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Iridium-Catalyzed C-C Bond Formation: Development of Crotylation and Methallylation Reactions through Transfer Hydrogenation

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Iridium-Catalyzed C-C Bond Formation: Development of Crotylation and Methallylation Reactions through Transfer Hydrogenation

by

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Abstract

Iridium-Catalyzed C-C Bond Formation: Development of Crotylation and Methallylation Reactions through Transfer Hydrogenation

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Under the conditions of transfer hydrogenation utilizing chromatographically purified *ortho*-cyclometallated iridium C,O-benzoate precatalysts, enantioselective carbonyl crotylation and methallylation can be performed in the absence of stoichiometric metallic reagents and stoichiometric chiral modifiers. In the case of carbonyl crotylation, use of a preformed precatalyst rather than an in situ generated catalyst results in lower reaction temperatures, providing generally higher diastereoselectivity and yields. By utilizing a more reactive leaving group in chloride over acetate on our methallyl donor, the inherently shorter lifetime of the olefin π-complex is compensated for, giving our group's first report of reactivity utilizing 1,1-disubstituted allyl donors.

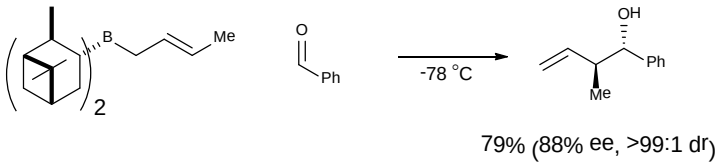
Table of Contents

Chapter 1

1.1 Part One: Second-Generation Conditions for Enantioselective Iridium-Catalyzed Carbonyl Crotylation

1.1.1 Background

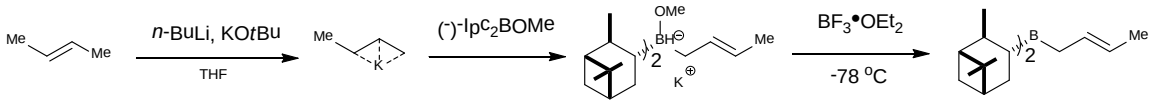
Through the past several decades, carbonyl crotylation has evolved into an indispensible method for the construction of polypropionate units in natural products.[1] Of the methods practically utilized for crotylation, most involve the use of chirally modified, preformed metal reagents. Such reagents have been generated using a diverse set of metals, including boron-crotyl reagents, titanium-crotyl reagents, and silicon-crotyl reagents.[2] While often well developed and applicable across a broad substrate scope, most of these chirally-modified crotyl-metal reagents generate stoichiometric byproducts and require multi-step synthesis for preparation. One of the most commonly utilized crotylation protocols in total synthesis, Brown's method, illustrates these difficulties (Scheme 1).



Scheme 1: Brown Crotylation

The crotylating reagent is prepared by potassiation of butane with Schlosser's base and subsequent transmetalation to boron. The process requires stoichiometric reagents such as *n*-BuLi, KO*t*-Bu, and Ipc_2BOMe, adding both complexity and cost to the process as

well as generating waste (Scheme 2).[3]

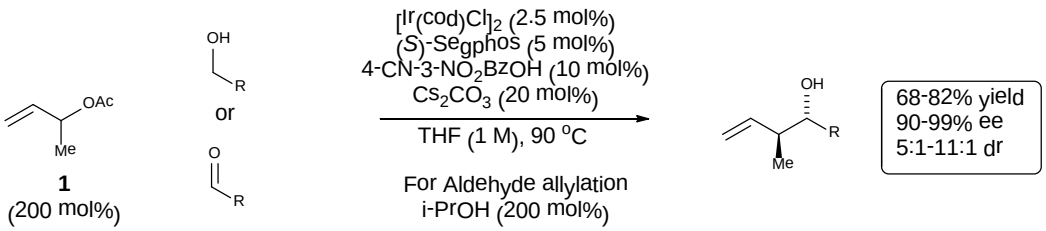


Scheme 2: Preparation of Brown's Crotylborane

In addition, for each crotyl transfer two equivalents of isopinocampheol are produced. As both the product and isopinocampheol are secondary alcohols, these reactions can often lead to difficult isolation issues.

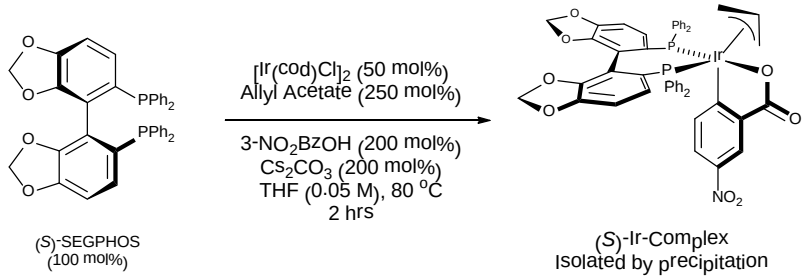
As an attempt to resolve these issues, catalytic protocols for carbonyl crotylation have been developed. A wide range of both Lewis acids and bases have been developed to create a chiral environment prior to addition, leading to enantioselective products. While these protocols successfully avoid the use of chirally modified crotyl-metal reagents, they still depend on use of preformed crotyl-metal reagents, leading to stoichiometric metallic byproducts.[2]

In 2009, Krische and coworkers reported an iridium-catalyzed transfer-hydrogenative enantioselective carbonyl crotylation employing α-methyl allyl acetate, **1**, as a crotyl donor.[4] The catalytic transformation represented a significant paradigm shift as no stoichiometric organometallic reagents or chiral auxiliaries are required to achieve high yield and enantioselectivity. In addition, the transformation can be performed from either the alcohol or aldehyde oxidation level, greatly widening the substrate scope (Scheme 3).



Scheme 3: First reported Krische group crotylation

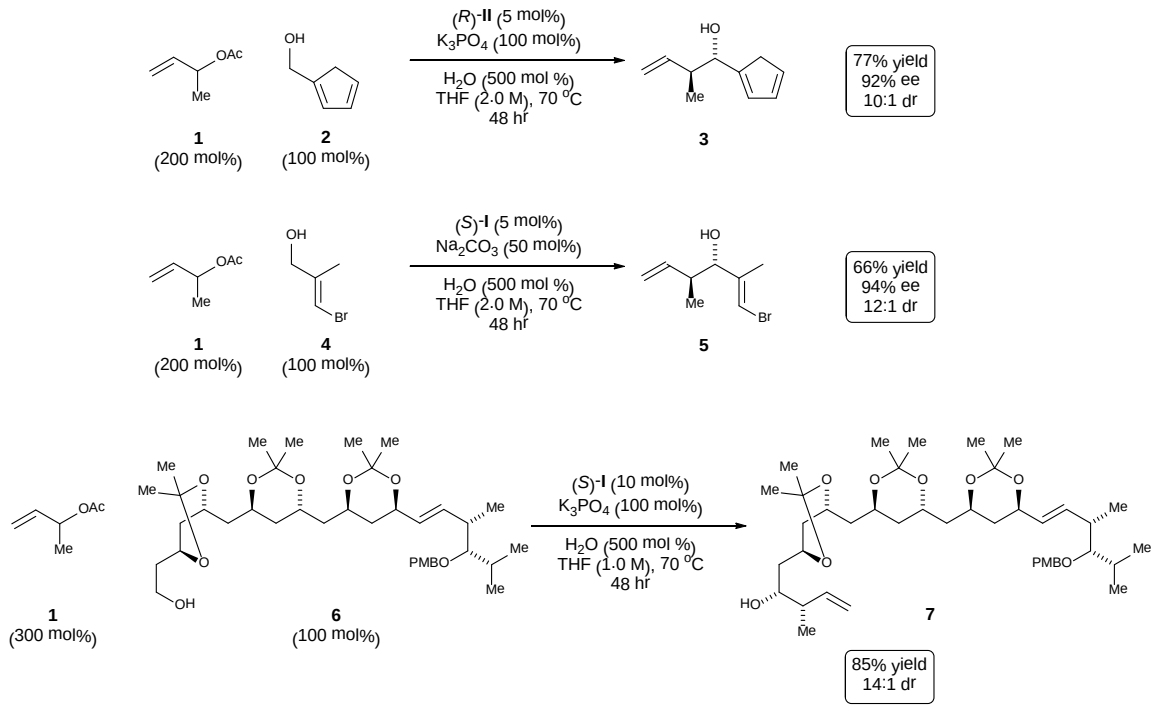
The key to this transformation is the *ortho*-cyclometallated iridium catalyst generated in situ from $[Ir(cod)Cl]_2$, 4-cyano-3-nitrobenzoic acid, chiral ligand (*S*)-SEGPHOS, and α-methyl allyl acetate. While the in situ method for formation of said catalyst was simple and effective, a protocol for assembly of a single component precatalyst was discovered which promised improved results (Scheme 4).



Scheme 4: Preformed precatalyst assembly

With the use of this precatalyst, first published in the Krische group's work on reverse prenylation[5], lower temperatures were found necessary for reactivity than those using the in situ method. Because of this advantage, crotylation using a single component precatalyst was explored.

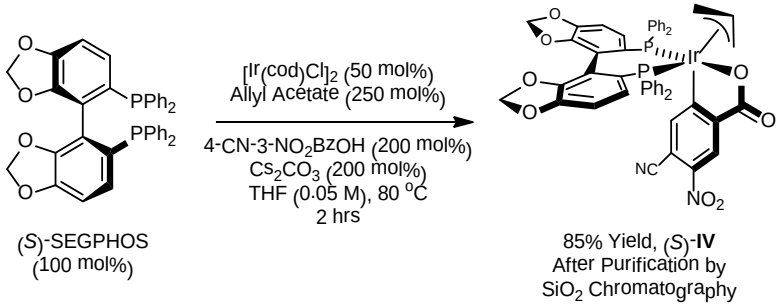
While exploring reactivity using these preformed precatalysts, an important additive was also discovered. Somewhat surprisingly, addition of a small amount of water (500 mol%) lead to increased yield and selectivity. In addition, the lower temperature of reaction further increased yield and diastereomeric ratio over reactions using in situ generated catalyst. Overall, three examples were published of crotylation using the preformed catalyst (Scheme 5). Optimized conditions were individually found for fufuryl alcohol **2** to give crotylation product **3** in high yield and selectivity.[6] With similar optimization, key intermediates in the core structures of cytotrienin A[7] and roxaticin[8], **4** and **6** respectively, gave products of crotylation **5** and **7** with good results . While all conditions were effective, none of the conditions were completely identical, leading to uncertainty over which protocol would give the best results over a wide substrate scope. In addition, the formation of the precatalyst by precipitation inherently lead to trapped impurities, resulting in a high degree of batch variability.



Scheme 5: Previous crotylation reactions using precatalyst

1.1.2 Optimization

With the discovery by a fellow group member of the precatalyst's ability to be subjected to flash chromatography and purified, the batch variability of the catalyst was greatly reduced (Scheme 6).

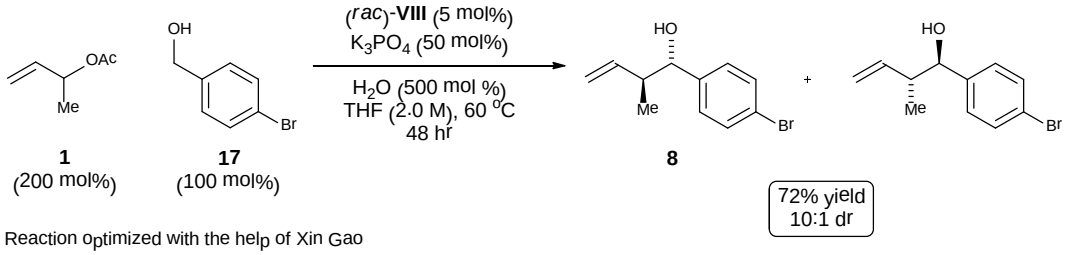


Scheme 6: Chromatographically purified catalyst (*S*)-**IV**

As a result, the decision to establish a general protocol for crotylation was made. In order to establish such conditions, an optimization was undertaken to gauge how previously established conditions would hold up over a larger substrate scope. Adjustment of each reaction condition was performed with the goal of maximizing product yield and diastereomeric ratio. Utilizing 4-bromobenzyl alcohol, **17**, as our model substrate, we quickly established THF to be our preferred solvent, in agreement with previous work. After choosing THF, we screened a variety of inorganic bases, finding that tribasic potassium phosphate gave higher yield and diastereoselectivity than sodium carbonate or sodium bicarbonate.

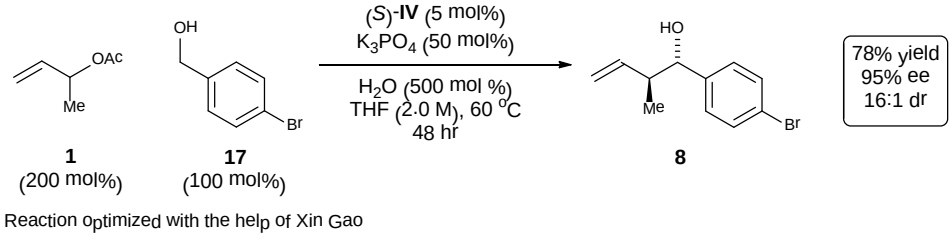
With tribasic potassium phosphate identified as the most effective base for our reaction, we screened the effects of base loading. We found that our diastereoselectivity was highest using 50 mol%, which is once again in agreement with a previously established set of conditions. In addition, we found that our ideal concentration was 2M, giving a slight increase in diastereoselectivity over 1M conditions. Finally,we confirmed that 500 mol% water as an additive is the ideal amount, in agreement with all previously mentioned examples, as increased water loading leads to diminished yields and decreased water loading results in reduced diastereoselectivity. We completed our optimization by screening reaction temperature, finding that we could go as low as 60 °C

without diminishing yield. This low temperature predictably improved diastereoselectivity and gave us our optimized conditions (Scheme 7).



Scheme 7: Optimized conditions using racemic catalyst

The next issue to tackle was confirming that our crotylation conditions would retain the enantioselectivity of past examples upon utilization of a chiral ligand. After a screen of chiral ligands, we confirmed that (*S*)-SEGPHOS gave high enantioselectivity. To our delight, we also observed an increase in reaction yield and diastereoselectivity upon use of the chiral catalyst as well. Our final conditions gave the product of crotylation **8** in 78% yield, 16:1 diastereomeric ratio, and 95% enantiomeric excess (Scheme 8). Pleased that these results represented a significant improvement over previously reported results, we generated examples to demonstrate the scope of our conditions.



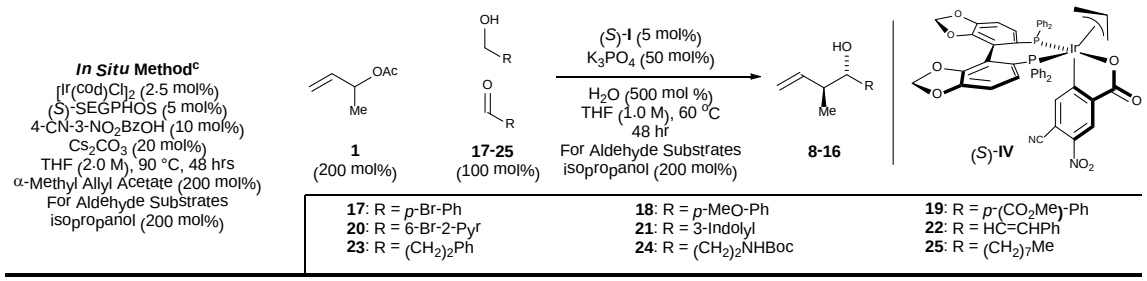
Scheme 8: Optimized conditions using chiral catalyst

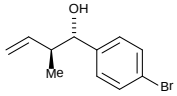
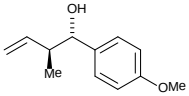
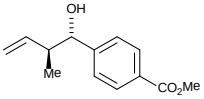
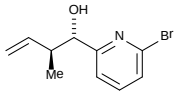
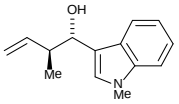
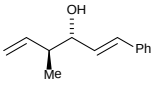
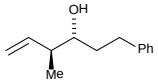
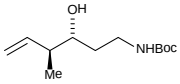
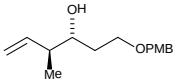
1.1.3 Substrate Scope

Utilizing the optimized conditions including catalyst (*S*)-**IV** (5 mol%), α-methyl allyl acetate **1** (200 mol%), tribasic potassium phosphate (50 mol%), and water (500 mol%) in THF (2 M) at 60 °C, crotylation took place with a wide range of substrates with good reactivity. Benzylic alcohols underwent crotylation in good yields, with alcohols **17-19,** and **21** resulting in crotylation products **8-10** and **12**. Moderate to high improvements in enantioselectivity, yield, and diastereomeric ratio were observed for all examples over results from first generation in situ reactions of the same substrates. Crotylation product **11** was also observed in the reation of alcohol **20**, giving moderate yield and high enantioselectivity and diastereomeric ratio for a substrate with no observed product using in situ reaction conditions. Utilizing allylic alcohol **22**, similar improvements to yield, enantioselectivity, and diastereomeric ratio were observed, giving product of crotylation **13**.

The same conditions were also utilized for aliphatic alcohol substrates, with alcohols **23** and **25** resulting in the corresponding crotylation products **14** and **16**. Slight but consistent improvements to yield and enantioselectivity were observed along with a large improvement to diastereomeric ratio. Crotylation product **15** was also observed in the reaction of alcohol **24** at increased temperature, 70 °C, in good yield, enantioselectivity, and diastereomeric ratio for a substrate with no observed product using

in situ reaction conditions. In the presence of isopropanol (200 mol%), the corresponding benzylic and aliphatic aldehydes underwent crotylation in comparably improved isolated yield, enantiomeric excess, and diastereomeric ratio. As with previous in situ methods, our conditions displayed crotylation of equal facility from either the alcohol or aldehyde oxidation level (Table 1).



			
Alcohol **Aldehyde**	Preformed (*S*)-**IV** 78% Yield **8**, 16:1 dr, 95% ee 82% Yield **8**, 17:1 dr, 98% ee[b]	Preformed (*S*)-**IV** 91% Yield **9**, 10:1 dr, 94% ee 89% Yield **9**, 12:1 dr, 98% ee[b]	Preformed (*S*)-**IV** 78% Yield **10**, 11:1 dr, 97% ee 81% Yield **10**, 13:1 dr, 98% ee[b]
Alcohol **Aldehyde**	*In Situ* (*S*)-**IV**[c] 73% Yield **8**, 8:1 dr, 95% ee 78% Yield **8**, 11:1 dr, 97% ee	*In Situ* (*S*)-**IV**[c] 67% Yield **9**, 5:1 dr, 90% ee 75% Yield **9**, 7:1 dr, 97% ee	*In Situ* (*S*)-**IV**[c] 70% Yield **10**, 7:1 dr, 95% ee 80% Yield **10**, 11:1 dr, 96% ee
			
Alcohol **Aldehyde**	Preformed (*S*)-**IV** 50% Yield **11**, 14:1 dr, 98% ee 75% Yield **11**, >20:1 dr, 97% ee[b]	Preformed (*S*)-**IV** 75% Yield **12**, 7:1 dr, 97% ee 74% Yield **12**, 10:1 dr, 98% ee[b]	Preformed (*S*)-**IV**[a] 72% Yield **13**, 10:1 dr, 92% ee 77% Yield **13**, 10:1 dr, 98% ee[b]
Alcohol **Aldehyde**	*In Situ* (*S*)-**IV**[c] no product observed	*In Situ* (*S*)-**IV**[c] 73% Yield **12**, 5:1 dr, 95% ee 78% Yield **12**, 6:1 dr, 97% ee	*In Situ* (*S*)-**IV**[c] 61% Yield **13**, 7:1 dr, 86% ee 66% Yield **13**, 8:1 dr, 98% ee
			
Alcohol **Aldehyde**	Preformed (*S*)-**IV** 71% Yield **14**, >20:1 dr, 98% ee 71% Yield **14**, >20:1 dr, 98% ee[b]	Preformed (*S*)-**IV**[a] 71% Yield **15**, >20:1 dr, 97% ee 66% Yield **15**, >20:1 dr, 99% ee[b]	Preformed (*S*)-**IV** 76% Yield **16**, 15:1 dr, 97% ee 76% Yield **16**, >20:1 dr, 99% ee[b]
Alcohol **Aldehyde**	*In Situ* (*S*)-**IV**[c] 69% Yield **14**, 7:1 dr, 98% ee 71% Yield **14**, 11:1 dr, 98% ee	*In Situ* (*S*)-**IV**[c] no product observed	*In Situ* (*S*)-**IV**[c] 73% Yield **16**, 7:1 dr, 95% ee 88% Yield **16**, 7:1 dr, 95% ee

[a] reactions run at 70 °C [b] aldehyde examples performed by Xin Gao [c] see reference 4

Table 1: Second generation Iridium-catalyzed crotylation using chromatographically purified precatalyst[9]

1.1.4 Summary

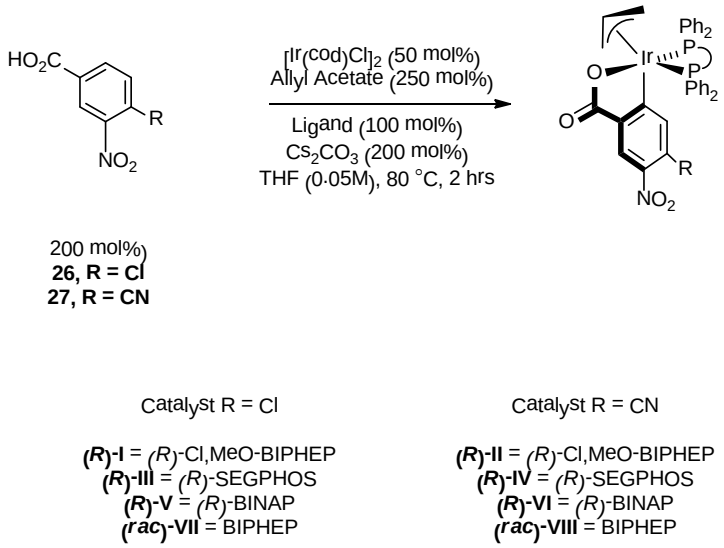
In summary, a standard set of conditions useful for a broad range of substrates has been established utilizing iridium precatalyst (*S*)-**IV**. This chromatographically purified single-component precatalyst promotes alcohol-mediated carbonyl crotylation at a significantly lower tempereature than previous conditions involving in situ catalyst preparation, resulting in generally higher yields and slightly enhanced enantioselectivity. In addition, the scope of the reaction was successfully expanded to substrates found unreactive under first generation conditions. Overall, this work represents both a simplification of procedure and improvement of yield, enantioselectivity, and substrate scope in the development of Krische research group methodology towards crotylation.

1.2 Part Two: 1,1-Disubstituted Olefins as Allyl Donors in Iridium Catalyzed Methallylation

1.2.1 Background

As described in the previous chapter, the Krische group has reported great success in the fields of allylation and crotylation utilizing *ortho*-cyclometallated iridium catalysts generated both in situ and, in the aforementioned case of crotylation, through a preformed precatalyst (Scheme 9). Benzylic, allylic, and aliphatic alcohols are transformed to the

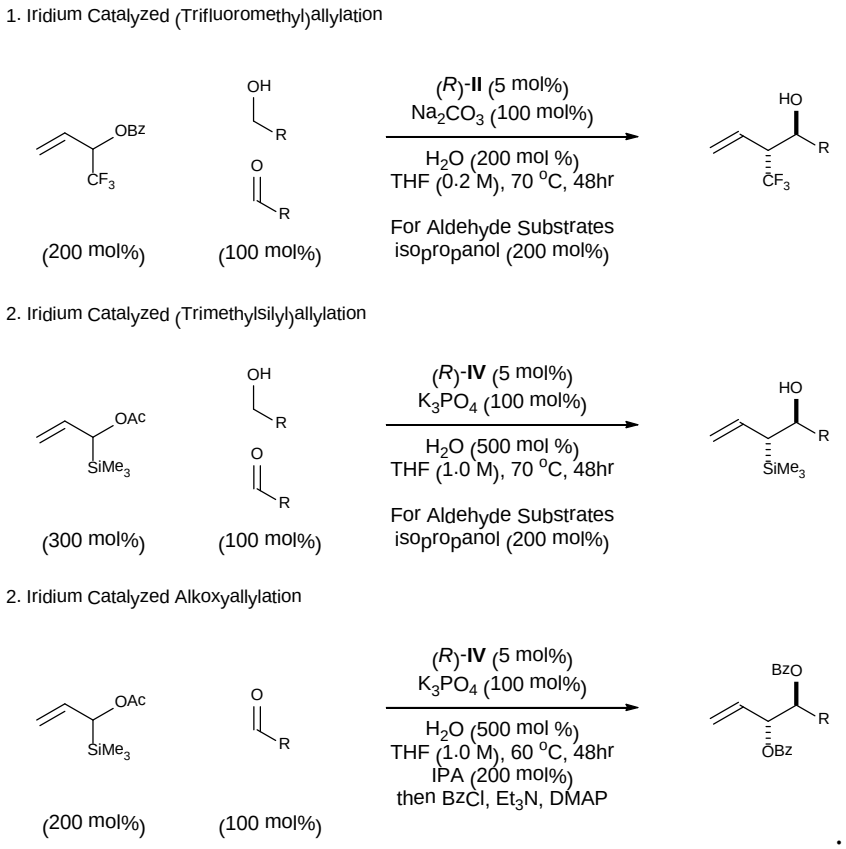
corresponding homoallylic alcohols with uniformly high levels of enantioselectivity. Under identical conditions with the addition of isopropanol as the terminal reductant, aldehydes undergo the same transformation. This protocol avoids both cryogenic conditions and stoichiometric use of chiral or metallic reagents.[10]



Scheme 9: *ortho*-cyclometallated iridium precatalysts

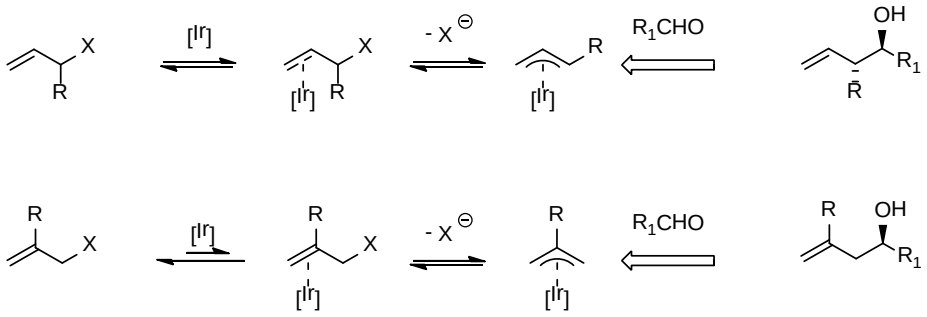
Since the development of these early reactions, the Krische group has developed a diverse range of reactions utilizing α-substituted allyl donors. Beyond crotylation[4,9], diastereo- and enantioselective processes such as α-(trifluoromethyl)allylation[11], α-(trimethylsilyl)allylation[12], α-(hydroxymethyl)allylation[13] can all be performed. While these processes all show high tolerance of substitution at the α position, coupling reactions using multiply substituted alkenes have been much more difficult to develop (Scheme 10).

To understand the difficulties inherent in coupling allyl-type moieties with multiply substituted olefins, one must consider the proposed reaction mechanism. In the the iridium-catalyzed crotylation, the reaction is postulated to take place through a substituted π-allyl iridium intermediate, resulting in complete branched regioselectivity accompanied by fair to complete levels of *anti*-diastereoselectivity. This proposed



Scheme 10: General reactions schemes for several group developed couplings using α-substituted allyl donors.

addition occurs with allylic inversion from the primary (*E*)-σ-allyl haptomer.[4] 1,1- or 1,2-substituents are proposed to render the alkene a poor ligand for the iridium center due to steric hinderence, resulting in no observed participation in the carbonyl addition process. This is supported in the literature by examples of decreased stability in late transition metal-olefin π-complexes with increasing degrees of olefin substitution.[14] As olefin coordination is a prerequisite to ionization, the observed success with monosubstituted allyl donors likely stems from the shorter lifetime of iridium-olefin π-complexes with higher degrees of substitution (Scheme 11). The goal of this research was to probe the limitations of iridium transfer hydrogenation coupling utilizing a 1,1-substituted allyl donor.



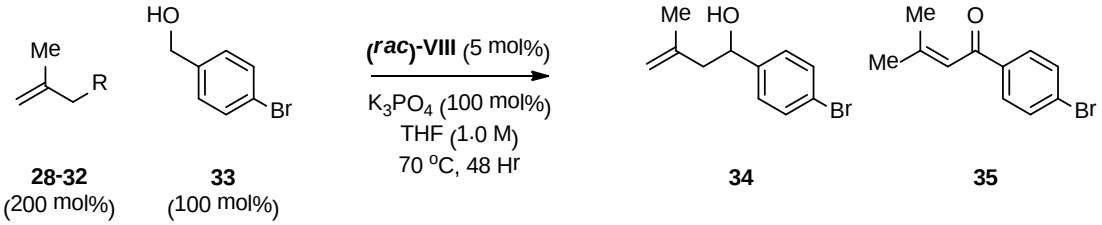
Scheme 11: Difficulties presented by 1,1 disubstituted allyl donor over monosubstituted

1.2.2 Discovery

As previously described, an explanation for the poor reactivity of 1,1-substituted allyl donors can be a short lifetime of the iridium-olefin π-complex, giving ionization too small of a timeframe to efficiently occur. A natural solution to such a problem would be to cause a faster ionization event due to the use of a better leaving group. To test this

premise, the methallylation reaction was chosen as a simple yet useful system employing a 1,1-disubstituted allyl donor. While examples have been reported in the literature, there have been very few studies devoted exclusively to enantioselective carbonyl methallylation compared to analogous allylation and crotylation reactions.[15,16] Due to this fact, a study was initiated to explore whether methallylation could be achieved through iridium catalysis using methallyl donors with a better leaving group.

To explore this premise, methallyl acetate **28**, benzoate **29**, mesylate **30**, carbonate **31**, and chloride **32** were reacted under conditions similar to aforementioned iridium catalyzed transfer hydrogenation crotylation conditions utilizing a preformed catalyst. While **28**, **29**, **30**, and **31** were not observed to participate in carbonyl addition, a relatively high rate of conversion was observed using methallyl chloride **32**. Employing (*rac*)-**VIII** as the catalyst, prepared from $[Ir(cod)Cl]_2$, BIPHEP, allyl acetate, and 4-cyano-3-nitrobenzoic acid, methallyl chloride reacted with benzylic alcohol to give methallylation product **34** in 72% yield after 48 hours at 70 °C (Table 2). While extremely promising, this initial experiment also revealed a major side-reaction in the oxidation of methallylation product **34** to form the undesired conjugated enone **35**. The formation of enone **35**, while a surprise, corroborates the reduced coordination ability of the methyl-substituted homoallylic olefin when compared to unsubstituted olefin products of allylation or crotylation. This reduced coordination ability is thought to induce β-hydride elimination to form a transient β,γ-enone that isomerizes to the thermodynamically preferred conjugated enone **35**.



28-32 (200 mol%) **33** (100 mol%) **34** **35**

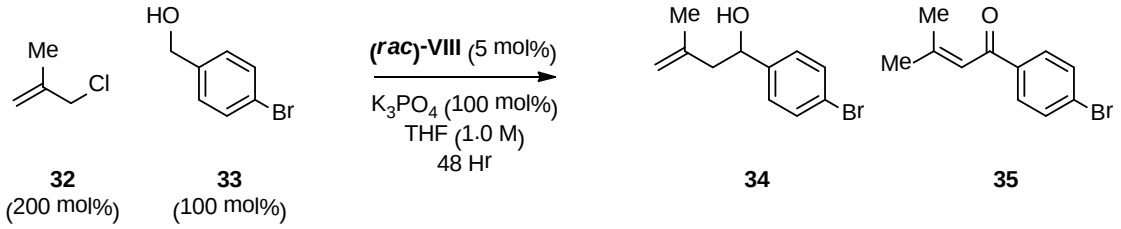
Entry	Leaving Group (R)	Yield (%) 34	35
1	**28,** R = OAc	-	-
2	**29,** R = OBz	-	-
3	**30,** R = OMs	-	-
4	**31,** R = OBoc	-	-
5	**32,** R = Cl	72	24

Reaction was discovered by Abbas Hassan

Table 2: Initial discovery of methallylation using methallyl chloride.

1.2.3 Reaction Optimization

After initial discovery, the reaction was fully optimized through adjustment of each reaction condition with the goal of maximizing product yield while also minimizing the byproduct enone. Through a screen of reaction temperatures, we observed a great reduction in the ratio of produced enone byproduct **35** to methallylation product **34** with a relatively small reduction in yield (Table 3). In order to explore further suppression of the enone byproduct, however, further optimization was carried out at 70 °C.



32 (200 mol%) **33** (100 mol%) **34** **35**

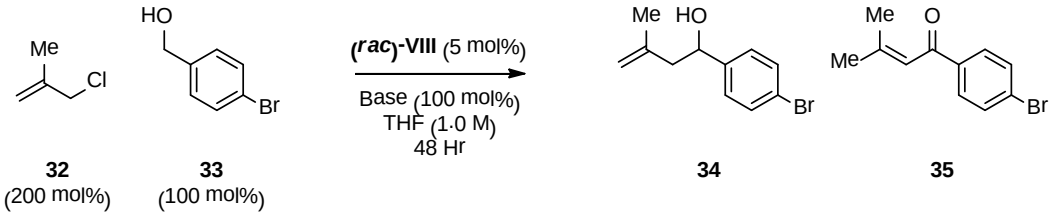
Entry	Temperature (°C)	Yield (%) **34**	**35**
1	90	73	20
2	80	74	23
3	70	72	24
4	60	67	17
5	50	63	5

Reaction was optimized with the help of Abbas Hassan

Table 3: Temperature effect.

The next variable explored was the effect of the reaction solvent. We observed that non-polar solvents such as toluene and hexane gave appreciable amounts of product, but had a much lower ratio of product to enone byproduct than our initial reaction. Additionally, the chlorinated solvent dichloroethane was observed to give only trace amounts of product or byproduct **35**. Oxygenated solvents such as THF and 1,4-dioxane were both found to be effective, with THF showing much higher product yield but 1,4-dioxane displaying a lower amount of enone byproduct **35**. Due to the significantly higher product yield, we decided to continue forward with THF as our solvent of choice (Table 4, Entries 1-5). After choosing THF, we screened a variety of organic and inorganic bases, finding that tribasic potassium phosphate gave much higher product

yields than candidates such as sodium carbonate, sodium acetate, or 2,6-lutidine (Table 4, Entries 5-8).



32 (200 mol%) **33** (100 mol%) **34** **35**

Entry	Base	Solvent	Yield (%) **34**	**35**
1	K_3PO_4	Toluene	37	15
2	K_3PO_4	Hexane	33	22
3	K_3PO_4	DCE	-	-
4	K_3PO_4	Dioxane	59	9
5	K_3PO_4	THF	72	24
6	Na_2CO_3	THF	21	-
7	NaOAc	THF	-	-
8	2,6-Lutidine	THF	-	-

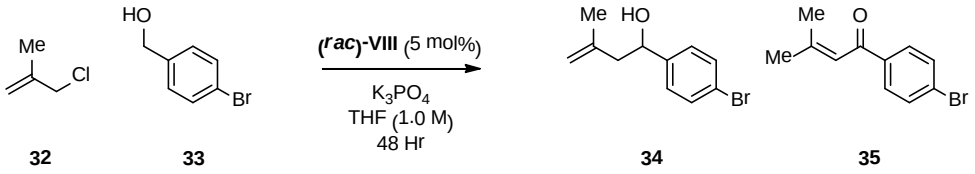
Reaction was optimized with the help of Abbas Hassan

Table 4: Solvent and base effects.

After selection of tribasic potassium phosphate as the most effective base for our reaction, we screened the effects of base loading on our reaction. With descending molar ratios of base (75 mol% and 50 mol%), we observed a reduction in enone byproduct **35** (12% and 0% respectively). However, this reduction of byproduct came at the expense of product yield (Table 5, Entries 1-5). When the molar ratio of the base was increased

above 100%, observed yield was diminished, most likely as a result of product decomposition.

With optimal base and base stoichiometry in hand, we moved on to exploration of the molar ratio of our allyl donor, methallyl chloride. With increased loading (300 mol%), we observed a reduced amount of enone byproduct **35**, 16% (Table 5, Entry 6). This increased loading of methallyl chloride was not an issue due to the commercial availability and relatively low cost of methallyl chloride. With all of our variables optimized, we decided to rescreen a lower temperature reaction as 50 °C had shown the lowest production of enone byproduct upon initial investigation. To our delight, reaction yield of **34** at 50 °C exceeded reaction yield of **34** at 70 °C with a significant reduction in enone byproduct **35** (Table 5, Entry 7). With this result, we were satisfied with our reaction conditions of 50 °C, 100 mol% tribasic potassium phosphate, and 300 mol% methallyl chloride.



32 **33** **34** **35**

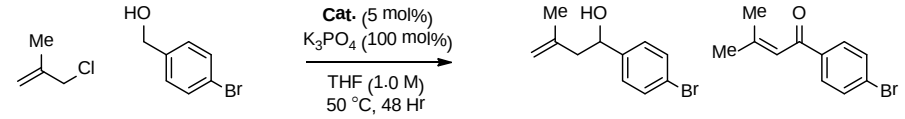
Entry	Methallyl Chloride	K_3PO_4 (mol%)	T (°C)	Yield (%) **34**	**35**
1	200	50	70	25	-
2	200	75	70	60	12
3	200	100	70	72	24
4	200	125	70	68	17
5	200	150	70	40	-
6	300	100	70	74	16
7	300	100	50	76	5

Reaction was optimized with the help of Abbas Hassan

Table 5: Effects of tribasic potassium phosphate and methallyl chloride loading.

The next issue to tackle was enantioselectivity. In previous reactions utilizing chiral *ortho*-cyclometallated iridium *C,O*-benzoates to catalyze carbonyl additions, we saw very high levels of enantioselectivity. Due to this fact, we believed that a screening of axially chiral diphosphine ligands would produce successful results. To our delight, several chiral ligands gave excellent enantioselectivity. Catalyst modified by (*R*)-SEGPHOS, (*R*)-**IV**, furnished methallylation product **34** in 63% yield and 96 % enantiomeric excess, albeit with 32% yield of the enone byproduct **35**. (*R*)-BINAP modified catalyst, (*R*)-**VI**, displayed a lower level of enone byproduct **35** but also displayed a lower level of enantioselectivity (85% ee). Due to the relatively low cost and high availability of BINAP, an effort was made to improve enantioselectivity by varying reaction conditions with no success. Finally, a balance was struck with (*R*)-Cl,MeO-BIPHEP modified catalyst, *(R)*-**II**, giving both a high level of enantioselectivity (94% ee)

and a high yield of **34** (84%), albeit accompanied by a significant amount of enone byproduct **35** (12%). Making the observation that our yields had significantly increased using catalyst *(R)*-**II**, we discovered that a shorter reaction time did not have a negative impact on yield (Table 6).



32 (300 mol%) **33** (100 mol%) **34** **35**

Entry	Ligand-catalyst	Time (h)	Yield **34**	Yield **35**
1	(*R*)-SEGPHOS-(***R***)-**IV**	48	63%, 96% ee	32%
2	(*R*)-BINAP-(***R***)-**VI**	48	84%, 85% ee	14%
3	(*R*)-Cl,MeO-BIPHEP-(***R***)-**II**	48	84%, 94% ee	12%
4	(*R*)-Cl,MeO-BIPHEP-(***R***)-**II**	24	83%, 96% ee	12%

Reaction was optimized with the help of Abbas Hassan

Table 6: Screening of chiral ligands.

1.2.4 Substrate Scope

Utilizing the optimized conditions including catalyst (*R*)-**II** (5 mol%), methallyl chloride (300 mol%), and tribasic potassium phosphate (100 mol%) in THF (1.0 M) at 50 °C, methallylation took place with a wide range of substrates with good reactivity. Benzylic alcohols underwent methallylation in good yields, with piperonyl alcohol **50** resulting in a 78% isolated yield of product **42** and 95% ee, heteroaryl alcohol **51** resulting in methallylation product **43** in 87% isolated yield and 96% ee, and

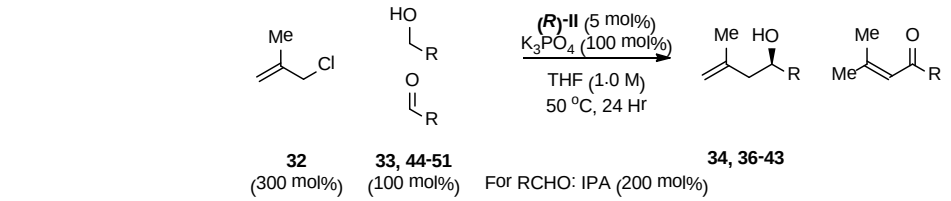
aforementioned 4-bromobenzyl alcohol **33** resulting in methallylation product **34** in 83% isolated yield and 96% ee. The same conditions carried over to aliphatic alcohols, with nonanol **44**, cyclohexane methanol **47**, mono-protected propanediol **45** and mono-protected neopentyl glycol **44** resulting in the corresponding products of methallylation (**36**, **39**, **37**, and **38**, respectively) in fair to excellent yields with uniformly high levels of enantioselectivity. In addition, aliphatic alcohols showed a much lower propensity to form the aforementioned enone byproducts with only trace amounts forming in all cases. Allylic systems, however, showed high levels of enone byproduct formation under standard conditions, To suppress evident over oxidation in these systems, reactions of cinnamyl alcohol **48** and geraniol **49** were performed under standard conditions with an additional 200 mol% isopropanol to give products **40** and **41** in good isolated yield and high enantiomeric excess (Table 7).

In the presence of isopropanol (200 mol%), the corresponding benzylic and aliphatic aldehydes underwent methallylation in comparable isolated yields and enantiomeric excess. As with allylic alcohols, allylic aldehydes required additional isopropanol (400 mol%) but also gave comparable isolated yields and enantiomeric excess. These reactions displayed methallylation of equal facility from either the alcohol or aldehyde oxidation level (Table 7).

1.2.5 Summary

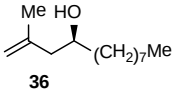
In summary, the scope of carbonyl addition chemistry in the Krische research group was successfully expanded to allyl donors containing a 1,1-disubstitution pattern in

the form of the methallylation reaction. We postulated that methallyl acetate did not serve as an efficient allyl donor due to the decreased stability and therefore shorter lifetime of the resultant iridium-olefin π-complex that precedes formation of the π-allyliridium complex requisite for carbonyl addition. Through moving away from acetate to a more reactive leaving group in methallyl chloride, we believe the ionization to form the π-allyliridium species is faster, directly compensating for the shorter lifetime of the more highly substituted olefin π-complex. With this discovery in hand, highly enantioselective methallylation is achieved from the alcohol or aldehyde oxidation levels in the absence of stoichiometric chiral or metallic reagents.

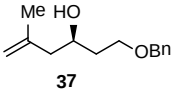


32 (300 mol%) **33, 44-51** (100 mol%) For RCHO: IPA (200 mol%) **34, 36-43**

44: R = $(CH_2)_7Me$ **45**: R = $(CH_2)_2OBn$ **46**: R = $C(CH_3)_2CH_2OPMB$
47: R = C_6H_{11} **48**: R = HC=CHPh **49**: R = $HC{=}C(CH_3)(CH_2)_2CH{=}C(CH_3)_2$
33: R = *p*-BrPh **50**: R = piperonyl **51**: R = 2-benzothienyl



36



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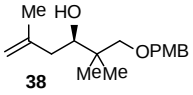
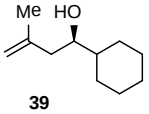


38

Alcohol:	80% Yield (>1% enone), 95% ee[c]	69% Yield (>1% enone), 96% ee[c]	90% Yield (>1% enone), 94% ee
Aldehyde:	75% Yield (>1% enone), 97% ee[c]	55% Yield (>1% enone), 95% ee[c]	91% Yield (>1% enone), 97% ee



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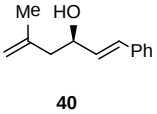
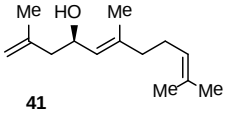
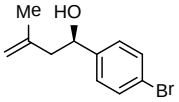


40



41

Alcohol:	72% Yield (>1% enone), 92% ee[c]	72% Yield (12% enone), 92% ee[a]	80% Yield (>1% enone), 94% ee[a]
Aldehyde:	74% Yield (>1% enone), 91% ee[c]	74% Yield (13% enone), 91% ee[b]	75% Yield (6% enone), 93% ee[b]



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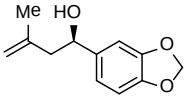

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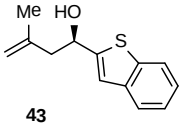


43

Alcohol:	83% Yield (14% enone), 96% ee[c]	78% Yield (5% enone), 95% ee	87% Yield (5% enone), 96% ee
Aldehyde:	90% Yield (8% enone), 95% ee[c]	85% Yield (10% enone), 96% ee	91% Yield (5% enone), 95% ee

[a] Reaction was carried out with 200 mol% IPA. [b] Reaction was carried out with 400 mol% IPA. [c] Reaction was performed by Abbas Hassan.

Table 7: Substrate scope of Iridium catalyzed methallylation reaction

1.3 Experimental Section

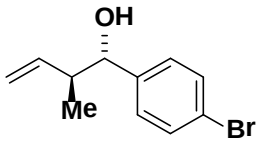
1.3.1 Representative Synthesis of Catalyst: Preparation of (*S*)-IV

To a mixture of $[Ir(cod)Cl]_2$ (87.3 mg, 0.13 mmol, 100 mol%), (*S*)-SEGPHOS (159 mg, 0.26 mmol, 200 mol%), Cs_2CO_3 (169 mg, 0.52 mmol, 400 mol%), 4-CN-3-NO_2BzOH (100 mg, 0.52 mmol, 400 mol%) and allyl acetate (65 mg, 0.65 mmol, 500 mol%) in a sealed tube under an atmosphere of N_2 was added THF (2.6 mL, 0.05 M). The reaction

mixture was stirred for 30 minutes at ambient temperature and heated for 1.5 hours at 80 ^{o}C. Upon cooling to ambient temperature, the reaction mixture was diluted with CH_2Cl_2 (10 mL), filtered through a celite plug, washed with CH_2Cl_2 (50 mL) and concentrated *in vacuo*. The residue was purified by flash chromatography (SiO_2, 20% Et_2O/CH_2Cl_2) and concentrated *in vacuo*. The light yellow gum was dissolved in THF (3 mL). Rapid addition of hexanes (50 mL) to the stirred solution resulted in precipitation of a bright yellow powder, which was collected by gravity filtration. Removal of trace solvents *in vacuo* delivered (*S*)-**IV** (228 mg, 0.221 mmol) in 85% yield.

1.3.2 Experiment details of crotylation from alcohol oxidation level

(*1S,2S*)-1-(4-bromophenyl)-2-methylbut-3-en-1-ol

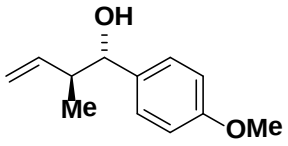


8

An oven-dried sealed tube under an atmosphere of N_2 was charged with (4-bromophenyl)methanol **17** (37.4 mg, 0.20 mmol, 100 mol%), (*S*)-**IV** (10.3 mg, 0.01 mmol, 5 mol%), K_3PO_4 (21.5 mg, 0.10 mmol, 50 mol%), THF (0.1 mL, 2.0 M), and H_2O (18 μL, 1.0 mmol, 500 mol%). But-3-en-2-yl acetate **1** (45.6 mg, 0.40 mmol, 200 mol%) was added and the mixture was allowed to stir at ambient temperature for 0.5 hr, at which point the reaction vessel was placed in an oil bath at 60 ^{o}C and was allowed to stir for 48 hr. The reaction mixture was concentrated *in vacuo*. Purification of the residue by column chromatography (SiO_2; ethyl acetate: hexanes, 1:20 with 0.1% TEA) provided **8** (37.6 mg, 0.156 mmol) as a colorless oil in 78% yield (16:1 dr).

TLC (SiO_2): R_f = 0.4 (ethyl acetate: hexanes, 1:5). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.46 (d, *J* = 8.0 Hz, 2H), 7.18 (d, *J* = 8.0 Hz, 2H), 5.81-5.71 (m, 1H), 5.22-5.16 (m, 2H), 4.32 (d, *J* = 7.6 Hz, 1H), 2.45-2.37 (m, 1H), 2.20 (br s, 1H), 0.87 (d, *J* = 6.8 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ141.4, 140.1, 131.3, 128.6, 121.4, 117.3, 77.1, 46.4, 16.4 **HPLC**: (Chiralpak AS-H/AS-H column, hexanes:*i*-PrOH = 98:2, 0.5 mL/min, 230 nm), t_{minor} = 27.9 min, t_{major} = 31.8 min; ee = 97%

(*1S,2S*)-1-(4-methoxyphenyl)-2-methylbut-3-en-1-ol



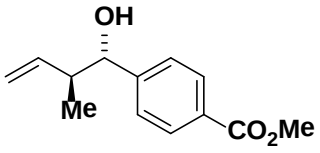
9

An oven-dried sealed tube under an atmosphere of N_2 was charged with (4-methoxyphenyl)methanol **18** (27.6 mg, 0.20 mmol, 100 mol%), (*S*)-**IV** (10.3 mg, 0.01 mmol, 5 mol%), K_3PO_4 (21.5 mg, 0.10 mmol, 50 mol%), THF (0.1 mL, 2.0 M), and H_2O (18 μL, 1.0 mmol, 500 mol%). But-3-en-2-yl acetate **1** (45.6 mg, 0.40 mmol, 200 mol%) was added and the mixture was allowed to stir at ambient temperature for 0.5 hr, at which point the reaction vessel was placed in an oil bath at 60 ^oC and was allowed to stir for 48 hr. The reaction mixture was concentrated *in vacuo*. Purification of the residue by column chromatography (SiO_2; ethyl acetate: hexanes, 1:20 with 0.1% TEA) provided **9** (35.0 mg, 0.182 mmol) as a colorless oil in 91% yield (10:1 dr).

TLC (SiO_2): R_f = 0.4 (ethyl acetate: hexanes, 1:5). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.25 (d, *J* = 8.0 Hz, 2H), 6.87 (d, *J* = 8.0 Hz, 2H), 5.86-5.76 (m, 1H), 5.23-5.16 (m, 2H), 4.29 (d, *J*

= 8.4 Hz, 1H), 3.80 (s, 3H), 2.48-2.42 (m, 1H), 2.15 (br s, 1H), 0.83 (d, *J* = 6.8 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ159.3, 141.2, 134.8, 128.2, 117.0, 113.9, 77.7, 55.5, 46.7, 16.8. **HPLC**: (Chiralpak AD-H/AD-H column, hexanes:*i*-PrOH = 95:5, 0.5 mL/min, 230 nm), t_{minor} = 40.2 min, t_{major} = 47.6 min; ee = 95%.

Methyl 4-((*1S,2S*)-1-hydroxy-2-methylbut-3-enyl)benzoate



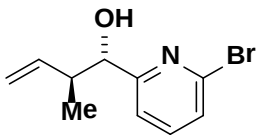
10

An oven-dried sealed tube under an atmosphere of N_2 was charged with methyl 4-(hydroxymethyl)benzoate **19** (33.2 mg, 0.20 mmol, 100 mol%), (*S*)-**IV** (10.3 mg, 0.01 mmol, 5 mol%), K_3PO_4 (21.5 mg, 0.10 mmol, 50 mol%), THF (0.1 mL, 2.0 M), and H_2O (18 μL, 1.0 mmol, 500 mol%). But-3-en-2-yl acetate **1** (45.6 mg, 0.40 mmol, 200 mol%) was added and the mixture was allowed to stir at ambient temperature for 0.5 hr, at which point the reaction vessel was placed in an oil bath at 60 ^{o}C and was allowed to stir for 48 hr. The reaction mixture was concentrated *in vacuo*. Purification of the residue by column chromatography (SiO_2; ethyl acetate: hexanes, 1:20 with 0.1% TEA) provided **10** (34.4 mg, 0.156 mmol) as a colorless oil in 78% yield (11:1 dr).

TLC (SiO_2): R_f = 0.4 (ethyl acetate: hexanes, 1:5). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.97 (d, *J* = 8.0 Hz, 2H), 7.36 (d, *J* = 8.0 Hz, 2H), 5.79-5.69 (m, 1H), 5.17-5.12 (m, 2H), 4.40 (d, *J* = 7.2 Hz, 1H), 3.88 (s, 3H), 2.49-2.36 (m, 2H), 0.86 (d, *J* = 6.8 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ167.2, 147.9, 140.1, 129.7, 129.6, 127.0, 117.5, 77.3, 52.3, 46.5, 16.6.

HPLC: (Chiralpak AD-H column, hexanes:*i*-PrOH = 95:5, 0.5 mL/min, 254 nm), t_{minor} = 27.1 min, t_{major} = 32.3 min; ee = 98%.

(*1S*,*2S*)-1-(6-bromopyridin-2-yl)-2-methylbut-3-en-1-ol

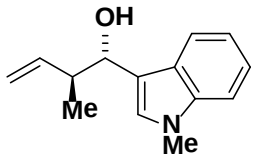


11

An oven-dried sealed tube under an atmosphere of N_2 was charged with (6-bromopyridin-2-yl)methanol **20** (37.6 mg, 0.20 mmol, 100 mol%), (*S*)-**IV** (10.3 mg, 0.01 mmol, 5 mol%), K_3PO_4 (21.5 mg, 0.10 mmol, 50 mol%), THF (0.1 mL, 2.0 M), and H_2O (18 μL, 1.0 mmol, 500 mol%). But-3-en-2-yl acetate **1** (45.6 mg, 0.40 mmol, 200 mol%) was added and the mixture was allowed to stir at ambient temperature for 0.5 hr, at which point the reaction vessel was placed in an oil bath at 60 ^oC and was allowed to stir for 48 hr. The reaction mixture was concentrated *in vacuo*. Purification of the residue by column chromatography (SiO_2; ethyl acetate: hexanes, 1:20 with 0.1% TEA) provided **11** (24.2 mg, 0.100 mmol) as a colorless oil in 50% yield (14:1 dr).

TLC (SiO_2): R_f = 0.3 (ethyl acetate: hexanes, 1:5). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.53 (t, *J* = 7.6 Hz, 1H), 7.38 (d, *J* = 7.6 Hz, 1H), 7.25 (d, *J* = 8.0 Hz, 1H), 5.73 (dt, *J* = 17.2, 10.4, 1H), 5.10-4.99 (m, 2H), 4.58 (t, *J* = 5.2 Hz, 1H), 3.28 (d, *J* = 6.0 Hz, 1H), 2.72-2.64 (m, 1H), 1.06 (d, *J* = 6.8 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 162.8, 141.0, 138.7, 138.6, 126.7, 120.0, 116.5, 44.6, 16.1. **HPLC**: (Chiralcel OD-H column, hexanes:*i*-PrOH = 95:5, 0.5 mL/min, 210 nm), t_{major} = 12.1 min, t_{minor} = 16.8 min ; ee = 98%.

(*1S,2S*)-2-methyl-1-(1-methyl-1*H*-indol-3-yl)but-3-en-1-ol

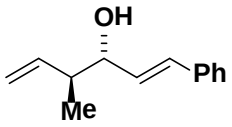


12

An oven-dried sealed tube under an atmosphere of N_2 was charged with (1-methyl-1*H*-indol-3-yl)methanol **21** (32.2 mg, 0.20 mmol, 100 mol%), (*S*)-**IV** (10.3 mg, 0.01 mmol, 5 mol%), K_3PO_4 (21.5 mg, 0.10 mmol, 50 mol%), THF (0.1 mL, 2.0 M), and H_2O (18 μL, 1.0 mmol, 500 mol%). But-3-en-2-yl acetate **1** (45.6 mg, 0.40 mmol, 200 mol%) was added and the mixture was allowed to stir at ambient temperature for 0.5 hr, at which point the reaction vessel was placed in an oil bath at 60 ^oC and was allowed to stir for 48 hr. The reaction mixture was concentrated *in vacuo*. Purification of the residue by column chromatography (SiO_2; ethyl acetate: hexanes, 1:20 with 0.1% TEA) provided **12** (32.3 mg, 0.150 mmol) as a colorless oil in 75% yield (7:1 dr).

TLC (SiO_2): R_f = 0.4 (ethyl acetate: hexanes, 1:5). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.62 (d, *J* = 8.0 Hz, 1H), 7.34 (d, *J* = 8.4 Hz, 1H), 7.26 (t, *J* = 8.0 Hz, 1H), 7.14 (t, *J* = 8.0 Hz, 1H), 6.48 (s, 1H), 5.98-5.88 (m, 1H), 5.33-5.25 (m, 2H), 4.60 (d, *J* = 8.4 Hz, 1H), 3.81 (s, 3H), 2.86-2.78 (m, 1H), 2.22 (br s, 1H), 1.03 (d, *J* = 6.8 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 140.7, 140.3, 138.2, 127.5, 121.9, 120.9, 119.8, 117.4, 109.4, 100.8, 71.4, 44.3, 30.7, 17.5. **HPLC**: (Chiralcel OJ-H column, hexanes:*i*-PrOH = 93:7, 0.5 mL/min, 254 nm), t_{major} = 53.3 min, t_{minor} = 66.0 min; ee = 98%.

(*3R,4S,E*)-4-methyl-1-phenylhexa-1,5-dien-3-ol

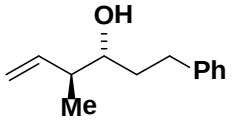


13

An oven-dried sealed tube under an atmosphere of N_2 was charged with *trans*-cinnamyl alcohol **22** (26.8 mg, 0.20 mmol, 100 mol%), (*S*)-**IV** (10.3 mg, 0.01 mmol, 5 mol%), K_3PO_4 (21.5 mg, 0.10 mmol, 50 mol%), THF (0.1 mL, 2.0 M), and H_2O (18 μL, 1.0 mmol, 500 mol%). But-3-en-2-yl acetate **1** (45.6 mg, 0.40 mmol, 200 mol%) was added and the mixture was allowed to stir at ambient temperature for 0.5 hr, at which point the reaction vessel was placed in an oil bath at 70 ^oC and was allowed to stir for 48 hr. The reaction mixture was concentrated *in vacuo*. Purification of the residue by column chromatography (SiO_2; ethyl acetate: hexanes, 1:20 with 0.1% TEA) provided **13** (27.1 mg, 0.144 mmol) as a colorless oil in 72% yield (10:1 dr).

TLC (SiO_2): R_f = 0.3 (ethyl acetate:hexanes, 1:10). **^{1}H NMR** (400 MHz, CDCl3): δ 7.41-7.23 (m, 5H), 6.61 (d, *J* = 16.0 Hz, 1H), 6.21 (dd, *J* = 16.0, 7.2 Hz, 1H), 5.88-5.78 (m, 1H), 5.21-5.16 (m, 2H), 4.06 (t, *J* = 6.8 Hz, 1H), 2.41-2.35 (m, 1H), 1.99 (br s, 1H), 1.06 (d, *J* = 6.8 Hz, 3H).
^{13}C NMR (100 MHz, CDCl3): δ 140.4, 136.9, 132.0, 130.4, 128.8, 127.9, 126.8, 117.0, 76.4, 44.9, 16.3. **HPLC**: (Chiralpak AS-H/AS-H column, hexanes:*i*-PrOH = 98:2, 0.5 mL/min, 254 nm), t_{minor} = 26.8 min, t_{major} = 31.5 min; ee = 93%.

(*3R,4S*)-4-methyl-1-phenylhex-5-en-3-ol

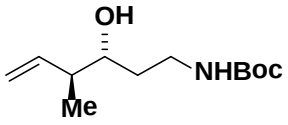


14

An oven-dried sealed tube under an atmosphere of N_2 was charged with 3-phenylpropan-1-ol **23** (27.2 mg, 0.20 mmol, 100 mol%), (*S*)-**IV** (10.3 mg, 0.01 mmol, 5 mol%), K_3PO_4 (21.5 mg, 0.10 mmol, 50 mol%), THF (0.1 mL, 2.0 M), and H_2O (18 μL, 1.0 mmol, 500 mol%). But-3-en-2-yl acetate **1** (45.6 mg, 0.40 mmol, 200 mol%) was added and the mixture was allowed to stir at ambient temperature for 0.5 hr, at which point the reaction vessel was placed in an oil bath at 60 ^oC and was allowed to stir for 48 hr. The reaction mixture was concentrated *in vacuo*. Purification of the residue by column chromatography (SiO_2; ethyl acetate: hexanes, 1:20 with 0.1% TEA) provided **14** (27.0 mg, 0.142 mmol) as a colorless oil in 71% yield (>20:1 dr).

TLC (SiO_2): R_f = 0.4 (ethyl acetate: hexanes, 1:5). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.31-7.17 (m, 5H), 5.80-5.70 (m, 1H), 5.15-5.10 (m, 2H), 3.43-3.40 (m, 1H), 2.89-2.81 (m, 1H), 2.72-2.64 (m, 1H), 2.26-2.20 (m, 1H), 1.89-1.80 (m, 1H), 1.75-1.62 (m, 2H), 1.03 (d, *J* = 6.8 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 142.6, 140.4, 128.7, 128.6, 126.0, 116.8, 74.2, 44.6, 36.4, 32.4, 16.5. **HPLC**: (Chiralcel OD-H column, hexanes:*i*-PrOH = 97:3, 0.7 mL/min, 254 nm), t_{minor} = 11.5 min, t_{major} = 18.7 min; ee = 99%.

***tert*-butyl (*3R,4S*)-3-hydroxy-4-methylhex-5-enylcarbamate**

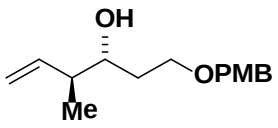


15

An oven-dried sealed tube under an atmosphere of N_2 was charged with *tert*-butyl 3-hydroxypropylcarbamate **24** (35.0 mg, 0.20 mmol, 100 mol%), (*S*)-**IV** (10.3 mg, 0.01 mmol, 5 mol%), K_3PO_4 (21.5 mg, 0.10 mmol, 50 mol%), THF (0.1 mL, 2.0 M), and H_2O (18 μL, 1.0 mmol, 500 mol%). But-3-en-2-yl acetate **1** (45.6 mg, 0.40 mmol, 200 mol%) was added and the mixture was allowed to stir at ambient temperature for 0.5 hr, at which point the reaction vessel was placed in an oil bath at 70 ^oC and was allowed to stir for 48 hr. The reaction mixture was concentrated *in vacuo*. Purification of the residue by column chromatography (SiO_2; ethyl acetate: hexanes, 1:20 with 0.1% TEA) provided **15** (32.6 mg, 0.142 mmol) as a colorless oil in 71% yield (>20:1 dr).

TLC (SiO_2): R_f = 0.5 (ethyl acetate:hexanes, 1:3). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 5.76 (dtd, *J* = 17.2, 10.0, 0.4 Hz, 1H), 5.12-5.05 (m, 2H), 4.91 (br, 1H), 3.48-3.41 (m, 2H), 3.20-3.11 (m, 1H), 2.58 (d, *J* = 2.8 Hz, 1H), 2.30-2.17 (m, 1H), 1.72-1.64 (m, 1H), 1.54-1.45 (m, 1H), 1.44 (s, 9H), 1.03 (d, *J* = 6.8 Hz,3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 156.7, 140.4, 116.1, 79.3, 72.6, 44.2, 37.7, 34.2, 28.4, 16.2. **HPLC**: Enantiomeric excess was determined by HPLC analysis of the 4-nitrobenzoate derivative of the product (Chiralcel OJ-H column, hexanes:*i*-PrOH = 98:2, 0.75 mL/min, 254 nm), t_{minor} = 24.4 min, t_{major} = 28.1 min; ee = 96%.

(*3R,4S*)-1-(4-methoxybenzyloxy)-4-methylhex-5-en-3-ol



16

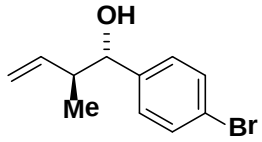
An oven-dried sealed tube under an atmosphere of N_2 was charged with 3-(4-methoxybenzyloxy)propan-1-ol **25** (39.2 mg, 0.20 mmol, 100 mol%), (*S*)-**IV** (10.3 mg, 0.01 mmol, 5 mol%), K_3PO_4 (21.5 mg, 0.10 mmol, 50 mol%), THF (0.1 mL, 2.0 M), and

H_2O (18 μL, 1.0 mmol, 500 mol%). But-3-en-2-yl acetate **1** (45.6 mg, 0.40 mmol, 200 mol%) was added and the mixture was allowed to stir at ambient temperature for 0.5 hr, at which point the reaction vessel was placed in an oil bath at 60 ^{o}C and was allowed to stir for 48 hr. The reaction mixture was concentrated *in vacuo*. Purification of the residue by column chromatography (SiO_2; ethyl acetate: hexanes, 1:20 with 0.1% TEA) provided **16** (38.1 mg, 0.152 mmol) as a colorless oil in 76% yield (15:1 dr).

TLC (SiO_2): R_f = 0.5 (ethyl acetate:hexanes, 1:4). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.26-7.24 (m, 2H), 6.90-6.86 (m, 2H), 5.80 (dt, *J* = 17.2, 10.0 Hz, 1H), 5.09-5.02 (m, 2H), 4.45 (s, 2H), 3.80 (s, 3H), 3.71-3.61 (m, 3H), 2.79 (d, *J* = 2.8, 1H), 2.23 (qt, *J* = 6.8, 0.8 Hz, 1H), 1.74-1.70 (m, 2H), 1.03 (d, *J* = 6.8 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 159.2, 140.5, 130.1, 129.3, 115.4, 113.8, 74.3, 73.0, 68.9, 55.3, 44.0, 33.5, 15.8. **HPLC**: Enantiomeric excess was determined by HPLC analysis of the 4-nitrobenzoate derivative of the product (Chiralcel AD-H column, hexanes:*i*-PrOH = 98:2, 1.0 mL/min, 210 nm), t_{minor} = 15.4 min, t_{major} = 17.9 min; ee = 97%.

1.3.3 Experiment details of crotylation from aldehyde oxidation level

(*1S,2S*)-1-(4-bromophenyl)-2-methylbut-3-en-1-ol



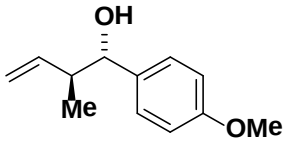
8

An oven-dried sealed tube under an atmosphere of N_2 was charged with 4-bromobenzaldehyde **17** (37.0 mg, 0.20 mmol, 100 mol%), (*S*)-**IV** (10.3 mg, 0.01 mmol, 5

mol%), K_3PO_4 (21.5 mg, 0.10 mmol, 50 mol%), THF (0.1 mL, 2.0 M), isopropanol (31 μL, 0.4 mmol, 200 mol%), and H_2O (18 μL, 1.0 mmol, 500 mol%). But-3-en-2-yl acetate **1** (45.6 mg, 0.40 mmol, 200 mol%) was added and the mixture was allowed to stir at ambient temperature for 0.5 hr, at which point the reaction vessel was placed in an oil bath at 60 ^oC and was allowed to stir for 48 hr. The reaction mixture was concentrated *in vacuo*. Purification of the residue by column chromatography (SiO_2; ethyl acetate: hexanes, 1:20 with 0.1% TEA) provided **8** (39.5 mg, 0.164 mmol) as a colorless oil in 82% yield (17:1 dr).

HPLC: (Chiralpak AS-H/AS-H column, hexanes:*i*-PrOH = 98:2, 0.5 mL/min, 230 nm), t_{minor} = 27.9 min, t_{major} = 31.8 min; ee = 98%

(*1S,2S*)-1-(4-methoxyphenyl)-2-methylbut-3-en-1-ol



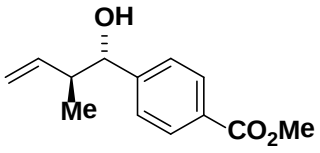
9

An oven-dried sealed tube under an atmosphere of N_2 was charged with 4-methoxybenzaldehyde **18** (27.2 mg, 0.20 mmol, 100 mol%), (*S*)-**IV** (10.3 mg, 0.01 mmol, 5 mol%), K_3PO_4 (21.5 mg, 0.10 mmol, 50 mol%), THF (0.1 mL, 2.0 M), isopropanol (31 μL, 0.4 mmol, 200 mol%), and H_2O (18 μL, 1.0 mmol, 500 mol%). But-3-en-2-yl acetate **1** (45.6 mg, 0.40 mmol, 200 mol%) was added and the mixture was allowed to stir at ambient temperature for 0.5 hr, at which point the reaction vessel was placed in an oil bath at 60 ^oC and was allowed to stir for 48 hr. The reaction mixture was concentrated *in vacuo*. Purification of the residue by column chromatography (SiO_2; ethyl acetate:

hexanes, 1:20 with 0.1% TEA) provided **9** (34.2 mg, 0.178 mmol) as a colorless oil in 89% yield (12:1 dr).

HPLC: (Chiralpak AD-H/AD-H column, hexanes:*i*-PrOH = 95:5, 0.5 mL/min, 230 nm), t_{minor} = 40.2 min, t_{major} = 47.6 min; ee = 98%.

Methyl 4-((*1S,2S*)-1-hydroxy-2-methylbut-3-enyl)benzoate

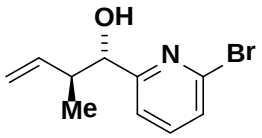


10

An oven-dried sealed tube under an atmosphere of N_2 was charged with methyl 4-formylbenzoate **19** (32.8 mg, 0.20 mmol, 100 mol%), (*S*)-**IV** (10.3 mg, 0.01 mmol, 5 mol%), K_3PO_4 (21.5 mg, 0.10 mmol, 50 mol%), THF (0.1 mL, 2.0 M), isopropanol (31 μL, 0.4 mmol, 200 mol%), and H_2O (18 μL, 1.0 mmol, 500 mol%). But-3-en-2-yl acetate **1** (45.6 mg, 0.40 mmol, 200 mol%) was added and the mixture was allowed to stir at ambient temperature for 0.5 hr, at which point the reaction vessel was placed in an oil bath at 60 ^oC and was allowed to stir for 48 hr. The reaction mixture was concentrated *in vacuo*. Purification of the residue by column chromatography (SiO_2; ethyl acetate: hexanes, 1:20 with 0.1% TEA) provided **10** (35.7 mg, 0.162 mmol) as a colorless oil in 81% yield (11:1 dr).

HPLC: (Chiralpak AD-H column, hexanes:*i*-PrOH = 95:5, 0.5 mL/min, 254 nm), t_{minor} = 27.1 min, t_{major} = 32.3 min; ee = 98%.

(*1S,2S*)-1-(6-bromopyridin-2-yl)-2-methylbut-3-en-1-ol

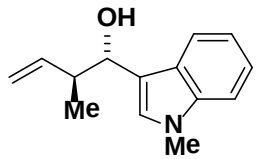


11

An oven-dried sealed tube under an atmosphere of N_2 was charged with 6-bromopicolinaldehyde **20** (37.2 mg, 0.20 mmol, 100 mol%), (*S*)-**IV** (10.3 mg, 0.01 mmol, 5 mol%), K_3PO_4 (21.5 mg, 0.10 mmol, 50 mol%), THF (0.1 mL, 2.0 M), isopropanol (31 μL, 0.4 mmol, 200 mol%), and H_2O (18 μL, 1.0 mmol, 500 mol%). But-3-en-2-yl acetate **1** (45.6 mg, 0.40 mmol, 200 mol%) was added and the mixture was allowed to stir at ambient temperature for 0.5 hr, at which point the reaction vessel was placed in an oil bath at 60 ^oC and was allowed to stir for 48 hr. The reaction mixture was concentrated *in vacuo*. Purification of the residue by column chromatography (SiO_2; ethyl acetate: hexanes, 1:20 with 0.1% TEA) provided **11** (36.3 mg, 0.150 mmol) as a colorless oil in 75% yield (>20:1 dr).

HPLC: (Chiralcel OD-H column, hexanes:*i*-PrOH = 95:5, 0.5 mL/min, 210 nm), t_{major} = 12.1 min, t_{minor} = 16.8 min ; ee = 97%.

(*1S,2S*)-2-methyl-1-(1-methyl-1*H*-indol-3-yl)but-3-en-1-ol

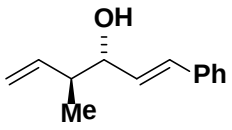


12

An oven-dried sealed tube under an atmosphere of N_2 was charged with 1-methyl-1*H*-indole-3-carbaldehyde **21** (31.8 mg, 0.20 mmol, 100 mol%), (*S*)-**IV** (10.3 mg, 0.01 mmol, 5 mol%), K_3PO_4 (21.5 mg, 0.10 mmol, 50 mol%), THF (0.1 mL, 2.0 M), isopropanol (31 μL, 0.4 mmol, 200 mol%), and H_2O (18 μL, 1.0 mmol, 500 mol%). But-3-en-2-yl acetate **1** (45.6 mg, 0.40 mmol, 200 mol%) was added and the mixture was allowed to stir at ambient temperature for 0.5 hr, at which point the reaction vessel was placed in an oil bath at 60 ^oC and was allowed to stir for 48 hr. The reaction mixture was concentrated *in vacuo*. Purification of the residue by column chromatography (SiO_2; ethyl acetate: hexanes, 1:20 with 0.1% TEA) provided **12** (31.9 mg, 0.148 mmol) as a colorless oil in 75% yield (10:1 dr).

HPLC: (Chiralcel OJ-H column, hexanes:*i*-PrOH = 93:7, 0.5 mL/min, 254 nm), t_{major} = 53.3 min, t_{minor} = 66.0 min; ee = 98%.

(*3R,4S,E*)-4-methyl-1-phenylhexa-1,5-dien-3-ol



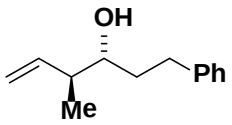
13

An oven-dried sealed tube under an atmosphere of N_2 was charged with *trans*-cinnamyl aldehyde **22** (26.4 mg, 0.20 mmol, 100 mol%), (*S*)-**IV** (10.3 mg, 0.01 mmol, 5 mol%), K_3PO_4 (21.5 mg, 0.10 mmol, 50 mol%), THF (0.1 mL, 2.0 M), isopropanol (31 μL, 0.4 mmol, 200 mol%), and H_2O (18 μL, 1.0 mmol, 500 mol%). But-3-en-2-yl acetate **1** (45.6 mg, 0.40 mmol, 200 mol%) was added and the mixture was allowed to stir at ambient

temperature for 0.5 hr, at which point the reaction vessel was placed in an oil bath at 70 ^{o}C and was allowed to stir for 48 hr. The reaction mixture was concentrated *in vacuo*. Purification of the residue by column chromatography (SiO_2; ethyl acetate: hexanes, 1:20 with 0.1% TEA) provided **13** (29.0 mg, 0.154 mmol) as a colorless oil in 77% yield (10:1 dr).

HPLC: (Chiralpak AS-H/AS-H column, hexanes:*i*-PrOH = 98:2, 0.5 mL/min, 254 nm), t_{minor} = 26.8 min, t_{major} = 31.5 min; ee = 98%.

(*3R,4S*)-4-methyl-1-phenylhex-5-en-3-ol

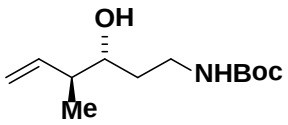


14

An oven-dried sealed tube under an atmosphere of N_2 was charged with 3-phenylpropanal **23** (26.8 mg, 0.20 mmol, 100 mol%), (*S*)-**IV** (10.3 mg, 0.01 mmol, 5 mol%), K_3PO_4 (21.5 mg, 0.10 mmol, 50 mol%), THF (0.1 mL, 2.0 M), isopropanol (31 μL, 0.4 mmol, 200 mol%), and H_2O (18 μL, 1.0 mmol, 500 mol%). But-3-en-2-yl acetate **1** (45.6 mg, 0.40 mmol, 200 mol%) was added and the mixture was allowed to stir at ambient temperature for 0.5 hr, at which point the reaction vessel was placed in an oil bath at 60 ^{o}C and was allowed to stir for 48 hr. The reaction mixture was concentrated *in vacuo*. Purification of the residue by column chromatography (SiO_2; ethyl acetate: hexanes, 1:20 with 0.1% TEA) provided **14** (27.0 mg, 0.142 mmol) as a colorless oil in 71% yield (>20:1 dr).

HPLC: (Chiralcel OD-H column, hexanes:*i*-PrOH = 97:3, 0.7 mL/min, 254 nm), t_{minor} = 11.2 min, t_{major} = 17.4 min; ee = 98%.

***tert*-butyl (*3R,4S*)-3-hydroxy-4-methylhex-5-enylcarbamate**

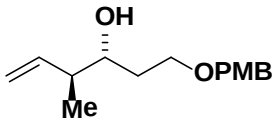


15

An oven-dried sealed tube under an atmosphere of N_2 was charged with *tert*-butyl 3-oxopropylcarbamate **24** (34.6 mg, 0.20 mmol, 100 mol%), (*S*)-**IV** (10.3 mg, 0.01 mmol, 5 mol%), K_3PO_4 (21.5 mg, 0.10 mmol, 50 mol%), THF (0.1 mL, 2.0 M), isopropanol (31 μL, 0.4 mmol, 200 mol%), and H_2O (18 μL, 1.0 mmol, 500 mol%). But-3-en-2-yl acetate **1** (45.6 mg, 0.40 mmol, 200 mol%) was added and the mixture was allowed to stir at ambient temperature for 0.5 hr, at which point the reaction vessel was placed in an oil bath at 70 ^oC and was allowed to stir for 48 hr. The reaction mixture was concentrated *in vacuo*. Purification of the residue by column chromatography (SiO_2; ethyl acetate: hexanes, 1:20 with 0.1% TEA) provided **15** (30.3 mg, 0.142 mmol) as a colorless oil in 66% yield (>20:1 dr).

HPLC: Enantiomeric excess was determined by HPLC analysis of the 4-nitrobenzoate derivative of the product (Chiralcel OJ-H column, hexanes:*i*-PrOH = 98:2, 0.75 mL/min, 254 nm), t_{minor} = 24.4 min, t_{major} = 28.1 min; ee = 99%.

(*3R,4S*)-1-(4-methoxybenzyloxy)-4-methylhex-5-en-3-ol



16

An oven-dried sealed tube under an atmosphere of N_2 was charged with 3-(4-methoxybenzyloxy)propanal **25** (38.8 mg, 0.20 mmol, 100 mol%), (*S*)-**IV** (10.3 mg, 0.01 mmol, 5 mol%), K_3PO_4 (21.5 mg, 0.10 mmol, 50 mol%), THF (0.1 mL, 2.0 M), isopropanol (31 μL, 0.4 mmol, 200 mol%), and H_2O (18 μL, 1.0 mmol, 500 mol%). But-3-en-2-yl acetate **1** (45.6 mg, 0.40 mmol, 200 mol%) was added and the mixture was allowed to stir at ambient temperature for 0.5 hr, at which point the reaction vessel was placed in an oil bath at 60 ^oC and was allowed to stir for 48 hr. The reaction mixture was concentrated *in vacuo*. Purification of the residue by column chromatography (SiO_2; ethyl acetate: hexanes, 1:20 with 0.1% TEA) provided **16** (38.1 mg, 0.152 mmol) as a colorless oil in 76% yield (>20:1 dr).

HPLC: Enantiomeric excess was determined by HPLC analysis of the 4-nitrobenzoate derivative of the product (Chiralcel AD-H column, hexanes:*i*-PrOH = 98:2, 1.0 mL/min, 210 nm), t_{minor} = 15.4 min, t_{major} = 17.9 min; ee = 99%.

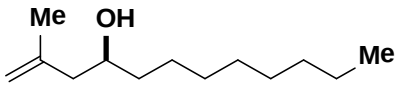
1.3.4 Representative Synthesis of Catalyst: Synthesis of (*R*)-II

To a mixture of $[Ir(cod)Cl]_2$ (134.3 mg, 0.20 mmol, 100 mol%), (*R*)-Cl,MeO-BIPHEP (260.6 mg, 0.40 mmol, 200 mol%), Cs_2CO_3 (260.6 mg, 0.80 mmol, 400 mol%), 4-Cl-3-NO_2BzOH (161.2 mg, 0.89 mmol, 400 mol%) and allyl acetate (100.1 mg, 1.0 mmol, 500 mol%) in a sealed tube under N_2 atmosphere was added THF (4.0 mL, 0.05 M). The reaction mixture was stirred for 30 min at ambient temperature and heated for 1.5 hr at 80 oC, at which point the reaction mixture was allowed to cool to ambient temperature. The reaction mixture was filtered and washed with THF (10 mL). The filtrate was

concentrated *in vacuo* and purified by flash column chromatography (dichloromethane:ether, 3:1). The purified catalyst was precipitated from THF (2 mL) and hexane (50 mL) to give a yellow precipitate, which was collected by filtration and dried under vacuum to provide **(*R*)-II** (344.0 mg, 0.320 mmol) in 80% yield.

1.3.5 Experiment details of Methallylation from Alcohol Oxidation Level

(S)-2-methyldodec-1-en-4-ol



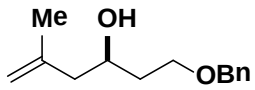
36

To a resealable pressure tube equipped with a magnetic stir bar was added ***(R)*-II** (10.7 mg, 0.01 mmol, 5 mol%) and dry potassium phosphate (42.4 mg, 0.20 mmol, 100 mol%). The tube was sealed with a rubber septum and purged with nitrogen. THF (0.2 mL, 1.0 M), alcohol **44** (28.5 mg, 0.20 mmol, 100 mol%) and β-methallyl chloride (54.3 mg, 0.60 mmol, 300 mol%) were added and the rubber septum was quickly replaced with a screw cap. The mixture was placed in an oil bath at 50 oC and was allowed to stir for 24 hr. The reaction mixture was concentrated *in vacuo*. Purification of by column chromatography (SiO_2; ethyl acetate: hexanes, 1:40 to 1:20) provided the desired product **36** (31.7 mg, 0.160 mmol) as a colorless oil in 80% yield.

TLC (SiO_2): Rf = 0.38 (ethyl acetate: hexanes, 1:9). **$[\alpha]_D^{25}$** = -8.0 (c = 1, CH2Cl2), literature value for *ent* **36**, +11.2 (c = 3.02, CCl4). **^{1}H NMR** (400 MHz, CDCl3): δ 4.90-4.87 (m, 1H), 4.81-4.78 (m, 1H), 3.75-3.68 (m, 1H), 2.21 (dd *J* = 13.5, 3.3 Hz, 1H), 2.08 (ddd, *J* = 13.7, 9.4, 0.7 Hz, 1H), 1.76 (s 3H), 1.68 (d, *J* = 1.7, 1H), 1.46-1.27 (m, 14H), 0.88 (t, *J* = 6.9 Hz, 3H). **^{13}C NMR** (100 MHz, CDCl3): δ 142.9, 113.4, 68.6, 46.2, 37.1, 31.9, 29.7, 29.6, 29.3, 25.7, 22.7, 22.4, 14.1 **FTIR** (neat): 3315, 2921, 2859, 2367, 2331,

1842, 1739, 1647, 1563, 1534, 1456, 1375, 1261, 1230, 1216, 1072, 1018, 887, 867, 846, 804, 758, 750, 721, 703, 669, 655 cm-1. **HPLC**: Enantiomeric excess was determined by HPLC analysis of the 4-nitrobenzoate derivative of the product, (Chiralcel OD-H-OD-H column, hexanes:*i*-PrOH = 99.5:0.5, 1 mL/min, 254 nm), tmajor = 35.8 min tminor = 41.9 min,; ee = 95%.

(R)-1-(benzyloxy)-5-methylhex-5-en-3-ol



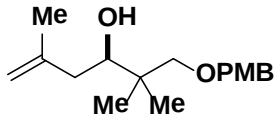
37

To a resealable pressure tube equipped with a magnetic stir bar was added ***(R)*-II** (10.7 mg, 0.01 mmol, 5 mol%) and dry potassium phosphate (42.4 mg, 0.20 mmol, 100 mol%). The tube was sealed with a rubber septum and purged with nitrogen. THF (0.2 mL, 1.0 M), alcohol **45** (33.2 mg, 0.20 mmol, 100 mol%) and β-methallyl chloride (54.3 mg, 0.60 mmol, 300 mol%) were added and the rubber septum was quickly replaced with a screw cap. The mixture was placed in an oil bath at 50 oC and was allowed to stir for 24 hr. The reaction mixture was concentrated *in vacuo*. Purification of by column chromatography (SiO_2; ethyl acetate: hexanes, 1:10 to 1:5) provided the desired product **37** (30.4 mg, 0.138 mmol) as a colorless oil in 69% yield.

TLC (SiO_2): Rf = 0.35 (ethyl acetate: hexanes, 1:4). **$[\alpha]_D^{25}$** = -2.0 (c = 1, CH2Cl2), literature value -3.39o (c = 0.5, CHCl3). **^{1}H NMR** (400 MHz, CDCl3): δ 7.37-7.27 (m, 5H), 4.85-4.84 (m, 1H), 4.78-4.77 (m, 1H), 4.53 (s, 2H), 4.01-3.94 (m, 1H), 3.75-3.70 (m, 1H), 3.68-3.63 (m, 1H) 2.73 (d, *J* = 2.5 Hz, OH), 2.24-2.14 (m, 2H), 1.82-1.70 (m, 2H), 1.75 (s, 3H). **^{13}C NMR** (100 MHz, CDCl3): δ 142.7, 138.0, 128.4, 127.7, 127.6, 113.1, 73.3, 68.7, 68.2, 46.0, 36.2, 22.5. **FTIR** (neat): 3441, 3066, 3025, 2920, 2859, 2347, 2335, 1722, 1495, 1453, 1365, 1275, 1205, 1166, 1028, 891, 736, 697, 668 cm-1.

HPLC: (Chiralcel AS-H column, hexanes:*i*-PrOH = 95:05, 0.5 mL/min, 254 nm), tminor = 8.7 min, tmajor = 9.5 min; ee = 96

(R)-1-(4-methoxybenzyloxy)-2,2,5-trimethylhex-5-en-3-ol

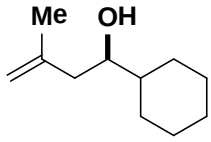


38

To a resealable pressure tube equipped with a magnetic stir bar was added ***(R)*-II** (10.7 mg, 0.01 mmol, 5 mol%) and dry potassium phosphate (42.4 mg, 0.20 mmol, 100 mol%). The tube was sealed with a rubber septum and purged with nitrogen. THF (0.2 mL, 1.0 M), alcohol **46** (44.9 mg, 0.20 mmol, 100 mol%) and β-methallyl chloride (54.3 mg, 0.60 mmol, 300 mol%) were added and the rubber septum was quickly replaced with a screw cap. The mixture was placed in an oil bath at 50 oC and was allowed to stir for 24 hr. The reaction mixture was concentrated *in vacuo*. Purification of by column chromatography (SiO_2; ethyl acetate: hexanes, 1:10 to 1:5) provided the desired product **38** (50.1 mg, 0.180 mmol) as a colorless oil in 90% yield.

TLC (SiO_2): Rf = 0.31 (ethyl acetate: hexanes, 1:10). **$[\alpha]_D^{25}$** = +2.0 (c = 1, CH2Cl2). **^{1}H NMR** (400 MHz, CDCl3): δ 7.25-7.22 (m, 2H), 6.89-6.85 (m, 2H), 4.86-4.84 (m, 1H), 4.80-4.78 (m, 1H), 4.44 (s, 2H), 2.94 (s, 3H), 3.64-3.60 (m, 1H), 3.35 (d, J = 8.86, 1H), 3.27 (d, J = 8.86, 1H), 3.47 (d, J = 3.47, 1H), 2.17 (d, J = 13.7 Hz, 1H), 2.03 (ddd, J = 13.72, 10.66, 0.47 Hz, 1H), 1.77 (s, 3H), 0.92 (s, 3H), 0.91 (s, 3H). **^{13}C NMR** (100 MHz, CDCl3): δ 159.1, 143.8, 130.2, 129.1, 113.7, 112.6, 78.9, 74.9, 73.2, 55.3, 40.3, 38.3, 22.5, 22.3, 19.7. **FTIR** (neat): 3484, 3068, 2958, 2933, 2914, 2857, 1646, 1612, 1586, 1513, 1465, 1439, 1362, 1301, 1247, 1207, 1173, 1088, 1036, 889, 820, 756 cm-1. **HRMS** (ESI) Calcd. for C17H26O3Na [M+Na]+: 301.17742, Found: 301.1773. **HPLC**: (Chiralcel OD-H column, hexanes:*i*-PrOH = 95:5, 0.5 mL/min, 220 nm), tminor = 13.2 min, tmajor = 13.8 min; ee = 94%.

(R)-1-cyclohexyl-3-methylbut-3-en-1-ol

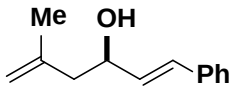


39

To a resealable pressure tube equipped with a magnetic stir bar was added ***(R)*-II** (10.7 mg, 0.01 mmol, 5 mol%) and dry potassium phosphate (42.4 mg, 0.20 mmol, 100 mol%). The tube was sealed with a rubber septum and purged with nitrogen. THF (0.2 mL, 1.0 M), alcohol **47** (22.8 mg, 0.20 mmol, 100 mol%) and β-methallyl chloride (54.3 mg, 0.60 mmol, 300 mol%) were added and the rubber septum was quickly replaced with a screw cap. The mixture was placed in an oil bath at 50 oC and was allowed to stir for 24 hr. The reaction mixture was concentrated *in vacuo*. Purification of by column chromatography (SiO_2; ethyl acetate: hexanes, 1:20 to 1:10) provided the desired product **39** (24.3 mg, 0.144 mmol) as a colorless oil in 72% yield.

TLC (SiO_2): Rf = 0.45 (ethyl acetate: hexanes, 1:10). **[α]$_D^{25}$** = -5.0o (c = 1, CH2Cl2), literature value for *ent* **39**, +2.0 (c = 1.4, CCl4). **^{1}H NMR** (400 MHz, CDCl3): δ 4.90-4.88 (m, 1H), 4.81- 4.80 (m, 1H), 3.50-3.45 (m, 1H), 2.24 (ddd, *J* = 13.6, 20.0, 0.4 Hz, 1H) 2.06 (ddd, *J* = 13.6, 10, 0.4 Hz, 1H), 1.89-1.84 (m, 1H), 1.80-1.73 (m, 2H), 1.76 (dd, *J* = 0.4, 0.4 Hz, 3H), 1.71-1.64 (m, 3H), 1.40-1.30 (m, 1H), 1.28-0.99 (m, 5H). **^{13}C NMR** (100 MHz, CDCl3): δ 143.3, 113.5, 72.4, 43.4, 43.0, 29.0, 28.2, 26.6, 26.3, 26.2, 22.2. **FTIR** (neat): 3422, 3074, 2978, 2852, 1644, 1449, 1396, 1374, 1259, 1173, 1142, 1100, 1086, 1060, 1044, 986, 953, 864, 842 cm-1. **HPLC**: Enantiomeric excess was determined by HPLC analysis of the 4-nitrobenzoate derivative of the product, (Chiralcel AS-H column, hexanes:*i*-PrOH = 99:01, 0.5 mL/min, 254 nm), tmajor = 9.1 min, tminor = 10.1 min; ee = 92%.

(R,E)-5-methyl-1-phenylhexa-1,5-dien-3-ol

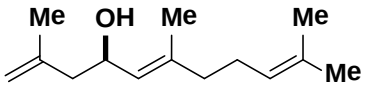


40

To a resealable pressure tube equipped with a magnetic stir bar was added ***(R)*-II** (10.7 mg, 0.01 mmol, 5 mol%) and dry potassium phosphate (42.4 mg, 0.20 mmol, 100 mol%). The tube was sealed with a rubber septum and purged with nitrogen. THF (0.2 mL, 1.0 M), alcohol **48** (26.8 mg, 0.20 mmol, 100 mol%), β-methallyl chloride (54.3 mg, 0.60 mmol, 300 mol%), and isopropanol (31 μL, 0.40 mmol, 200 mol %) were added and the rubber septum was quickly replaced with a screw cap. The mixture was placed in an oil bath at 50 oC and was allowed to stir for 24 hr. The reaction mixture was concentrated *in vacuo*. Purification of by column chromatography (SiO_2; ethyl acetate: hexanes, 1:12 to 1:7) provided the oxidized product (4.5mg, 0.024 mmol) as a colorless oil in 12% yield and the desired product **40** (30.1 mg, 0.160 mmol) as a colorless oil in 80% yield.

TLC (SiO_2): Rf = 0.31 (ethyl acetate: hexanes, 1:4). **$[\alpha]_D^{25}$** = +24.0 (c = 1, CH2Cl2), literature value +19.0 (c = 1.44, CH2Cl2).**^{1}H NMR** (400 MHz, CDCl3): δ 7.4-7.22 (m, 5H), 6.64 (dd, *J* = 15.9, 1.2 Hz, 1H), 6.24 (dd, *J* = 15.9, 6.3 Hz, 1H), 4.94-4.86 (m, 2H), 4.47-4.42 (m, 1H), 2.39- 2.29 (m, 2H), 1.87 (bs, 1H), 1.81 (t, *J* = 1.1 Hz, 3H). **^{13}C NMR** (100 MHz, CDCl3): δ 142.0, 136.7, 131.7, 130.1, 128.5, 127.6, 126.4, 114.1, 69.9, 46.2, 22.5. **FTIR** (neat): 3371, 3076, 3026, 2931, 1647, 1599, 1494, 1448, 1274, 1099, 1070, 1046, 965, 891, 747, 740 cm-1. **HPLC**: (Chiralcel OD-H column, hexanes:*i*-PrOH = 90:10, 1 mL/min, 254 nm), tmajor = 7.1 min, tminor = 12.0 min; ee = 94%.

(R,E)-2,6,10-trimethylundeca-1,5,9-trien-4-ol

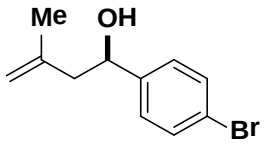


41

To a resealable pressure tube equipped with a magnetic stir bar was added ***(R)*-II** (10.7 mg, 0.01 mmol, 5 mol%) and dry potassium phosphate (42.4 mg, 0.20 mmol, 100 mol%). The tube was sealed with a rubber septum and purged with nitrogen. THF (0.2 mL, 1.0 M), alcohol **49** (30.9 mg, 0.20 mmol, 100 mol%), β-methallyl chloride (54.3 mg, 0.60 mmol, 300 mol%), and isopropanol (31 μL, 0.40 mmol, 200 mol %) were added and the rubber septum was quickly replaced with a screw cap. The mixture was placed in an oil bath at 50 oC and was allowed to stir for 24 hr. The reaction mixture was concentrated *in vacuo*. Purification of by column chromatography (SiO_2; ethyl acetate: hexanes, 1:40 to 1:20) provided the desired product **41** (33.3 mg, 0.160 mmol) as a colorless oil in 80% yield.

TLC (SiO_2): Rf = 0.40 (ethyl acetate: hexanes, 1:10). **$[\alpha]_D^{25}$** = +13.0 (c = 1, CH2Cl2), literature value +19.2 (c = 6.5, CH2Cl2). **^{1}H NMR** (400 MHz, CDCl3): δ 5.19 (dq, *J* = 8.4, 1.3 Hz, 1H), 5.11-5.06 (m, 1H), 4.88-4.80 (m, 2H), 4.51 (dt, *J* = 8.5, 4.8 Hz, 1H), 4.45 (ddd, *J* = 13.7, 8.6, 0.9, 1H), 2.19-2.14 (m, 1H), 2.13-1.99 (m, 4H), 1.78 (t, *J* = 0.9, 3H), 1.70 (d, *J* = 1.4 Hz, 3H), 1.68 (d, *J* = 1.1 Hz, 3H), 1.60 (s, 3H). **^{13}C NMR** (100 MHz, CDCl3): δ 142.4, 138.6, 131.6, 127.1, 123.9, 66.0, 46.2, 39.5, 26.3, 25.7, 22.5, 17.7, 16.6. **FTIR** (neat): 3362, 3074, 2967, 2916, 2855, 2322, 1647, 1442, 1375, 1261, 1201, 1139, 1105, 1046, 1008, 979, 887 cm-1. **HPLC**: Enantiomeric excess was determined by HPLC analysis of the 4-nitrobenzoate derivative of the product, (Chiralcel OJ-H/AS-H column, hexanes:*i*-PrOH = 99:1, 0.4 mL/min, 254 nm), tmajor = 22.6 min, tminor = 24.2 min; ee = 94%.

(R)-1-(4-bromophenyl)-3-methylbut-3-en-1-ol

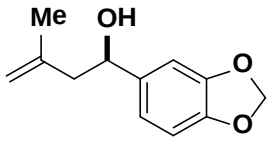


34

To a resealable pressure tube equipped with a magnetic stir bar was added alcohol **33** (37.4 mg, 0.20 mmol, 100 mol%), ***(R)*-II** (10.7 mg, 0.01 mmol, 5 mol%) and dry potassium phosphate (42.4 mg, 0.20 mmol, 100 mol%). The tube was sealed with a rubber septum and purged with nitrogen. THF (0.2 mL, 1.0 M) and β-methallyl chloride (54.3 mg, 0.60 mmol, 300 mol%) were added and the rubber septum was quickly replaced with a screw cap. The mixture was placed in an oil bath at 50 oC and was allowed to stir for 24 hr. The reaction mixture was concentrated *in vacuo*. Purification of by column chromatography (SiO_2; ethyl acetate: hexanes, 1:10 to 1:5) provided the oxidized product (6.7 mg, 0.028 mmol) as white solid in 14% yield and the desired product **34** (40.0 mg, 0.166 mmol) as white solid in 83% yield.

TLC (SiO_2): Rf = 0.30 (ethyl acetate: hexanes, 1:5). **m.p.**: 72-73 oC. **$[\alpha]_D^{25}$** = +45.0o (c = 1, CH2Cl2). **^{1}H NMR** (400 MHz, CDCl3): δ 7.47 (d, *J* = 8.8 Hz, 2H), 7.25 (d, *J* = 8.8 Hz 2H), 4.94- 4.93 (m, 1H), 4.85-4.84 (m, 1H), 4.78-4.75 (m, 1H), 2.39-2.36 (m, 2H), 2.18 (d, *J* = 2.4 Hz, 1H), 1.79 (s, 3H). **^{13}C NMR** (100 MHz, CDCl3): δ 143.0, 142.0, 131.5, 127.5, 121.2, 114.5, 70.7, 48.4, 22.3. **FTIR** (neat): 3358, 3075, 2976, 2934, 1900, 1803, 1648, 1592, 1488, 1472, 1406, 1373, 1336, 1304, 1202, 1169, 1046, 1008, 902, 874, 822, 803, 718 cm-1. **HPLC**: (Chiralcel OJ-H column, hexanes:*i*-PrOH = 95:05, 1 mL/min, 254 nm), tminor = 8.7 min, tmajor = 9.5 min; ee = 96%.

(R)-1-(benzo[d][1,3]dioxol-5-yl)-3-methylbut-3-en-1-ol

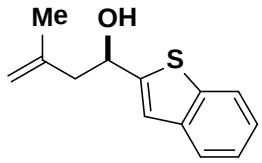


42

To a resealable pressure tube equipped with a magnetic stir bar was added alcohol **50** (30.4 mg, 0.20 mmol, 100 mol%), ***(R)*-II** (10.7 mg, 0.01 mmol, 5 mol%) and dry potassium phosphate (42.4 mg, 0.20 mmol, 100 mol%). The tube was sealed with a rubber septum and purged with nitrogen. THF (0.2 mL, 1.0 M) and β-methallyl chloride (54.3 mg, 0.60 mmol, 300 mol%) were added and the rubber septum was quickly replaced with a screw cap. The mixture was placed in an oil bath at 50 oC and was allowed to stir for 24 hr. The reaction mixture was concentrated *in vacuo*. Purification of by column chromatography (SiO_2; ethyl acetate: hexanes, 1:20 to 1:10) provided the oxidized product (2.0 mg, 0.010 mmol) as a colorless oil in 5% yield and the desired product **42** (32.2 mg, 0.156 mmol) as a colorless oil in 78% yield.

TLC (SiO_2): Rf = 0.28 (ethyl acetate: hexanes, 1:4). **$[\alpha]_D^{25}$** = +50.0 (c = 1, CH2Cl2). **^{1}H NMR** (400 MHz, CDCl3): δ 6.90 (dt, *J* = 1.69, 0.44 Hz, 1H), 6.82 (ddd, *J* = 8.0, 1.7, 0.57 Hz, 1H), 6.77 (dd, *J* = 8.0, 0.32 Hz, 1H), 5.95 (s, 2H), 4.93-4.83 (m, 2H), 4.73 (dd, *J* = 8.4, 5.1, 1H), 2.44-2.34 (m, 2H), 2.07 (bs, 1H), 1.79 (t, *J* = 1.0, 3H). **^{13}C NMR** (100 MHz, CDCl3): δ 147.7, 146.8, 142.3, 138.1, 119.1, 114.1, 108.0, 106.3, 101.0, 71.2, 48.3, 22.3. **FTIR** (neat): 3408, 3076, 2897, 1726, 1646, 1609, 1503, 1487, 1442, 1376, 1187, 1124, 1094, 1209, 1186, 1124, 1094, 1010, 932, 896, 810, 783, 750, 727 cm-1. **HPLC**: (Chiralcel OJ-H column, hexanes:*i*-PrOH = 95:5, 1 mL/min, 280 nm), tminor = 15.3 min, tmajor = 16.6 min; ee = 94%.

(R)-1-(benzo[b]thiophen-2-yl)-3-methylbut-3-en-1-ol



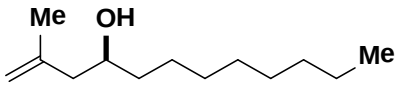
43

To a resealable pressure tube equipped with a magnetic stir bar was added alcohol **51** (32.8 mg, 0.20 mmol, 100 mol%), ***(R)*-II** (10.7 mg, 0.01 mmol, 5 mol%) and dry potassium phosphate (42.4 mg, 0.20 mmol, 100 mol%). The tube was sealed with a rubber septum and purged with nitrogen. THF (0.2 mL, 1.0 M) and β-methallyl chloride (54.3 mg, 0.60 mmol, 300 mol%) were added and the rubber septum was quickly replaced with a screw cap. The mixture was placed in an oil bath at 50 oC and was allowed to stir for 24 hr. The reaction mixture was concentrated *in vacuo*. Purification of by column chromatography (SiO_2; ethyl acetate: hexanes, 1:20 to 1:10) provided the oxidized product (2.2 mg, 0.010 mmol) as a white solid in 5% yield and the desired product **43** (38.0 mg, 0.174 mmol) as a white solid in 87% yield.

TLC (SiO_2): Rf = 0.25 (ethyl acetate: hexanes, 1:4). **m.p.:** 78-80 oC. **$[\alpha]_D^{25}$** = +36.1 (c = 1, CH2Cl2). **^{1}H NMR** (400 MHz, CDCl3): δ 7.83-7.81 (m, 1H), 7.73-7.71 (m, 1H), 7.36-7.28 (m, 2H), 7.22 (t, *J* = 0.74, 1H), 5.16 (t, *J* = 6.76, 1H), 4.97-4.90 (m, 2H), 2.65-2.57 (m, 2H), 2.32 (bs, 1H), 1.12 (t, *J* = 1.1 Hz, 1H). **^{13}C NMR** (100 MHz, CDCl3): δ 148.6, 141.5, 139.5, 139.2, 124.2, 124.1, 123.4, 122.4, 120.0, 114.7, 68.1, 47.9, 22.4. **FTIR** (neat): 3556, 3069, 2966, 2937, 1643, 1457, 1438, 1376, 1326, 1275, 1261, 1155, 1118, 1054, 973, 946, 899, 876, 845, 831, 754, 728, 669 cm-1. **HRMS** (CI) Calcd. for C13H14OS [M]+: 218.0766, Found: 218.0765. **HPLC**: (Chiralcel OJ-H column, hexanes:*i*-PrOH = 95:5, 1 mL/min, 254 nm), tminor = 19.8 min, tmajor = 26.0 min; ee = 96%

1.3.6 Experiment details of Methallylation from Aldehyde Oxidation Level

(S)-2-methyldodec-1-en-4-ol

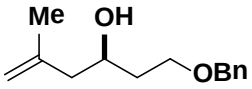


36

To a resealable pressure tube equipped with a magnetic stir bar was added ***(R)*-II** (10.7 mg, 0.01 mmol, 5 mol%) and dry potassium phosphate (42.4 mg, 0.20 mmol, 100 mol%). The tube was sealed with a rubber septum and purged with nitrogen. THF (0.2 mL, 1.0 M), aldehyde **44** (28.4 mg, 0.20 mmol, 100 mol%), β-methallyl chloride (54.3 mg, 0.60 mmol, 300 mol%), and isopropanol (31 μL, 0.40 mmol, 200 mol%) were added and the rubber septum was quickly replaced with a screw cap. The mixture was placed in an oil bath at 50 oC and was allowed to stir for 24 hr. The reaction mixture was concentrated *in vacuo*. Purification of by column chromatography (SiO_2; ethyl acetate: hexanes, 1:40 to 1:20) provided the desired product **36** (29.8 mg, 0.150 mmol) as a colorless oil in 75% yield.

HPLC: Enantiomeric excess was determined by HPLC analysis of the 4-nitrobenzoate derivative of the product, (Chiralcel OD-H-OD-H column, hexanes:*i*-PrOH = 99.5:0.5, 1 mL/min, 254 nm), tmajor = 36.2 min tminor = 42.3 min,; ee = 97%.

(R)-1-(benzyloxy)-5-methylhex-5-en-3-ol



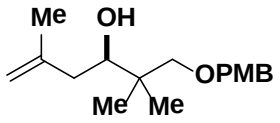
37

To a resealable pressure tube equipped with a magnetic stir bar was added ***(R)*-II** (10.7 mg, 0.01 mmol, 5 mol%) and dry potassium phosphate (42.4 mg, 0.20 mmol, 100 mol%). The tube was sealed with a rubber septum and purged with nitrogen. THF (0.2 mL, 1.0

M), aldehyde **45** (32.8 mg, 0.20 mmol, 100 mol%), β-methallyl chloride (54.3 mg, 0.60 mmol, 300 mol%) and isopropanol (31 μL, 0.40 mmol, 200 mol%) were added and the rubber septum was quickly replaced with a screw cap. The mixture was placed in an oil bath at 50 oC and was allowed to stir for 24 hr. The reaction mixture was concentrated *in vacuo*. Purification of by column chromatography (SiO_2; ethyl acetate: hexanes, 1:9 to 1:5) provided the desired product **37** (24.2 mg, 0.110 mmol) as a colorless oil in 55% yield.

HPLC: (Chiralcel AS-H column, hexanes:*i*-PrOH = 95:05, 0.5 mL/min, 254 nm), tminor = 10.0 min, tmajor = 11.0 min; ee = 97%.

(R)-1-(4-methoxybenzyloxy)-2,2,5-trimethylhex-5-en-3-ol

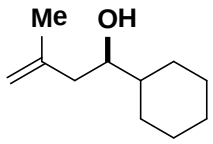


38

To a resealable pressure tube equipped with a magnetic stir bar was added ***(R)*-II** (10.7 mg, 0.01 mmol, 5 mol%) and dry potassium phosphate (42.4 mg, 0.20 mmol, 100 mol%). The tube was sealed with a rubber septum and purged with nitrogen. THF (0.2 mL, 1.0 M), aldehyde **46** (44.5 mg, 0.20 mmol, 100 mol%), β-methallyl chloride (54.3 mg, 0.60 mmol, 300 mol%), and isopropanol (31 μL, 0.40 mmol, 200 mol%) were added and the rubber septum was quickly replaced with a screw cap. The mixture was placed in an oil bath at 50 oC and was allowed to stir for 24 hr. The reaction mixture was concentrated *in vacuo*. Purification of by column chromatography (SiO_2; ethyl acetate: hexanes, 1:10 to 1:5) provided the desired product **38** (50.7 mg, 0.182 mmol) as a colorless oil in 91% yield.

HPLC: (Chiralcel OD-H column, hexanes:*i*-PrOH = 95:5, 0.5 mL/min, 220 nm), tminor = 12.0 min, tmajor = 12.6 min; ee = 97%.

(R)-1-cyclohexyl-3-methylbut-3-en-1-ol

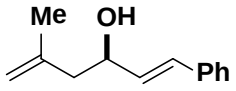


39

To a resealable pressure tube equipped with a magnetic stir bar was added ***(R)*-II** (10.7 mg, 0.01 mmol, 5 mol%) and dry potassium phosphate (42.4 mg, 0.20 mmol, 100 mol%). The tube was sealed with a rubber septum and purged with nitrogen. THF (0.2 mL, 1.0 M), aldehyde **47** (22.4 mg, 0.20 mmol, 100 mol%), β-methallyl chloride (54.3 mg, 0.60 mmol, 300 mol%) and isopropanol (31 μL, 0.40 mmol, 200 mol%) were added and the rubber septum was quickly replaced with a screw cap. The mixture was placed in an oil bath at 50 oC and was allowed to stir for 24 hr. The reaction mixture was concentrated *in vacuo*. Purification of by column chromatography (SiO_2; ethyl acetate: hexanes, 1:20) provided the desired product **39** (24.9 mg, 0.148 mmol) as a colorless oil in 74% yield.

HPLC: Enantiomeric excess was determined by HPLC analysis of the 4-nitrobenzoate derivative of the product, (Chiralcel AS-H column, hexanes:*i*-PrOH = 99:01, 0.5 mL/min, 254 nm), tmajor = 8.9 min, tminor = 9.7 min; ee = 91%.

(R,E)-5-methyl-1-phenylhexa-1,5-dien-3-ol (4.33)

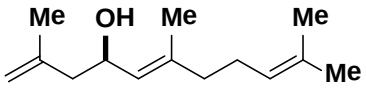


40

To a resealable pressure tube equipped with a magnetic stir bar was added ***(R)*-II** (10.7 mg, 0.01 mmol, 5 mol%) and dry potassium phosphate (42.4 mg, 0.20 mmol, 100 mol%). The tube was sealed with a rubber septum and purged with nitrogen. THF (0.2 mL, 1.0 M), aldehyde **48** (26.4 mg, 0.20 mmol, 100 mol%), β-methallyl chloride (54.3 mg, 0.60 mmol, 300 mol%), and isopropanol (62 μL, 0.80 mmol, 400 mol%) were added and the rubber septum was quickly replaced with a screw cap. The mixture was placed in an oil bath at 50 oC and was allowed to stir for 24 hr. The reaction mixture was concentrated *in vacuo*. Purification of by column chromatography (SiO_2; ethyl acetate: hexanes, 1:12 to 1:7) provided the oxidized product (4.8 mg, 0.026 mmol) as a colorless oil in 13% yield and the desired product **40** (30.9 mg, 0.164 mmol) as a colorless oil in 82% yield.

HPLC: (Chiralcel OD-H column, hexanes:*i*-PrOH = 90:10, 1 mL/min, 254 nm), tmajor = 7.1 min, tminor = 12.0 min; ee = 95%.

(R,E)-2,6,10-trimethylundeca-1,5,9-trien-4-ol



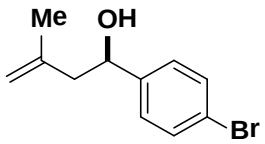
41

To a resealable pressure tube equipped with a magnetic stir bar was added ***(R)*-II** (10.7 mg, 0.01 mmol, 5 mol%) and dry potassium phosphate (42.4 mg, 0.20 mmol, 100 mol%). The tube was sealed with a rubber septum and purged with nitrogen. THF (0.2 mL, 1.0 M), aldehyde **49** (30.4 mg, 0.20 mmol, 100 mol%), β-methallyl chloride (54.3 mg, 0.60 mmol, 300 mol%), and isopropanol (62 μL, 0.80 mmol, 400 mol%) were added and the rubber septum was quickly replaced with a screw cap. The mixture was placed in an oil bath at 50 oC and was allowed to stir for 24 hr. The reaction mixture was concentrated *in vacuo*. Purification of by column chromatography (SiO_2; ethyl acetate: hexanes, 1:40 to

1:20) provided the oxidized product (2.5 mg, 0.012 mmol) as a colorless oil in 6% yield and the desired product **41** (31.3 mg, 0.150 mmol) as a colorless oil in 75% yield.

HPLC: Enantiomeric excess was determined by HPLC analysis of the 4-nitrobenzoate derivative of the product, (Chiralcel OJ-H/AS-H column, hexanes:*i*-PrOH = 99:1, 0.4 mL/min, 254 nm), tmajor = 25.0 min, tminor = 27.0 min; ee = 93%.

(R)-1-(4-bromophenyl)-3-methylbut-3-en-1-ol

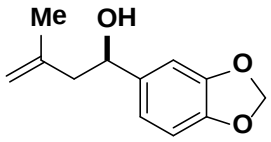


34

To a resealable pressure tube equipped with a magnetic stir bar was added aldehyde **33** (37.0 mg, 0.20 mmol, 100 mol%), ***(R)*-II** (10.7 mg, 0.01 mmol, 5 mol%) and dry potassium phosphate (42.4 mg, 0.20 mmol, 100 mol%). The tube was sealed with a rubber septum and purged with nitrogen. THF (0.2 mL, 1.0 M), β-methallyl chloride (54.3 mg, 0.60 mmol, 300 mol%) and isopropanol (31 μL, 0.40 mmol, 200 mol%) were added and the rubber septum was quickly replaced with a screw cap. The mixture was placed in an oil bath at 50 oC and was allowed to stir for 24 hr. The reaction mixture was concentrated *in vacuo*. Purification of by column chromatography (SiO_2; ethyl acetate: hexanes, 1:10 to 1:5) provided the oxidized product (3.8 mg, 0.016 mmol) as white solid in 14% yield and the desired product **34** (43.5 mg, 0.180 mmol) as white solid in 83% yield.

HPLC: (Chiralcel OJ-H column, hexanes:*i*-PrOH = 95:05, 1 mL/min, 254 nm), tminor = 8.7 min, tmajor = 9.5 min; ee = 95%.

(R)-1-(benzo[d][1,3]dioxol-5-yl)-3-methylbut-3-en-1-ol

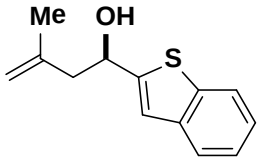


42

To a resealable pressure tube equipped with a magnetic stir bar was added aldehyde **50** (30.0 mg, 0.20 mmol, 100 mol%), ***(R)*-II** (10.7 mg, 0.01 mmol, 5 mol%) and dry potassium phosphate (42.4 mg, 0.20 mmol, 100 mol%). The tube was sealed with a rubber septum and purged with nitrogen. THF (0.2 mL, 1.0 M), β-methallyl chloride (54.3 mg, 0.60 mmol, 300 mol%), and isopropanol (31μL, 0.40 mmol, 200 mol%) were added and the rubber septum was quickly replaced with a screw cap. The mixture was placed in an oil bath at 50 oC and was allowed to stir for 24 hr. The reaction mixture was concentrated *in vacuo*. Purification of by column chromatography (SiO_2; ethyl acetate: hexanes, 1:20 to 1:10) provided the oxidized product (4.0 mg, 0.020 mmol) as a colorless oil in 10% yield and the desired product **42** (35.1 mg, 0.170 mmol) as a colorless oil in 85% yield.

HPLC: (Chiralcel OJ-H column, hexanes:*i*-PrOH = 95:5, 1 mL/min, 280 nm), tminor = 14.3 min, tmajor = 15.6 min; ee = 96%.

(R)-1-(benzo[b]thiophen-2-yl)-3-methylbut-3-en-1-ol (4.37)



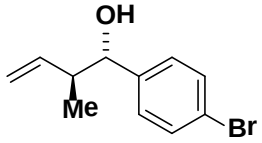
43

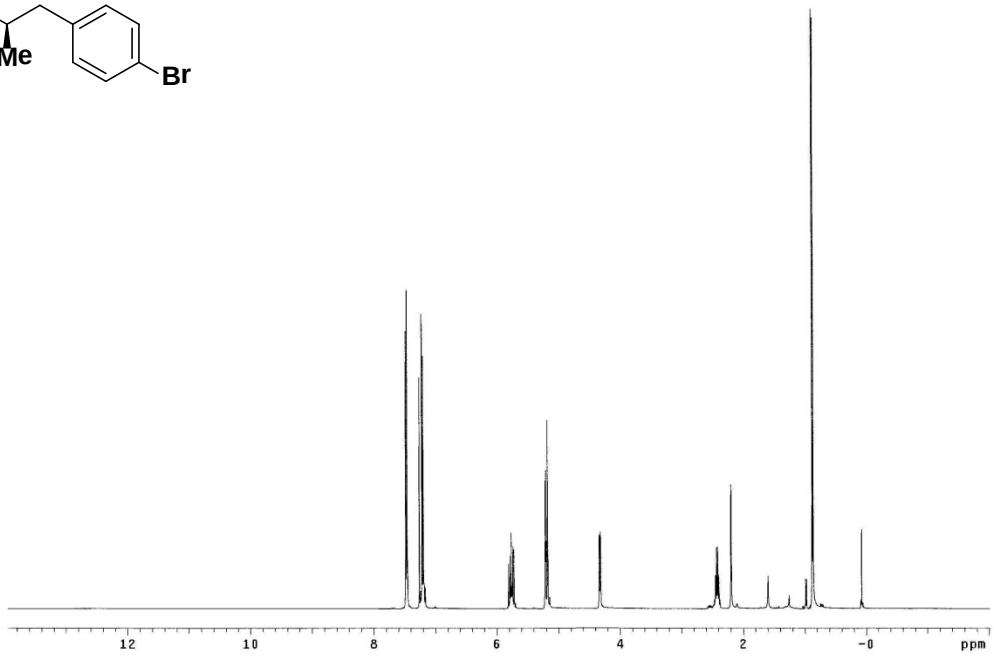
To a resealable pressure tube equipped with a magnetic stir bar was added aldehyde **51** (32.4 mg, 0.20 mmol, 100 mol%), ***(R)*-II** (10.7 mg, 0.01 mmol, 5 mol%) and dry potassium phosphate (42.4 mg, 0.20 mmol, 100 mol%). The tube was sealed with a rubber septum and purged with nitrogen. THF (0.2 mL, 1.0 M), β-methallyl chloride (54.3 mg, 0.60 mmol, 300 mol%), and isopropanol (31 μL, 0.40 mmol, 200 mol%) were added and the rubber septum was quickly replaced with a screw cap. The mixture was placed in an oil bath at 50 oC and was allowed to stir for 24 hr. The reaction mixture was concentrated *in vacuo*. Purification of by column chromatography (SiO_2; ethyl acetate: hexanes, 1:20 to 1:10) provided the oxidized product (2.2 mg, 0.010 mmol) as white solid in 5% yield and the desired product **43** (39.7 mg, 0.182 mmol) as a white solid in 91% yield.

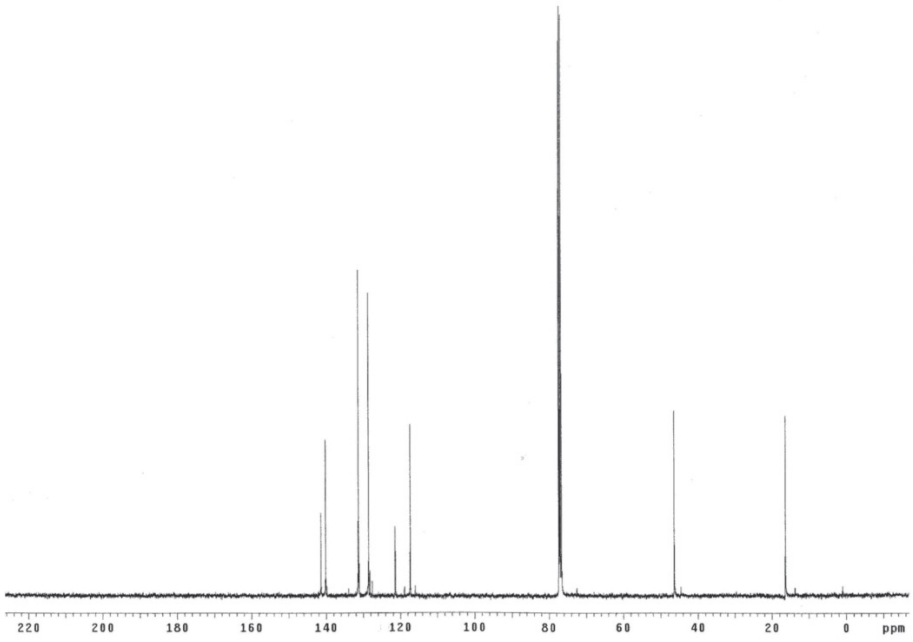
HPLC: (Chiralcel OJ-H column, hexanes:*i*-PrOH = 95:5, 1 mL/min, 254 nm), tminor = 19.8 min, tmajor = 26.3 min; ee = 96%.

Appendix: NMR Spectra of New Compounds

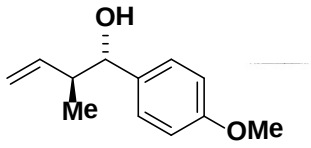
(*1S,2S*)-1-(4-bromophenyl)-2-methylbut-3-en-1-ol (8)

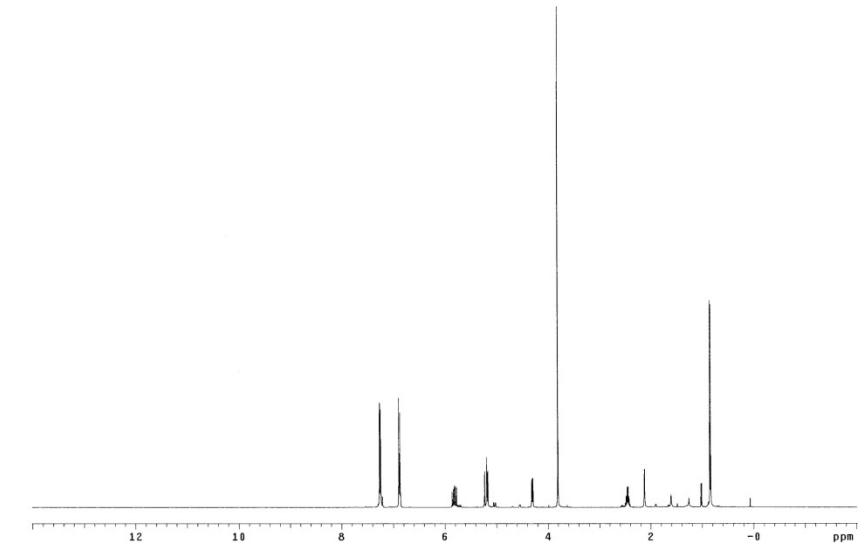


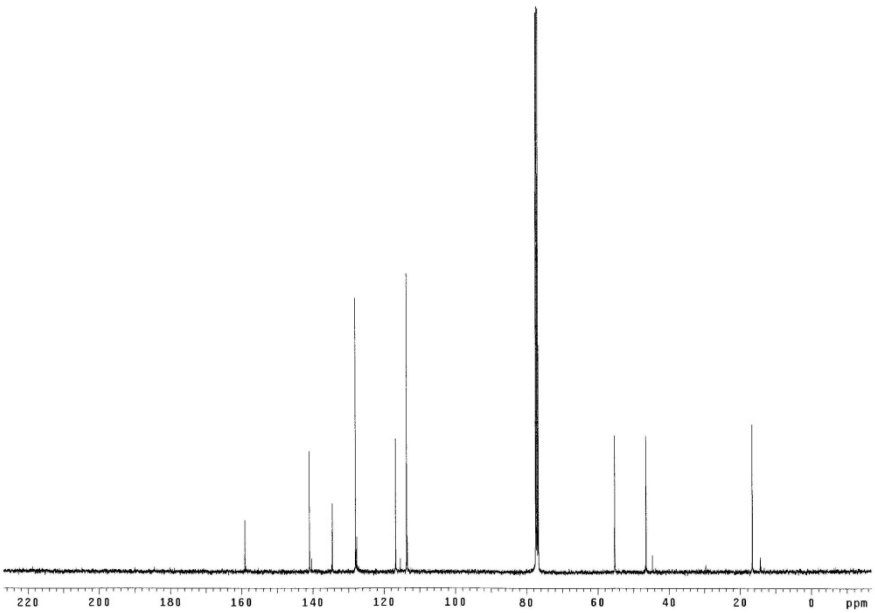




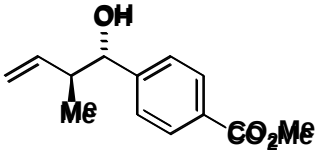
(*1S,2S*)-1-(4-methoxyphenyl)-2-methylbut-3-en-1-ol (9)

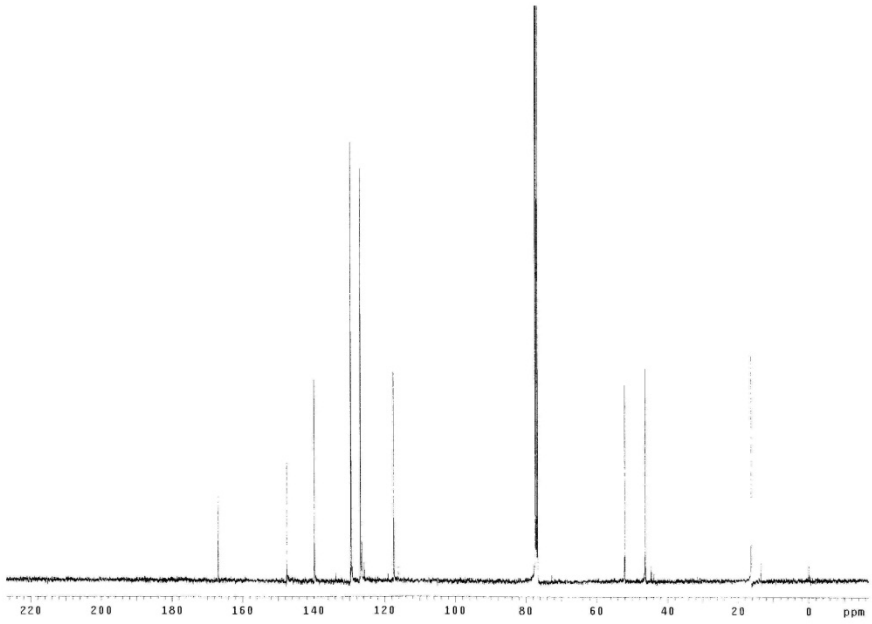




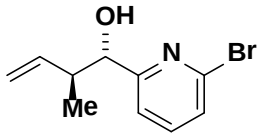


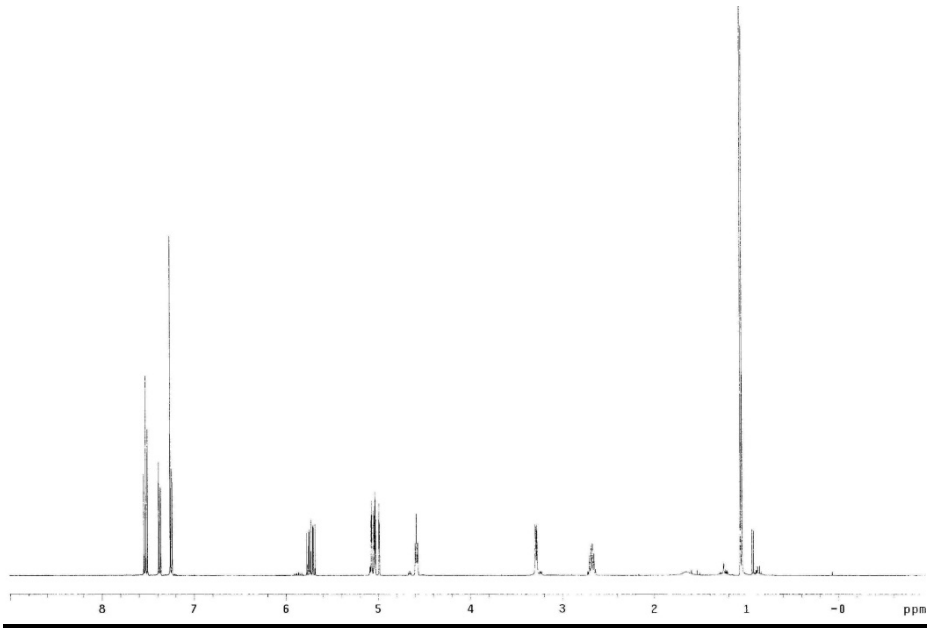
Methyl 4-((*1S*,*2S*)-1-hydroxy-2-methylbut-3-enyl)benzoate (10)

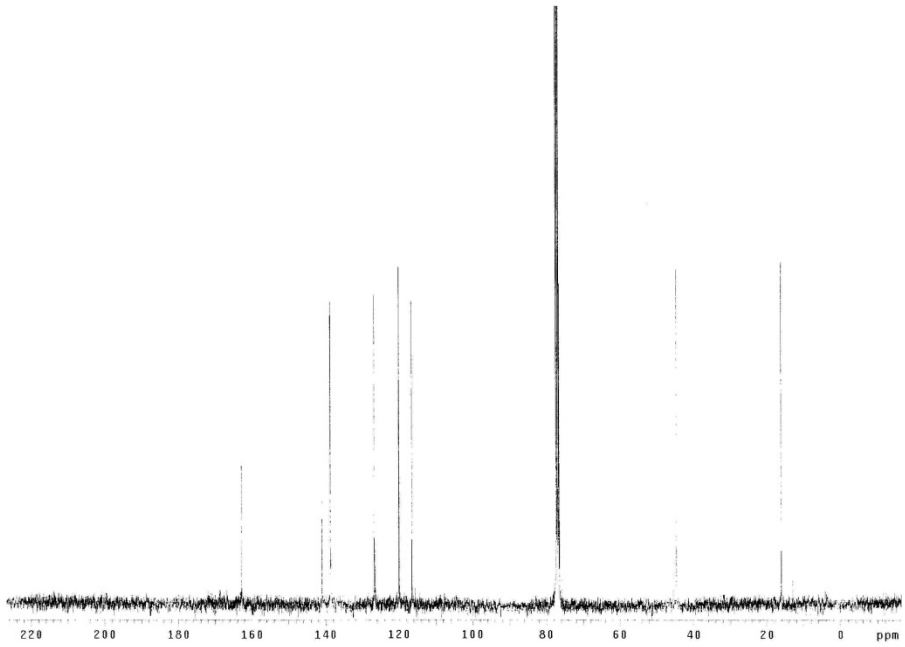




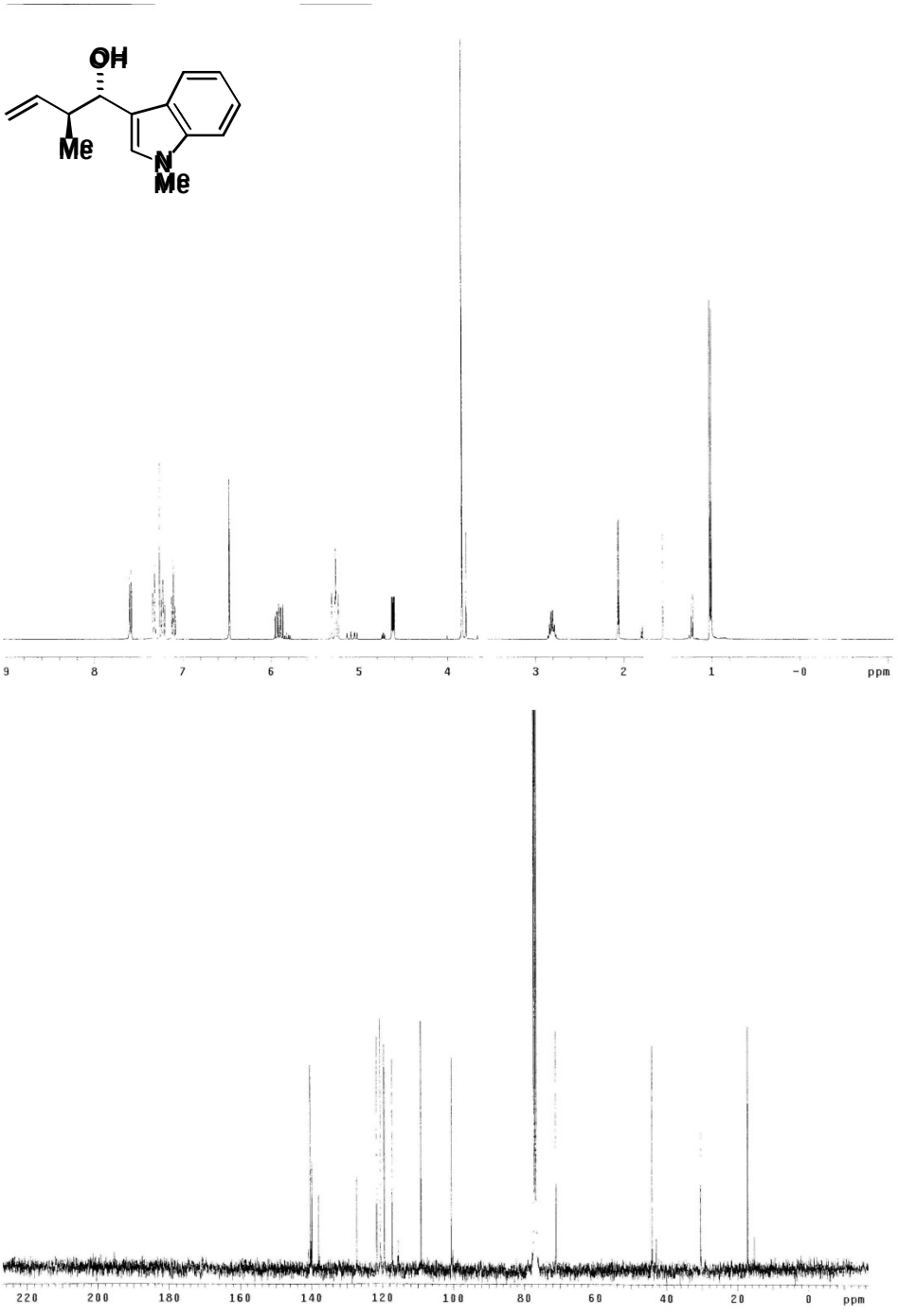
(*1S,2S*)-1-(6-bromopyridin-2-yl)-2-methylbut-3-en-1-ol (11)



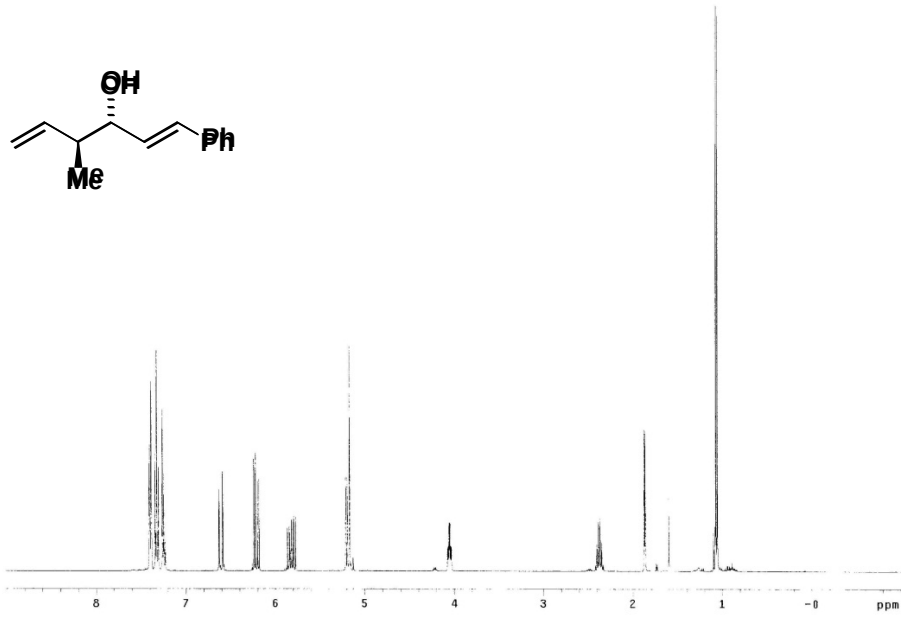


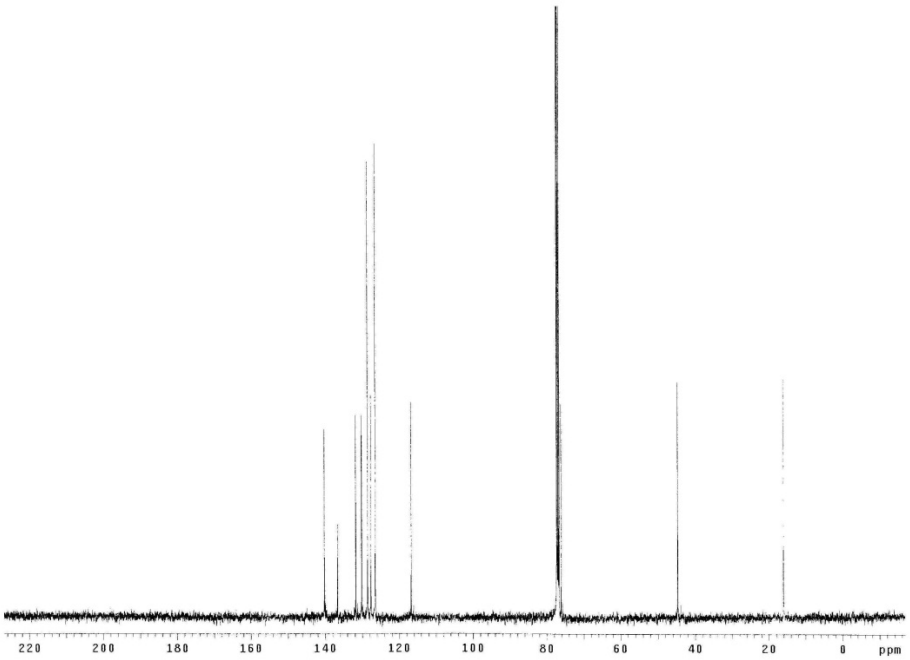


(*1S*,*2S*)-2-methyl-1-(1-methyl-1*H*-indol-3-yl)but-3-en-1-ol (12)

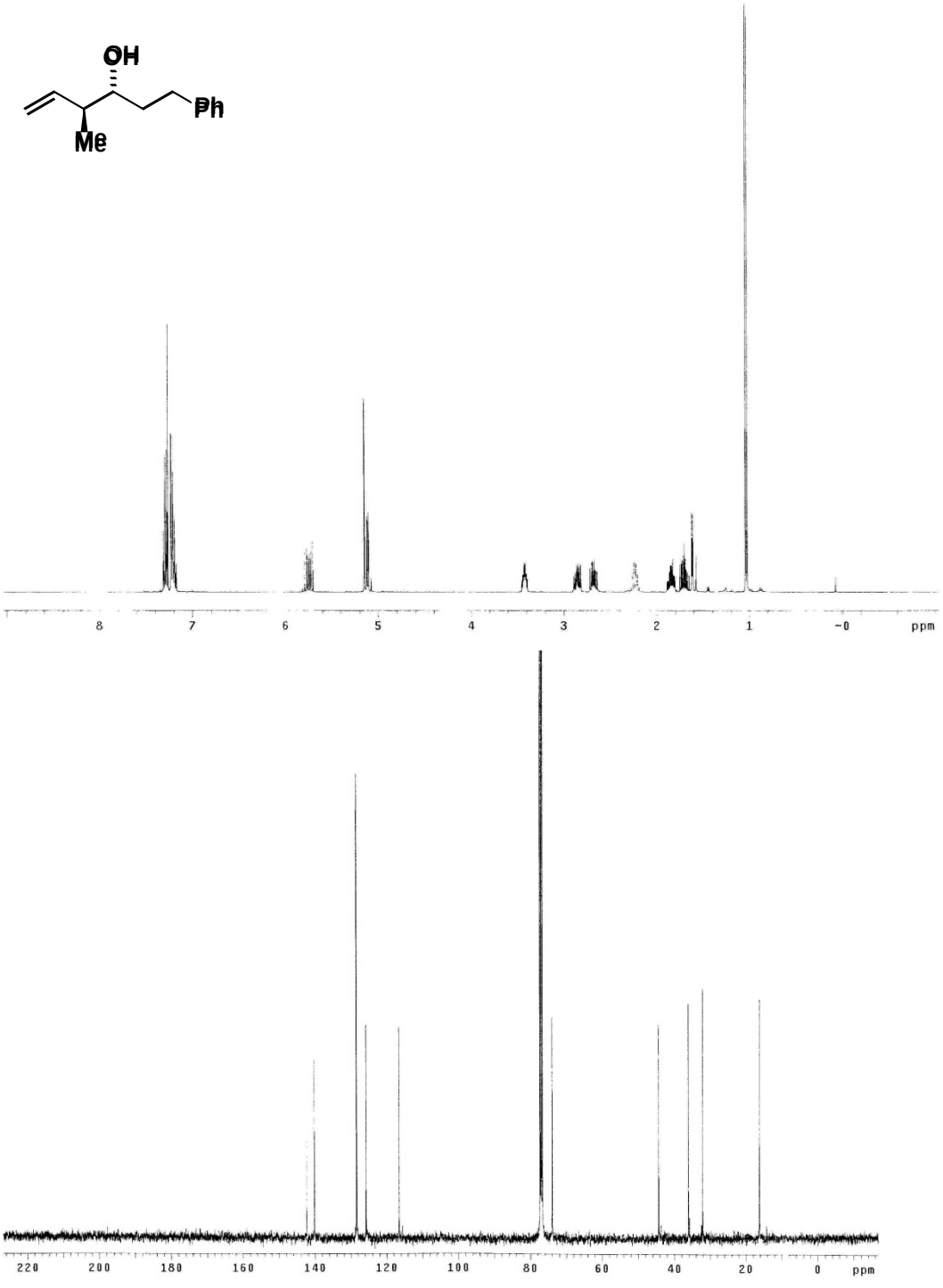


(*3R,4S,E*)-4-methyl-1-phenylhexa-1,5-dien-3-ol (13)

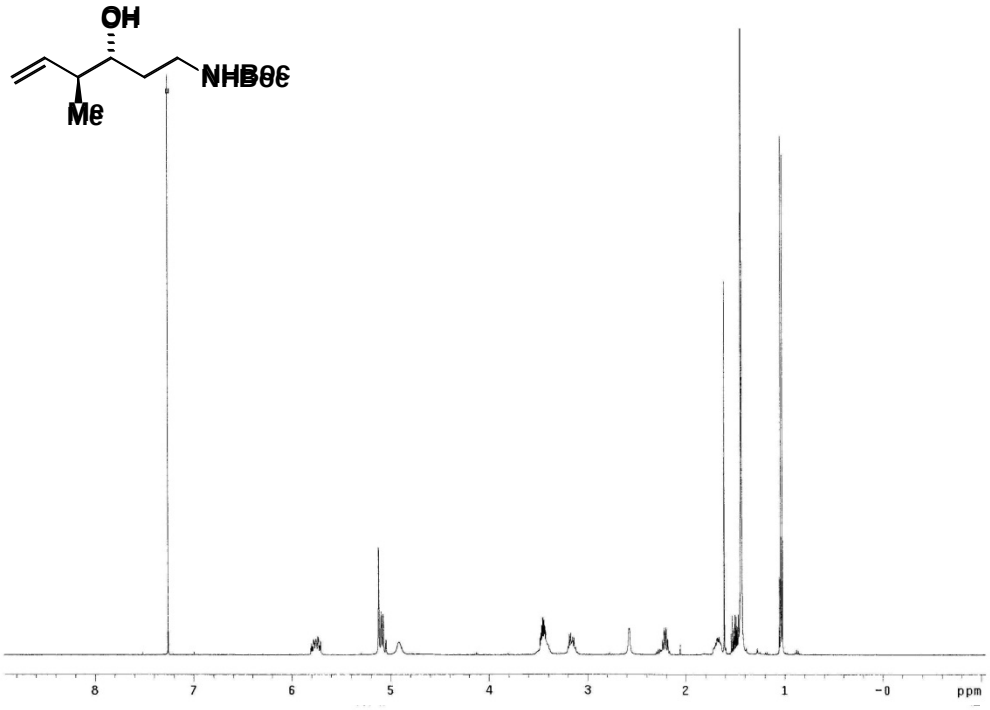


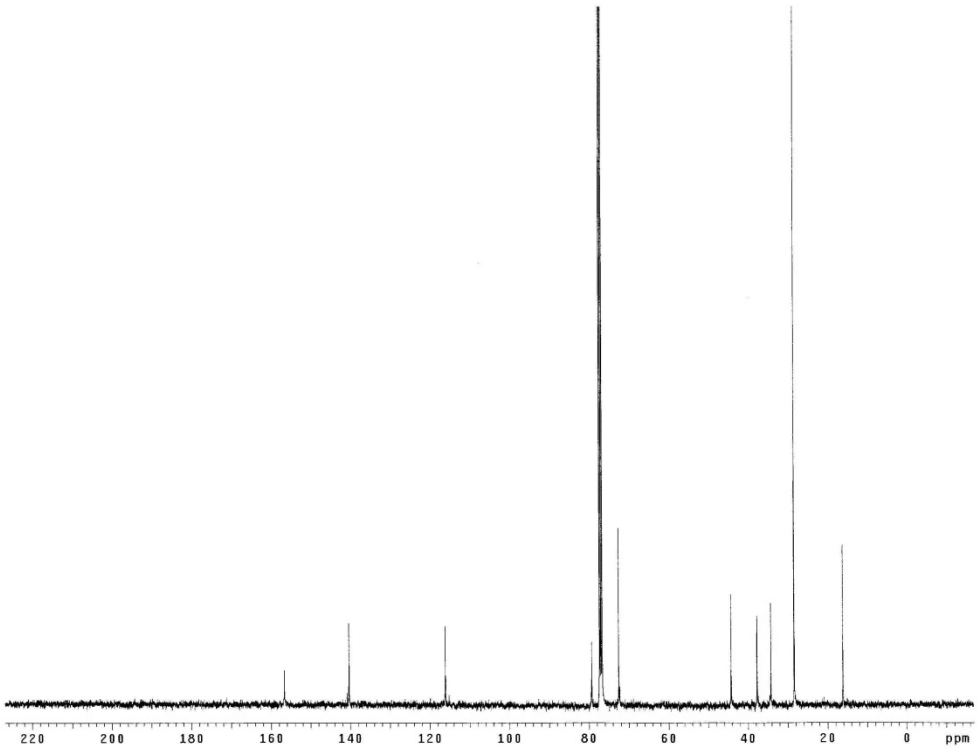


(*3R,4S*)-4-methyl-1-phenylhex-5-en-3-ol (14)

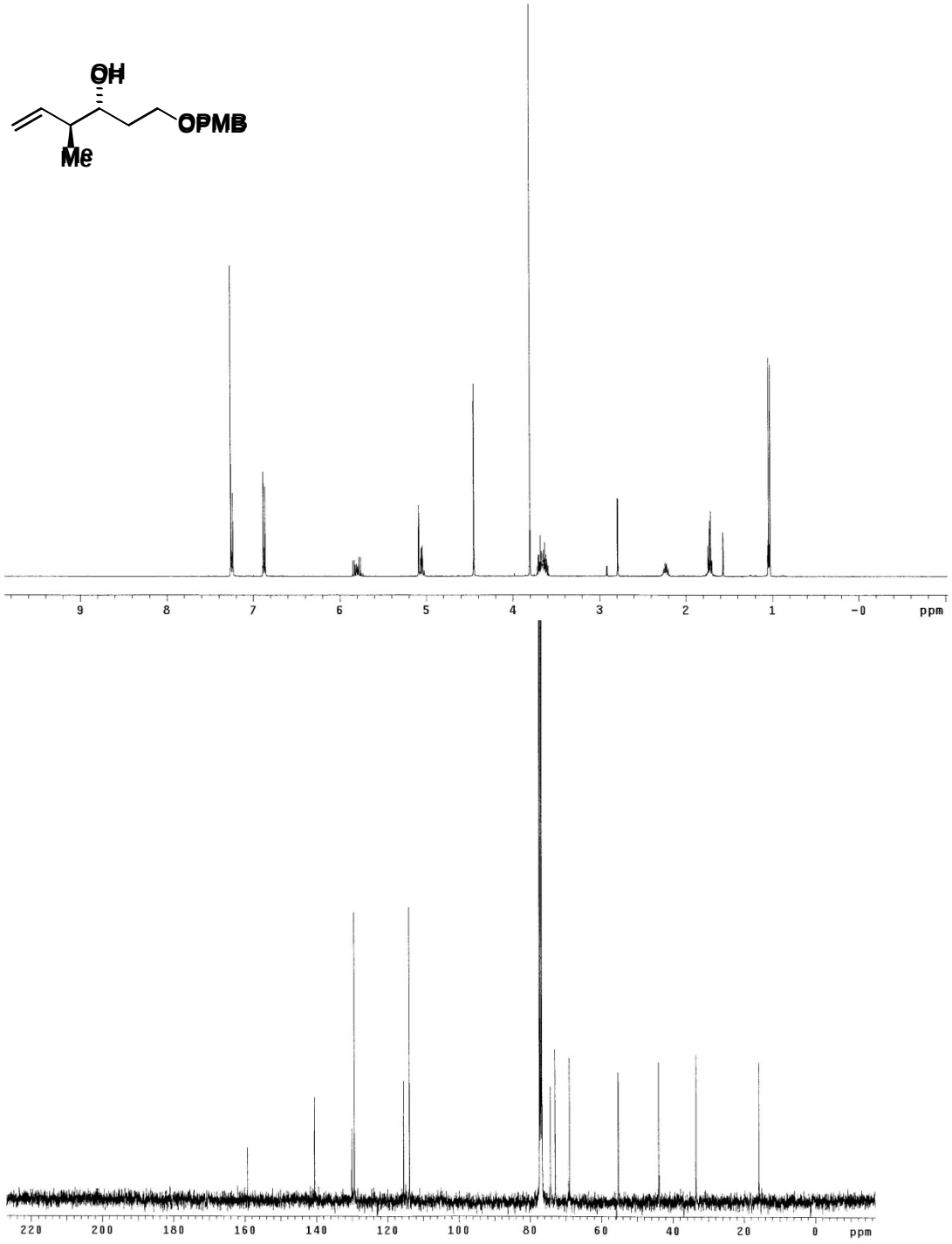


***tert*-butyl (*3R,4S*)-3-hydroxy-4-methylhex-5-enylcarbamate (15)**

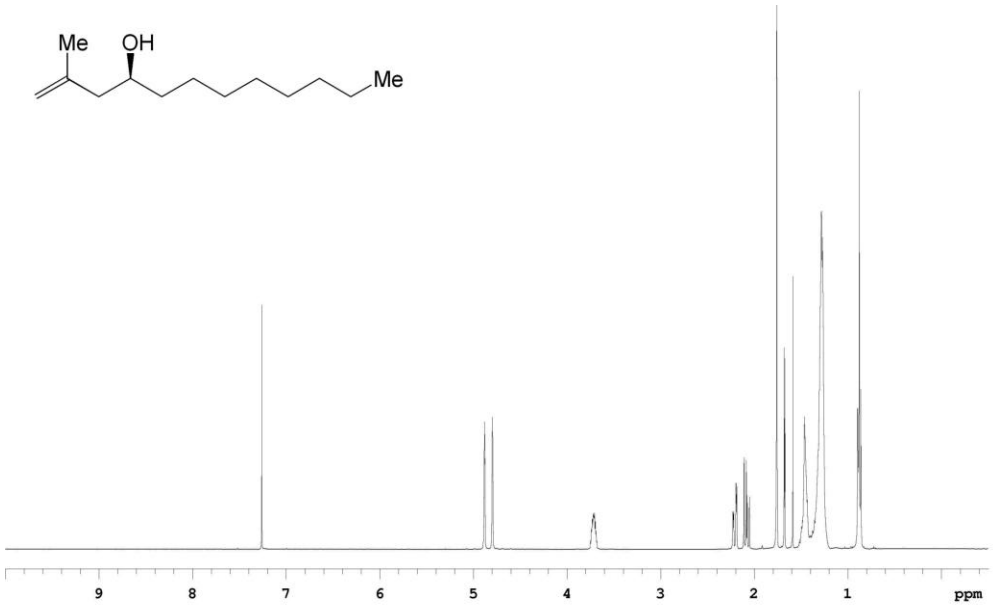


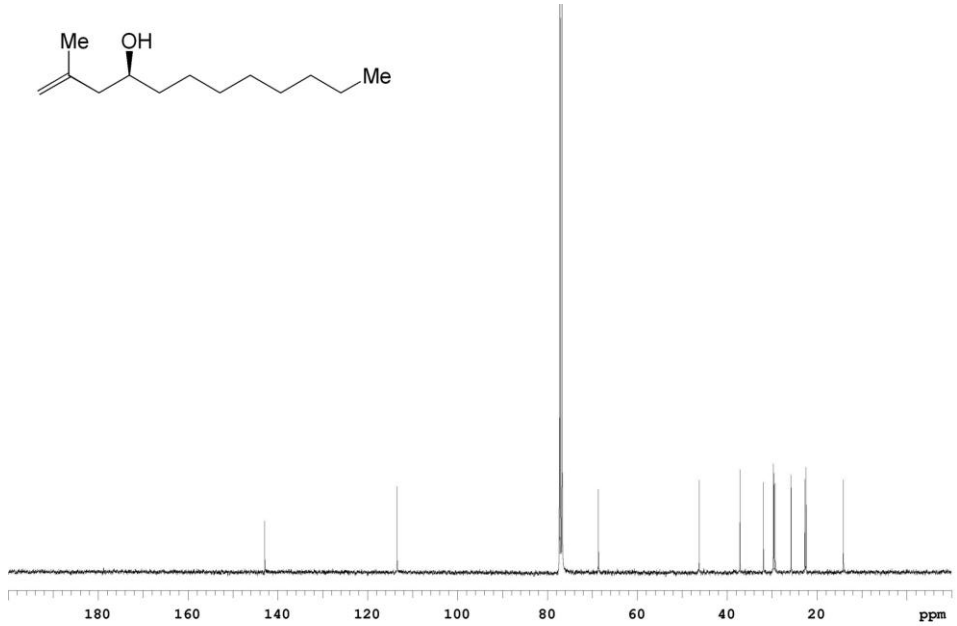


(*3R,4S*)-1-(4-methoxybenzyloxy)-4-methylhex-5-en-3-ol (16)

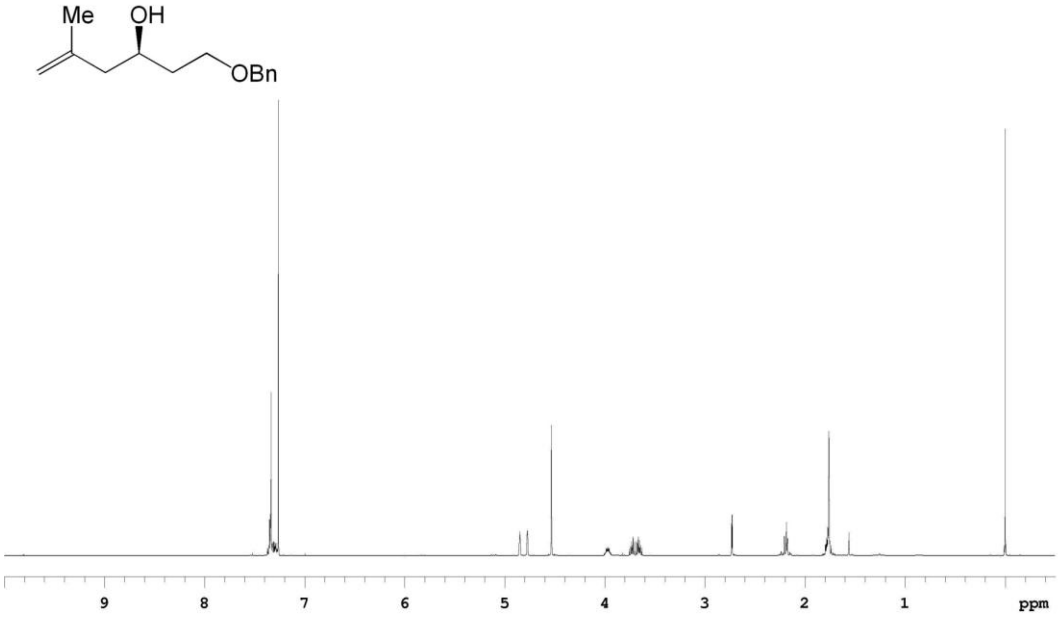


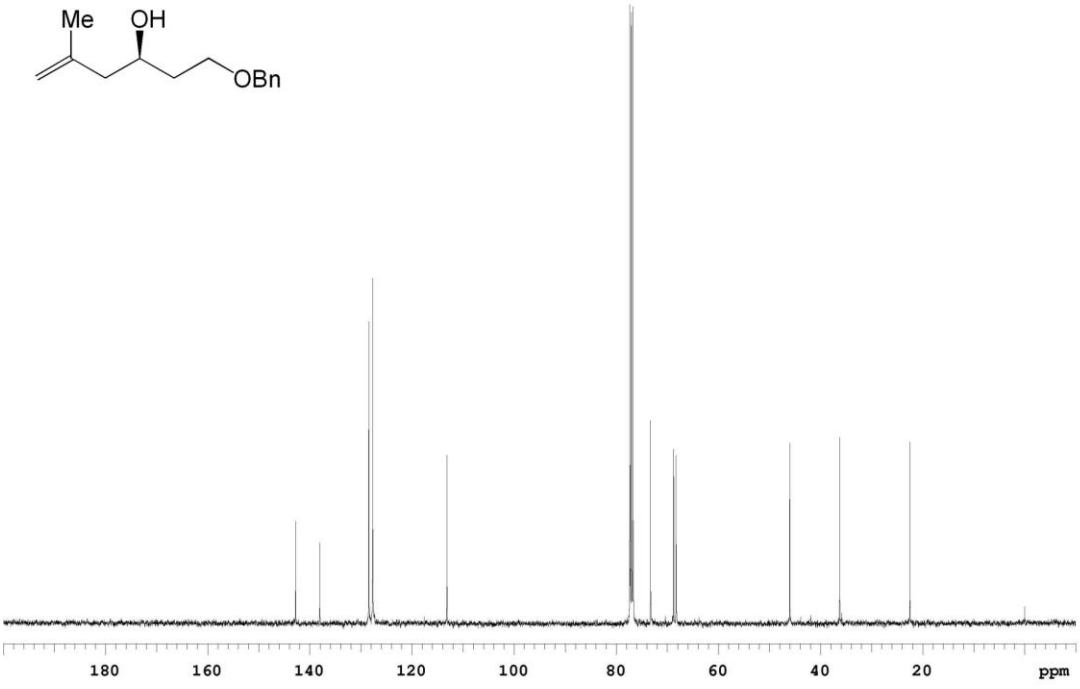
(S)-2-methyldodec-1-en-4-ol (36)



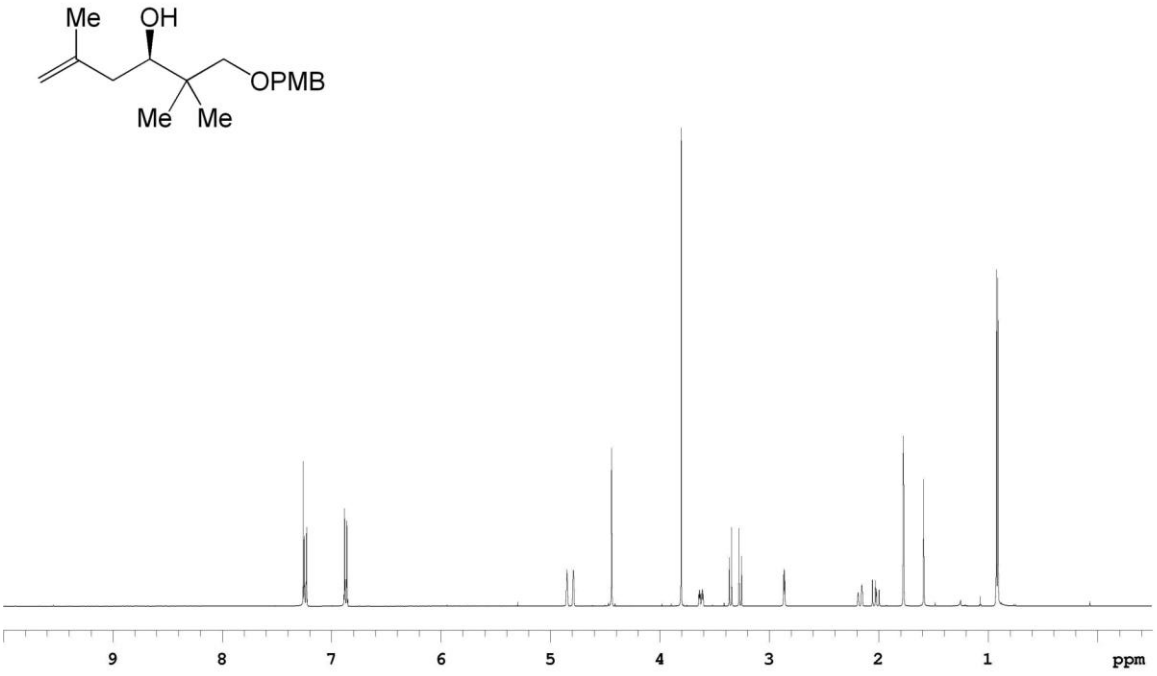


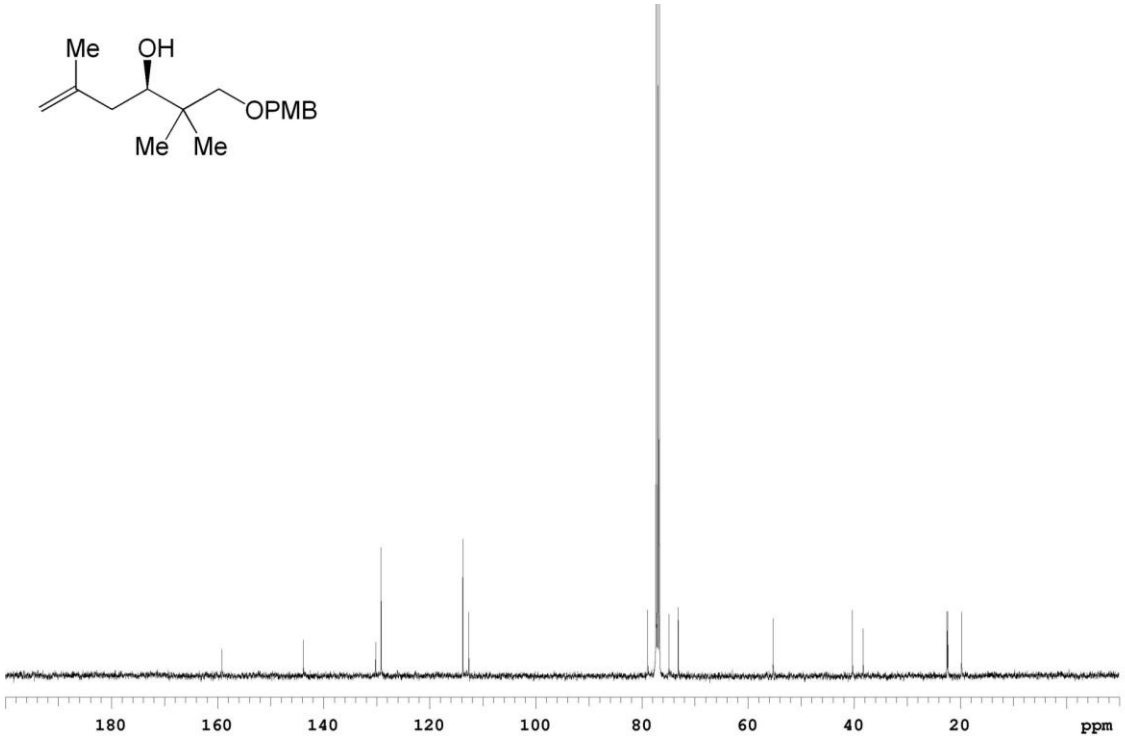
(R)-1-(benzyloxy)-5-methylhex-5-en-3-ol (37)



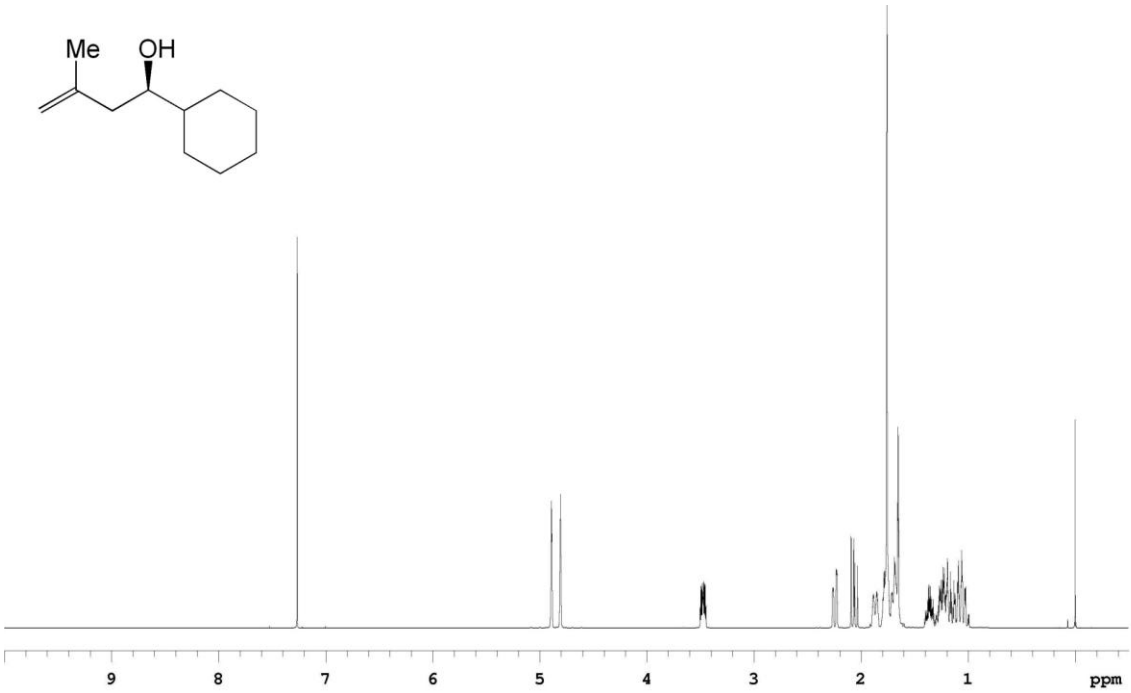


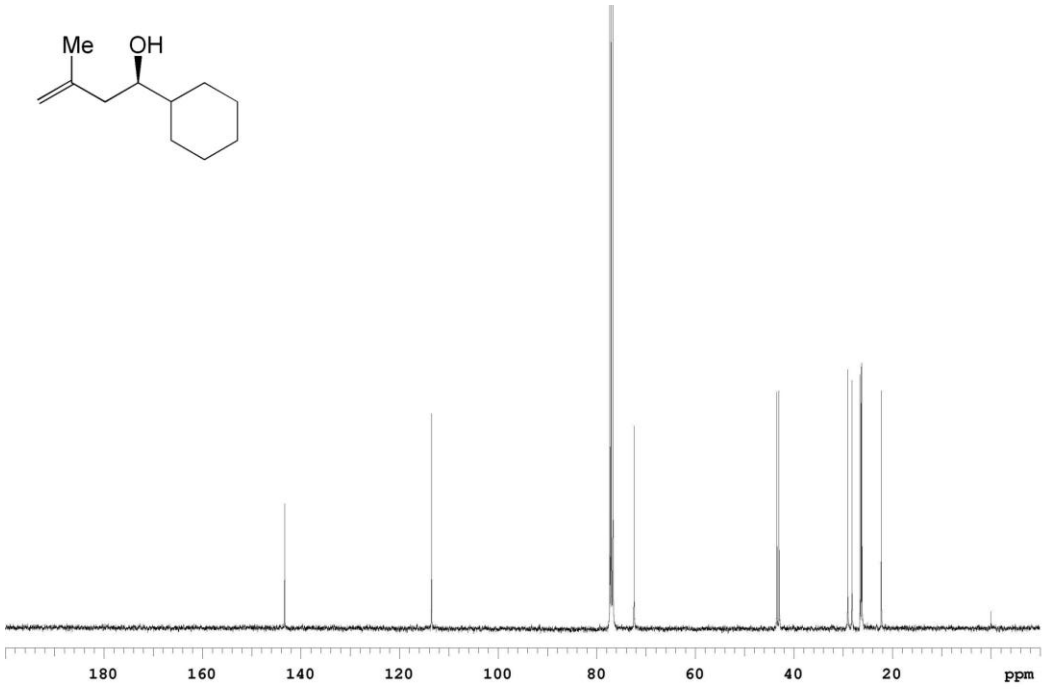
(R)-1-(4-methoxybenzyloxy)-2,2,5-trimethylhex-5-en-3-ol (38)



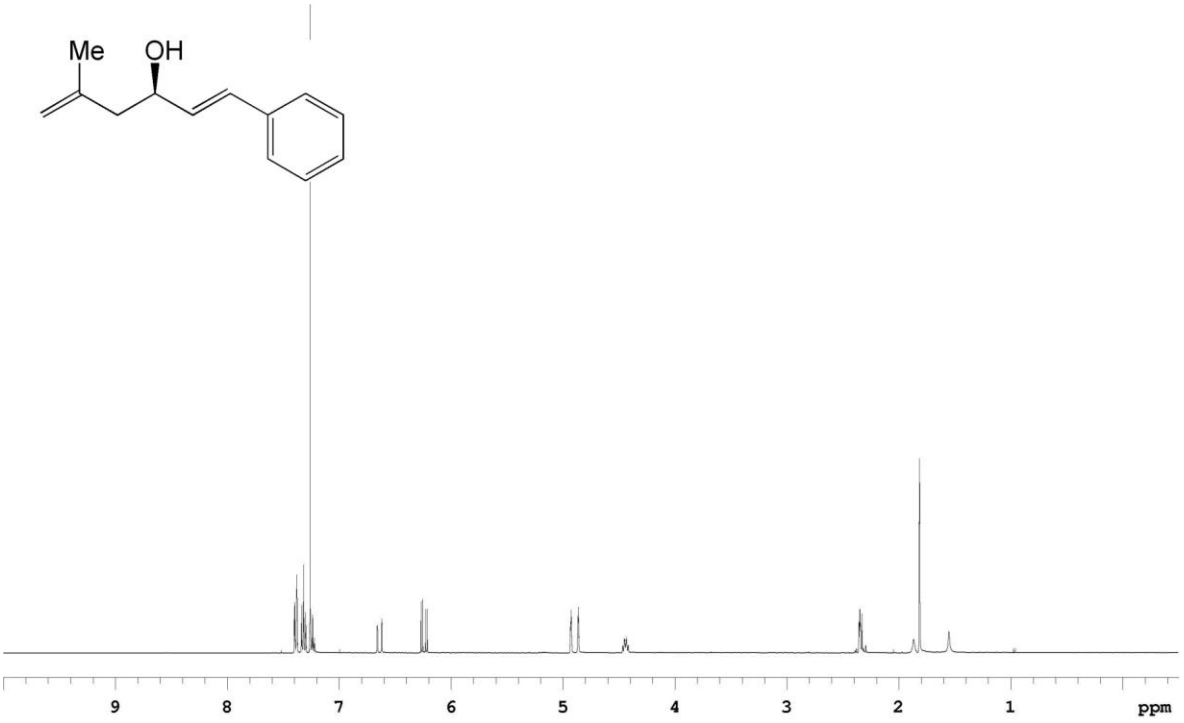


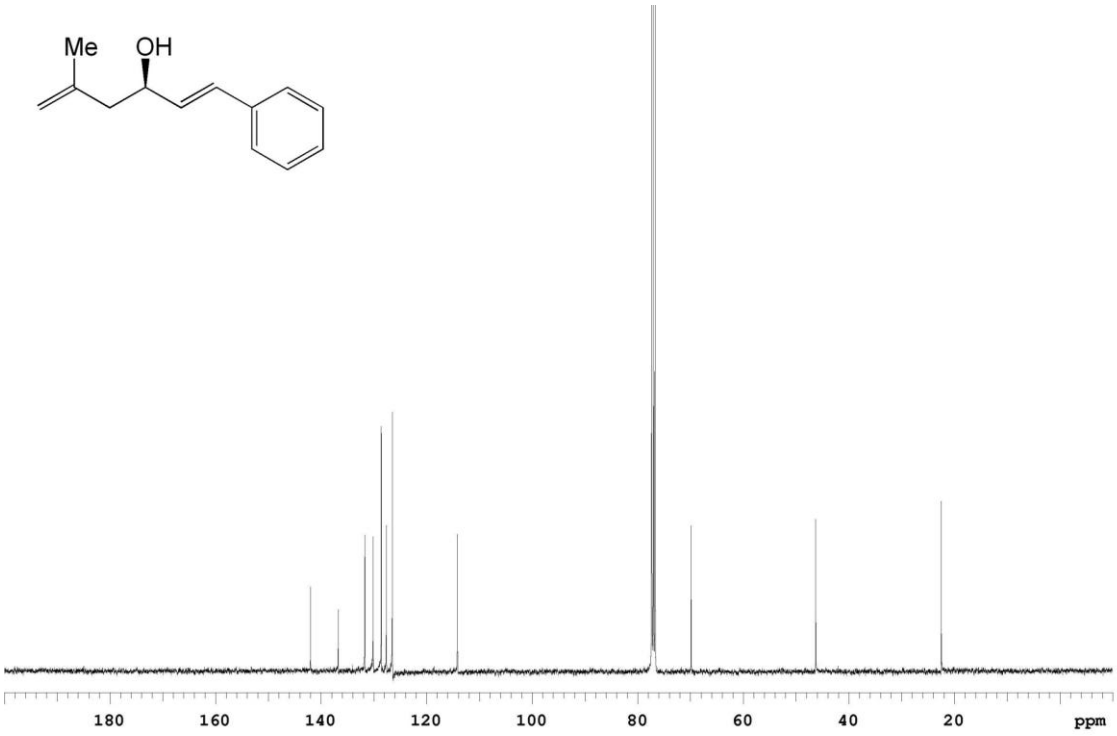
(R)-1-cyclohexyl-3-methylbut-3-en-1-ol (39)



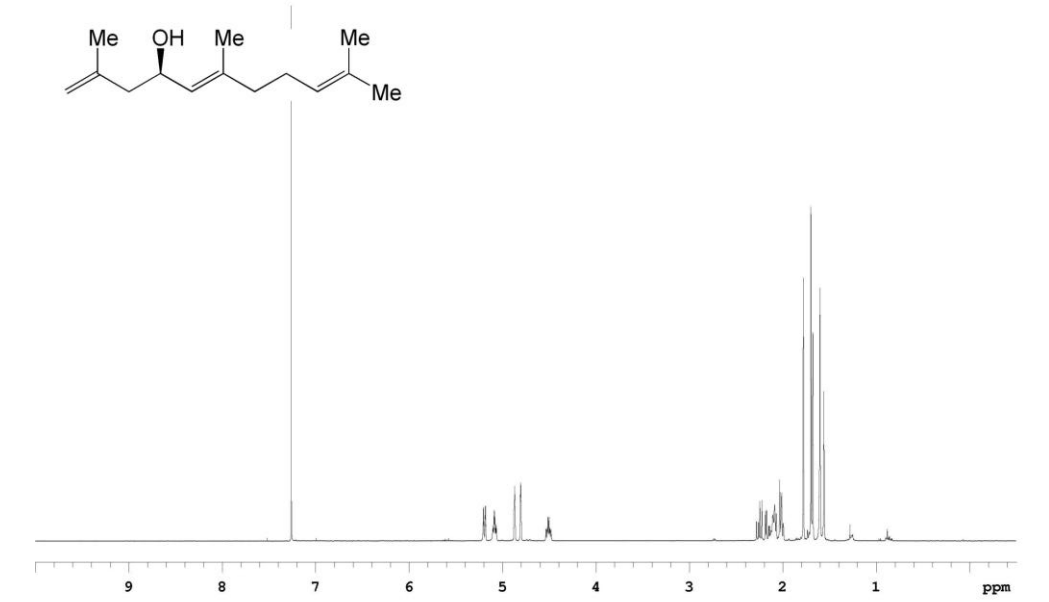


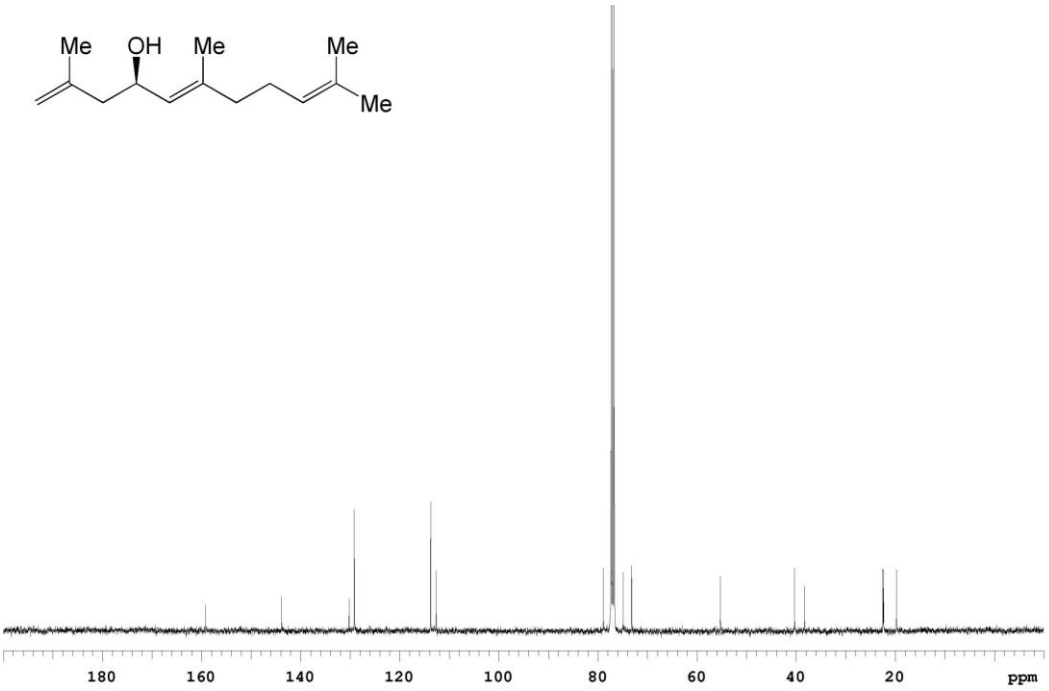
(R,E)-5-methyl-1-phenylhexa-1,5-dien-3-ol (40)



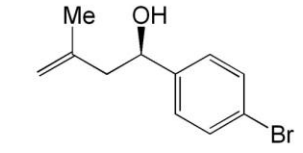


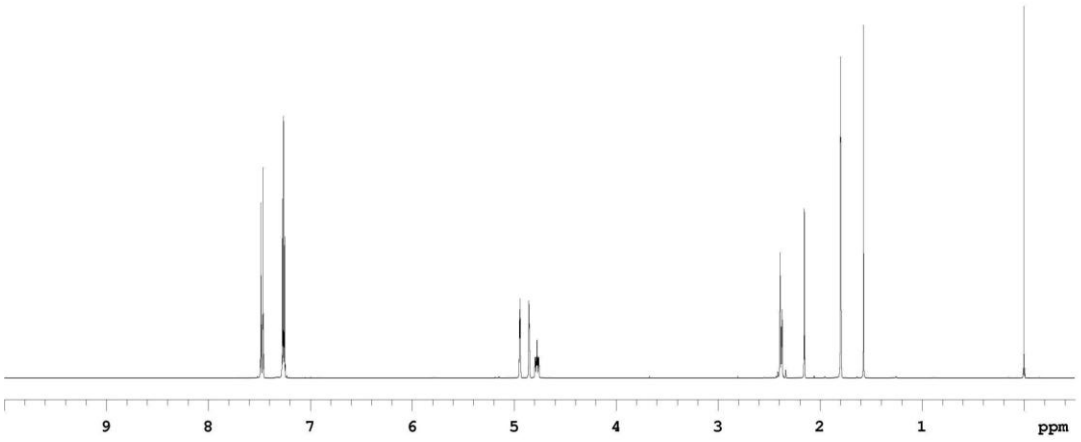
(R,E)-2,6,10-trimethylundeca-1,5,9-trien-4-ol (41)

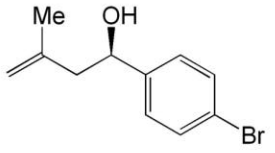




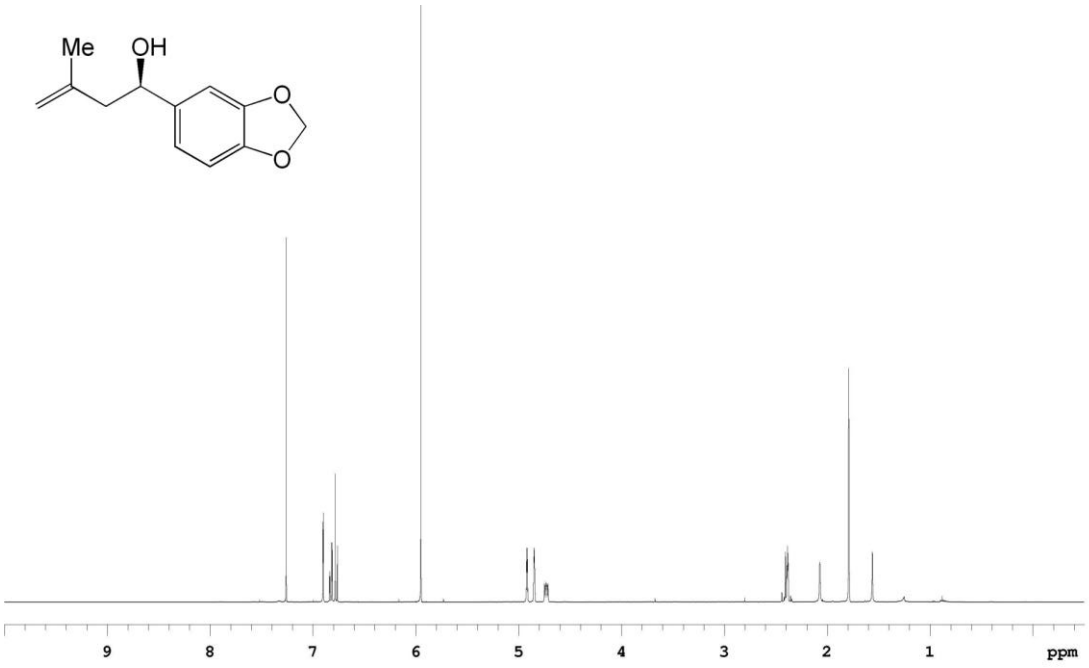
(R)-1-(4-bromophenyl)-3-methylbut-3-en-1-ol (34)

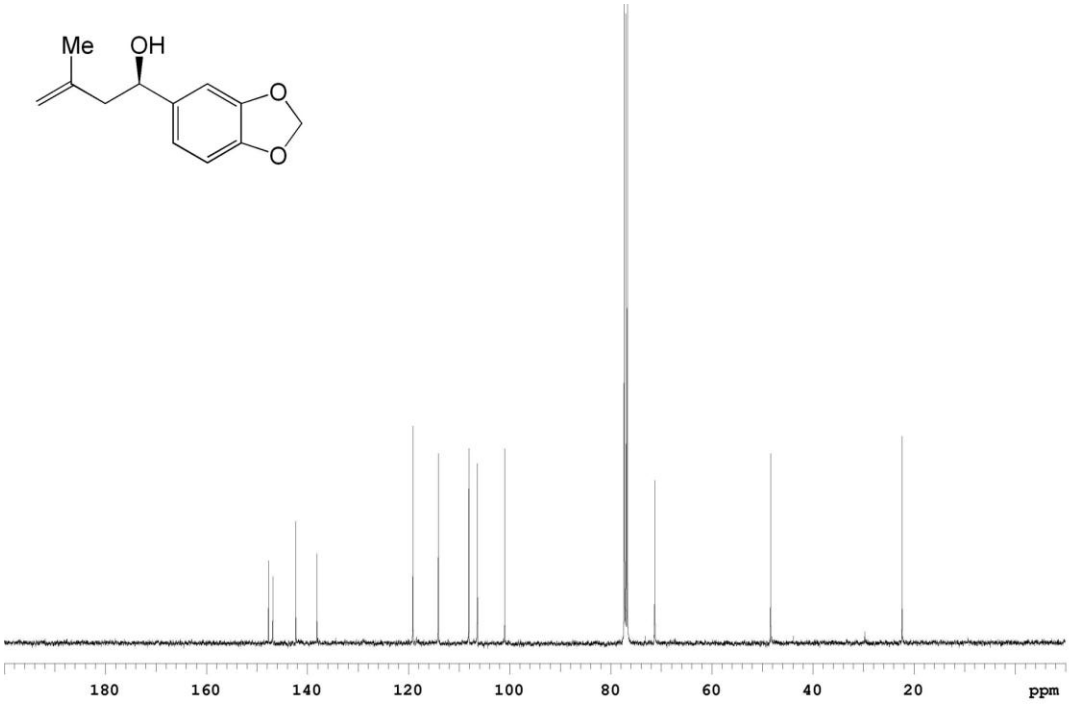




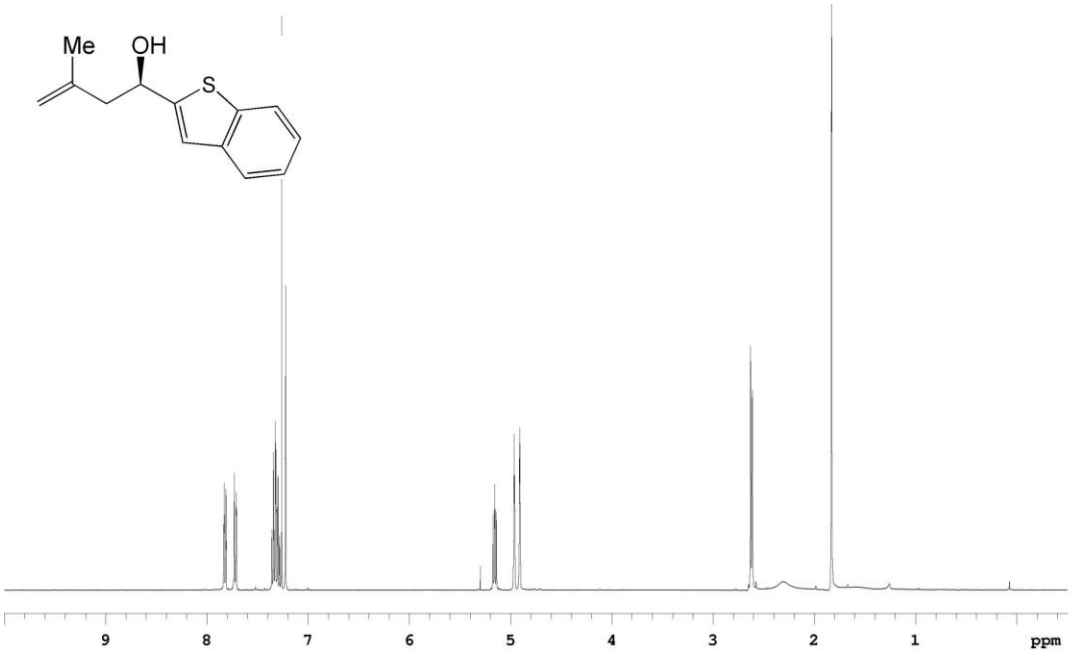


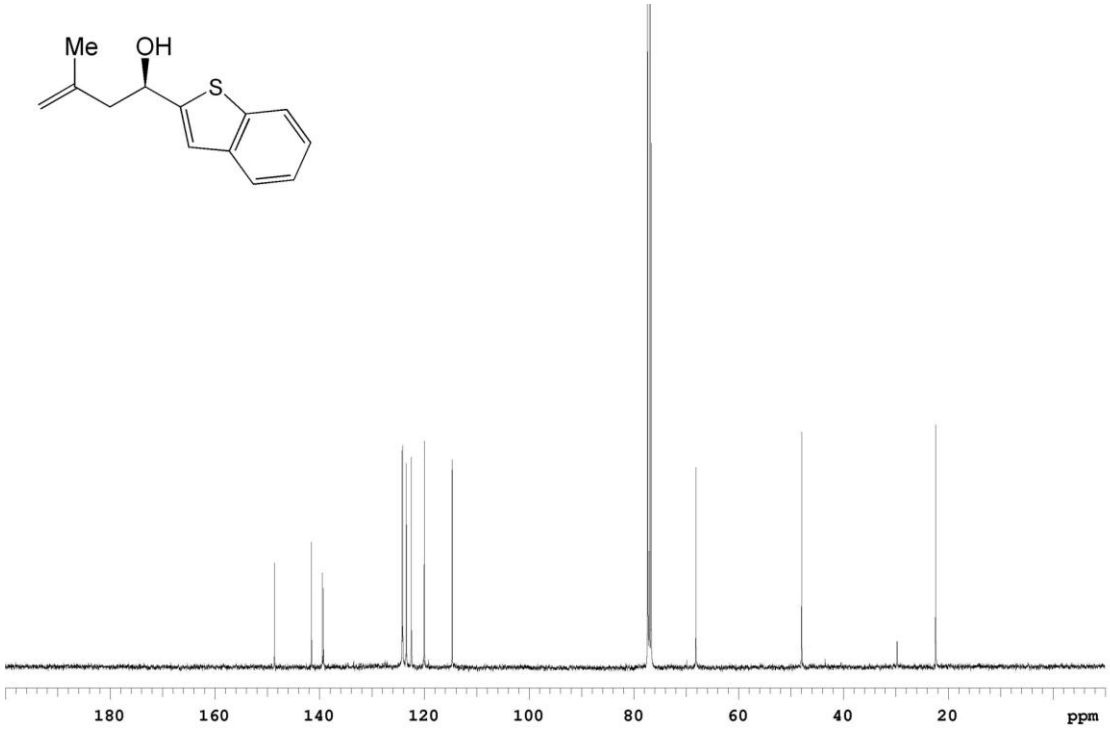
(R)-1-(benzo[d][1,3]dioxol-5-yl)-3-methylbut-3-en-1-ol (42)





(R)-1-(benzo[b]thiophen-2-yl)-3-methylbut-3-en-1-ol (43)





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