Summary and conclusions

We have accomplished the selective 1,3-isomerization of secondary and tertiary allylic alcohols that possess 1-aryl substituents, via catalysis by rhenium complex **1**, to form allylic alcohols with conjugated di- and trisubstituted alkene components. Two competing reaction pathways were proposed for the isomerization of these substrates: a concerted reaction via a chair-like transition state and a stepwise reaction that involved the formation of an allylic cation. This latter pathway was undesirable because it led to the formation of numerous condensation and dehydration products, but it could generally be averted with the use of the proper reaction temperature and solvent. Ether was

universally the optimal solvent for this isomerization reaction, but the appropriate reaction temperature varied widely from substrate to substrate.

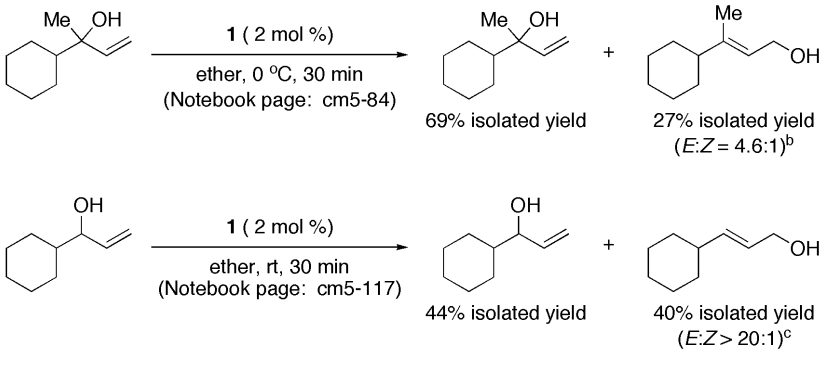
The 1,3-isomerization of all secondary allylic alcohols proceeded with high *E*-selectivity. This selectivity was independent of the alkene geometry of the starting material and could be rationalized, for all substrates, through examination of the proposed chair-like transition state. Both electron-rich and electron-deficient substrates participated readily in this isomerization reaction, but the latter substrates were less reactive. This trend was consistent with the buildup of a partial positive charge in the allyl moiety in the proposed chair-like transition state. Highly electron-rich allylic alcohols containing heterocyclic 1-substituents were generally too reactive, exhibiting extensive side product formation, while substrates with highly electron deficient allyl systems, such as α-hydroxy esters, underwent little reaction at all with catalyst **1**.

2-Phenylbut-3-en-2-ol underwent this 1,3-isomerization reaction to generate an allylic alcohol with a trisubstituted alkene component. This substrate was more prone to generate side products, and its isomerization reaction was less *E*-selective, than was the corresponding secondary alcohol substrate. However, we were still able to obtain a desirable yield and *E*-selectivity with the use of a higher catalyst loading, a low reaction temperature, and a long reaction time (10-18 hours). These reaction conditions were somewhat undesirable, but they were the best that could be obtained without adding anything else to the reaction. We will, however, revisit the 1,3-isomerization reaction of 2-phenylbut-3-en-2-ol in section 3.3, where we explore the use of reaction additives.

3.3. Use of Protecting Group Additives

While achievement of the selective 1,3-isomerization reactions with catalyst **1** that were presented in section 3.2 was exciting, this reaction still exhibited a severe limitation: it could only selectively form products that possessed conjugated alkenes. When allylic alcohols without 1-aryl substituents were employed under our optimal reaction conditions, product mixtures were obtained, although the side reactions that we had observed for the substrates possessing conjugated allyl systems (see section 3.2) were much less prevalent (Scheme 3.3.1).[viii] For these substrates, the reaction equilibrium

Scheme 3.3.1. 1,3-isomerization of allylic alcohols that lack 1-aryl substituents: thermodynamic product mixtures result.[a]

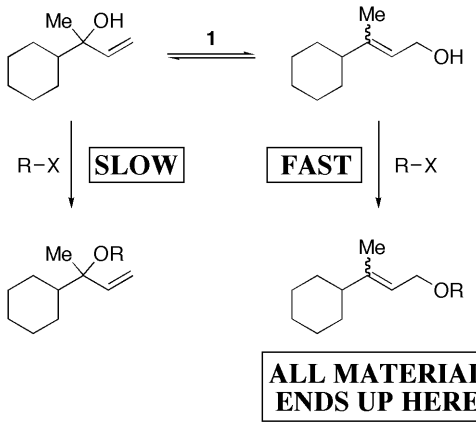


[a] 3.0 mmol scale, 0.2M. [b] Determined by GC. [c] Determined by ^{1}H NMR.

favored the formation of tertiary alcohols over primary ones, and it favored secondary alcohols very slightly over primary ones.[10,12b,21] We envisioned, however, that we could capitalize on the greater reactivity of primary alcohols, relative to tertiary alcohols, by adding a trapping reagent to this reaction. As illustrated in Scheme 3.3.2, such a reagent would selectively react with the primary alcohol substrate, thus continuously siphoning it out of the reaction equilibrium and driving the reaction to the right.

[viii] The use of longer reaction times did not change the product ratio. The use of lower temperatures lowered the amount of observed 1,3-isomerization.

Scheme 3.3.2. Addition of a trapping reagent (R–X) to the reaction of catalyst 1 with tertiary allylic alcohols possessing monosubstituted alkene components.

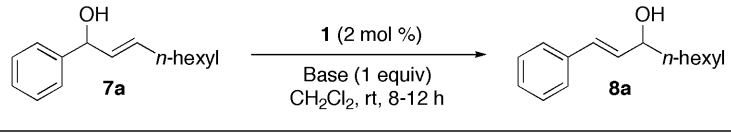


3.3.1. Search for a suitable trapping reagent

Our initial idea for a suitable trapping reagent was a trialkyl silyl chloride. This type of reagent requires the presence of a base in order to react with alcohols. We already knew that even small amounts of amine bases such as NEt_2 and $N(n\text{-}Pr)_3$ would completely deactivate **1**, presumably via coordination, because we had employed these two bases to quench all of the isomerization reactions reported in section 3.2. We therefore screened a number of more bulky bases, which should be less likely to coordinate to **1**, in order to determine their compatibility with catalyst **1** in the isomerization of alcohol **7a**. As shown in Scheme 3.3.3, every amine base that we screened completely deactivated catalyst **1**, even under our most reactive conditions (CH_2Cl_2, rt). Inorganic bases, such as $NaHCO_3$ and K_2CO_3, lowered the reactivity of **1**, but they did not completely attenuate it. Unfortunately these inorganic bases proved to be inefficient at promoting the reaction of alcohols with trialkyl silyl chlorides.[ix]

[ix] Notebook page: cm5-86.

Scheme 3.3.3. Screen of base compatibility with catalyst 1 in the 1,3-isomerization of alcohol 7a.[a,b,c,d]

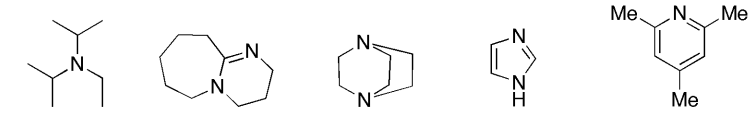


Base:

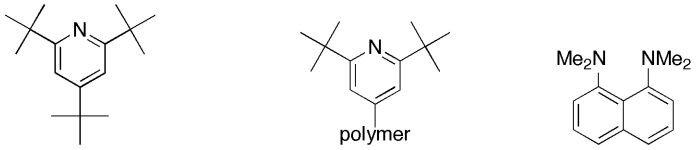
$NaHCO_3$: 16% **8a**; 84% side products

K_2CO_3: 14% **8a**; 86% side products

Every base shown below resulted in **no reaction**:



Hunig's base | DBU | DABCO | imidazole | 2,4,6-collidine



2,4,6-tri-*tert*-butylpyridine | 2,6-di-*tert*-butylpyridine, polymer-bound | Proton Sponge

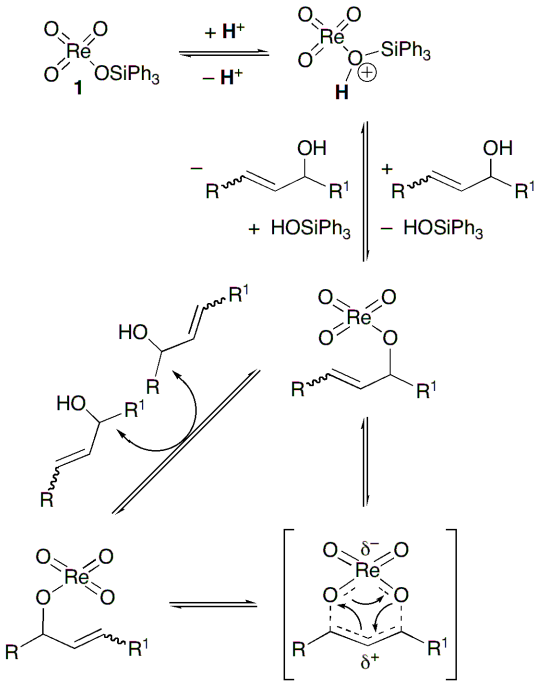
[a] 0.2 mmol scale, 0.2M. [b] Reactions quenched with NEt_3. [c] Crude reaction mixtures analyzed by ^1H NMR. [d] See notebook pages: cm5-66, cm5-68, and cm5-77.

It was especially surprising that 2,4,6-tri-*tert*-butylpyridine deactivated catalyst **1**, because this base is most likely too hindered to be able to coordinate to the rhenium moiety of **1**. This result suggests that this 1,3-isomerization reaction may require a proton source. Either $HOSiPh_3$ or perrhenic acid (derived from the hydrolysis of **1**) could serve as this proton source. It is possible that protonation is needed in order for the anionic $OSiPh_3$ moiety to dissociate from **1** at the beginning of the reaction, thus initiating the entry of **1** into the catalytic cycle, as illustrated in Scheme 3.3.4.[x] A second possibility is that protonation is necessary for the achievement of catalyst turnover, as

[x] It should be noted that, in all of these reactions, catalyst **1** contained a small amount of free $HOSiPh_3$ (see experimental section). This free $HOSiPh_3$ could conceivably serve as an acid in these reactions.

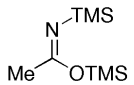
shown in Scheme 3.3.5. At this point, both of these statements are purely speculative and warrant further mechanistic studies.

Scheme 3.3.4. Proposed mechanism for the need for acid to initiate the entry of complex 1 into the catalytic cycle of the 1,3-isomerization of an allylic alcohol.

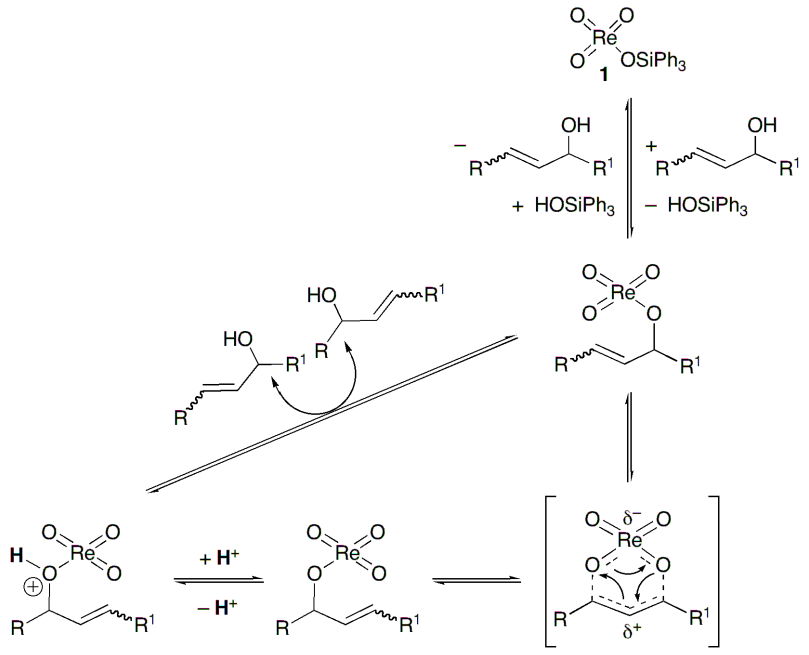


Returning to the goal of identifying a suitable trapping reagent for this isomerization reaction, the use of N,O-bis(trimethylsilyl)acetamide (BSA, Figure 3.3.1) circumvented the above-mentioned problem. BSA is able to deliver a trimethylsilyl group to an alcohol without the aid of an additional base. As shown in Table 3.3.1, the addition of BSA (1.2 equiv) promoted the selective 1,3-isomerization of various tertiary allylic alcohols.[19] Thus it appeared that the side products of BSA-promoted silylation reactions, namely acetamide and its derivatives, did not significantly diminish the reactivity of catalyst **1**, unlike the amine bases (Scheme 3.3.3). These results also indicated that, as we had anticipated, silylation by BSA was

Figure 3.3.1. BSA



Scheme 3.3.5. Proposed mechanism for the need for acid to allow catalyst turnover of complex 1 during the 1,3-isomerization of an allylic alcohol.



faster for the primary alcohols than for the tertiary alcohols, allowing the isomer containing the primary alcohol to be selectively and irreversibly silylated and subsequently isolated in high yield following deprotection.[xi]

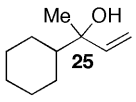
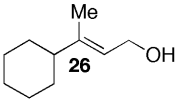
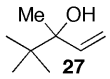
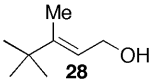
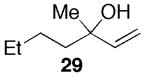
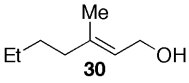
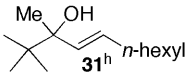
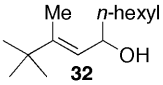
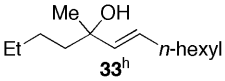
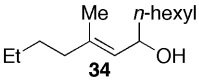
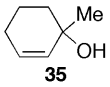
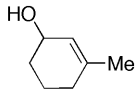
3.3.2. Scope of BSA-assisted isomerization of tertiary allylic alcohols

The BSA-assisted isomerization reactions were significant because they allowed, for the first time, reactions in which the product contained a *non-conjugated* alkene component to proceed to near completion. For example, substrate **25** isomerized to alcohol **26** in only 29% yield in the presence of catalyst **1** (Table 3.3.1, entry 1), but **26** was isolated in 89% yield when BSA was employed as a reaction additive (entry 3). It was noteworthy that the favored regioisomer (i.e., the primary alcohol) in these BSA-

[xi] Trimethylsilyl allylic ethers undergo 1,3-isomerization at room temperature with **1**, though at a slower rate than allylic alcohols.[17] We did not, however, observe significant 1,3-isomerization of the trimethylsilyl allylic ethers formed during our reactions.

assisted isomerization reactions was actually the thermodynamically *disfavored* regioisomer, as described at the beginning of section 3.3.

Table 3.3.1. 1,3-isomerization of tertiary allylic alcohols to form non-conjugated, trisubstituted alkenes.[a,b]

entry	substrate	equiv BSA	mol % **1**	temp. (°C)	time (h)	product	isolated[c] yield (%)	*E*:*Z*[d]	notebook page
1	 **25**	0	2	0	0.5	 **26**	29[e]	4.7 : 1	cm5-196
2[f]	 **27**	1.2	5	0	0.8	 **28**	79	> 99 : 1	cm5-225
3	**25**	1.2	2	0	0.5	**26**	89	4.7 : 1	cm5-197
4[g]	 **29**	1.2	2	0	0.5	 **30**	93	1.8 : 1	cm5-232
5	 **31**[h]	1.2	5	rt	24	 **32**	49	27 : 1	cm6-140
6	 **33**[h]	1.2	5	rt	0.5	 **34**	50	2.1 : 1	cm5-246
7	 **35**	1.2	5	rt	30	 **36**	50	------	cm5-255

[a] 0.4 mmol scale, ether, 0.2M. [b] See ref. 19. [c] Determined after deprotection via K_2CO_3/MeOH. [d] Determined by GC. [e] 71% of **25** recovered. [f] 1.6 mmol scale. [g] 4.0 mmol scale. [h] *E*:*Z* > 20:1 (^{1}H NMR).

These reactions were also significant because they generated trisubstituted alkenes. As we had observed in section 3.2, all of these reactions were *E*-selective. This selectivity increased with increasing steric demand of the substituent attached to the tertiary alcohol (e.g., entries 2-4: *t*-Bu >> Cy > *n*-Bu). For comparison, the A-values of *t*-Bu, Cy, and Et are 4.9, 2.15, and ca. 1.75 kcal/mol, respectively.[20] The addition of BSA did not, however, *improve* the *E*-selectivity in these reactions, relative to the *E*-selectivity that was observed in the reactions that employed **1** alone (compare entries 1 and 3). Because silylation by BSA presumably traps the kinetic product of these reactions, this

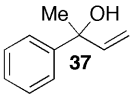
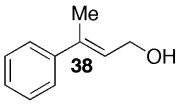
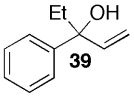
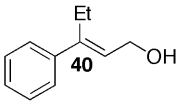
observation suggested that the kinetic and the thermodynamic *E*:*Z* product ratios were the same for the substrates listed in Table 3.3.1.

The use of BSA as a reaction additive also promoted the isomerization of tertiary allylic alcohols to form secondary alcohols (Table 3.3.1, entries 5-7). The yields in these reactions were only 50% at best, but these results were still significant because the reaction of these substrates with catalyst **1** in the absence of BSA rapidly resulted in the formation of complex mixtures of various dehydration products, with little or no formation of the desired 1,3-regioisomer.[xii] It thus appeared that the larger number of alkyl substituents attached to their allyl systems rendered these substrates electron-rich enough to become more subject to side reactions, which were competitive with the silylation of the secondary alcohol products. As we had observed for the analogous substrates possessing monosubstituted alkene components (entries 2 and 4), the *E*-selectivity in these reactions was dependent upon the size of the substituents on the allylic alcohol (entries 5-6).

Finally, the use of BSA as a reaction additive greatly improved the results obtained for the isomerization of tertiary alcohols possessing 1-aryl substituents, such as 2-phenylbut-3-en-2-ol. As discussed in section 3.2.2, 2-phenylbut-3-en-2-ol isomerized to near completion in the absence of BSA, since its 1,3-regioisomer contained a conjugated alkene. However, this isomerization could only proceed without significant side reactions or loss of *E*-selectivity at low reaction temperatures (≤ –40 °C), which necessitated the use of long reaction times and a higher catalyst loading, as shown in Table 3.3.2 (entry 1).[19] 2-Phenylbut-3-en-2-ol (**37**) readily underwent various side

[xii] Notebook page: cm5-216.

Table 3.3.2. 1,3-Isomerization of tertiary allylic alcohols to form conjugated, trisubstituted alkenes.[a,b]

entry	substrate	BSA (equiv.)	mol % **1**	temp. (°C)	time (h)	product	isolated yield (%)	*E*:*Z*[c]	notebook page
1	 **37**	0	4	–40	16	 **38**	83	18 : 1	cm5-63
2		0	2	–10	0.5		67	8.7 : 1	cm5-122
3		1.2	2	–10	0.5		92[d]	23 : 1	cm5-152
4	 **39**	0	4	–30	29	 **40**	83	1.3 : 1	cm5-203
5		0	2	–10	0.5		25	1.2 : 1	cm5-153
6		1.2	2	–10	0.5		90[d]	5.4 : 1	cm5-149

[a] 0.4 mmol scale, ether, 0.2M. [b] See ref. 19. [c] Determined by GC. [d] Determined after deprotection via K_2CO_3/MeOH.

reactions, as well as E/Z-isomerization, at higher temperatures (entry 2). The addition of BSA dramatically improved this reaction, resulting in both a higher yield of product **38** and higher *E*-selectivity, with the use of a lower catalyst loading, a higher reaction temperature, and, most notably, a significantly shorter reaction time (entry 3). A similar trend was observed in the isomerization of 3-phenylpent-1-en-3-ol (**39**), although the addition of BSA brought about a much less-pronounced improvement in *E*-selectivity in this case (entries 4-6). It appeared that, for the isomerization of 1-aryl substrates like **37** and **39**, silylation by BSA trapped out the *E*-isomer of the primary alcohol, which we have presumed to be the kinetic product, before subsequent dehydration and/or *E*/*Z*-isomerization could occur. This situation contrasted that observed for the non-conjugated substrates, in which the addition of BSA did not improve the *E*-selectivity (Table 3.3.1, compare entries 1 and 3).

We briefly explored the use of other protecting group additives, using alcohol **25** as a model substrate. Table 3.3.3 lists the results of the reaction of **25** and **1** in the presence of (a) BSA, (b) bis(trimethylsilyl)trifluoromethyl acetamide (BSTFA, Figure 3.3.2), which is a more-reactive analog of BSA, and (c) triethylsilyl chloride (TESCl) plus Proton Sponge. In

Figure 3.3.2. BSTFA

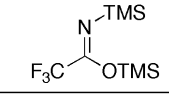
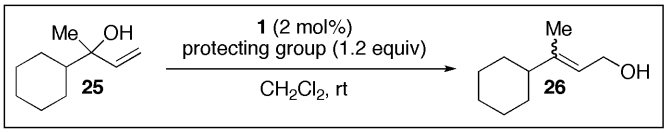


Table 3.3.3. 1,3-Isomerization of 2-cyclohexylbut-3-en-2-ol (25): use of various protecting group additives.[a,b]



entry	protecting group	time (h)	**25**:**26**[c]	side products	*E*:*Z*[d]	notebook page
1	BSA	3.5	1:8	few	4.6:1	cm5-92
2	BSTFA	3	1:2.4	many	4.7:1	cm5-93
3	TESCl[e]	16	1.1:1	few	3.9:1	cm5-89

[a] 0.2 mmol scale, 0.2M. [b] All values calculated after deprotection via TBAF.
[c] Determined by ^{1}H NMR. [d] Determined by GC. [e] 1.5 equiv Proton Sponge also used.

these reactions, CH_2Cl_2 was employed as the solvent in order to maximize both the solubility and the reactivity of the various reagents. The use of BSTFA formed a product mixture containing **25**:**26** =1:2.4, as well as a significant amount of side products (Table 3.3.3, entry 2). This result indicated that BSTFA was inferior to BSA as an additive for this isomerization reaction (compare entries 1 and 2). The use of TESCl led to a product mixture containing **25**:**26** = 1.1:1 (entry 3). In addition to the low conversions to **26**, equal or lower *E*-selectivities were also observed in the isomerization reactions that were accompanied by these two alternative protecting groups, as shown in Table 3.3.3. Therefore we concluded that BSA was the most favorable reaction additive.

We did not expect TESCl to be an effective additive, because of our previous observation that the presence of Proton Sponge completely deactivated catalyst **1** (Scheme 3.3.3). Therefore it was actually quite surprising that the isomerization reaction shown in entry 3 of Table 3.3.2 proceeded at all.[xiii] The presence of TESCl should propagate the formation of HCl over the course of this reaction, which could then serve as an acid source and may have prevented the complete deactivation of **1**. Thus in

[xiii] In this reaction, the order of addition was **1**, then Proton Sponge, then TESCl, and finally **25**.

hindsight, it is possible that the addition of a silylating reagent to the reactions shown in Scheme 3.3.3, which involved the addition of amine bases, may have prevented complete catalyst deactivation in these cases as well. Unfortunately, these control experiments were not performed.

3.3.3. Secondary-to-primary allylic alcohol isomerization

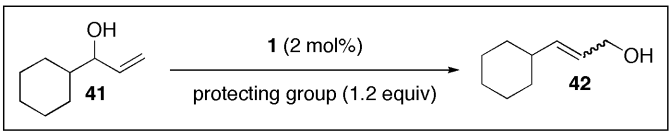
Encouraged by the results of BSA addition to the 1,3-isomerization reactions involving tertiary alcohols, we thought that this reaction strategy could also be applied to the isomerization of secondary alcohols to form primary alcohols that contained non-conjugated alkene components. We had previously observed that these reactions were highly *E*-selective, much more so than those of the corresponding tertiary alcohols (Scheme 3.3.1), and thus we envisioned this reaction as a new route to synthesize disubstituted alkenes with high *E*-selectivity.

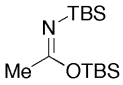
Table 3.3.4 lists the results of these studies, which employed 1-cyclohexylprop-2-en-1-ol (**41**) as a model substrate. Unfortunately, not only did the addition of BSA fail to drive these isomerization reactions toward product formation, it also appeared to completely deactivate catalyst **1** (compare entries 1 and 2). Only at higher reaction temperatures in certain solvents was any isomerization to product **42** observed at all (entries 4 and 6-7), and in all of these cases the extent of isomerization to **42** was much lower than that observed in the control experiment (entry 1). It is possible that BSA was simply silylating alcohol **41** in these reactions, before the 1,3-isomerization to form **42** could occur.[xiv] However, the use of *tert*-butyldimethylsilyl N,O-bis(*tert*-

[xiv] In all of the reactions shown in entries 2-7 of Table 3.3.4, at least some silylation of the **41** was observed. The extent of silylation was never quantified, due to the similarity of the silylated and the non-silylated alcohols with respect to ^{1}H NMR and the instability of the silylated products to silica gel chromatography.

butyldimethylsilyl)acetamide as a silylating reagent resulted in no silylation of **41**, but catalyst **1** was still completely deactivated in its presence (entry 8). This result suggested that these silylating reagents were actually deactivating **1**, rather than simply silylating the starting material.

Table 3.3.4. 1,3-Isomerization of 1-cyclohexylprop-2-en-1-ol (41): use of various protecting group additives.[a]



entry	protecting group	solvent	temp. (°C)	time (h)	conversion to **42** (%)[b]	*E*:*Z*	notebook page
1[c]	none	ether	rt	0.5	40[d]	> 20:1[e]	cm5-117
2	BSA	ether	rt	67	0	------	cm5-134
3	BSA	CH_2Cl_2	rt	67	0	------	cm5-134
4	BSA	CH_2Cl_2	40	15.5	2	N. D.	cm5-137
5	BSA	THF	60	14.5	0	------	cm5-146
6	BSA	toluene	60	14.5	< 27	N. D.	cm5-146
7	BSA	C_6H_6	60	14.5	< 32	N. D.	cm5-146
8		ether	rt	46.5	0[f]	------	cm5-170
9		ether	0	0.5	quantitative unselective protection[g]	N. D.	cm5-169

[a] 0.2 mmol scale, 0.2M. [b] Calculated after deprotection via TBAF. [c] 3.0 mmol scale. [d] Isolated yield, also 44% of **41** was recovered. [e] Determined by ^{1}H NMR. [f] Very little protection was observed. [g] Isomerization did occur, final ratios not calculated.

We do not know why BSA deactivated catalyst **1** in the reactions of the secondary alcohols but not in those of the tertiary alcohols. A possible, though unsubstantiated, explanation for this observation is that BSA actually reacted with **1** to generate a new rhenium species, which was a less active catalyst than **1** itself. Because tertiary alcohols are more reactive than secondary ones, the tertiary alcohols would still be able to react

with this new catalyst, while the less-reactive secondary alcohols would not. BSA could promote silyl group exchange with **1**, replacing the triphenylsilyl group of **1** with a trimethylsilyl group. Osborn has reported that this trimethylsilyl analog of **1** is a less active catalyst than **1** itself in 1,3-allylic alcohol isomerization reactions.[14] Thus Osborn's results support this hypothesis, but the mechanistic studies required to speak more conclusively about the interference of BSA with the isomerization of secondary alcohols were not performed.

We also investigated the effects of adding 3,4-dihydro-2*H*-pyran, a protecting group whose reaction with allylic alcohol substrates is *acid*-catalyzed, to the 1,3-isomerization reaction involving substrate **41**. As shown in entry 9 of Table 3.3.4, the use of this protecting group did not deactivate catalyst **1**, but it did result in the rapid, quantitative, and, unfortunately, unselective protection of both **41** and **42**. Thus this protecting group was also unsuitable for promoting the selective 1,3-isomerization of alcohol **41**.

We did, however, make an interesting observation regarding the acidic properties of catalyst **1** during these studies. The protection of an alcohol via reaction with 3,4-dihydro-2*H*-pyran normally requires the use of an acid catalyst, but in our case this reaction proceeded readily with only the addition of **1** (Table 3.3.4, entry 9). Furthermore, we observed that the protection of **41** and **42** via reaction with 3,4-dihydro-2*H*-pyran using *p*-toluenesulfonic acid as the acid catalyst was quite slow in ether, requiring more than 3 hours to reach completion.[xv] Conversely, in the presence of **1**, this protection reaction was complete in less than 30 minutes. Likewise, the addition of BSA

[xv] Notebook page: cm5-163.

to a mixture of **41**, **42**, and **1** in ether resulted in the quantitative silylation of both **41** and **42** within 15 minutes, even though the silylation of these substrates by BSA (without **1**) was observed to be both slow and selective for **42** in ether.[xvi] In addition, the presence of *p*-toluenesulfonic acid did not affect the reaction of **1** with alcohol **41** at all.[xvii] All of these observations, as well as our previous observations that amine bases completely deactivate catalyst **1** (Scheme 3.3.3), strongly suggest that either **1** or one of its decomposition products serves as an acid catalyst in this 1,3-isomerization reaction.

3.3.4. Summary and conclusions

We have demonstrated that the addition of BSA greatly improves certain 1,3-allylic alcohol isomerization reactions. The most successful substrates for these BSA-assisted reactions were tertiary allylic alcohols that possessed monosubstituted alkene components. The products of these reactions contained trisubstituted *E*-alkenes, which formed with varying levels of stereoselectivity, depending upon the steric demands of the substituents on the tertiary alcohol. This reaction strategy efficiently generated products containing both conjugated and non-conjugated alkenes. The use of the BSA additive was moderately successful in promoting the selective 1,3-isomerization of tertiary allylic alcohols possessing disubstituted alkene components, and it was unsuccessful at promoting this reaction when secondary allylic alcohols were used as the starting material.

We observed that amine bases, even sterically hindered ones, completely deactivated catalyst **1**, whereas *p*-toluenesulfonic acid did not affect its reactivity. Additionally, we saw that **1** served as a very efficient catalyst for both the BSA-promoted

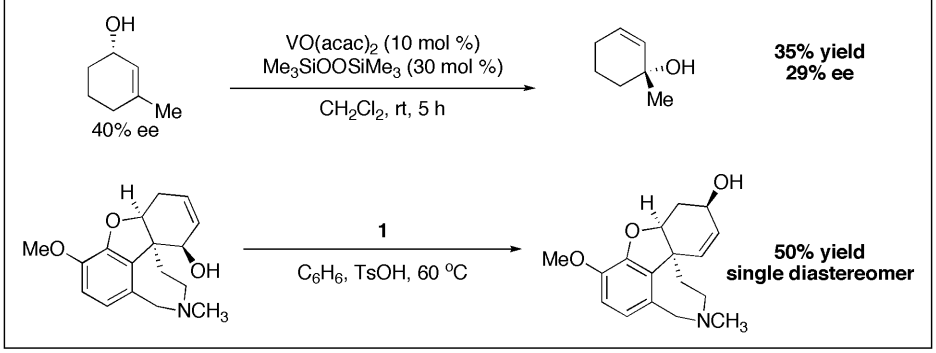
[xvi] Notebook pages: cm5-119 and cm5-147.
[xvii] Notebook page: cm5-164.

silylation of allylic alcohols and the addition of allylic alcohols to 3,4-dihydro-2*H*-pyran. Though further studies are greatly needed before conclusive statements can be made to explain these results, our current observations suggest that (a) either catalyst **1** or one of its decomposition products (e.g., $HOSiPh_3$ or perrhenic acid) can operate as an efficient general acid catalyst, and (b) this acidic quality of **1** may be essential to its catalytic activity in the 1,3-isomerization of allylic alcohols.

3.4. Chirality Transfer

Since all of the allylic alcohols employed during our studies possessed a stereogenic center, we wondered if chirality could be transferred during the 1,3-isomerization of nonracemic allylic alcohols. Such a reaction would be quite useful, because in many cases one isomer of a given allylic alcohol will be easier to synthesize in enantioenriched form than the other. As shown in Scheme 3.4.1, this type of chirality transfer had already been observed in the 1,3-isomerization of cyclic nonracemic allylic alcohols, both with catalyst **1**[22] and with $VO(acac)_2$.[10] We chose to explore the chirality transfer in the isomerization reactions of secondary allylic alcohols bearing 1-phenyl substituents, because these substrates required the simplest reaction conditions and consistently exhibited high *E*-stereoselectivity (see section 3.2).

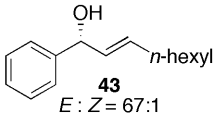
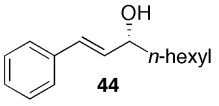
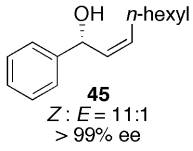
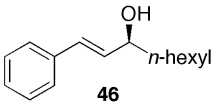
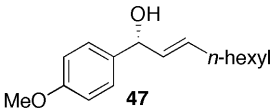
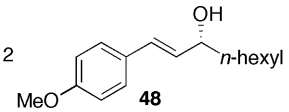
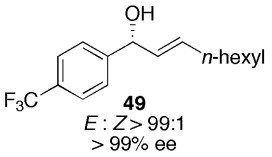
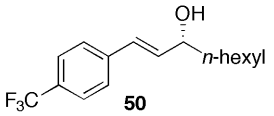
Scheme 3.4.1. 1,3-Isomerization of chiral, nonracemic cyclic allylic alcohols.[10, 22]



3.4.1. Formation of enantioenriched secondary allylic alcohols

Table 3.4.1 lists the results of the isomerization of enantioenriched 1-phenyl allylic alcohols bearing various substituents.[19] Substrates **43** and **45**, which possessed an unsubstituted 1-phenyl substituent, underwent this isomerization reaction with only a small loss (ca. 10%) of enantiopurity (entries 3-5). Higher retention of enantiopurity was

Table 3.4.1. 1,3-Isomerization of chiral, nonracemic allylic alcohols.[a,b,c]

entry	substrate	temp. (°C)	time (h)	product[d]	isolated yield (%)	ee (%)	predicted ee (%)[e]	notebook page
1[f]	 **43** *E* : *Z* = 67:1, 99% ee	–50	0.5	 **44**	96	65	96	cm5-269
2[f]		–50	2		96	57	96	cm5-270
3		–78	0.2		38[g]	87	96	cm5-282
4		–78	2		93	81	96	cm6-10
5	 **45** *Z* : *E* = 11:1, > 99% ee	–78	2	 **46**	92	72	> 82	cm5-300
6	 **47** *E* : *Z* > 20:1[h], 89% ee	–78	2	 **48**	72[i]	1	> 80	cm6-105
7	 **49** *E* : *Z* > 99:1, > 99% ee	–50	1	 **50**	99	95	> 97	cm6-119

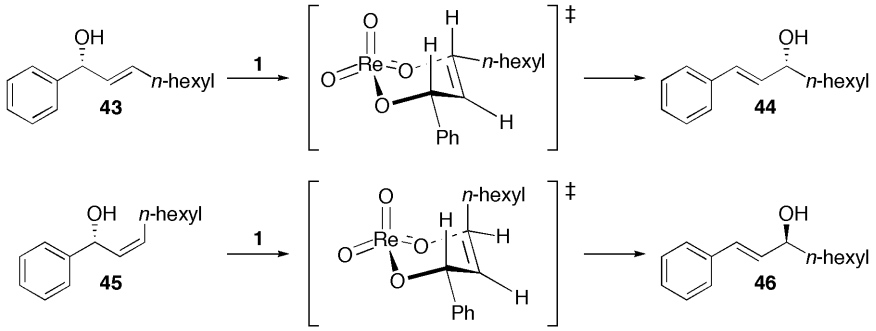
[a] 0.4 mmol scale, 3 mol % **1**, ether, 0.2M. [b] Unless otherwise noted, *E*:*Z* was determined by GC, and ee was determined by chiral HPLC. [c] See ref. 19. [d] *E*:*Z* > 20:1 (^{1}H NMR). [e] Calculated from *E*:*Z* and ee of the starting material. [f] 2 mol % **1**. [g] 57% **43** recovered. [h] Determined by ^{1}H NMR. [i] 2% **47** recovered.

observed when the reaction was performed at –78 °C, rather than at –50 °C (compare entries 1-2 and entries 3-4). Because side product formation in this reaction was completely suppressed at –50 °C (see Table 3.2.1, entry 22), the fact that an even lower reaction temperature was needed to minimize racemization strongly suggested that a competing reaction pathway other than that involving discrete allylic cation formation

(which has been assumed to be responsible for the formation of side products) was responsible for the observed partial loss of enantiopurity in these reactions. Subsequent loss of enantiopurity did not appear to occur to a significant extent over time (compare entries 1-2 and entries 3-4).[xviii]

The most interesting observation that was made during these studies was that the absolute configuration of the products shown in Table 3.4.1 was controlled by the alkene geometry of the respective starting materials. For example, the isomerization of alcohol **43**, which possessed *E*-stereochemistry, led to the formation of (*R*)-product **44**, while the isomerization of the *Z*-analog of **43** (alcohol **45**) led to the formation of the (*S*)-enantiomer of **44** (product **46**). This observation can be rationalized by consideration of the chair-like transition states that have been proposed for each of these reactions, which are illustrated in Scheme 3.4.2. Because the absolute stereochemistry of the products

Scheme 3.4.2. 1,3-Isomerization of the *E*- and *Z*-isomers of a chiral, nonracemic allylic alcohol leads to the formation of opposite enantiomers of the product.



[xviii] Differences of up to ca. 5% in ee were observed for a given reaction under the same conditions. For example, we performed the reaction shown in Table 3.4.1, entry 4 on a separate occasion and observed a 98% yield with an 84% ee (notebook page: cm5-263). It appeared that the observed ee in these reactions was extremely sensitive to the reaction conditions, and variables such as catalyst loading and concentration were not reproduced with a high level of rigor from reaction to reaction. Therefore the small difference between entries 1 and 2, and between entries 3 and 4, are likely within reasonable error.

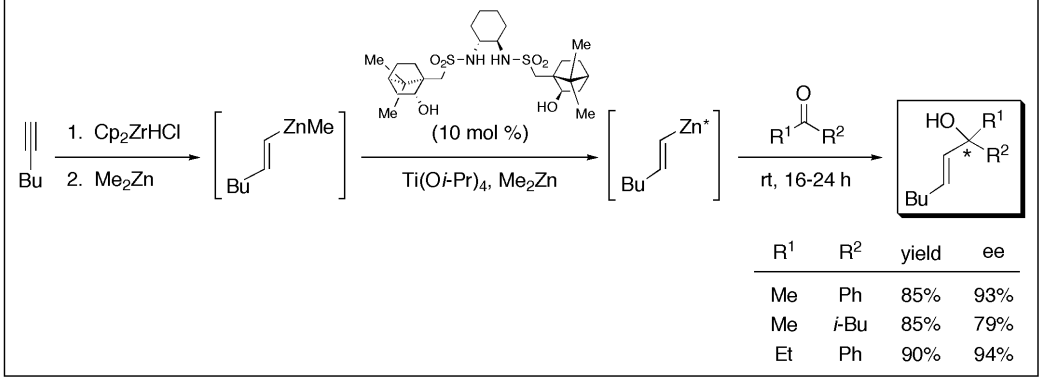
predicted by this model matched that of the observed products of this reaction, the results presented in entries 1-5 of Table 3.4.1 provided strong experimental evidence to support this proposed reaction mechanism.

As a first approximation, we hypothesized that the minor loss of enantiopurity that was exhibited in the isomerization reactions shown in entries 3-5 of Table 3.4.1 was the result of a competing reaction pathway that involved an allylic cation (see Scheme 3.1.2). To test this hypothesis, we evaluated the extent of chirality transfer present in the isomerization of both electron-rich and electron-deficient analogs of substrate **43**. The electron-rich analog, methoxy-substituted substrate **47** underwent the isomerization reaction with essentially *no* transfer of chirality (Table 3.4.1, entry 6). The electron-deficient analog, trifluoromethyl-substituted substrate **49**, on the other hand, exhibited nearly quantitative chirality transfer in this reaction (entry 7). In fact, substrate **49** isomerized with a high transfer of chirality even at –50 °C. These results were completely consistent with our hypothesis regarding the involvement of a competing allylic cation pathway, as substrate **47** should favor this pathway, while **49** should not.

3.4.2. Formation of enantioenriched tertiary allylic alcohols

Another potentially useful application of this methodology involves the formation of enantioenriched tertiary allylic alcohols. These substrates are quite difficult to synthesize in enantiopure form. Only a few examples of the use of enantioselective catalysis to form these substrates are known. These examples involve the asymmetric addition of vinyl groups to ketones, which is illustrated in Scheme 3.4.3.[23] This reaction only works efficiently if the two substituents on the ketone differ greatly in steric bulk, and thus its substrate scope is limited. We envisioned that the 1,3-isomerization of chiral,

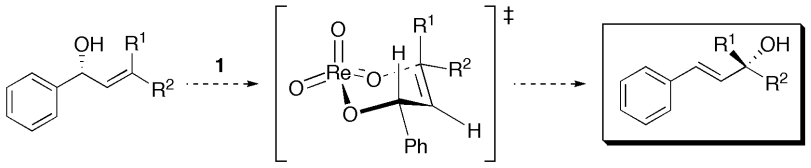
Scheme 3.4.3. Catalytic asymmetric addition of vinyl groups to ketones.[23]



R^1	R^2	yield	ee
Me	Ph	85%	93%
Me	*i*-Bu	85%	79%
Et	Ph	90%	94%

nonracemic secondary allylic alcohols possessing trisubstituted alkene components could be employed to generate enantioenriched tertiary allylic alcohols, as illustrated in Scheme 3.4.4. Enantioenriched secondary allylic alcohols are much easier to synthesize than are enantioenriched tertiary ones.[24] The advantage of the reaction strategy presented in Scheme 3.4.4, relative to the asymmetric vinylation of ketones, lies in the fact that, for the former, the two substituents on the tertiary alcohol product (R^1 and R^2) can theoretically be anything, since the absolute stereochemistry of the product is set by the alkene geometry of the starting material.

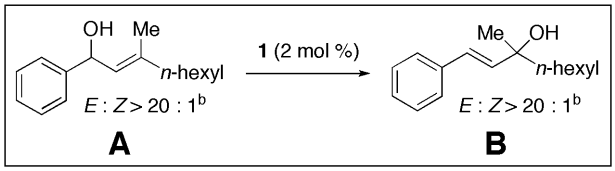
Scheme 3.4.4. Formation of enantioenriched, tertiary allylic alcohols via the 1,3-isomerization of chiral, nonracemic secondary allylic alcohols.



Because we had not yet investigated the reactivity of substrates of the form shown in Scheme 3.4.4 with catalyst **1**, we first looked at the reactivity of a racemic model substrate, (*E*)-3-methyl-1-phenylnon-2-en-1-ol. Table 3.4.2 lists the results of these studies. As expected, the isomerization of this substrate was more prone to side product formation than was that of its disubstituted analog, substrate **7a** (see section 3.2), because

the allyl moiety of (*E*)-3-methyl-1-phenylnon-2-en-1-ol was more electron-rich than that of **7a**. Again, the use of low reaction temperatures was necessary to prevent the occurrence of extensive side reactions. Surprisingly, ether proved to be a poor solvent for the isomerization of this substrate (Table 3.4.2, entries 2-4), with THF and CH_2Cl_2 giving much more desirable results (entries 5-8). Only THF permitted selective product formation at –78 °C (entry 6). This solvent trend was notably different from that observed with the analogous secondary alcohol substrate **7a** (see Table 3.2.1). As before, the isomerization of (*E*)-3-methyl-1-phenylnon-2-en-1-ol proceeded with high *E*-stereoselectivity.

Table 3.4.2. 1,3-isomerization of (*E*)-3-methyl-1-phenylnon-2-en-1-ol.[a]

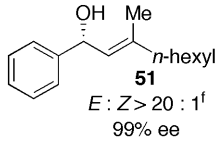
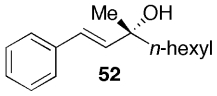
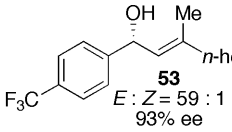
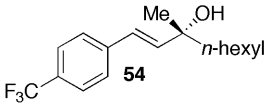


entry	solvent	temp.	time	A (%)[b]	B (%)[b]	side products (%)[b]	notebook page
1	toluene	–50 °C	30 min	0	20	80	cm6-35
2	ether	–50 °C	6 min	25	25	50	cm6-22
3	ether	–50 °C	30 min	0	45	55	cm6-22
4[c]	ether	–78 °C	2 h	0	62	38	cm6-123
5	THF	–50 °C	30 min	0	90	10	cm6-35
6[c]	**THF**	**–78 °C**	**2 h**	**0**	**> 95**	**< 5**	**cm6-123**
7	**CH_2Cl_2**	**–50 °C**	**30 min**	**0**	**100**	**0**	**cm6-39**
8[c]	CH_2Cl_2	–78 °C	2 h	0	50	50	cm6-123

[a] 0.2 mmol scale, 0.2 M. [b] Determined by ^{1}H NMR. [c] 3 mol % **1**.

Table 3.4.3 lists the results of the isomerization reactions of the enantioenriched secondary allylic alcohols with trisubstituted alkene components. The isomerization of (*R*,*E*)-3-methyl-1-phenylnon-2-en-1-ol (**51**) resulted in almost no chirality transfer, even at –78 °C (entries 1-2). We suspected that enantiopurity loss might be problematic for

Table 3.4.3. 1,3-Isomerization of chiral, nonracemic allylic alcohols to form tertiary alcohols.[a,b]

entry	substrate	temp. (°C)	time (h)	product[c]	isolated yield (%)	ee (%)	predicted ee (%)[d]	notebook page
1 2[e]	 **51** *E* : *Z* > 20 : 1[f] 99% ee	–50 –78	0.5 2	 **52**	74 81	2 9	> 89 > 89	cm6-95 cm6-128
3[g]	 **53** *E* : *Z* = 59 : 1 93% ee	–50	0.5	 **54**	95	58	90	cm6-121

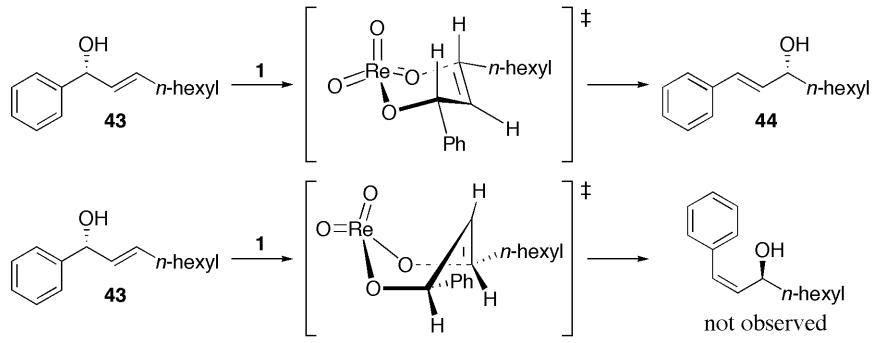
[a] 0.4 mmol scale, 2 mol % **1**, THF, 0.2M. [b] Unless otherwise noted, *E*:*Z* was determined by GC, and ee was determined by chiral HPLC. [c] *E*:*Z* > 20:1 (^{1}H NMR). [d] Calculated from *E*:*Z* and ee of the starting material. [e] 4 mol% **1**. [f] Determined by ^{1}H NMR. [g] Ether used as solvent.

substrate **51**, due to the extra substituent on its allyl moiety, which rendered the substrate more electron-rich. It was surprising, however, that a single methyl group made that significant of a difference, as the isomerization of the analogous enantioenriched disubstituted substrate (alcohol **43**) proceeded with approximately 80% ee (Table 3.4.1, entry 4). Adding an electron-withdrawing trifluoromethyl substituent to **51** (alcohol **53**) allowed this isomerization reaction to proceed with significantly higher selectivity, resulting in a product with 58% ee (entry 3), although this ee was again much smaller than that of the analogous substrate possessing a disubstituted alkene (alcohol **49**, see Table 3.4.1, entry 7).

It was tempting to attribute the lack of efficient chirality transfer in the isomerization of these chiral, nonracemic allylic alcohols bearing trisubstituted alkene components to their partial reaction through the competing allylic cation pathway (see Scheme 3.1.2). However, as aforementioned, the lack of side product formation, which would be indicative of such a reaction pathway, in these reactions questioned the likelihood of such a scenario. An alternative explanation was that the chair-like structure

of the transition state underwent a ring flip, which would form a boat-like structure and thus invert the stereocenter. Further analysis of this proposal revealed that this boat-like transition state would generate the *Z*-isomer of the product, as illustrated for substrate **43** in Scheme 3.4.5. We never observed the *Z*-product in any of these reactions, and thus the

Scheme 3.4.5. 1,3-Isomerization via a boat-like, rather than a chair-like, transition state leads to inversion of both the stereocenter and the alkene geometry.



possibility that competing boat-like transitions states were responsible for the partial racemization of these substrates was eliminated. A third possible explanation suggests that, in the presence of catalyst **1**, these allylic alcohols undergo a series of intermolecular S_N2/S_N2'-type reactions. As shown with substrate **51** in Scheme 3.4.6, this reaction pathway would result in the racemization of both the product and the starting material, without ever forming a discrete allylic cation. Because this reaction pathway involves the interaction of two substrate molecules, it should be discouraged by carrying out the isomerization reaction at a lower concentration.

Scheme 3.4.6. Possible racemization pathway, via an S_N2/S_N2'-type reaction, for the interaction of alcohol 51 with catalyst 1.

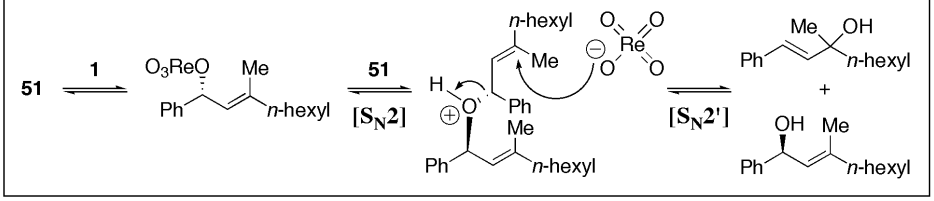


Table 3.4.4 illustrates our investigation of the isomerization of selected chiral, nonracemic allylic alcohols under dilute reaction conditions. These conditions did not have a significant effect on the reaction of methoxy-substituted substrate **47** (entry 1), but they did significantly increase the selectivity of the isomerization of substrates **43** and **53**, increasing the ee of the product by 12% and 33%, respectively (entries 2-3). Unfortunately these dilute reaction conditions also severely decreased the rate of these two isomerization reactions, resulting in very low conversions to product (11% and 18%, respectively). While these results do suggest that the racemization mechanism shown in Scheme 3.4.6 may be operative in these reactions, more quantitative studies need to be performed in order to confirm this hypothesis.

Table 3.4.4. 1,3-Isomerization of chiral, nonracemic allylic alcohols under dilute reaction conditions.[a]

			0.2 M			0.02 M		
entry	substrate	product[b]	isolated yield (%)	ee (%)[c]	notebook page	isolated yield (%)	ee (%)[c]	notebook page
1	**47**	**48**	72[d]	1	cm6-105	82[e]	0	cm6-114
2	**43**[f]	**44**	93	81	cm6-10	11[g]	93	cm6-118
3	**53**	**54**	95	58	cm6-121	18[h]	91	cm6-113

[a] Same reaction conditions as given for corresponding reactions in Tables 3.4.1 and 3.4.3. [b] *E*:*Z* > 20:1 (^{1}H NMR). [c] Determined by chiral HPLC. [d] 2% **47** recovered. [e] 9% **47** recovered. [f] > 99% ee (chiral HPLC). [g] 88% **43** (> 99% ee) recovered. [h] 81% **53** recovered.

3.4.3. Summary and conclusions

We have observed that chirality can be transferred during the 1,3-isomerization of chiral, nonracemic secondary allylic alcohols at low reaction temperatures. The extent of chirality transfer was highly dependent upon both the reaction conditions and the electronic nature of the substrate. Electron-deficient substrates transferred chirality to a far greater extent than did electron-rich substrates. Isomerization reactions that formed tertiary alcohols transferred chirality much less efficiently than those that formed

secondary ones, presumably because the former possessed more electron-rich allyl systems. To date, only one substrate, alcohol **49**, has undergone this isomerization reaction with > 90% ee. We also demonstrated that the absolute stereochemistry of the products of these reactions depended upon the alkene geometry of the starting material and could be predicted from the structure of the chair-like transition state that has been suggested for this reaction. This observation provided our strongest piece of experimental evidence to support this proposed reaction mechanism.

3.5. General Summary and Conclusions

Over the course of this project, we have developed two different reaction strategies to efficiently promote the selective 1,3-isomerization of allylic alcohols with catalyst **1**: conjugated product synthesis and BSA-promoted product trapping. Our procedures featured low catalyst loadings and short reaction times, and they delivered the product isomers in high yields and with high *E*-stereoselectivities for a variety of allylic alcohols. This reaction has enabled the synthesis of allylic alcohols with conjugated or non-conjugated, di- or trisubstituted, and electron-rich or electron-deficient alkene components.

This isomerization reaction has a much broader substrate scope that it did when we began working on this project. There is still, however, room for improvement. The isomerization of tertiary alcohols to form secondary alcohols, and the isomerization of secondary alcohols to form primary ones, do not proceed efficiently with **1** alone or with the use of BSA as an additive, but they could conceivably be promoted with the use of other trapping reagents. The latter reaction would be especially beneficial, as it proceeds with high *E*-selectivity and could therefore be employed in the stereoselective

transformation of aldehydes into *E*-alkenes (via vinylmagnesium bromide addition, followed by 1,3-isomerization). With respect to chirality transfer, these reactions currently only proceed with high enantiomeric excess when highly electron-deficient substrates are employed. It is likely that the development of a new catalyst, one that less readily transforms the alcohol moiety into a leaving group, will be necessary to improve this aspect of the reaction.

The fundamental reaction properties that we have observed during these studies, namely (a) the lower reactivity and the higher stereoselectivity exhibited by electron-deficient substrates, (b) the dependence of *E*-selectivity on the steric bulk surrounding tertiary alcohols, and (c) the correlation between the alkene geometry and the absolute configuration of enantioenriched allylic alcohols, are all consistent with the proposed chair-like transition state that contains a partially cationic allyl moiety. However, the side product formation and the imperfect chirality transfer that we have also observed indicate that competing reaction pathways, possibly involving allylic cation formation, are operative as well. Thus we conclude that a mechanistic continuum operates for these 1,3-allylic alcohol isomerization reactions. The actual mechanism lies somewhere between that of the ordered, six-membered ring transition state and that of the discrete allylic cation, and it will more closely resemble one or the other, depending upon both the reaction conditions and the electronic properties of the allylic alcohol substrate.

3.6. Experimental Section

3.6.1. Specific experimental procedures and characterization data

Triphenylsilyl perrhenate (**1**).[13] (Notebook page: cm4-227) In glove box, added Re_2O_7 (1.64 g, 3.4 mmol) and triphenylsilanol (2.06 g, 7.5 mmol) to a 100-mL round-bottomed

flask. Added dry toluene (24 mL) and let stir at room temperature for 1 hour. Still in glove box, filtered through Celite and removed solvent *in vacuo*. Dissolved in a small amount of dry ether and placed in the freezer (in the glove box) overnight. Obtained 1.81 g of **1** as white crystals after vacuum filtration (52% yield). A second crystallization from the remaining ether solution resulted in the isolation of 720 mg of **1**, again, as white crystals (total of 73% yield). ^{1}H NMR indicated that these crystals (from all batches) contained a small (< 5%) amount of triphenylsilanol. This impurity was never completely removed. **1** was stored over long periods of time (many months) in the freezer in the glove box. ^{1}H NMR (300 MHz, C_6D_6, ppm): δ 7.61 (triphenylsilanol, 6H, m), 7.38 (6H, m), 7.06 (9H, m), 7.06 (triphenylsilanol, 9H, m). HRMS (EI) calcd. for $C_{18}H_{15}O_4ReSi$: 510.0297, found: 510.0296.

(*E*)-3-cyclohexyl-1-phenylprop-2-en-1-ol (**2**). To a flame-dried, round-bottomed flask, under an argon atmosphere, added 1-phenyl-2-propenyl acetate (1.0 mL, 6.2 mmol), vinylcyclohexane (700 μL, 5.1 mmol), and CH_2Cl_2 (16 mL). Then added, via cannula transfer, a solution of $RuCl_2(PCy_3)(H_2IMes)CHPh$ (136 mg, 0.16 mmol) and CH_2Cl_2 (10 mL). Placed in a 45 °C oil bath and let stir overnight. Allowed to cool to room temperature, removed solvent *in vacuo*, and added 3.0M aqueous NaOH solution (1.2 mL, 3.6 mmol), THF (45 mL), and MeOH (9 mL). Let stir at room temperature for 3.5 hours. Added 40 mL aqueous NH_4Cl solution, extracted 3 times with 25 mL ether, and dried with Na_2SO_4. The product was purified via silica gel chromatography (8:2 pentane:ether) to obtain 636 mg of **2** as an orange oil (58% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 7.20 (5H, m), 5.63 (1H, dd, J = 15.5, 5.9 Hz), 5.51 (1H, ddd, J = 15.5,

6.5, 0.9 Hz), 5.05 (1H, d, *J* = 6.6 Hz), 1.9 (2H, m), 1.6 (5H, m), 1.1 (5H, m). ^{13}C NMR (300 MHz, $CDCl_3$, ppm): δ 143.6, 138.7, 130.0, 128.6, 127.6, 126.4, 75.5, 40.4, 32.92, 32.88, 26.3, 26.2. HRMS (EI) calcd. for $C_{15}H_{20}O$: 216.1514, found: 216.1507.

(*E*)-1-cyclohexyl-3-phenylprop-2-en-1-ol (**3**). In glove box, added **1** (2 mg, 0.004 mmol) to 4-mL vial. Removed from glove box, added ether (1 mL), placed in Cryotrol set to –50 °C, and let stir for approximately 10 minutes. Added **2** (43.1 mg, 0.2 mmol) via syringe and let stir at –50 °C for 30 minutes. Removed from Cryotrol, immediately added 20 μL triethylamine, and let stir until warmed to room temperature. Concentrated *in vacuo* and purified directly via silica gel chromatography (8:2 pentane:ether) to obtain 41.3 mg of **3** as a clear oil (96% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 7.3 (5H, m), 6.58 (1H, d, *J* = 15.9 Hz), 6.26 (1H, ddd, *J* = 15.8, 7.1, 1.1 Hz), 4.05 (1H, t, *J* = 6.6 Hz), 1.95 (1H, d, *J* = 13.5 Hz), 1.75 (5H, m), 1.55 (1H, m), 1.2 (5H, m). ^{13}C NMR (300 MHz, $CDCl_3$, ppm): δ 137.0, 131.4, 131.2, 128.8, 127.8, 126.6, 77.8, 44.1, 29.1, 28.8, 26.7, 26.32, 26.26. HRMS (EI) calcd. for $C_{15}H_{20}O$: 216.1514, found: 216.1516.

(*Z*)-3-cyclohexyl-1-phenylprop-2-en-1-ol (**4**). To a flame-dried, round-bottomed flask, under an argon atmosphere, added (*Z*)-(2-bromovinyl)cyclohexane[25] (374 mg, 2.0 mmol) and ether (10 mL). Placed in a dry ice/acetone bath and let stir for approximately 10 minutes. Added a 1.7M pentane solution of *t*-butyllithium (3 mL, 5.1 mmol) dropwise. Let stir at –78 °C for 1 hour. Added benzaldehyde (distilled from CaH_2, 200 μL, 2.0 mmol) via syringe, let stir at –78 °C for 20 minutes, removed dry ice/acetone bath, and let stir for 20 more minutes at room temperature. Slowly added 10 mL aqueous NH_4Cl

solution, extracted 3 times with ether, and dried with Na_2SO_4. Purified via silica gel chromatography (8:2 pentane:ether) to obtain 288 mg of **4**:3-cyclohexyl-1-phenylprop-2-yn-1-ol = 1.5:1 as a cloudy oil. To convert this mixture into pure **4**, it was added to Lindlar catalyst (5% Pd on $CaCO_3$, poisoned with Pb, 45 mg) and MeOH (3 mL), degassed via 3 freeze-pump-thaw cycles, and placed under a H_2 atmosphere for approximately 26 hours. The reaction solution was filtered through Celite, rinsing with ether, and purified via silica gel chromatography (8:2 pentane:ether) to obtain 165 mg of **4** as a clear oil (37% yield, ≥ 97% pure by GC). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 7.35 (5H, m), 5.5 (3H, m), 2.5 (1H, m), 1.7 (6H, m), 1.2 (5H, m). ^{13}C NMR (300 MHz, $CDCl_3$, ppm): δ 144.0, 138.6, 130.0, 128.7, 127.6, 126.1, 70.1, 37.1, 33.6, 33.3, 26.1, 26.0, 25.9. HRMS (EI) calcd. for $C_{15}H_{20}O$: 216.1514, found: 216.1519.

1-(2-Nitrophenyl)prop-2-en-1-ol (**5b**). To a flame-dried, round-bottomed flask, under an argon atmosphere, added 2-nitrobenzaldehyde (7.5 g, 50 mmol) and ether (100 mL). Placed in an ice bath and let stir for approximately 10 minutes. Added a 1.0M THF solution of vinylmagnesium bromide (100 mL, 100 mmol) dropwise, over approximately 30 minutes. Let stir at 0 °C for 1 hour, then slowly added 150 mL aqueous dilute HCl solution, extracted 3 times with 100 mL ether, and dried with Na_2SO_4. Purified via silica gel chromatography (7:3 hexanes:ethyl acetate) to obtain approximately 2 g of **5b** as a reddish-brown oil (ca. 20% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 7.92 (1H, dd, *J* = 8.1, 1.2 Hz), 7.77 (1H, dd, *J* = 7.8, 1.5 Hz), 7.65 (1H, td, *J* = 7.6, 1.2 Hz), 7.45 (1H, ddd, *J* = 8.3, 7.4, 1.5 Hz), 6.09 (1H, ddd, *J* = 17.3, 10.4, 5.3 Hz), 5.80 (1H, dt, *J* = 5.1, 1.5 Hz), 5.42 (1H, dt, *J* = 17.1, 1.4 Hz), 5.27 (1H, dt, *J* = 10.5, 1.4 Hz), 2.6 (1H, br). ^{13}C

NMR (300 MHz, $CDCl_3$, ppm): δ 148.5, 138.1, 137.7, 133.8, 129.1, 128.7, 124.8, 116.4, 70.2. HRMS (CI) calcd. for $C_9H_9NO_3 + NH_4$: 197.0926, found: 197.0918.

1-(2-Methoxyphenyl)prop-2-en-1-ol (**5c**). Followed procedure given for **5b**, with 5.5 mL (46 mmol) *o*-anisaldehyde, 90 mL (90 mmol) vinylmagnesium bromide (1.0M in THF), and 90 mL ether. Purified via silica gel chromatography (7:3 hexanes:ethyl acetate) to obtain 6.7 g of **5c** as a yellow oil (89% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 7.2 (2H, m), 6.85 (2H, m), 6.07 (1H, ddd, J = 17.3, 10.4, 5.6 Hz), 5.34 (1H, t, J = 5.7 Hz), 5.24 (1H, d, J = 17.4 Hz), 5.10 (1H, d, J = 10.5 Hz), 3.79 (3H, s), 2.70 (1H, d, J = 6.0 Hz). ^{13}C NMR (300 MHz, $CDCl_3$, ppm): δ 156.9, 139.6, 130.9, 129.0, 127.6, 121.1, 114.7, 110.9, 71.8, 55.6. HRMS (EI) calcd. for $C_{10}H_{12}O_2$: 164.0837, found: 164.0839.

(*E*)-3-(2-nitrophenyl)prop-2-en-1-ol (**6b**). Followed procedure given for **3**, with 71.9 mg (0.4 mmol) **5b**, 4 mg (0.008 mmol) **1**, 2 mL CH_2Cl_2, a reaction temperature of room temperature, and a reaction time of 30 minutes. Purified via silica gel chromatography (7:3 pentane:ether) to obtain 70.5 mg of **6b** as a yellow oil (98% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 7.90 (1H, dd, J = 8.3, 1.1 Hz), 7.80 (2H, m), 7.38 (1H, ddd, J = 8.4, 6.8, 2.0 Hz), 7.07 (1H, dt, J = 15.9, 1.7 Hz), 6.34 (1H, dt, J = 15.6, 5.3 Hz), 4.37 (2H, dd, J = 5.3, 1.7 Hz), 2.31 (1H, br). ^{13}C NMR (300 MHz, $CDCl_3$, ppm): δ 147.9, 134.3, 133.3, 132.7, 128.9, 128.3, 125.9, 124.7, 63.4. HRMS (EI) calcd. for $C_9H_9NO_3$: 179.0582, found: 179.0584.

(*E*)-3-(2-methoxyphenyl)prop-2-en-1-ol (**6c**). Followed procedure given for **3**, with 65.5 mg (0.4 mmol) **5c**, 4 mg (0.008 mmol) **1**, 2 mL ether, a reaction temperature of –50 °C, and a reaction time of 30 minutes. Purified via silica gel chromatography (8:2 to 7:3 pentane:ether) to obtain 42.3 mg of **6c** as an oil (65% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 7.45 (1H, dd, *J* = 7.7, 1.7 Hz), 7.25 (1H, ddd, *J* = 8.1, 7.4, 1.8 Hz), 6.93 (3H, m), 6.39 (1H, dt, *J* = 16.2, 5.9 Hz), 4.33 (1H, dd, *J* = 6.0, 1.5 Hz), 3.86 (3H, s), 1.74 (1H, br). ^{13}C NMR (300 MHz, $CDCl_3$, ppm): δ 156.9, 129.5, 128.9, 127.2, 126.3, 125.9, 120.8, 111.0, 64.4, 55.6. HRMS (EI) calcd. for $C_{10}H_{12}O_2$: 164.0837, found: 164.0837.

(*E*)-1-phenylnon-2-en-1-ol (**7a**). Followed procedure given for **2**, with 2.4 mL (15 mmol) 1-phenyl-2-propenyl acetate, 2.0 mL (12.7 mmol) 1-octene, 270 mg (0.32 mmol) $RuCl_2(PCy_3)(H_2IMes)CHPh$, and 40 mL CH_2Cl_2; then 3 mL (9.0 mmol) aqueous NaOH solution (3.0M), 20 mL MeOH, and 100 mL THF. Purified via silica gel chromatography (8:2 pentane:ether, 2 sequential columns) to obtain 1.5 g of **7a** as a yellow oil (54% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 7.35 (5H, m), 5.75 (2H, m), 5.18 (1H, dd, *J* = 6.0, 2.4 Hz), 2.07 (2H, dt, *J* = 6.7, 6.7 Hz), 1.91 (1H, d, *J* = 3.0 Hz), 1.3 (8H, m), 0.89 (3H, t, *J* = 6.6 Hz). ^{13}C NMR (300 MHz, $CDCl_3$, ppm): δ 143.6, 133.1, 132.4, 128.7, 127.7, 126.4, 75.4, 32.4, 31.9, 29.2, 29.1, 22.8, 14.3. HRMS (EI) calcd. for $C_{15}H_{22}O$: 218.1671, found: 218.1666.

(*E*)-1-(2-nitrophenyl)non-2-en-1-ol (**7b**). Followed procedure given for **2**, with 1.3 mL (7.6 mmol) 1-(2-nitrophenyl)allyl acetate, 1.0 mL (6.4 mmol) 1-octene, 135 mg (0.16 mmol) $RuCl_2(PCy_3)(H_2IMes)CHPh$, and 32 mL CH_2Cl_2; then 2 mL (6.0 mmol) aqueous

NaOH solution (3.0M), 12 mL MeOH, and 60 mL THF. Purified via silica gel chromatography (8:2 to 7:3 pentane:ether) to obtain 650 mg of **7b** as an orange oil (39% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 7.88 (1H, dd, *J* = 8.4, 1.2 Hz), 7.79 (1H, dd, *J* = 8.0, 1.4 Hz), 7.63 (1H, td, *J* = 7.6, 1.3 Hz), 7.43 (1H, ddd, *J* = 8.0, 7.3, 1.4 Hz), 5.8 (2H, m), 5.7 (1H, m), 2.41 (1H, br), 2.05 (2H, dt, *J* = 7.0, 7.0 Hz), 1.3 (8H, m), 0.88 (3H, t, *J* = 6.8 Hz). ^{13}C NMR (300 MHz, $CDCl_3$, ppm): δ 148.5, 138.4, 134.4, 133.5, 129.9, 128.7, 128.4, 124.7, 70.2, 32.4, 31.9, 29.1, 29.0, 22.8, 14.3. HRMS (EI) calcd. for $C_{15}H_{21}NO_3$ – H: 262.1438, found: 262.1439.

(*E*)-1-(2-methoxyphenyl)non-2-en-1-ol (**7c**). Followed procedure given for **2**, with 2.5 mL (14.5 mmol) 1-(2-methoxyphenyl)allyl acetate, 2.0 mL (12.7 mmol) 1-octene, 270 mg (0.32 mmol) $RuCl_2(PCy_3)(H_2IMes)CHPh$, and 40 mL CH_2Cl_2; then 3.5 mL (10.5 mmol) aqueous NaOH solution (3.0M), 25 mL MeOH, and 125 mL THF. Purified via silica gel chromatography (8:2 pentane:ether) to obtain 1.5 g of **7c** as a yellow oil (48% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 7.20 (2H, m), 6.86 (2H, m), 5.65 (2H, m), 5.28 (1H, d, *J* = 5.7 Hz), 3.79 (3H, s), 2.68 (1H, d, *J* = 6.0 Hz), 1.97 (2H, m), 1.25 (8H, m), 0.80 (3H, t, *J* = 6.8 Hz). ^{13}C NMR (300 MHz, $CDCl_3$, ppm): δ 156.9, 132.4, 131.8, 131.2, 128.7, 127.6, 121.0, 110.9, 71.9, 55.6, 32.5, 31.9, 29.3, 29.1, 22.8, 14.3. HRMS (EI) calcd. for $C_{16}H_{24}O_2$: 248.1776, found: 248.1780.

(*E*)-1-phenylnon-1-en-3-ol (**8a**). Followed procedure given for **3**, with 84.8 mg (0.4 mmol) **7a**, 4 mg (0.008 mmol) **1**, 2 mL ether, a reaction temperature of –50 °C, and a reaction time of 30 minutes. Purified via silica gel chromatography (8:2 pentane:ether) to

obtain 83.6 mg of **8a** as a clear oil (99% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 7.35 (5H, m), 6.60 (1H, d, *J* = 15.9 Hz), 6.25 (1H, dd, *J* = 15.9, 6.9 Hz), 4.30 (1H, dt, *J* = 6.3, 6.3 Hz), 1.65 (3H, m), 1.4 (8H, m), 0.91 (3H, t, *J* = 6.8 Hz). ^{13}C NMR (300 MHz, $CDCl_3$, ppm): δ 137.0, 132.8, 130.4, 128.8, 127.8, 126.7, 73.3, 37.6, 32.0, 29.5, 25.6, 22.8, 14.3. HRMS (EI) calcd. for $C_{15}H_{22}O$: 218.1671, found: 218.1670.

(*E*)-1-(2-nitrophenyl)non-1-en-3-ol (**8b**). Followed procedure given for **3**, with 104.8 mg (0.4 mmol) **7b**, 4 mg (0.008 mmol) **1**, 2 mL ether, a reaction temperature of room temperature, and a reaction time of 30 minutes. Purified via silica gel chromatography (1:1 pentane:ether) to obtain 104.2 mg of **8b** as a reddish oil (99% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 7.91 (1H, dd, *J* = 8.3, 0.8 Hz), 7.57 (2H, m), 7.38 (1H, ddd, *J* = 8.4, 6.8, 2.0 Hz), 7.02 (1H, dd, *J* = 15.6, 0.6 Hz), 6.20 (1H, dd, *J* = 15.9, 6.6 Hz), 4.33 (1H, dt, *J* = 6.2, 6.2 Hz), 2.1 (1H, br), 1.65 (2H, m), 1.35 (8H, m), 0.88 (3H, t, *J* = 6.8 Hz). ^{13}C NMR (300 MHz, $CDCl_3$, ppm): δ 148.0, 138.3, 133.2, 132.8, 128.9, 128.2, 125.4, 124.7, 77.7, 37.3, 31.9, 29.4, 25.5, 22.8, 14.3. HRMS (EI) calcd. for $C_{15}H_{21}NO_3$ – H: 262.1438, found: 262.1439.

(*E*)-1-(2-methoxyphenyl)non-1-en-3-ol (**8c**). Followed procedure given for **3**, with 99.2 mg (0.4 mmol) **7c**, 4 mg (0.008 mmol) **1**, 2 mL ether, a reaction temperature of –50 °C, and a reaction time of 30 minutes. Purified via silica gel chromatography (8:2 pentane:ether) to obtain 68.1 mg of **8c** as a clear oil (69% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 7.45 (1H, dd, *J* = 7.5, 1.8 Hz), 7.24 (1H, m), 6.90 (3H, m), 6.24 (1H, dd, *J* = 16.1, 7.1 Hz), 4.29 (1H, dt, *J* = 6.6, 6.6 Hz), 3.86 (3H, s), 1.5 (11H, m), 0.90 (3H, t, *J*

= 6.8 Hz). ^{13}C NMR (300 MHz, $CDCl_3$, ppm): δ 156.9, 133.5, 128.9, 127.0, 125.9, 125.2, 120.8, 111.0, 73.8, 55.6, 37.5, 32.0, 29.5, 25.7, 22.8, 14.3. HRMS (EI) calcd. for $C_{16}H_{24}O_2$: 248.1776, found: 248.1783.

(*E*)-1-(4-(trifluoromethyl)phenyl)non-2-en-1-ol (**9a**). *Step 1*: To a flame-dried, round-bottomed flask, under an argon atmosphere, added 1-octyne (6.5 mL, 44 mmol) and ether (120 mL). Placed in a dry ice/acetone bath and let stir for approximately 10 minutes. Added a 1.6M hexanes solution of *n*-butyllithium (24 mL, 38 mmol) dropwise and let stir at –78 °C for 30 minutes. Added, at –78 °C, a solution of α,α,α-trifluoro-*p*-tolualdehyde (4 mL, 30 mmol) and ether (30 mL) dropwise. Let stir at –78 °C for 1 hour, then removed dry ice/acetone bath and let slowly warm to room temperature. Quenched by slowly adding 100 mL aqueous NH_4Cl solution, extracted 3 times with 100 mL ether, and dried with Na_2SO_4. Purified via silica gel chromatography (7:3 pentane:ether) to obtain 8.7 g of 1-(4-(trifluoromethyl)-phenyl)non-2-yn-1-ol as a pale yellow oil (99% yield, contained a very small amount of 1-octyne). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 7.65 (4H, m), 5.51 (1H, d, *J* = 6.0 Hz), 2.28 (2H, td, *J* = 7.1, 1.9 Hz), 2.28 (1H, br), 1.4 (8H, m), 0.90 (3H, t, *J* = 6.9 Hz). ^{13}C NMR (300 MHz, $CDCl_3$, ppm): δ 145.2, 133.9 (q, *J* = 129 Hz), 127.1, 125.7, (q, *J* = 15.0 Hz), 124.3 (q, *J* = 1082 Hz), 88.7, 79.5, 64.4, 31.5, 28.8, 28.7, 22.7, 19.0, 14.2. HRMS (EI) calcd. for $C_{16}H_{19}F_3O$: 284.1388, found: 284.1390. *Step 2*: To a flame-dried, round-bottomed flask, under an argon atmosphere, added 1-(4-(trifluoromethyl)-phenyl)non-2-yn-1-one (see **49**, Step 2, 1.88 g, 6.66 mmol) and THF (50 mL). Placed in an ice bath and added a 1.0M THF solution of lithium aluminum hydride (20 mL, 20 mmol) dropwise. Immediately removed ice bath and let

stir at room temperature for 84 hours. Placed in an ice bath and let stir for approximately 10 minutes, then slowly added 30 mL EtOAc and a few scoops of $Na_2SO_4 \bullet 10H_2O$. Removed ice bath and let stir at room temperature for approximately 20 minutes. Filtered through Celite, rinsing with ether. Purified via silica gel chromatography (7:3 pentane:ether) to obtain 1.4 g of **9a** as a yellow oil (73% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 7.61 (2H, d, *J* = 8.4 Hz), 7.50 (2H, d, *J* = 8.1 Hz), 5.81 (1H, dt, *J* = 15.3, 6.7 Hz), 5.62 (1H, ddt, *J* = 15.3, 6.9, 1.4 Hz), 5.23 (1H, dd, *J* = 6.9, 3.0 Hz), 2.07 (2H, dt, *J* = 6.9 Hz), 1.95 (1H, d, *J* = 3.3 Hz), 1.3 (8H, m), 0.89 (3H, t, *J* = 6.8 Hz). ^{13}C NMR (300 MHz, $CDCl_3$, ppm): δ 147.4 (d, *J* = 4.5 Hz), 134.2, 131.9, 129.8 (q, *J* = 129 Hz), 126.6, 125.5 (q, *J* = 15.0 Hz), 124.4, (q, *J* = 1081 Hz), 74.9, 32.4, 31.8, 29.1, 29.0, 22.8, 14.2. HRMS (EI) calcd. for $C_{16}H_{21}F_3O$: 286.1544, found: 286.1552.

(*E*)-1-(4-methoxyphenyl)non-2-en-1-ol (**9b**). Followed procedure given for **9a**, with: *Step 1*: 10 mL (67.7 mmol) 1-octyne, 31 mL (49.6 mmol) *n*-butyllithium (1.6M in hexanes), 5 mL (41.2 mmol) *p*-anisaldehyde, and 60 mL ether. Purified via silica gel chromatography (8:2 pentane:ether) to obtain 9.96 g of 1-(4-methoxyphenyl)non-2-yn-1-ol[26] as a light yellow oil (98% yield). *Step 2*: 3 mL (13 mmol) 1-(4-methoxyphenyl)non-2-yn-1-ol, 39 mL (39 mmol) lithium aluminum hydride (1.0M in THF), 100 mL THF, and a reaction time of 68 hours. Purified via silica gel chromatography (8:2 pentane:ether) to obtain 2.35 g of **9b** as an oil (73% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 7.30 (2H, d, *J* = 8.7 Hz), 6.89 (2H, d, *J* = 8.7 Hz), 5.71 (2H, m), 5.13 (1H, dd, *J* = 5.9, 3.2 Hz), 3.81 (3H, s), 2.06 (2H, dt, *J* = 6.7, 6.7 Hz), 1.86 (1H, br), 1.34 (8H, m), 0.89 (3H, t, *J* = 6.8 Hz). ^{13}C NMR (300 MHz, $CDCl_3$, ppm): δ 159.2, 135.9, 132.7,

132.5, 127.7, 114.0, 75.0, 55.5, 32.4, 31.9, 29.3, 29.1, 22.8, 14.3. HRMS (EI) calcd. for $C_{16}H_{24}O_2$: 248.1776, found: 248.1787.

(*E*)-1-(4-(trifluoromethyl)phenyl)non-1-en-3-ol (**10a**). Followed procedure given for **3**, with 114.6 mg (0.4 mmol) **9a**, 6 mg (0.012 mmol) **1**, 2 mL ether, a reaction temperature of –50 °C, and a reaction time of 1 hour. Purified via silica gel chromatography (8:2 pentane:ether) to obtain 112.9 mg of **10a** as an oil (98% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 7.57 (2H, d, *J* = 8.4 Hz), 7.47 (2H, d, *J* = 8.4 Hz), 6.62 (1H, d, *J* = 15.9 Hz), 6.33 (1H, dd, *J* = 15.9, 6.0 Hz), 4.32 (1H, dt, *J* = 6.2, 6.2 Hz), 1.79 (1H, br), 1.65 (2H, m), 1.35 (8H, m), 0.90 (3H, t, *J* = 7.1 Hz). ^{13}C NMR (300 MHz, $CDCl_3$, ppm): δ 140.5 (d, *J* = 5.4 Hz), 135.5, 129.6 (q, *J* = 129 Hz), 128.8, 126.8, 125.7 (q, *J* = 15.4 Hz), 124.4, (q, *J* = 1081 Hz), 72.9, 37.6, 32.0, 29.4, 25.6, 22.8, 14.3. HRMS (EI) calcd. for $C_{16}H_{21}F_3O$: 286.1544, found: 286.1537.

(*E*)-1-(4-methoxyphenyl)non-1-en-3-ol (**10b**). Followed procedure given for **3**, with 99.2 mg (0.4 mmol) **9b**, 4 mg (0.008 mmol) **1**, 2 mL ether, a reaction temperature of –50 °C, and a reaction time of 30 minutes. Purified via silica gel chromatography (8:2 pentane:ether) to obtain 67.5 mg of **10b** as an oil (68% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 7.32 (2H, d, *J* = 8.4 Hz), 6.86 (2H, d, *J* = 9.0 Hz), 6.51 (1H, d, *J* = 15.9 Hz), 6.09 (1H, dd, *J* = 16.1, 7.1 Hz), 4.25 (1H, dt, *J* = 6.6, 6.6 Hz), 3.81 (3H, s), 1.74 (1H, br), 1.5 (10H, m), 0.90 (3H, t, *J* = 6.8 Hz). ^{13}C NMR (300 MHz, $CDCl_3$, ppm): δ 159.4, 130.7, 130.0, 129.7, 127.8, 114.2, 73.5, 55.5, 37.6, 32.0, 29.4, 25.6, 22.8, 14.3. HRMS (EI) calcd. for $C_{16}H_{24}O_2$: 248.1776, found: 248.1768.

(*Z*)-1-(4-nitrophenyl)non-2-en-1-ol (**11**). *Step 1*: Followed procedure given for **9a** (Step 1), with 27 mL (183 mmol) 1-octyne, 100 mL (160 mmol) *n*-butyllithium (1.6M in hexanes), 18.6 g (123 mmol) 4-nitrobenzaldehyde, and 300 mL THF. Purified via silica gel chromatography (8:2 pentane:ether) to obtain 29 g of 1-(4-nitrophenyl)non-2-yn-1-ol as a red oil (90% yield). Dissolved in hexanes and kept under vacuum (ca. 0.03 torr) overnight to isolate this product as an orange solid. ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 8.23 (2H, d, *J* = 8.7 Hz), 7.72 (2H, dd, *J* = 8.9, 0.5 Hz), 5.55 (1H, d, *J* = 5.1 Hz), 2.36 (1H, d, *J* = 5.7 Hz), 2.27 (2H, td, *J* = 7.1, 2.1 Hz), 1.5 (2H, m), 1.31 (6H, m), 0.89 (3H, t, *J* = 6.9 Hz). ^{13}C NMR (300 MHz, $CDCl_3$, ppm): δ 148.3, 147.8, 127.5, 123.9, 89.2, 79.1, 64.0, 31.4, 28.7, 28.6, 22.7, 19.0, 14.2. HRMS (EI) calcd. for $C_{15}H_{19}NO_3$: 261.1365, found: 261.1350. *Step 2*: To a round-bottomed flask, added 1-(4-nitrophenyl)non-2-yn-1-ol (784 mg, 3.0 mmol), Lindlar catalyst (5% Pd on $CaCO_3$, poisoned with Pb, 30 mg), and EtOAc (30 mL). Evacuated flask (aspirator vacuum) and placed under a H_2 atmosphere, stirring at 1000 rpm at room temperature. Kept under static H_2 atmosphere and stopped reaction by evacuating flask after a little over 1 equivalent of H_2 had been consumed (monitored by displacement of water in an attached buret, took approximately 1 hour). Filtered through Celite, rinsing with EtOAc, and purified via silica gel chromatography (8:2 pentane:ether) to obtain 789 mg of **11** as an orange oil (99% yield, *Z*:*E* > 20:1 by ^{1}H NMR). ^{1}H NMR (300 MHz, C_6D_6, ppm): δ 7.88 (2H, dt, *J* = 9.0, 2.2 Hz), 7.09 (2H, dtd, *J* = 9.0, 2.2, 0.9 Hz), 5.31 (2H, m), 5.16 (1H, dd, *J* = 7.7, 2.3 Hz), 1.9 (2H, m), 1.25 (1H, br), 1.25 (8H, m), 0.90 (3H, t, *J* = 6.8 Hz). ^{13}C NMR (300 MHz, C_6D_6, ppm): δ 151.0, 147.4, 132.9, 131.6, 126.6, 123.6, 68.7, 32.0, 29.8, 29.2, 27.9, 23.0, 14.3. HRMS (EI) calcd. for $C_{15}H_{21}NO_3$: 263.1521, found: 263.1522.

(*E*)-1-(4-nitrophenyl)non-1-en-3-ol (**12**). Followed procedure given for **3**, with 105.2 mg (0.4 mmol) **11**, 4 mg (0.008 mmol) **1**, 2 mL ether, a reaction temperature of 0 °C, and a reaction time of 30 min. Purified via silica gel chromatography (8:2 pentane:ether) to obtain 98.5 mg of **12** as a yellow oil (94% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 8.16 (2H, dt, *J* = 9.0, 2.3 Hz), 7.49 (2H, dt, *J* = 9.0, 2.3 Hz), 6.66 (1H, d, *J* = 15.9 Hz), 6.42 (1H, dd, *J* = 16.1, 6.2 Hz), 4.34 (1H, dtd, *J* = 6.3, 6.3, 1.0 Hz), 1.90 (1H, br), 1.46 (10H, m), 0.88 (3H, t, *J* = 6.8 Hz). ^{13}C NMR (300 MHz, $CDCl_3$, ppm): δ 147.0, 143.6, 137.8, 127.8, 127.1, 124.2, 72.7, 37.5, 31.9, 29.4, 25.5, 22.8, 14.2. HRMS (EI) calcd. for $C_{15}H_{21}NO_3$: 263.1521, found: 263.1517.

(*E*)-1-(thiophen-2-yl)non-2-en-1-ol (**13**). Followed procedure given for **9a**, with: *Step 1*: 5 mL (34 mmol) 1-octyne, 16 mL (26 mmol) *n*-butyllithium (1.6M in hexanes), 2 mL (22 mmol) 2-thiophene-carboxaldehyde, and 30 mL ether. Purified via silica gel chromatography (8:2 pentane:ether) to obtain 3.4 g (69% yield) of 1-(thiophen-2-yl)non-2-yn-1-ol[27] as a bright yellow oil (contained ca. 15% 2-thiophene-carboxaldehyde). *Step 2*: 3.4 g (15.3 mmol) 1-(thiophen-2-yl)non-2-yn-1-ol, 50 mL (50 mmol) lithium aluminum hydride (1.0M in THF), 120 mL THF, and a reaction time of 28 hours. Purified via silica gel chromatography (8:2 pentane:ether) to obtain 2.3 g of **13** as a yellow oil (67% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 7.26 (1H, m), 6.98 (2H, m), 5.80 (2H, m), 5.39 (1H, m), 2.08 (3H, m), 1.34 (8H, m), 0.89 (3H, t, *J* = 6.9 Hz). ^{13}C NMR (300 MHz, $CDCl_3$, ppm): δ 147.9, 133.7, 131.6, 126.9, 125.2, 124.2, 71.3, 32.3, 31.9, 29.1, 29.0, 22.8, 14.3. HRMS (EI) calcd. for $C_{13}H_{20}OS$: 224.1235, found: 224.1233.

(*E*)-1-(thiophen-2-yl)non-1-en-3-ol (**14**). Followed procedure given for **3**, with 89.9 mg (0.4 mmol) **13**, 4 mg (0.008 mmol) **1**, 2 mL ether, a reaction temperature of –50 °C, and a reaction time of 15 minutes. Purified via silica gel chromatography (8:2 pentane:ether) to obtain 82.9 mg of **14** as an oil (92% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 7.16 (1H, m), 6.96 (2H, m), 6.71 (1H, dd, *J* = 15.8, 0.8 Hz), 6.07 (1H, dd, *J* = 15.9, 6.6 Hz), 4.24 (1H, dt, *J* = 6.6, 6.6 Hz), 1.76 (1H, br), 1.6 (2H, m), 1.35 (8H, m), 0.90 (3H, t, *J* = 6.8 Hz). ^{13}C NMR (300 MHz, $CDCl_3$, ppm): δ 142.1, 132.5, 127.5, 125.9, 124.4, 123.5, 73.0, 37.5, 32.0, 29.4, 25.6, 22.8, 14.3. HRMS (EI) calcd. for $C_{13}H_{20}OS$: 224.1235, found: 224.1229.

(*E*)-1-(1-tosyl-1*H*-indol-3-yl)non-2-en-1-ol (**15**). Followed procedure given for **9a** (Step 1), with 1 mL (5.9 mmol) (*E*)-1-iodooct-1-ene,[28] 3.0 mL (4.8 mmol) *n*-butyllithium (1.6M in hexanes), 1.2 g (4.0 mmol) 1-tosyl-1*H*-indole-3-carbaldehyde,[29] and 20 mL THF. Purified via silica gel chromatography (6:4 pentane:ether) to obtain 500.8 mg of **15** as a sticky yellow substance (30% yield). **15** decomposed if not used within ca. 1 week. ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 7.98 (1H, d, *J* = 8.1 Hz), 7.78 (2H, d, *J* = 8.4 Hz), 7.62 (1H, d, *J* = 7.8 Hz), 7.53 (1H, d, *J* = 0.9 Hz), 7.3 (4H, m), 5.8 (2H, m), 5.39 (1H, m), 2.35 (3H, s), 2.08 (2H, dt, *J* = 6.7, 6.7 Hz), 1.84 (1H, d, *J* = 4.2 Hz), 1.35 (8H, m), 0.89 (3H, t, *J* = 7.2 Hz). ^{13}C NMR (300 MHz, $CDCl_3$, ppm): δ 145.1, 135.8, 135.5, 134.4, 130.7, 130.1, 129.2, 127.1, 125.02, 124.97, 123.3, 123.1, 120.8, 113.9, 69.3, 32.4, 31.9, 29.2, 29.1, 22.8, 21.8, 14.3. HRMS (EI) calcd. for $C_{24}H_{29}NO_3S$: 411.1868, found: 411.1864.

(*E*)-1-(1-tosyl-1*H*-indol-3-yl)non-1-en-3-ol (**16**). Followed procedure given for **3**, with 82.2 mg (0.2 mmol) **15**, 2 mg (0.004 mmol) **1**, 1 mL ether, a reaction temperature of –50 °C, and a reaction time of 30 minutes. Purified via silica gel chromatography (6:4 pentane:ether) to obtain 54.3 mg of **16** as a yellow oil (66% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 7.69 (1H, d, *J* = 8.1 Hz), 7.4 (3H, m), 6.95 (3H, m), 6.82 (2H, d, *J* = 7.8 Hz), 6.32 (1H, d, *J* = 16.2 Hz), 5.99 (1H, dd, *J* = 16.1, 6.8 Hz), 3.98 (1H, dt, *J* = 6.2, 6.2 Hz), 1.95 (3H, s) 1.95 (1H, br), 1.2 (10H, m), 0.57 (3H, t, *J* = 6.8 Hz). ^{13}C NMR (300 MHz, $CDCl_3$, ppm): δ 145.1, 135.6, 135.1, 134.2, 130.0, 129.1, 126.9, 125.0, 124.0, 123.6, 120.7, 120.5, 120.2, 113.8, 73.4, 37.6, 31.9, 29.4, 25.6, 22.7, 21.6, 14.2. HRMS (FAB) calcd. for $C_{24}H_{29}NO_3S$: 411.1868, found: 411.1852.

(*E*)-1-(furan-2-yl)non-2-en-1-ol (**17**). Followed procedure given for **9a** (Step 1), with 2 g (8.4 mmol) (*E*)-1-iodooct-1-ene,[28] 4.5 mL (7.2 mmol) *n*-butyllithium (1.6M in hexanes), 0.5 mL (6.0 mmol) 2-furaldehyde, and 30 mL ether. Purified via silica gel chromatography (7:3 pentane:ether) to obtain 1.19 g of **17**:furaldehyde = 8:1 as a bright yellow oil (90% yield). Re-purified via silica gel chromatography (8:2 pentane:ether) to obtain 814 mg of pure **17** as a yellow-orange oil (65% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 7.40 (1H, dd, *J* = 2.0, 0.8 Hz), 6.34 (1H, dd, *J* = 3.0, 1.8 Hz), 6.24 (1H, dt, *J* = 3.6, 0.8 Hz), 5.8 (2H, m), 5.18 (1H, t, *J* = 5.3 Hz), 2.10 (2H, dt, *J* = 6.3, 6.3 Hz), 1.96 (1H, d, *J* = 4.8 Hz), 1.35 (8H, m), 0.89 (3H, t, *J* = 6.8 Hz). ^{13}C NMR (300 MHz, $CDCl_3$, ppm): δ 155.9, 142.5, 134.6, 128.7, 110.4, 106.5, 68.9, 32.4, 31.9, 29.13, 29.06, 22.8, 14.3.

1-(Thiophen-2-yl)prop-2-en-1-ol (**18**). To a flame-dried, round-bottomed flask, under an argon atmosphere, added 2-thiophene-carboxaldehyde (5 mL, 54.5 mmol) and ether (100 mL). Placed in an ice bath and added a 1.0M THF solution of vinylmagnesium bromide (100 mL, 100 mmol) dropwise. Removed ice bath shortly thereafter and let stir at room temperature for 2 hours. Slowly added 100 mL aqueous NH_4Cl solution, extracted 3 times with 100 mL ether, and dried with Na_2SO_4. Purified via silica gel chromatography (7:3 pentane:ether) to obtain ca. 7 g of **18** as a yellow oil (92% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 7.55 (1H, m), 7.27 (2H, m), 6.41 (1H, ddd, *J* = 17.2, 10.3, 5.9 Hz), 5.7 (2H, m), 5.53 (1H, dt, *J* = 10.5, 1.2 Hz), 2.47 (1H, br). ^{13}C NMR (300 MHz, $CDCl_3$, ppm): δ 146.8, 139.5, 127.0, 125.5, 124.6, 116.0, 71.2. HRMS (EI) calcd. for C_7H_8OS: 140.0296, found: 140.0291.

(*E*)-3-(thiophen-2-yl)prop-2-en-1-ol (**19**). Followed procedure for **3**, with 112.2 mg (0.8 mmol) **18**, 8 mg (0.016 mmol) **1**, 4 mL THF, a reaction temperature of –50 °C, and a reaction time of 30 min. Purified via silica gel chromatography (7:3 pentane:ether) to obtain 78.2 mg of **19** as an oil (70% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 7.16 (1H, m), 6.96 (2H, m), 6.74 (1H, d, *J* = 15.6 Hz), 6.20 (1H, dt, *J* = 15.6, 5.8 Hz), 4.26 (*E*-isomer, 1.93H, dd, *J* = 5.7, 1.2 Hz), 3.64 (*Z*-isomer, 0.067H, d, *J* = 6.9 Hz), 2.16 (1H, br). ^{13}C NMR (300 MHz, $CDCl_3$, ppm): δ 141.9, 128.3, 127.5, 126.0, 124.5, 124.4, 63.4. HRMS (EI) calcd. for C_7H_8OS: 140.0296, found: 140.0288.

1-(1-Tosyl-1*H*-indol-3-yl)prop-2-en-1-ol (**20**). Followed procedure given for **18**, with 8 g (27 mmol) 1-tosyl-1*H*-indole-3-carbaldehyde,[29] 100 mL (100 mmol) vinylmagnesium

bromide (1.0M in THF), and 50 mL THF. Purified via silica gel chromatography (1:1 pentane:ether) and recrystallized purified material from MeOH to obtain 4.5 g of **20** as a fine white powder (51% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 7.98 (1H, d, *J* = 8.1 Hz), 7.78 (2H, d, *J* = 8.1 Hz), 7.65 (1H, d, *J* = 7.8 Hz), 7.54 (1H, s), 7.33 (1H, t, *J* = 7.2 Hz), 7.24 (3H, m), 6.17 (1H, m), 5.45 (1H, m), 5.45 (1H, d, *J* = 16.8 Hz), 5.30 (1H, d, *J* = 10.5 Hz), 2.35 (3H, s), 1.93 (1H, d, *J* = 3.9 Hz). ^{13}C NMR (300 MHz, $CDCl_3$, ppm): δ 145.2, 138.8, 135.8, 135.5, 130.1, 129.0, 127.1, 125.1, 124.2, 123.5, 123.4, 120.7, 116.6, 113.9, 69.1, 21.8. HRMS (FAB) calcd. for $C_{18}H_{17}NO_3S$: 327.0929, found: 327.0940.

(*E*)-3-(1-tosyl-1*H*-indol-3-yl)prop-2-en-1-ol (**21**). Followed procedure given for **3**, with 131 mg (0.4 mmol) **20**, 3 mg (0.006 mmol) **1**, 2 mL THF, a reaction temperature of –50 °C, and a reaction time of 10 minutes. Purified via silica gel chromatography (2:1 pentane:ether) to obtain 72.9 mg of **21** as a fluffy white solid (56% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 8.00 (1H, d, *J* = 8.1 Hz), 7.74 (3H, m), 7.59 (1H, s), 7.30 (2H, m), 7.19 (2H, d, *J* = 8.1 Hz), 6.68 (1H, dd, *J* = 16.1, 0.8 Hz), 6.44 (1H, dt, *J* = 16.2, 5.6 Hz), 4.35 (2H, dd, *J* = 5.7, 1.2 Hz), 2.31 (3H, s), 1.83 (1H, br). ^{13}C NMR (300 MHz, $CDCl_3$, ppm): δ 145.2, 135.7, 135.2, 130.1, 130.0, 129.2, 127.0, 125.1, 124.2, 123.7, 121.8, 120.5, 120.2, 113.9, 64.0, 21.7. HRMS (FAB) calcd. for $C_{18}H_{17}NO_3S$: 327.0929, found: 327.0933.

1-(Furan-2-yl)prop-2-en-1-ol (**22**). Followed procedure given for **18**, with 2 mL (24 mmol) 2-furaldehyde, 50 mL (50 mmol) vinylmagnesium bromide (1.0M in THF), and

50 mL ether. Purified via silica gel chromatography (7:3 pentane:ether) to obtain 2.7 g of **22** as a yellow oil (91% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 7.41 (1H, m), 6.35 (1H, m), 6.26 (1H, d, *J* = 3.0 Hz), 6.13 (1H, ddd, *J* = 17.2, 10.3, 5.8 Hz), 5.43 (1H, dt, *J* = 17.4, 1.3 Hz), 5.30 (1H, dt, *J* = 10.5, 1.2 Hz), 5.23 (1H, t, *J* = 4.8 Hz), 2.17 (1H, d, *J* = 4.8 Hz). ^{13}C NMR (300 MHz, $CDCl_3$, ppm): δ 155.2, 142.7, 137.0, 116.7, 110.5, 106.9, 68.8. HRMS (EI) calcd. for $C_7H_8O_2$: 124.0524, found: 124.0529.

1-(1-((2-(Trimethylsilyl)ethoxy)methyl)-1*H*-indol-3-yl)prop-2-en-1-ol (**23**). *Step 1*: To a flame-dried, round-bottomed flask, under an argon atmosphere, added 60% sodium hydride (1.4 g, 35 mmol) and THF (60 mL). Placed in an ice bath and let stir for approximately 10 minutes. Added indole-3-carboxaldehyde (5 g, 34 mmol), as a solid, in portions. Removed ice bath shortly thereafter and let stir at room temperature for 1 hour. Reaction initially looked like a strawberry smoothie. It became red and less cloudy over time. After the hour had passed, returned to the ice bath and let stir for approximately 10 minutes. Added 2-(trimethylsilyl)ethoxymethyl chloride (6 mL, 34 mmol) in portions. Reaction immediately turned cloudy and tan. Removed ice bath shortly after completing the addition, then let stir at room temperature for 3 hours. Added 60 mL aqueous $NaHCO_3$ solution, extracted 3 times with 70 mL ether, and dried with Na_2SO_4. Purified via silica gel chromatography (1:1 pentane:ether) to obtain 10.1 g of 1-((2-(trimethylsilyl)ethoxy)methyl)-1*H*-indole-3-carbaldehyde as an orange oil. ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 10.06 (1H, s), 8.31 (1H, m), 7.80 (1H, s), 7.55 (1H, m), 7.36 (2H, m), 5.58 (2H, s), 3.55 (2H, t), 0.90 (2H, t), 0.00 (9H, s). ^{13}C NMR (300 MHz, $CDCl_3$, ppm): δ 185.1, 138.3, 137.4, 125.8, 124.6, 123.6, 122.3, 119.2, 110.9, 76.7, 66.8,

17.9, –1.3. HRMS (FAB) calcd. for $C_{15}H_{21}NO_2Si$ + H: 276.1420, found: 276.1419. *Step 2*: Followed procedure given for **18**, with 10 g (36 mmol) 1-((2-(trimethylsilyl)-ethoxy)methyl)-1*H*-indole-3-carbaldehyde, 100 mL (100 mmol) vinylmagnesium bromide (1.0M in THF), and 100 mL ether. Purified via silica gel chromatography (1:1 pentane:ether) to obtain 6.8 g of **23** as a yellow oil (62% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 7.76 (1H, dt, *J* = 7.8, 0.9 Hz), 7.49 (1H, dt, *J* = 8.4, 0.9 Hz), 7.27 (1H, m), 7.18 (2H, m), 6.27 (1H, ddd, *J* = 17.1, 10.2, 5.7 Hz), 5.55 (1H, m), 5.48 (1H, dt, *J* = 17.4, 1.4 Hz), 5.46 (2H, s), 5.27 (1H, dt, *J* = 10.2, 1.5 Hz), 3.50 (2H, dd, *J* = 9.3, 6.9 Hz), 1.93 (1H, d, *J* = 4.5 Hz), 0.90 (2H, dd, *J* = 8.1, 8.1 Hz), –0.04 (9H, s). ^{13}C NMR (300 MHz, $CDCl_3$, ppm): δ 139.9, 137.4, 127.1, 125.9, 122.8, 120.4, 120.1, 118.2, 115.1, 110.4, 75.8, 69.2, 66.1, 17.9, –1.2. HRMS (EI) calcd. for $C_{17}H_{25}NO_2Si$: 303.1655, found: 303.1664.

(*E*)-methyl 4-hydroxybut-2-enoate (**24**).[30] *Step 1*: To a flame-dried, round-bottomed flask, under an argon atmosphere, added, via cannula transfer, a solution of $RuCl_2(PCy_3)(H_2IMes)CHPh$ (100 mg, 0.12 mmol) and CH_2Cl_2 (30 mL). Added (*Z*)-2,2,3,3,10,10,11,11-octamethyl-4,9-dioxa-3,10-disiladodec-6-ene (2 mL, 6.2 mmol) and methyl acrylate (2.2 mL, 24.4 mmol) via syringe. Placed in a 45 °C oil bath and let stir overnight. Concentrated *in vacuo* and purified directly via silica gel chromatography (19:1 hexanes:ethyl acetate) to obtain (*E*)-methyl 4-(*tert*-butyldimethylsilyloxy)but-2-enoate as a brown oil (contained impurities, < 43% yield, based on the 57% recovered (*Z*)-2,2,3,3,10,10,11,11-octamethyl-4,9-dioxa-3,10-disiladodec-6-ene). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 7.02 (1H, dt), 6.12 (1H, dt), 4.35 (2H, dd), 3.75 (3H, s), 0.91 (9H,

s), 0.09 (6H, s). *Step 2*: To a flame-dried, round-bottomed flask, under an argon atmosphere, added (*E*)-methyl 4-(*tert*-butyldimethylsilyloxy)but-2-enoate (ca. 1.2 g, 5.2 mmol), a 1.0M THF solution of tetrabutylammonium fluoride (6.2 mL, 6.2 mmol), and THF (45 mL). Let stir at room temperature for 1 hour. Added 40 mL aqueous NH_4Cl solution, extracted 3 times with 50 mL ether, and dried with Na_2SO_4. Purified via silica gel chromatography (1:1 pentane:ether) to obtain 341 mg of **24** as a clear, colorless oil (56% yield).

2-Cyclohexylbut-3-en-2-ol (**25**). To a flame-dried, round-bottomed flask, under an argon atmosphere, added cyclohexyl methyl ketone (9 mL, 70 mmol) and ether (100 mL). Placed in an ice bath and let stir for approximately 15 minutes. Added a 1.0M THF solution of vinylmagnesium bromide (100 mL, 100 mmol) dropwise. Let sir for 30 minutes at 0 °C, then removed ice bath and let stir for 1 hour at room temperature. Placed in an ice bath, slowly added 100 mL aqueous NH_4Cl solution, extracted 3 times with 100 mL ether, and dried with Na_2SO_4. Purified via silica gel chromatography (8:2 pentane:ether) to obtain 8.0 g of **25**:1,3-dicyclohexyl-3-hydroxybutan-1-one (the self-aldol product) = 7.7:1 as a slightly yellow liquid. Transferred to a round-bottomed flask, added a 3.0M aqueous solution of NaOH (17 mL, 51 mmol), THF (100 mL), and MeOH (20 mL). Let stir at room temperature overnight. Added aqueous NH_4Cl solution, extracted 3 times with 60 mL ether, and dried with Na_2SO_4. Purified via silica gel chromatography (9:1 to 8:2 pentane:ether) to obtain 4.3 g of **25** as an oil (40% yield). ^1H NMR (300 MHz, $CDCl_3$, ppm): δ 7.55 (2H, m), 7.40 (2H, m), 7.30 (1H, m), 6.22 (1H, dd, J = 17.3, 10.7 Hz), 5.34 (1H, dd, J = 17.4, 1.2 Hz), 5.19 (1H, dd, J = 10.8, 1.1 Hz),

1.93 (1H, br), 1.70 (3H, s). ^{13}C NMR (300 MHz, $CDCl_3$, ppm): δ 146.6, 145.1, 128.5, 127.2, 125.4, 112.6, 75.0, 29.6. HRMS (EI) calcd. for $C_{10}H_{18}O$: 154.1358, found: 154.1353.

(*E*)-3-cyclohexylbut-2-en-1-ol (**26**). In glove box, added **1** (4 mg, 0.008 mmol) to 4-mL vial. Removed from glove box, added ether (2 mL) and *N*,*O*-bis(trimethylsilyl)-acetamide (120 μL, 0.485 mmol). Placed in an ice bath and let stir for approximately 10 minutes. Added **25** (61.9 mg, 0.4 mmol) via syringe and let stir at 0 °C for 30 minutes. Removed from ice bath, immediately added 20 μL triethylamine, and removed solvent *in vacuo*. Added anhydrous MeOH (2 mL) and K_2CO_3 (110 mg, 0.8 mmol), then let stir at room temperature for 1 hour. Added 2 mL aqueous NH_4Cl solution, extracted several times with CH_2Cl_2, and dried with Na_2SO_4. Purified via silica gel chromatography (8:2 pentane:ether) to obtain 55.1 mg of **26** as an oil (89% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 5.38 (1H, t, J = 6.8 Hz), 4.15 (2H, d, J = 6.6 Hz), 1.7 (7H, m), 1.64 (3H, s), 1.2 (5H, m). ^{13}C NMR (300 MHz, $CDCl_3$, ppm): δ 144.9, 121.7, 59.6, 47.3, 31.9, 26.8, 26.5, 14.8. HRMS (EI) calcd. for $C_{10}H_{18}O$: 154.1358, found: 154.1352.

3,4,4-Trimethylpent-1-en-3-ol (**27**). Followed procedure given for **25**, with 6.5 mL (52.2 mmol) pinacolone, 100 mL (100 mmol) vinylmagnesium bromide (1.0M in THF), and 100 mL ether; then 12 mL (36 mmol) 3.0M aqueous NaOH solution, 100 mL THF, and 20 mL MeOH. Purified via silica gel chromatography (9:1 pentane:ether) to obtain 2.66 g of **27** as a yellow oil (40% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 6.09 (1H, dd, J = 17.6, 10.7 Hz), 5.23 (1H, dd, J = 17.4, 1.5 Hz), 5.09 (1H, dd, J = 11.0, 1.7 Hz), 1.41

(1H, br), 1.25 (3H, s), 0.95 (9H, s). ^{13}C NMR (300 MHz, $CDCl_3$, ppm): δ 143.5, 112.5, 77.5, 37.4, 25.5, 23.5. HRMS (EI) calcd. for $C_8H_{16}O$: 128.1201, found: 128.1196.

(*E*)-3,4,4-trimethylpent-2-en-1-ol (**28**). Followed procedure given for **26**, with 205 mg (1.6 mmol) **27**, 470 μL (1.9 mmol) *N*,*O*-bis(trimethylsilyl)-acetamide, 41 mg (0.08 mmol) **1**, 8 mL ether, a reaction temperature of 0 °C, and a reaction time of 50 minutes; then 442 mg (3.2 mmol) K_2CO_3 and 8 mL anhydrous MeOH. Purified via silica gel chromatography (8:2 pentane:ether) to obtain 162 mg of **28** as an oil (79% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 5.45 (1H, tq, *J* = 6.5, 1.1 Hz), 4.19 (2H, dd, *J* = 6.5, 0.8 Hz), 1.66 (3H, m), 1.45 (1H, br), 1.05 (9H, s). ^{13}C NMR (300 MHz, $CDCl_3$, ppm): δ 147.3, 120.6, 60.2, 36.3, 29.0, 13.0. HRMS (EI) calcd. for $C_8H_{16}O$: 128.1201, found: 128.1207.

3-Methylhept-1-en-3-ol (**29**). Followed procedure given for **25**, with 6.5 mL (53 mmol) 2-hexanone, 100 mL (100 mmol) vinylmagnesium bromide (1.0M in THF), and 100 mL ether; then 13 mL (39 mmol) 3.0M aqueous NaOH solution, 100 mL THF, and 20 mL MeOH. Purified via silica gel chromatography (8:2 pentane:ether) to obtain 4.51 g of **29** as a yellow oil (67% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 5.93 (1H, dd, *J* = 17.3, 10.7 Hz), 5.21 (1H, dd, *J* = 17.4, 1.2 Hz), 5.05 (1H, dd, *J* = 10.7, 1.4 Hz), 1.55 (2H, m), 1.45 (1H, br), 1.3 (4H, m), 1.28 (3H, s), 0.91 (3H, t, *J* = 6.9 Hz). ^{13}C NMR (300 MHz, $CDCl_3$, ppm): δ 145.5, 111.7, 73.5, 42.3, 27.9, 26.3, 23.3, 14.3. HRMS (EI) calcd. for $C_8H_{16}O$: 128.1201, found: 128.1204.

3-Methylhept-2-en-1-ol (**30**). Followed procedure given for **26**, with 513 mg (4.0 mmol) **29**, 1.185 mL (4.794 mmol) *N*,*O*-bis(trimethylsilyl)-acetamide, 41 mg (0.08 mmol) **1**, 20 mL ether, a reaction temperature of 0 °C, and a reaction time of 30 minutes; then 1.1 g (7.96 mmol) K_2CO_3 and 20 mL anhydrous MeOH. Purified via silica gel chromatography (7:3 pentane:ether) to obtain 476.7 mg of **30** as an oil (93% yield). (***E*-isomer**): ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 5.40 (1H, td, *J* = 6.9, 0.9 Hz), 4.15 (2H, d, *J* = 6.9 Hz), 2.01 (2H, t, *J* = 7.4 Hz), 1.67 (3H, s), 1.3 (5H, m), 0.90 (3H, t, *J* = 7.1 Hz). ^{13}C NMR (300 MHz, $CDCl_3$, ppm): δ 140.4, 123.3, 59.6, 39.4, 30.1, 22.6, 16.3, 14.2. HRMS (EI) calcd. for $C_8H_{16}O$: 128.1201, found: 128.1195. (***Z*-isomer**): ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 5.42 (1H, tt, *J* = 7.1, 0.8 Hz), 4.13 (2H, dd, *J* = 7.2, 0.9 Hz), 2.08 (2H, t, *J* = 7.4 Hz), 1.74 (3H, dt, *J* = 1.1, 1.1 Hz), 1.35 (5H, m), 0.91 (3H, t, *J* = 7.1 Hz). ^{13}C NMR (300 MHz, $CDCl_3$, ppm): δ 140.8, 124.1, 59.3, 31.9, 30.7, 23.7, 22.8, 14.2. HRMS (EI) calcd. for $C_8H_{16}O$: 128.1201, found: 128.1195.

(*E*)-2,2,3-trimethylundec-4-en-3-ol (**31**). To a flame-dried, round-bottomed flask, under an argon atmosphere, added **27** (1 mL, 8.58 mmol), 1-octene (2.7 mL, 17.2 mmol), and CH_2Cl_2. Then added, via cannula transfer, a solution of $RuCl_2(PCy_3)(H_2IMes)CHPh$ (300 mg, 0.35 mmol) and 5 mL CH_2Cl_2. Placed in a 45 °C oil bath and let stir overnight. Allowed to cool to room temperature, removed solvent *in vacuo*, and purified twice via silica gel chromatography (9:1 pentane:ether; then 7:3 pentane:ether) to obtain 1.07 g of **31** as a yellow-gold oil (59% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 5.67 (1H, d, *J* = 15.6 Hz), 5.59 (1H, dt, *J* = 15.6, 5.9 Hz), 2.05 (2H, dt, *J* = 6.7, 6.7 Hz), 1.57 (1H, br), 1.3 (8H, m), 1.24 (3H, s), 0.94 (9H, s), 0.89 (3H, t, *J* = 7.1 Hz). ^{13}C NMR (300 MHz,

$CDCl_3$, ppm): δ 135.1, 128.8, 77.0, 37.6, 32.7, 31.9, 29.7, 29.1, 25.6, 23.8, 22.9, 14.3. HRMS (EI) calcd. for $C_{14}H_{28}O$ – H: 211.2056, found: 211.2065.

(*E*)-2,2,3-trimethylundec-3-en-5-ol (**32**). Followed procedure given for **26**, with 85.3 mg (0.4 mmol) **31**, 120 μL (0.485 mmol) *N*,*O*-bis(trimethylsilyl)-acetamide, 10 mg (0.02 mmol) **1**, 2 mL ether, a reaction temperature of room temperature, and a reaction time of 24 hours; then 110 mg (0.8 mmol) K_2CO_3 and 2 mL anhydrous MeOH. Purified via silica gel chromatography (9:1 pentane:ether) to obtain 41.4 mg of **32** as a clear oil (49% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 5.23 (1H, dd, *J* = 8.4, 1.2 Hz), 4.37 (1H, m), 1.69 (3H, d, *J* = 0.9 Hz), 1.29 (10H, m), 1.05 (9H, s), 0.89 (3H, t, *J* = 6.8 Hz). ^{13}C NMR (300 MHz, $CDCl_3$, ppm): δ 146.5, 125.2, 69.3, 38.1, 36.3, 32.1, 29.5, 29.2, 25.7, 22.8, 14.3, 13.3. HRMS (EI) calcd. for $C_{14}H_{28}O$: 212.2140, found: 212.2131.

(*E*)-5-methyltridec-6-en-5-ol (**33**). Followed procedure given for **31**, with 1 mL (7.80 mmol) **29**, 2.5 mL (15.9 mmol) 1-octene, 300 mg (0.35 mmol) $RuCl_2(PCy_3)(H_2IMes)CHPh$, and 40 mL CH_2Cl_2. Purified 3 times via silica gel chromatography (9:1 pentane:ether; then 7:3 pentane:ether; then 8:2 pentane:ether) to obtain 913 mg of **33** as a yellow oil (55% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 5.60 (1H, dt, *J* = 15.6, 6.2 Hz), 5.50 (1H, d, *J* = 15.6 Hz), 2.03 (2H, dt, *J* = 6.7, 6.7 Hz), 1.4 (14H, m), 1.26 (3H, s), 0.90 (3H, t, *J* = 6.9 Hz), 0.89 (3H, t, *J* = 6.9 Hz). ^{13}C NMR (300 MHz, $CDCl_3$, ppm): δ 137.2, 128.2, 73.0, 42.8, 32.5, 31.9, 29.6, 29.0, 28.2, 26.5, 23.4, 22.9, 14.3. HRMS (EI) calcd. for $C_{14}H_{28}O$: 212.2140, found: 212.2130.

5-Methyltridec-5-en-7-ol (**34**). Followed procedure given for **26**, with 84.9 mg (0.4 mmol) **33**, 120 μL (0.485 mmol) *N*,*O*-bis(trimethylsilyl)-acetamide, 10 mg (0.02 mmol) **1**, 2 mL ether, a reaction temperature of room temperature, and a reaction time of 30 minutes; then 110 mg (0.8 mmol) K_2CO_3 and 2 mL anhydrous MeOH. Purified via silica gel chromatography (8:2 pentane:ether) to obtain 42.8 mg of **34** as an oil (50% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 5.16 (1H, d, *J* = 9.2 Hz), 4.36 (1H, m), 2.09 (*Z*-isomer, 0.6H, dt, *J* = 7.0, 7.0 Hz), 2.01 (*E*-isomer, 1.4H, t, *J* = 7.1 Hz), 1.72 (*Z*-isomer, 1H, d, *J* = 1.5 Hz), 1.68 (*E*-isomer, 2H, d, *J* = 1.2 Hz), 1.37 (14H, m), 0.92 (6H, m). ^{13}C NMR (300 MHz, $CDCl_3$, ppm): δ 139.6, 139.1, 128.8, 128.1, 68.9, 68.5, 39.5, 38.03, 38.00, 32.2, 32.1, 30.8, 30.1, 29.5, 25.74, 25.67, 23.6, 23.0, 22.85, 22.83, 22.5, 16.7, 14.3, 14.23, 14.19. HRMS (EI) calcd. for $C_{14}H_{28}O$: 212.2140, found: 212.2141.

1-Methylcyclohex-2-enol (**35**).[31] To a flame-dried, round-bottomed flask, under an argon atmosphere, added cyclohex-2-en-1-one (5 mL, 51.6 mmol) and ether (100 mL). Placed in an ice bath and let stir for approximately 10 minutes. Added a 3.0M ether solution of methylmagnesium bromide (34 mL, 102 mmol) dropwise over approximately 20 minutes. Let stir for 2 hours. Did not maintain ice bath. Returned to ice bath, slowly added 100 mL aqueous NH_4Cl solution, extracted 3 times with 100 mL ether, and dried with Na_2SO_4. Purified via silica gel chromatography (7:3 pentane:ether) to obtain 3.66 g of **35** as a yellow oil (63% yield).

3-Methylcyclohex-2-enol (**36**).[32] Followed procedure given for **26**, with 45.0 mg (0.4 mmol) **35**, 120 μL (0.485 mmol) *N*,*O*-bis(trimethylsilyl)-acetamide, 10 mg (0.02 mmol)

1, 2 mL ether, a reaction temperature of room temperature, and a reaction time of 30 hours; then 110 mg (0.8 mmol) K_2CO_3 and 2 mL anhydrous MeOH. Purified via silica gel chromatography (8:2 pentane:ether) to obtain 22.3 mg of **36** as an oil (50% yield).

2-Phenylbut-3-en-2-ol (**37**). Followed procedure given for **25**, with 6 mL (51.4 mmol) acetophenone, 100 mL (100 mmol) vinylmagnesium bromide (1.0M in THF), and 100 mL ether; then 9 mL (27 mmol) 3.0M aqueous NaOH solution, 50 mL THF, and 10 mL MeOH. Purified via silica gel chromatography (8:2 pentane:ether) to obtain 2.23 g of **37** as a yellow oil (29% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 7.55 (2H, m), 7.40 (2H, m), 7.30 (1H, m), 6.22 (1H, dd, *J* = 17.3, 10.7 Hz), 5.34 (1H, dd, *J* = 17.4, 1.2 Hz), 5.19 (1H, dd, *J* = 10.8, 1.1 Hz), 1.93 (1H, br), 1.70 (3H, s). ^{13}C NMR (300 MHz, $CDCl_3$, ppm): δ 146.6, 145.1, 128.5, 127.2, 125.4, 112.6, 75.0, 29.6. HRMS (EI) calcd. for $C_{10}H_{12}O$: 148.0888, found: 148.0885.

3-Phenylbut-2-en-1-ol (**38**). Followed procedure given for **26**, with 59.4 mg (0.4 mmol) **37**, 120 μL (0.485 mmol) *N*,*O*-bis(trimethylsilyl)-acetamide, 4 mg (0.008 mmol) **1**, 2 mL ether, a reaction temperature of –10 °C, and a reaction time of 30 minutes; then 110 mg (0.8 mmol) K_2CO_3 and 2 mL anhydrous MeOH. Purified via silica gel chromatography (8:2 pentane:ether) to obtain 54.4 mg of **38** as an oil (92% yield). (***E*-isomer**): ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 7.45 (2H, m), 7.34 (3H, m), 6.01 (1H, dt, *J* = 6.68, 1.4 Hz), 4.40 (2H, d, *J* = 6.6 Hz), 2.12 (3H, s), 1.74 (1H, br). ^{13}C NMR (300 MHz, $CDCl_3$, ppm): δ 143.0, 138.0, 128.5, 127.5, 126.7, 126.0, 60.1, 16.2. HRMS (EI) calcd. for $C_{10}H_{12}O$: 148.0888, found: 148.0887. (***Z*-isomer**): ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 7.35

(3H, m), 7.21 (2H, m), 5.74 (1H, dt, *J* = 7.05, 1.3 Hz), 4.10 (2H, dd, *J* = 6.9, 1.2 Hz), 2.12 (3H, s), 1.53 (1H, br). ^{13}C NMR (300 MHz, $CDCl_3$, ppm): δ 141.0, 140.4, 128.3, 127.9, 127.4, 126.3, 60.5, 25.5. HRMS (EI) calcd. for $C_{10}H_{12}O$: 148.0888, found: 148.0891.

3-Phenylpent-1-en-3-ol (**39**). Followed procedure given for **25**, with 11 mL (83 mmol) propiophenone, 100 mL (100 mmol) vinylmagnesium bromide (1.0M in THF), and 100 mL ether. Did not perform NaOH treatment. Purified twice via silica gel chromatography (8:2 pentane:ether; then 9:1 pentane:ether) to obtain 8.14 g of **39** as an oil (60% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 7.39 (2H, m), 7.25 (2H, m), 7.18 (1H, m), 6.12 (1H, dd, *J* = 17.3, 10.7 Hz), 5.22 (1H, dd, *J* = 17.3, 1.1 Hz), 5.09 (1H, dd, *J* = 10.8, 1.2 Hz), 1.85 (2H, m), 1.79 (1H, br), 0.77 (3H, t, *J* = 7.4 Hz). ^{13}C NMR (300 MHz, $CDCl_3$, ppm): δ 145.6, 144.3, 128.4, 127.0, 125.6, 112.9, 34.8, 8.1. HRMS (EI) calcd. for $C_{11}H_{14}O$: 162.1045, found: 162.1049.

(*E*)-3-phenylpent-2-en-1-ol (**40**). Followed procedure given for **26**, with 65.1 mg (0.4 mmol) **39**, 120 μL (0.485 mmol) *N*,*O*-bis(trimethylsilyl)-acetamide, 4 mg (0.008 mmol) **1**, 2 mL ether, a reaction temperature of –10 °C, and a reaction time of 30 minutes; then 110 mg (0.8 mmol) K_2CO_3 and 2 mL anhydrous MeOH. Purified via silica gel chromatography (8:2 pentane:ether) to obtain 58.4 mg of **40** as an oil (90% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 7.45 (5H, m), 5.96 (1H, t, *J* = 6.9 Hz), 4.47 (2H, d, *J* = 6.9 Hz), 2.66 (2H, dt, *J* = 7.5, 7.5 Hz), 1.85 (1H, br), 1.11 (3H, t, *J* = 7.5 Hz). The following minor peaks correspond to the *Z*-isomer: δ 7.22 (d), 5.79 (tt, *J* = 6.9, 1.4 Hz), 4.16 (d, *J* = 6.9 Hz), 2.5 (dt). ^{13}C NMR (300 MHz, $CDCl_3$, ppm): δ 145.0, 142.1, 128.5,

127.4, 126.6, 126.4, 59.8, 23.4, 14.1. HRMS (EI) calcd. for $C_{11}H_{14}O$: 162.1045, found: 162.1043.

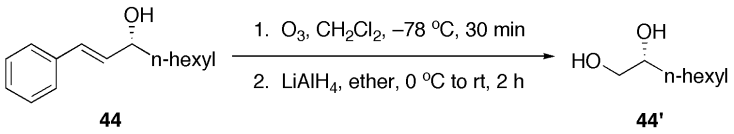
1-Cyclohexylprop-2-en-1-ol (**41**).[33] Followed procedure given for **25**, with 8 mL (66.5 mmol) cyclohexanecarboxaldehyde, 100 mL (100 mmol) vinylmagnesium bromide (1.0M in THF), and 100 mL ether. Did not perform NaOH treatment. Purified via silica gel chromatography (8:2 pentane:ether) to obtain 3.86 g of **41** as a cloudy oil (41% yield).

3-Cyclohexylprop-2-en-1-ol (**42**).[34] Followed procedure given for **3**, with 390 μL (3 mmol) **41**, 31 mg (0.061 mmol) **1**, 15 mL ether, a reaction temperature of room temperature, and a reaction time of 30 min. Purified via silica gel chromatography (6:4 pentane:ether) to obtain 350 mg of **42**:**41** = 1:1.1 as an oil (40% yield).

(*R*,*E*)-1-phenylnon-2-en-1-ol (**43**). *Step 1*: Followed procedure given for **9a** (Step 1), with 14 mL (95 mmol) 1-octyne, 40 mL (64 mmol) *n*-butyllithium (1.6M in hexanes), 6 mL (59 mmol) benzaldehyde (distilled from CaH_2), and 100 mL ether. Purified via silica gel chromatography (8:2 pentane:ether) to obtain 10.6 g of 1-phenylnon-2-yn-1-ol[27] as a light yellow oil (83% yield). *Step 2*: To a flame-dried, round-bottomed flask, under an argon atmosphere, added 1-phenylnon-2-yn-1-ol (10.4 g, 48 mmol), 85% manganese(IV) oxide (49 g, 479 mmol), and benzene (200 mL). Let stir at room temperature for 18.5 hours, then filtered through Celite, rinsing with ether. Purified via silica gel chromatography (9:1 pentane:ether) to obtain 8.95 g of 1-phenylnon-2-yn-1-one[27] as a

yellow oil (87% yield). *Step 3*: To a 3-neck, round-bottomed flask, added 4 Å molecular sieves (pellets, 2.5 g) and flame-dried under vacuum. Let cool to room temperature, placed under an argon atmosphere, added 1-phenylnon-2-yn-1-one (2 mL, 9.9 mmol) and THF (50 mL). Let stir at room temperature for 3 hours. Added a 1.0M toluene solution of (*S*)-2-methyl-CBS-oxazaborolidine (25 mL, 25 mmol) and placed in a dry ice/ethylene glycol:ethanol (8:2) bath. (Note: cold bath becomes solid, so flask should be placed in bath prior to dry ice addition.) When temperature had reached –30 to –40 °C range, added a 2.0M THF solution of borane-methyl sulfide complex (25 mL, 50 mmol) dropwise, over approximately 15 minutes. Let stir at –30 to –40 °C for 3 hours, then, *very* slowly, added 40 mL MeOH and let warm to room temperature. Diluted with 150 mL ether, washed twice with 75 mL aqueous NH_4Cl solution, twice with 75 mL aqueous $NaHCO_3$ solution, and twice with 75 mL brine, then dried with Na_2SO_4. Purified via silica gel chromatography (8:2 pentane:ether) to obtain 1.87 g of (*S*)-1-phenylnon-2-yn-1-ol as a yellow oil (87% yield). Enantiomeric excess was determined to be 99% by chiral HPLC (OD-H column, 4% *i*-PrOH in hexanes, 1 mL/min). *Step 4*: Followed procedure given for **9a** (Step 2), with 880 mg (4 mmol) (*S*)-1-phenylnon-2-yn-1-ol (99% ee), 12 mL (12 mmol) lithium aluminum hydride (1.0M in THF), 30 mL THF, and a reaction time of 42 hours. Purified via silica gel chromatography (8:2 pentane:ether) to obtain 649 mg of **43** as a slightly yellow oil (74% yield). Spectral data same as for **7a**. Enantiomeric excess was determined to be 99% by chiral HPLC (OD-H column, 2% *i*-PrOH in hexanes, 1 mL/min). $[\alpha]_D = -34.2$ (28 °C, $CHCl_3$, c = 1.0). Literature value[24e] for *S*-enantiomer of **19** (94% ee, 20 °C, $CHCl_3$, c = 2.0) = +34.4.

(*R*,*E*)-1-phenylnon-1-en-3-ol **(44).** Followed procedure given for **3**, with **43** (87.3 mg, 0.4 mmol), **1** (6 mg, 0.012 mmol), ether (2 mL), a reaction temperature of –78 °C, and a reaction time of 2 hours. Purified via silica gel chromatography (8:2 pentane:ether) to obtain 81.2 mg of **44** as a white solid (93% yield). Spectral data same as for **8a**. Enantiomeric excess determined to be 81% by chiral HPLC (OJ column, 3% *i*-PrOH in hexanes, 1 mL/min). $[\alpha]_D$ = –18.6 (29-30 °C, EtOH, c = 2.5). Absolute stereochemistry confirmed by conversion of **44** to **44'** according to the following procedure: To a 25-mL



44 **44'**

round-bottomed flask, added **44** (84% ee, 85 mg, 0.4 mmol) and CH_2Cl_2 (5 mL). Placed in a dry ice/acetone bath and bubbled O_3 through the solution. Monitored by TLC, and when all of **44** had been consumed (about 30 minutes), stopped the O_3 flow, purged with N_2 for 5 minutes, and placed in an ice bath under an argon atmosphere. Added ether (5 mL), and then slowly added a 1.0M ether solution of lithium aluminum hydride (1.2 mL, 1.2 mmol). Removed ice bath and let stir for 2 hours. Replaced ice bath, slowly added 3 mL ethyl acetate and a little $Na_2SO_4 \bullet H_2O$, removed ice bath, and let stir for 15 minutes. Filtered through Celite, rinsing with ether. Purified via silica gel chromatography (100% ether) to obtain 18.5 mg of **44'** (32% yield). $[\alpha]_D$ = +7.8 (28 °C, EtOH, c = 0.9). Literature value[35] for the *S*-enantiomer of **44'** (>99% ee, 25 °C, EtOH, c = 0.33) = –15.4.

(*R*,*Z*)-1-phenylnon-2-en-1-ol **(45)**. *Step 1*: To a flame-dried, round-bottomed flask, under an argon atmosphere, added (*S*)-1-phenylnon-2-yn-1-ol (synthesis described for **43**, Step 3, 1 mL, 4.58 mmol), CH_2Cl_2 (12 mL), and *N*,*O*-bis(trimethylsilyl)-acetamide (1.7

mL, 6.88 mmol). Let stir at room temperature for 2 hours. *Step 2:* Removed solvent and excess reagent *in vacuo*, added Lindlar catalyst (5% Pd on $CaCO_3$, poisoned with Pb, 380 mg) and MeOH (12 mL). Degassed via 3 freeze-pump-thaw cycles and placed under a H_2 atmosphere (balloon). Let stir at room temperature for 1.5 hours. Filtered through Celite, rinsing with ether. Dried with Na_2SO_4 and removed solvent *in vacuo*. *Step 3*: Transferred to a round-bottomed flask, added K_2CO_3 (1.2 g, 8.68 mmol) and anhydrous MeOH (12 mL). Let stir at room temperature for 1 hour. Added aqueous NH_4Cl solution, extracted several times with CH_2Cl_2, and dried with Na_2SO_4. Crude ^{1}H NMR showed *Z*:*E* = 3:1. Purified via silica gel chromatography (9:1 pentane:ether) to obtain (with the sacrifice of a lot of material) 276 mg of **45** as an oil (28% yield, *Z*:*E* = 11:1, ca. 1% (*S*)-1-phenylnon-2-yn-1-ol). (Note: In hindsight, a better procedure for the synthesis of **45** would have been the one described herein for the synthesis of **11**.) ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 7.35 (5H, m), 5.6 (3H, m), 2.23 (2H, m), 2.02 (1H, br), 1.35 (8H, m), 0.92 (3H, t, *J* = 6.8 Hz). ^{13}C NMR (300 MHz, $CDCl_3$, ppm): δ 144.0, 132.6, 132.1, 128.7, 127.6, 126.1, 69.9, 31.9, 29.7, 29.2, 27.9, 22.8, 14.3. HRMS (EI) calcd. for $C_{15}H_{22}O$: 218.1671, found: 218.1672. Enantiomeric excess was determined to be >99% by chiral HPLC (OB-H column, 3% *i*-PrOH in hexanes, 1 mL/min). $[\alpha]_D$ = –136.0 (29 °C, $CHCl_3$, c = 1.1). Literature value[24f] for the *S*-enantiomer of **45** (90% ee, 20-28 °C, $CHCl_3$, c = 0.3-1.7) = +168.7.

(*S*,*E*)-1-phenylnon-1-en-3-ol (**46**). Followed procedure given for **3**, with 86.1 mg (0.39 mmol) **45**, 6 mg (0.012 mmol) **1**, 2 mL ether, a reaction temperature of –78 °C, and a reaction time of 2 hours. Purified via silica gel chromatography (8:2 pentane:ether) to

obtain 79.6 mg of **46** as a white solid (92% yield). Spectral data same as for **8a**. Enantiomeric excess determined to be 72% by chiral HPLC (OJ column, 3% *i*-PrOH in hexanes, 1 mL/min). $[\alpha]_D$ = +16.7 (29-30 °C, EtOH, c = 2.5).

(*R*,*E*)-1-(4-methoxyphenyl)non-2-en-1-ol (**47**). Followed procedure given for **43**, with: *Step 1*: Same reaction as for **9b** (Step 1). *Step 2*: 3 mL (13 mmol) 1-(4-methoxyphenyl)non-2-yn-1-ol, 13.3 g (130 mmol) manganese(IV) oxide (85%), 130 mL benzene, and a reaction time of 72 hours. Purified via silica gel chromatography (8:2 pentane:ether) to obtain 2.69 g of 1-(4-methoxyphenyl)non-2-yn-1-one[36] as a pale yellow oil (85% yield). *Step 3*: 1 mL (4.1 mmol) 1-(4-methoxyphenyl)non-2-yn-1-one, 8 mL (8 mmol) (*S*)-2-methyl-CBS-oxazaborolidine (1.0M in toluene), 10 mL (20 mmol) borane-methyl sulfide complex (2.0M in THF), 400 mg 4 Å molecular sieves (pellets), and 30 mL THF. Purified via silica gel chromatography (8:2 pentane:ether) to obtain 550 mg of (*S*)-1-(4-methoxyphenyl)non-2-yn-1-ol as an oil (54% yield). Enantiomeric excess determined to be 92% by chiral HPLC (OD-H column, 4% *i*-PrOH in hexanes, 1 mL/min, 220 nm). *Step 4*: 543 mg (2.2 mmol) (*S*)-1-(4-methoxyphenyl)non-2-yn-1-ol (92% ee), 7 mL (7 mmol) lithium aluminum hydride (1.0M in THF), 20 mL THF, and a reaction time of 68 hours. Purified via silica gel chromatography (8:2 pentane:ether) to obtain 439 mg of **47** as a yellow oil (80%). Spectral data same as for **9b**. Enantiomeric excess determined to be 89% by chiral HPLC (OD-H column, 3% *i*-PrOH in hexanes, 1 mL/min, 220 nm). $[\alpha]_D$ = –5.78 (23 °C, $CHCl_3$, c = 1.0).

(*R*,*E*)-1-(4-methoxyphenyl)non-1-en-3-ol (**48**). Followed procedure given for **3**, with 99.4 mg (0.4 mmol) **47**, 6 mg (0.012 mmol) **1**, 2 mL ether, a reaction temperature of –78 °C, and a reaction time of 2 hours. Purified via silica gel chromatography (8:2 pentane:ether) to obtain 72.0 mg of **48** as a clear oil (72% yield). Spectral data same as for **10b**. Enantiomeric excess determined to be 1% by chiral HPLC (OD-H column, 4% *i*-PrOH in hexanes, 1 mL/min).

(*R*,*E*)-1-(4-(trifluoromethyl)phenyl)non-2-en-1-ol (**49**). Followed procedure given for **43**, with: *Step 1*: Same reaction as for **9a** (Step 1). *Step 2*: 3 mL (11.6 mmol) 1-(4-(trifluoromethyl)phenyl)non-2-yn-1-ol, 12 g (117 mmol) manganese(IV) oxide (85%), 150 mL benzene, and a reaction time of 16.5 hours. Purified via silica gel chromatography (8:2 pentane:ether) to obtain 3.13 g of 1-(4-(trifluoromethyl)phenyl)non-2-yn-1-one as an orange oil (96% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 8.25 (2H, d, J = 8.1 Hz), 7.75 (2H, d, J = 8.1 Hz), 2.53 (2H, t, J = 7.2 Hz), 1.70 (2H, m), 1.40 (6H, m), 0.92 (3H, t, J = 7.1 Hz). ^{13}C NMR (300 MHz, $CDCl_3$, ppm): δ 177.1, 139.7, 135.2 (q, J = 130 Hz), 130.0, 125.8 (q, J = 15.0 Hz), 123.8 (q, J = 1085 Hz), 98.7, 80.0, 31.4, 28.9, 27.9, 22.7, 19.5, 14.2. HRMS (EI) calcd. for $C_{16}H_{17}F_3O$: 282.1231, found: 282.1223. *Step 3*: 1 mL (3.9 mmol) 1-(4-(trifluoromethyl)phenyl)non-2-yn-1-one, 12 mL (12 mmol) (*S*)-2-methyl-CBS-oxazaborolidine (1.0M in toluene), 10 mL (20 mmol) borane-methyl sulfide complex (2.0M in THF), 400 mg 4 Å molecular sieves (pellets), and 30 mL THF. Purified via silica gel chromatography (7:3 pentane:ether) to obtain 1.08 g of (*S*)-1-(4-(trifluoromethyl)-phenyl)non-2-yn-1-ol as a yellow oil (97% yield). Enantiomeric excess determined to be >99% by chiral HPLC (AD column, 2% *i*-PrOH in

hexanes, 1 mL/min, 220 nm). *Step 4*: 1.06 g (3.7 mmol) (*S*)-1-(4-(trifluoromethyl)-phenyl)non-2-yn-1-ol (>99% ee), 11 mL (11 mmol) lithium aluminum hydride (1.0M in THF), 30 mL THF, and a reaction time of 70.5 hours. Purified via silica gel chromatography (8:2 pentane:ether) to obtain 813 mg of **49** as a yellow oil (77%). Spectral data same as for **9a**. Enantiomeric excess determined to be >99% by chiral HPLC (OB-H column, 1% *i*-PrOH in hexanes, 1 mL/min, 220 nm). $[\alpha]_D = -42.38$ (24 °C, $CHCl_3$, c = 1.0).

(*R*,*E*)-1-(4-(trifluoromethyl)phenyl)non-1-en-3-ol (**50**). Followed procedure given for **3**, with 114.3 mg (0.4 mmol) **49**, 6 mg (0.012 mmol) **1**, 2 mL ether, a reaction temperature of –50 °C, and a reaction time of 1 hour. Purified via silica gel chromatography (8:2 pentane:ether) to obtain ca. 114 mg of **50** as a solid/ oil (99% yield). Spectral data same as for **10a**. Enantiomeric excess determined to be 95% by chiral HPLC (OD-H column, 1% *i*-PrOH in hexanes, 1 mL/min).). $[\alpha]_D = -7.7$ (24 °C, $CHCl_3$, c = 1.0).

(*R*,*E*)-3-methyl-1-phenylnon-2-en-1-ol (**51**). *Step 1*: To a flame-dried, round-bottomed flask, under an argon atmosphere, added bis(cyclopentadienyl)-zirconium dichloride (790 mg, 2.70 mmol), a 2.0M hexanes solution of trimethylaluminum (20 mL, 40 mmol), and CH_2Cl_2 (70 mL). Placed in water/ice/NH_4Cl bath (approximately –10 °C) and *slowly* added water (365 μL, 20.3 mmol) via syringe. Let stir for 10 minutes. Added a solution of 1-octyne (2 mL, 13.5 mmol) and CH_2Cl_2 (10 mL) dropwise, over 5 minutes. Let stir at ca. –10 °C for 10 minutes, then added a solution of iodine (4.1 g, 16.2 mmol) and THF (20 mL) dropwise, over 10 minutes. Let stir at ca. –10 °C for 15 minutes, then removed

cold bath and let slowly warm to room temperature. *Very slowly* added 5 mL aqueous K_2CO_3 solution, let stir for 15 minutes, then added $MgSO_4$ and filtered, rinsing with ether. Purified via silica gel chromatography (100% hexanes) to obtain 2.81 g of (*E*)-1-iodo-2-methyloct-1-ene[37] as a slightly yellow oil (83% yield). *Step 2*: Followed procedure given for **9a** (Step 1), with 1 mL (5.2 mmol) (*E*)-1-iodo-2-methyloct-1-ene, 3.2 mL (5.1 mmol) *n*-butyllithium (1.6M in hexanes), 0.5 mL (4.9 mmol) benzaldehyde (distilled from CaH_2), and 25 mL ether. Purified via silica gel chromatography (8:2 pentane:ether) to obtain 820 mg of (*E*)-3-methyl-1-phenylnon-2-en-1-ol[38] as an oil (72% yield). *Step 3*: Followed procedure given for **43** (Step 2), with: 903 mg (3.9 mmol) (*E*)-3-methyl-1-phenylnon-2-en-1-ol, 4.0 g (39 mmol) manganese(IV) oxide (85%), 40 mL benzene, and a reaction time of 71 hours. Purified via silica gel chromatography (9:1 pentane:ether) to obtain 593 mg of (*E*)-3-methyl-1-phenylnon-2-en-1-one[39] as a yellow oil (66% yield). *Step 4*: Followed procedure given for **43** (Step 3), with 571 mg (2.48 mmol) (*E*)-3-methyl-1-phenylnon-2-en-1-one, 5 mL (5 mmol) (*S*)-2-methyl-CBS-oxazaborolidine (1.0M in toluene), 6 mL (12 mmol) borane-methyl sulfide complex (2.0M in THF), 250 mg 4 Å molecular sieves (pellets), and 20 mL THF. Purified via silica gel chromatography (8:2 pentane:ether) to obtain 497 mg of **51** as a yellow oil (86% yield). Enantiomeric excess determined to be 99% by chiral HPLC (OD-H column, 1% *i*-PrOH in hexanes, 1 mL/min, 220 nm). $[\alpha]_D = -82.0$ (24 °C, $CHCl_3$, c = 0.94).

(*R*,*E*)-3-methyl-1-phenyldec-1-en-3-ol (**52**). Followed procedure given for **3**, with 92.8 mg (0.4 mmol) **51**, 8 mg (0.016 mmol) **1**, 2 mL THF, a reaction temperature of –78 °C, and a reaction time of 2 hours. Purified via silica gel chromatography (8:2 pentane:ether)

to obtain 74.8 mg of **52** as a clear oil (81% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 7.3 (5H, m), 6.58 (1H, d, *J* = 15.9 Hz), 6.28 (1H, d, *J* = 16.2 Hz), 1.6 (3H, m), 1.38 (3H, s), 1.3 (8H, m), 0.88 (3H, t, *J* = 6.8 Hz). ^{13}C NMR (300 MHz, $CDCl_3$, ppm): δ 137.3, 137.1, 128.8, 127.5, 127.2, 126.6, 73.5, 43.2, 32.0, 29.9, 28.4, 24.2, 22.8, 14.2. HRMS (EI) calcd. for $C_{17}H_{26}O$ –CH_2: 232.1827, found: 232.1818. Enantiomeric excess determined to be 9% by chiral HPLC (OJ column, 1% *i*-PrOH in hexanes, 1 mL/min).

(*R*,*E*)-3-methyl-1-(4-(trifluoromethyl)phenyl)non-2-en-1-ol (**53**). Followed procedure given for **51**, with: *Step 1*: Same reaction. *Step 2*: 1.4 mL (6.7 mmol) (*E*)-1-iodo-2-methyloct-1-ene, 4 mL (6.4 mmol) *n*-butyllithium (1.6M in hexanes), 750 μL (5.6 mmol) α,α,α-trifluoro-*p*-tolualdehyde, and 40 mL ether. Purified via silica gel chromatography (9:1 to 8:2 pentane:ether) to obtain 1.46 g of (*E*)-3-methyl-1-(4-(trifluoromethyl)-phenyl)non-2-en-1-ol as a yellow oil (87% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 7.60 (2H, d, *J* = 8.1 Hz), 7.50 (2H, d, *J* = 8.7 Hz), 5.55 (1H, dd, *J* = 8.7, 3.3 Hz), 5.36 (1H, dq, *J* = 8.9, 1.3 Hz), 2.04 (2H, t, *J* = 7.7 Hz), 1.82 (3H, d, *J* = 1.5 Hz), 1.82 (1H, m), 1.35 (8H, m), 0.88 (3H, t, *J* = 6.6 Hz). ^{13}C NMR (300 MHz, $CDCl_3$, ppm): δ 148.4 (d, *J* = 4.5 Hz), 140.5, 129.5 (q, *J* = 128 Hz), 126.8, 126.3, 125.5 (q, *J* = 15.1 Hz), 124.4 (q, *J* = 1081 Hz), 70.2, 39.7, 31.9, 29.1, 27.8, 22.8, 16.9, 14.2. HRMS (EI) calcd. for $C_{17}H_{23}F_3O$: 300.1701, found: 300.1709. *Step 3*: 810 mg (2.7 mmol) (*E*)-3-methyl-1-(4-(trifluoromethyl)phenyl)non-2-en-1-ol, 2.6 g (25 mmol) manganese(IV) oxide (85%), 50 mL benzene, and a reaction time of 65.5 hours. Purified via silica gel chromatography (9:1 pentane:ether) to obtain 602 mg of (*E*)-3-methyl-1-(4-(trifluoromethyl)phenyl)non-2-en-1-one as a yellow oil (75% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 8.02 (2H,

d, *J* = 8.1 Hz), 7.72 (2H, d, *J* = 8.4 Hz), 6.73 (1H, q, *J* = 1.2 Hz), 2.29 (2H, t, *J* = 7.7 Hz), 2.24 (3H, d, *J* = 1.2 Hz), 1.48 (8H, m), 0.91 (3H, t, *J* = 6.8 Hz). ^{13}C NMR (300 MHz, $CDCl_3$, ppm): δ 190.5, 163.2, 142.5, 133.7 (q, *J* = 129 Hz), 128.6, 125.7 (q, *J* = 14.7 Hz), 120.1, 124.0 (q, *J* = 1084 Hz), 41.9, 31.9, 29.2, 27.8, 22.8, 20.2, 14.3. HRMS (EI) calcd. for $C_{17}H_{21}F_3O$: 298.1544, found: 298.1558. *Step 4*: 582 mg (1.95 mmol) (*E*)-3-methyl-1-(4-(trifluoromethyl)phenyl)non-2-en-1-one, 4 mL (4 mmol) (*S*)-2-methyl-CBS-oxazaborolidine (1.0M in toluene), 5 mL (10 mmol) borane-methyl sulfide complex (2.0M in THF), 200 mg 4 Å molecular sieves (pellets), and 20 mL THF. Purified via silica gel chromatography (8:2 pentane:ether) to obtain 524 mg of **53** as a slightly yellow oil (89% yield). Enantiomeric excess determined to be 93% by chiral HPLC (OJ column, 1% *i*-PrOH in hexanes, 1 mL/min, 220 nm). $[\alpha]_D$ = –82.2 (24 °C, $CHCl_3$, c = 1.1).

(*R*,*E*)-3-methyl-1-(4-(trifluoromethyl)phenyl)non-1-en-3-ol (**54**). Followed procedure given for **3**, with 120.1 mg (0.4 mmol) **53**, 4 mg (0.008 mmol) **1**, 2 mL ether, a reaction temperature of –50 °C, and a reaction time of 30 minutes. Purified via silica gel chromatography (8:2 pentane:ether) to obtain 114.6 mg of **54** as a light yellow oil (95% yield). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 7.56 (2H, d, *J* = 8.4 Hz), 7.46 (2H, d, *J* = 8.4 Hz), 6.65 (1H, d, *J* = 15.9 Hz), 6.39 (1H, d, *J* = 15.9 Hz), 1.93 (1H, d, *J* = 0.6 Hz), 1.65 (2H, m), 1.41 (3H, s), 1.35 (8H, m), 0.89 (3H, t, *J* = 6.9 Hz). ^{13}C NMR (300 MHz, $CDCl_3$, ppm): δ 140.8, 139.7, 129.3 (q, *J* = 129 Hz), 126.7, 126.0, 125.6 (q, *J* = 15.3 Hz), 124.4 (q, *J* = 1081 Hz), 73.5, 43.1, 32.0, 30.0, 28.3, 24.2, 22.8, 14.2. HRMS (EI) calcd. for $C_{11}H_{23}F_3O$: 300.1701, found: 300.1708. Enantiomeric excess determined to be 58%

by chiral HPLC (OJ column, 1% *i*-PrOH in hexanes, 1 mL/min). $[\alpha]_D$ = +9.5 (25 °C, $CHCl_3$, c = 0.95).

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