Stereoselective Chelate-Controlled Addition of Grignard Reagents to Unsaturated Medium-Ring Heterocycles

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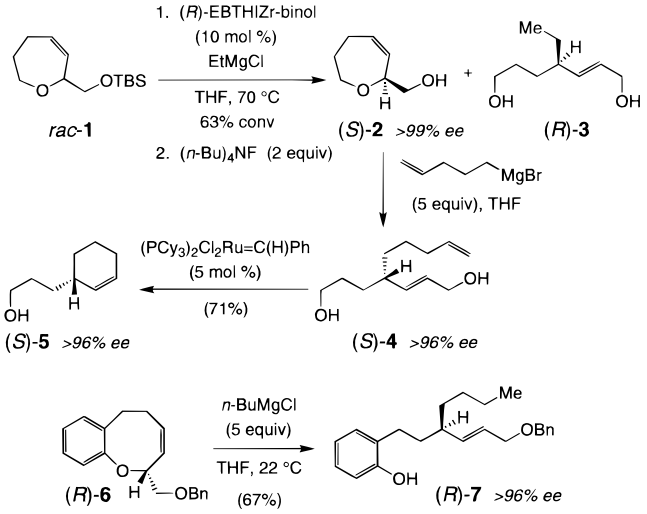
Various medium-ring heterocycles, bearing a C2-substituent that contains an accessible Lewis basic heteroatom, react with Grignard reagents with high levels of regio- and stereochemical control. The substrates can be prepared in the optically pure form by the Zr-catalyzed kinetic resolution; subsequent reaction with alkylmagnesium halides leads to the formation of optically pure alkylation products. The studies outlined herein probe the influence of the length and position of the heteroatom side chain on the facility and regio- and stereoselective outcome of the allylic substitution process. A catalytic procedure for the subsequent removal of the requisite heteroatom chelating group is presented.

Introduction

Addition of alkylmetals to alkenes represents an attractive and relatively unexplored method for regio- and stereoselective C−C bond formation.[1] Within this context, and in conjunction with programs in these laboratories[2] aimed at the development of metal-catalyzed alkylation of olefins,[3] we recently reported the initial results of our studies regarding a heteroatom-assisted[4] diastereoselective reaction between Grignard reagents and certain unsaturated medium ring heterocycles.[5] As illustrated in Scheme 1, the requisite optically pure seven-membered rings (e.g., (*S*)-**2**) may be accessed through the Zr-catalyzed kinetic resolution.[2f] The enantiomerically pure cyclic substrates thus obtained can be readily alkylated to afford chiral acyclic products (e.g., (*S*)-**4**) with excellent enantiopurity (>96% ee) and complete control of alkene regio- and stereochemistry (>98% trans). In addition to alcohols as the starting materials, the derived Bn, PMB, or MEM ethers can be effectively and selectively alkylated. Although not catalytic, these allylic substitutions complement the aforementioned Zr-catalyzed reaction, as alkylmetals other than Et-, *n*-Pr, and *n*-BuMgCl can be used.[2d] An advantage of this allylic substitution process is that a number of useful functional groups can be imported as part of the alkylmagnesium halide; such functionalities may be exploited for subsequent functionalization. The catalytic formation of unsaturated carbocycle (*S*)-**5**, shown in Scheme 1, through a subsequent catalytic ring-closing metathesis,[6] illustrates this point. As shown in Scheme 1, similar strategies may be applied to the corresponding oxocenes ((*R*)-**6** → (*R*)-**7**). Furans and pyrans, on the other hand, do not undergo alkylation under these reaction conditions.

Scheme 1



(1) For uncatalyzed examples of the addition of Grignard reagents to olefins, see: (a) Eisch, J. J. *J. Organomet. Chem.* **1980**, *200*, 101−117 and references therein. (b) Felkin, H.; Kaeseberg, C. *Tetrahedron Lett.* **1970**, 4587−4590 and references therein. (c) Richey, H. G.; Domalski, M. S. *J. Org. Chem.* **1981**, *46*, 3780−3783 and references therein. (d) Swiss, K. A.; Liotta, D. C.; Maryanoff, C. A. *J. Am. Chem. Soc.* **1990**, *112*, 9393−9394 and references therein.

(2) For Zr-catalyzed diastereoselective additions: (a) Houri, A. F.; Didiuk, M. T.; Xu, Z.; Horan, N. R.; Hoveyda, A. H. *J. Am. Chem. Soc.* **1993**, *115*, 6614−6624. (b) Morken, J. P.; Hoveyda, A. H. *J. Org. Chem.* **1993**, *58*, 4237−4244. For Zr-catalyzed enantioselective additions: (c) Morken, J. P.; Didiuk, M. T.; Hoveyda, A. H. *J. Am. Chem. Soc.* **1993**, *115*, 6697−6698. (d) Didiuk, M. T.; Johannes, C. W.; Morken, J. P.; Hoveyda, A. H. *J. Am. Chem. Soc.* **1995**, *117*, 7097−7104. Zr-catalyzed kinetic resolution through enantioselective allylic ether alkylation: (e) Morken, J. P.; Didiuk, M. T.; Visser, M. S.; Hoveyda, A. H. *J. Am. Chem. Soc.* **1994**, *116*, 3123−3124. (f) Visser, M. S.; Heron, N. M.; Didiuk, M. T.; Sagal, J. F.; Hoveyda, A. H. *J. Am. Chem. Soc.* **1996**, *118*, 4291−4298. (g) Visser, M. S.; Harrity, J. P. A.; Hoveyda, A. H. *J. Am. Chem. Soc.* **1996**, *118*, 3779−3780. (h) Harrity, J. P. A.; La, D. S.; Cefalo, D. R.; Visser, M. S.; Hoveyda, A. H. *J. Am. Chem. Soc.* **1998**, *120*, 2343−2351.

(3) For an example of a Cu-catalyzed addition of Grignard reagents to allylic ethers, see: (a) Gendreau, Y.; Normant, J. F. *Tetrahedron* **1979**, *35*, 1517−1521. For related Ni-catalyzed processes, see: (b) Consiglio, G.; Piccolo, O.; Roncetti, L.; Morandini, F. *Tetrahedron* **1986**, *42*, 2043−2053. (c) Didiuk, M. T.; Morken, J. P.; Hoveyda, A. H. *J. Am. Chem. Soc.* **1995**, *117*, 7273−7274. For an excellent recent review, see: (d) Consiglio, G.; Waymouth, R. M. *Chem. Rev.* **1989**, *89*, 257−276.

(4) For a review of directed reactions, see: Hoveyda, A. H.; Evans, D. A.; Fu, G. C. *Chem. Rev.* **1993**, *93*, 1307−1370.

(5) Heron, N. M.; Adams, J. A.; Hoveyda, A. H. *J. Am. Chem. Soc.* **1997**, *119*, 6205−6206.

(6) For recent reviews on the utility of olefin metathesis in organic synthesis, see: (a) Grubbs, R. H.; Miller, S. J.; Fu, G. C. *Acc. Chem. Res.* **1995**, *28*, 446−452 and references therein. (b) Schmalz, H.-G. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 1833−1836 and references therein. (c) Schuster, M.; Blechert, S. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 2036−2056. (d) Furstner, A. *Topics Catal.* **1997**, *4*, 285−299. (e) Armstrong, S. K. *J. Chem. Soc., Perkin Trans 1* **1998**, 371−388. (f) Grubbs, R. H.; Chang, S. *Tetrahedron* **1998**, *54*, 4413−4450.

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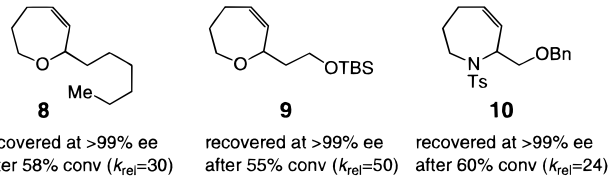
Chart 1



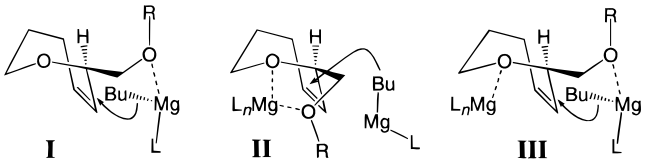
8 recovered at >99% ee after 58% conv (k_{rel}=30)

9 recovered at >99% ee after 55% conv (k_{rel}=50)

10 recovered at >99% ee after 60% conv (k_{rel}=24)

Conditions: 10 mol % (*R*)-(EBTHI)Zr-binol, 5 equiv EtMgCl, THF, 70 °C

Scheme 2



R=MgCl, Bn, PMB, MEM; L=halogen or alkyl

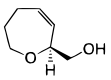
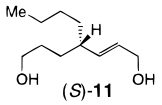
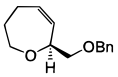
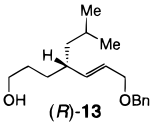
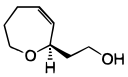
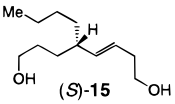
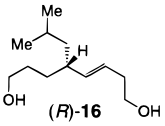
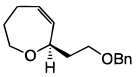
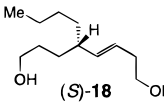
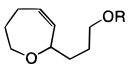
In this article, we address several general key issues related to this diastereoselective C−C bond forming reaction. Specifically, we will describe: (1) mechanistic aspects of the C−C bond-forming reaction, particularly where reactivity is dependent on the nature of the internal heteroatoms as well as the length and positioning of the side chain substituent; (2) stereoselective alkylation of substrates with directing groups that can be subsequently excised in a catalytic manner.

Results and Discussion

Structural Requirements for Effective Alkylation. All available data suggest that facile alkylation occurs when *both* the C2 side chain and the ring system bear Lewis basic heteroatoms that are available for efficient metal (Mg) coordination. Thus, as depicted in Chart 1, in contrast to substrates such as **2** (Scheme 1) or its corresponding Bn ether, 2-substituted oxepin **8**, silyl ether **9,** and cyclic amide **10** are inert to allylic substitution by alkylmagnesium halides (<2% conversion). As a result, since there is little or no uncatalyzed alkylation, these substrates can be resolved through the Zr-catalyzed kinetic resolution.[7]

In our preliminary report,[5] we proposed three possible general pathways through which the allylic substitution reaction could proceed (Scheme 2). The lack of reactivity of **10** in the absence of the chiral metallocene catalyst discredits the proposed mode of addition **I** (Scheme 2)[8] by suggesting that association of the ring heteroatom with a Lewis acidic metal is required (presumably to lower the energy of the σ^* orbital of the cleaving C−O bond). The question then arises whether the positive contribution of the side chain heteroatom is coupled with that of the heteroatom within the ring structure. That is, C−C bond formation and concomitant C−O rupture might be promoted by an internal bidentate chelate represented by **II**. Alternatively, the side chain oxygen may associate with the Grignard reagent to deliver the alkylmetal, while the ring heteroatom activates the allylic ether for reaction (mode **III**).

Table 1. The Influence of Side Chain Length on the Diastereoselective Alkylation Efficiency[a]

entry	substrate	Grignard reagent	temp, time	product	ee, yield (%)
1	 (*S*)-**2**	*n*-BuMgCl	22 °C, 24 h	 (*S*)-**11**	>96, 93
2	 (*S*)-**12**	*i*-BuMgCl	22 °C, 24 h	 (*R*)-**13**	>96, 87
3	 (*R*)-**14**	*n*-BuMgCl	22 °C, 13 h	 (*S*)-**15**	>96, 97
4		*i*-BuMgCl	22 °C, 13 h	 (*R*)-**16**	>96, 92
5		*n*-BuMgCl	22 °C, 13 h	NO REACTION	
6	 (*R*)-**17**	*n*-BuMgCl	70 °C, 56 h	 (*S*)-**18**	>96, 82
7	 *rac*-**19** (**a**, R=H or **b**, R=Bn)	*n*-BuMgCl	70 °C, 56 h	NO REACTION	

[a] Conditions: 5 equiv of RMgCl, THF. [b] Selectivity determined by analysis of the derived (*R*)-MTPA ester (TBS protection, ozonolysis, and reduction), in comparison with racemic materials (400 MHz ^{19}F NMR; entry 2 with ^{1}H NMR). [c] Isolated yield after silica gel chromatography.

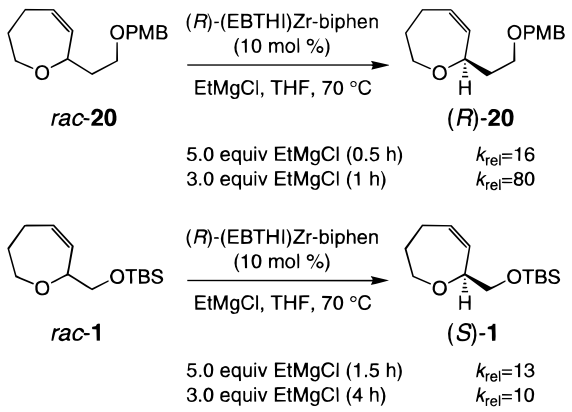
Variations in Reactivity as a Function of Side Chain Position and Length. To address the above questions and gain further insight into factors that allow facile alkylations, we carried out alkylations with substrates where the length and relative position of the heteroatom-containing side chain is varied. As shown in Table 1, oxepin (*S*)-**2** and its derived Bn ether (*S*)-**12** (entries 1 and 2) readily react with *n*-BuMgCl and *i*-BuMgCl to afford (*S*)-**11** and (*R*)-**13** in high yield and with excellent stereochemical control. As the examples illustrated in entries 3 and 4 (Table 1) indicate, when the C2 side chain is extended by one methylene unit ((*R*)-**14**), alkylation remains efficient. With the longer side chain, when the hydroxyl group is protected as a Bn ether unit, reaction efficiency suffers; there is <2% reaction with (*R*)-**17** at 22 °C within the same length of time that the parent alcohol ((*R*)-**14**) undergoes complete conversion. Nonetheless, as shown in entry 6, under more forcing conditions, (*R*)-**17** reacts with *n*-BuMgCl to provide (*S*)-**18** in >96% ee and 82% yield after silica gel chromatography. The influence of the Lewis basic heteroatom at the C2 side chain is lost when an additional methylene unit is incorporated: oxepin **19a** or its derived Bn ether **19b** are inert to the alkylation conditions.

Zr-Catalyzed Kinetic Resolution and Uncatalyzed Addition. The relatively slow rate of reaction of substrates such as **17** (entries 5 and 6, Table 1) with

(7) Relative rates were calculated by an equation reported previously: (a) Balavoine, G.; Moradpour, A.; Kagan, H. B. *J. Am. Chem. Soc.* **1974**, *96*, 5152−5158. (b) Martin, V. S.; Woodard, S. S.; Katsuki, T.; Yamada, Y.; Ikeda, M.; Sharpless, K. B. *J. Am. Chem. Soc.* **1981**, *103*, 6237−6240.

(8) In our initial report (ref 5), seven-membered ring substrates were proposed to react through a pseudo-chair conformer. However, closer inspection of models indicates that the related pseudo-boat conformers carry less torsional strain.

Scheme 3



Grignard reagents suggests that these heterocycles might be catalytically resolved by the Zr-catalyzed procedure without recourse to initial masking of the side chain heteroatom with a bulky protecting group (e.g., the TBS unit in (*S*)-**1** is removed to afford alkylation substrate (*S*)-**2** after the catalytic resolution). Indeed, as illustrated in Scheme 3, treatment of *rac*-**20** with 10 mol % (*R*)-(EBTHI)Zr-biphen[9] and 3.0 equiv of EtMgCl in THF (70 °C, 1 h) results in the recovery of (*R*)-**20** in >99% ee after 53% conversion (k_{rel} = 80). In contrast, the homologous (*S*)-**12** (or its derived PMB) cannot be resolved due to adventitious uncatalyzed alkylation.

It is noteworthy that the catalytic resolution of *rac*-**20** shown in Scheme 3 is carried out with *three* equiv EtMgCl, in contrast to five equiv typically used in our previous studies.[2e−g] This reduction in the amount of Grignard reagent was to minimize any adventitious uncatalyzed alkylation that may reduce the resolution efficiency, even if it occurs in minor amounts. As the data in Scheme 3 show, with lower amounts of EtMgCl (3.0 vs 5.0 equiv), the catalytic resolution is indeed more efficient (k_{rel} = 80 vs 16 for the resolution of *rac*-**20**). However, as also illustrated in Scheme 3, this trend does not apply to the catalytic resolution of all substrates. The catalytic resolution of *rac*-**1** is less efficient with lower amounts of the Grignard reagent. It is possible that with the slower reacting **1** (4 h vs 1 h for **20**), the uncatalyzed allylic substitution remains competitive with the metal-catalyzed process.

Variations in Reactivity as a Function of Positioning of the Chelating Group. To probe the influence of the position of the side chain that bears the chelating group, substrates **21**, **24**, and **27** (Table 2) were synthesized, and their reactivity under the standard alkylation conditions was investigated. The data presented in Table 2 suggest that a two-point chelation between a Mg and the substrate can alone promote alkylation. Whereas silyl ether **21a** is inert to the reaction conditions, **21b** and **21c** afford **22** and **23** in 93 and 50% isolated yield, respectively. The C−C bond-forming reaction with C7-substituted heterocycles **21b** and **21c** affords predominantly the S_N2-type products **23b** and **23c**, in contrast to C2-substituted substrates, where the S_N2' adducts are obtained exclusively (e.g., reaction of **2** in Scheme 1). Similar trends in selectivity are observed in

(9) Chin, B.; Buchwald, S. L. *J. Org. Chem.* **1996**, *61*, 5650−5651. Control experiments show that binol and biphen derivatives of the chiral Zr catalyst afford identical results in asymmetric carbomagnesation reactions.

Table 2. Effect of the Position of the Heteroatom Chelating Group on Alkylation Efficiency and Regioselectivity[a]

entry	substrate	regioselectivity[b]	products	yield (%)[c]
1	**21a** R=TBS	NO REACTION		--
2	**21b** R=H	**22**:**23** 1:8	**22**	93
3	**21c** R=Bn	**22**:**23** 1:8	**23**	50
4	**24a** R=H	**25**:**26** 1:8	**25**	92
5	**24b** R=PMB	NO REACTION	**26**	--
6	**27a** R=H	NO REACTION		
7	**27b** R=PMB	NO REACTION		

[a] Conditions: 5 equiv of *n*-BuMgCl, THF, 22 °C, 24 h. [b] Selectivity determined by analysis of the derived 400 MHz ^{1}H NMR spectra. [c] Isolated yield after silica gel chromatography; yield refers to total yield of all product isomers.

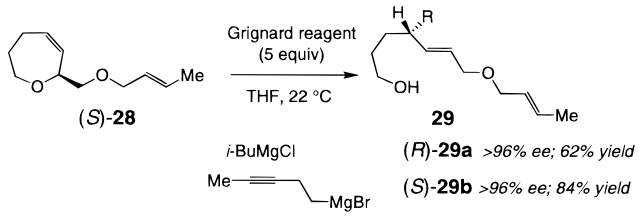
the alkylation of the homologous alcohol **24a**. However, in contrast to benzyl ether **21c**, **24b** is inert to the reaction conditions; this is presumably because the directing effect of the tethered heteroatom is completely abolished by the more remote positioning of the less Lewis basic OPMB.

There could be two reasons for the difference in regioselectivity in alkylations of substrates that bear a C2 (e.g., **2**) vs a C7 (e.g., **21b**,**c**) side chain: (1) With substrates bearing a substituent at the C2 position, S_N2-type products are not formed due to steric factors associated with the formation of a quaternary carbon center. (2) The S_N2-type product is formed predominantly in the reaction of **21b** and **21c**, because the C7 side chain heteroatom cannot reach and thus effectively deliver the alkylmetal reagent (assuming reactions occur via mode **III**, Scheme 2). To address the latter possibility and establish whether in the absence of two-point chelation, a suitably situated Lewis basic site alone can deliver the Grignard reagent and promote alkylation at the olefinic site, we examined the reactivity of oxepins **27a** and **27b** under a variety of conditions. As illustrated in Table 2 (entries 6 and 7), when the latter substrates were treated to Grignard reagents, in all cases, <5% alkylation product was detected.

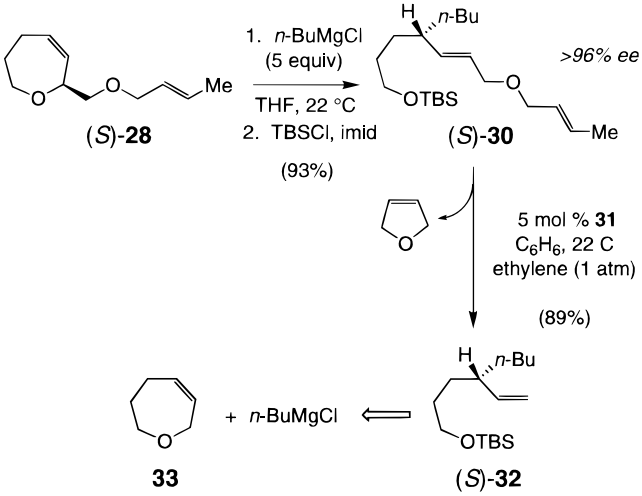
The above-mentioned observations suggest that the proposed mode of addition **II** (vs **I** and **III**, Scheme 2) represents a more plausible model that accounts for the required presence of accessible Lewis basic sites within the heterocyclic structure and the C2 side chain. That is, a two-point chelation serves to facilitate the cleavage of the ring C−O bond through activation by the bound Lewis acidic Mg, so that the incoming Grignard reagent can readily add to the C−C π bond and promote the allylic substitution. This mechanistic paradigm is supported by the fact that the less Lewis acidic dialkylmagnesium reagents are ineffective as alkylating agents (<2% reaction with Et_2Mg and **12** within similar reaction periods as used with EtMgBr).

The inertness of the derived pyran and furan ring systems, in contrast to the reactivity of oxepins and oxocins, is more difficult to explain with a reasonable

Scheme 4



Scheme 5



degree of certainty. This difference in reactivity may be partially attributed to the overlap of the reacting π cloud with the σ^* of the cleaving C−O bond within the more reactive conformers of the heterocycle. Such reaction-promoting overlap may be more easily accessible with the larger seven- and eight-membered rings.

Removal of the Chelating Group by Catalytic Ring-Closing Metathesis. One of the practical shortcomings of this, or any other, heteroatom-assisted reaction is that a Lewis basic site required for reaction may not be desired in the final product. Accordingly, an efficient method for the eventual removal of the directing unit would be desirable. Toward this end, we examined the ability of crotyl groups to serve as allylic substitution promoters. As illustrated in Scheme 4, medium-ring heterocycles that contain a crotyl unit within their C2 substituent are readily alkylated with high levels of stereochemical control (e.g., (*S*)-**28** → **29**). It must be noted that simple allyl units cannot be used, as they are easily cleaved by alkylmagnesium halides (direct S_N2' addition).

The advantage of alkylation products such as **29a**,**b** is that the required promoter group can then be easily removed by catalytic ring-closing metathesis. As an example, as depicted in Scheme 5, diastereoselective alkylation of (*S*)-**28** with *n*-BuMgCl, followed by protection of the primary alcohol, affords (*S*)-**30** in 93% yield and >96% ee. Subsequent treatment of (*S*)-**30** with 5 mol % $Mo(CHCMe_2Ph)(N(2,6\text{-}(i\text{-}Pr)_2C_6H_3))(OCMe(CF_3)_2)_2$ (**31**),[10] under 1 atm of ethylene, leads to the excision of the directing group and formation of (*S*)-**32** in 89% yield (>96% ee). It is worthy of note that, unlike the majority of reported examples, it is the released acyclic product—and not the cyclic system (2,5-dihydrofuran in this case)—that is the product of interest.

Several issues with regard to the metal-catalyzed excision of the directing arm of the heterocyclic substrate merit mention: (1) The catalytic ring-closing metathesis of substrates such as (*S*)-**30** is significantly more facile when the reaction is carried out under an atmosphere of ethylene, presumably due to the formation of the more active $Mo{=}CH_2$ system.[11] Thus, after the catalytic removal of the directing unit, the chiral unsaturated alcohol (*S*)-**32**, the formal (TBS protected) product of the enantioselective addition of the Grignard reagent to unfunctionalized heterocycle **33**, is obtained. (2) The less active $(PCy_3)_2Cl_2Ru{=}C(H)Ph$[12] delivers significantly lower yields (<5% conversion).

Conclusions

Diastereoselective alkylation of unsaturated oxepins and oxocenes can be promoted by an appropriately positioned Lewis basic directing group at the C2 position. Data summarized in Tables 1 and 2 suggest that a two-point binding involving both the heterocycle and the side chain heteroatom activates the allylic system to promote addition in an S_N2' fashion (mode **II**, Scheme 2). Although a chelating substituent is required for C−C bond formation, it can be easily removed by a subsequent Mo-catalyzed process (cf. Scheme 5).

The reactivity of these medium ring heterocycles toward Grignard reagents suggests that with an appropriately designed substrate, a variety of alkylmetals may be used to effect efficient and stereoselective C−C bond-forming reactions. Furthermore, more general and shorter synthesis schemes may involve the use of chiral Lewis acids in conjunction with less nucleophilic alkylmetal agents (e.g., alkylzinc reagents); such plans may also involve the utilization of a chiral metathesis catalyst[13] to access optically pure starting materials directly (without the need to proceed through a silyl ether such as **1**). Research along these lines should elevate stereoselective addition of alkylmetals to olefins to a practical and viable alternative that can be used in the preparation of optically pure materials.

Experimental Section

General. Infrared (IR) bands are characterized as broad (br), strong (s), medium (m), and weak (w), ν_{max} in cm^{-1}. ^1H NMR chemical shifts are reported in ppm from tetramethylsilane with the solvent resonance as the internal standard ($CHCl_3$: δ 7.26). Data are reported as follows: chemical shift, integration, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, br = broad, m = multiplet), coupling constants (Hz), and assignment. ^{13}C NMR spectra were recorded with complete proton decoupling. Chemical shifts are reported in ppm from tetramethylsilane with the solvent as the internal reference ($CDCl_3$: δ 77.0 ppm). Enantiomer ratios were determined by GLC with either a BETA-DEX 120 (30 m × 0.25 mm) chiral column by Supelco or an ALPHA-DEX GTA (20 × 0.25 mm) chiral column by Altech Assoc. or by ^1H NMR

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or ^{19}F NMR analysis of the derived (*R*)-MTPA ester. Microanalyses were performed by Robertson Microlit Laboratories (Madison, NJ).

All reactions were conducted in oven (135 °C) and flame-dried glassware under an inert atmosphere of dry argon. Tetrahydrofuran was distilled from sodium metal/benzophenone ketyl. All Grignard reagents were prepared from the appropriate alkyl halide purchased from Aldrich, which were distilled prior to use; Mg (turnings) were purchased from Strem and used without further purification. (*R*)-(EBTHI)Zr-binol and (*R*)-(EBTHI)Zr-biphen were prepared by the method of Buchwald.[14] Nonracemic (EBTHI)$ZrCl_2$ and (EBTHI)Zr-binol were stored under argon in a glovebox. $(PCy_3)_2Cl_2$-Ru=CHPh was prepared by the published methods.[15]

Representative Procedure for the Addition of Grignard Reagents to Cyclic Alkenes. A 5.0 mL flame-dried flask was charged with 30.0 mg (0.23 mmol) of (*S*)-**2**, 0.10 mL of THF, and 2.3 mL of freshly prepared 4-pentenylmagnesium bromide (1.17 mmol). The mixture was allowed to stir at 22 °C for 20 h. Reaction was quenched by the dropwise addition of a 1.0 mL portion of a saturated ammonium chloride solution; the mixture was subsequently washed with 3 × 25 mL of Et_2O. Combined organic layers were dried over $MgSO_4$, filtered, and concentrated in vacuo to afford a pale yellow oil. Silica gel chromatography (4:1 hexanes:EtOAc) afforded 34 mg of the alkylation product **4** (0.17 mmol, 76% yield).

Representative Procedure for the Zr-Catalyzed Kinetic Resolution. A 5.0 mL flame-dried flask with sidearm Teflon stopcock was charged with 30.0 mg (0.114 mmol) of **9**, 0.42 mL of THF, and 0.15 mL of freshly prepared EtMgCl (0.342 mmol). The precatalyst (*R*)-(EBTHI)Zr-biphen was added (6.2 mg, 1.14×10^{-2} mmol). The flask was equipped with a flame-dried reflux condenser and lowered into a 70 °C oil bath. The reaction was allowed to stir at 70 °C for approximately 60 min, at which time ^1H NMR analysis indicated that the reaction had reached 55% conversion. The reaction mixture was cooled to 0 °C in an ice bath, and excess EtMgCl was quenched by the dropwise addition of a 1.0 mL portion of a 1.0 M solution of aqueous HCl. The mixture was diluted with 15 mL of distilled H_2O and washed with 3 × 25 mL of Et_2O. The combined organic layers were dried over $MgSO_4$, filtered, and concentrated in vacuo to yield a pale yellow oil. Silica gel chromatography (9:1 hexanes:EtOAc) afforded 12.1 mg (0.046 mmol) of recovered (*R*)-**9** (0.046 mmol, 90% yield based on 55% conversion).

(*S*)-2-[(2-*tert*-Butyldimethylsiloxy)methyl]-2,5,6,7-tetrahydrooxepin (1). IR (KBr): 3007 (w), 2923 (m), 2845 (s), 1465 (m) cm^{-1}; ^1H NMR: δ 5.90−5.83 (1H, ddd, J = 11.2, 5.4, 2.4 Hz), 5.67−5.62 (1H, ddt, J = 11.3, 2.9, 1.4 Hz), 4.15−4.00 (2H, m), 3.75−3.67 (2H, m), 3.55 (1H, dd, J = 10.2, 6.4 Hz), 2.43−2.32 (1H, m), 2.25−2.15 (1H, m), 1.92−1.72 (2H, m), 0.84 (9H, s), 0.07 (6H, s); ^{13}C NMR: δ 133.1, 132.0, 79.2, 72.1, 66.7, 29.75, 27.8, 26.5, 19.0, −4.5, −4.6; HRCIMS $C_{13}H_{26}O_2Si$ requires 226.2535, found 226.2547.

(*S*)-2-(Hydroxymethyl)-2,5,6,7-tetrahydrooxepin ((*S*)-2). IR (KBr): 3408 (br), 2930 (s), 2860 (s), 1652 (w) cm^{-1}; ^1H NMR: δ 5.95−5.90 (1H, ddt, J = 11.1, 5.4, 2.4 Hz), 5.48−5.42 (1H, ddt, J = 11.2, 3.1, 1.3 Hz), 4.20−4.10 (1H, m), 3.78−3.75 (1H, dd, J = 7.0, 4.2 Hz), 3.75−3.72 (1H, dd, J = 7.6, 4.2 Hz), 3.64−3.55 (2H, m), 2.45−2.20 (2H, m), 1.95−1.73 (2H, m); ^{13}C NMR: δ 134.5, 130.5, 79.3, 72.5, 66.2, 29.8, 27.9. Anal. Calcd for $C_7H_{12}O_2$: C, 65.60; H, 9.44. Found: C, 65.35; H, 9.44.

(*S*)-(E)-1-(Hydroxymethyl)-4-(3-hydroxypropyl)nona-2,8-diene ((*S*)-4). IR (KBr): 3345 (br), 2936 (s), 2854 (s), 1671 (w), 1646 (m) cm^{-1}; ^1H NMR: δ 5.83−5.74 (1H, ddt, J = 16.8, 10.0, 6.8 Hz), 5.64−5.57 (1H, dt, J = 16.4, 6.8 Hz), 5.44−5.38 (1H, dd, J = 15.2, 8.8 Hz), 5.01−4.91 (2H, m), 4.10 (2H, t, J = 5.2 Hz), 3.63−3.61 (2H, m), 2.06−1.92 (3H, m), 1.58−1.18 (8H, m); ^{13}C NMR: δ 138.9, 136.9, 129.3, 114.4, 63.6, 62.9, 42.2, 34.6, 33.8, 31.1, 30.3, 26.5. Anal. Calcd for $C_{12}H_{22}O_2$: C, 72.68; H, 11.18. Found: C, 72.55; H, 11.07.

(*S*)-1-(3-Hydroxypropyl)cyclohex-2-ene ((*S*)-5). IR (KBr): 3332 (br), 3011 (w), 2930 (s), 2854 (m), 1652 (w) cm^{-1}; ^1H NMR: δ 5.68−5.64 (1H, m), 5.58−5.55 (1H, m), 3.65−3.62 (2H, t, J = 6.8 Hz), 2.06 (1H, m), 1.96 (2H, m), 1.82−1.16 (8H, m); ^{13}C NMR: δ 131.8, 127.1, 63.2, 34.9, 32.3, 30.1, 29.0, 25.3, 21.4; Anal. Calcd for $C_9H_{16}O$: C, 77.09; H, 11.50. Found: C, 77.02; H, 11.52. HRMS $C_9H_{15}O$ [M − H] requires 139.1123, found 139.1123.

2-[2-(*tert*-Butyldimethylsiloxy)ethyl]-2,5,6,7-tetrahydrooxepin (9). IR (KBr): 2957 (m), 2951 (m), 2856 (m), 1654 (w) cm^{-1}; ^1H NMR: δ 5.84−5.78 (1H, ddd, J = 11.2, 5.6, 2.4 Hz), 5.57−5.54 (1H, dt, J = 11.2, 1.6 Hz, vinylic CH), 4.20 (1H, m), 4.07−4.01 (1H, ddd, J = 11.6, 6.8, 4.4 Hz), 3.78−3.63 (3H, m), 2.38−2.34 (1H, m), 2.22−2.17 (1H, m), 1.85−1.72 (4H, m), 0.89 (9H, s, *t*-Bu), 0.06 (3H, s), 0.05 (3H, s); ^{13}C NMR: δ 135.5, 132.6, 75.0, 72.2, 60.2, 40.0, 29.9, 27.7, 26.6, −4.6. Anal. Calcd for $C_{14}H_{28}O_2Si$: C, 65.57; H, 11.00. Found: C, 65.87; H, 11.14.

2-[(Benzyloxy)methyl]-2,5,6,7-tetrahydro-*N*-tosylazepin (10). IR (KBr): 3032 (m), 2928 (s), 2867 (m), 1652 (w), 1597 (m) cm^{-1}; ^1H NMR: δ 7.74−7.72 (2H, d, J = 8.4 Hz), 7.32−7.30 (2H, m), 7.21−7.19 (3H, d, J = 6.0 Hz), 7.16−7.14 (2H, d, J = 8.8 Hz), 5.81−5.75 (1H, m), 5.56−5.21 (1H, m), 4.95 (1H, m), 4.46−4.43 (1H, d, J = 12.0 Hz), 4.38−4.34 (1H, d, J = 12.0 Hz), 3.78−3.71 (1H, dt, J = 14.0, 7.2 Hz), 3.23−3.16 (1H, dt, J = 14.4, 6.4 Hz), 3.56−3.51 (1H, dd, J = 10.4, 8.4 Hz), 3.48−3.44 (1H, dd, J = 10.4, 5.6 Hz), 2.36 (3H, s, Me), 2.20−2.00 (2H, m), 1.86−1.60 (2H, m); ^{13}C NMR: δ 140.4, 131.1, 129.2, 128.3, 127.9, 127.7, 127.6, 127.3, 94.3, 72.8, 69.7, 57.0, 43.4, 27.7, 24.9, 21.5, 20.1. Anal. Calcd for $C_{21}H_{25}NO_3S$: C, 67.90; H, 6.78. Found: C, 67.73; H, 6.64.

(*S*)-(*E*)-1-Hydroxy-4-butylhep-2-en-7-ol ((*S*)-11). IR (KBr): 3328 (br), 2954 (w), 2928 (m), 2869 (m), 1656 cm^{-1}; ^1H NMR: δ 5.60−5.54 (1H, dt, J = 15.4, 6.0 Hz), 5.41−5.35 (1H, dd, J = 15.4, 9.0 Hz), 4.08−4.06 (2H, d, J = 5.6 Hz), 3.62−3.53 (2H, m), 2.00−1.85 (1H, m), 1.56−1.11 (10H, m), 0.87−0.83 (3H, t, J = 7.0 Hz); ^{13}C NMR: δ 137.9, 129.8, 64.3, 63.6, 42.9, 35.6, 31.8, 31.1, 30.1, 23.5, 14.7; HRMS $C_{11}H_{22}O_2$ requires 186.1618, found 186.1602.

(*S*)-2-[(Benzyloxy)methyl]-2,5,6,7-tetrahydrooxepin ((*S*)-12). IR (KBr): 3018 (m), 2930 (s), 2860 (s), 1652 (w) cm^{-1}; ^1H NMR: δ 7.33−7.25 (5H, m), 5.90−5.83 (1H, ddt, J = 11.2, 5.4, 2.4 Hz), 5.57−5.53 (1H, dtd, J = 11.3, 3.1, 1.7 Hz), 4.62−4.60 (1H, d, J = 12.2 Hz), 4.56−4.53 (1H, d, J = 12.3 Hz), 4.13−4.07 (1H, ddd, J = 11.6, 6.8, 4.3 Hz), 3.75−3.69 (1H, ddd, J = 11.6, 7.1, 4.8 Hz), 3.55−3.51 (1H, dd, J = 10.0, 7.2 Hz), 3.46−3.43 (1H, dd, J = 10.1, 4.6 Hz), 2.42−2.35 (1H, m), 2.23−2.14 (1H, m), 1.88−1.70 (2H, m); ^{13}C NMR: δ 138.9, 133.8, 131.6, 128.9, 128.4, 128.2, 77.4, 74.1, 73.6, 72.3, 27.9, 27.8; HRMS $C_{14}H_{18}O_2$ requires 218.1303, found 218.1306.

(*R*)-E-1-(Benzyloxy)-4-isobutylhep-2-en-7-ol ((*R*)-13). IR (KBr): 3394 (br), 2950 (s), 2923 (s), 2864 (s), 1650 (w) cm^{-1}; ^1H NMR: δ 7.38−7.20 (5H, m), 5.59−5.52 (1H, dt, J = 15.6, 6.0 Hz), 5.43−5.37 (1H, dd, J = 15.6, 8.8 Hz), 4.49 (2H, s, $PhCH_2O$), 3.99−3.98 (2H, d, J = 6.0 Hz), 4.94−4.90 (1H, dd, J = 10.4, 2.4 Hz), 4.50 (2H, s), 3.99−3.98 (2H, d, J = 6.0 Hz), 3.61−3.58 (2H, t, J = 6.8 Hz), 2.09−2.01 (1H, m) 1.62−1.15 (7H, m) 0.87−0.86 (3H, d, J = 6.8 Hz), 0.85−0.83 (3H, d, J = 6.4 Hz); ^{13}C NMR: δ 139.6, 139.1, 129.0, 128.5, 128.2, 127.0, 72.4, 71.5, 63.7, 45.3, 40.9, 32.2, 31.2, 26.0, 24.2, 22.5; HRMS $C_{18}H_{28}O$ requires 276.2089, found 276.2088.

(*R*)-2-(Hydroxyethyl)-2,5,6,7-tetrahydrooxepin ((*R*)-14). IR (KBr): 3376 (br), 3018 (s), 2860 (s), 2930 (w), 2835 (w), 1652 (s) cm^{-1}; ^1H NMR: δ 5.86−5.79 (1H, m), 5.52−5.48 (1H, m), 4.31 (1H, m, $HOCH_2CH_2CHO$), 4.09−4.04 (1H, m), 3.88−3.67 (3H, m), 2.40−2.30 (1H, m), 2.23−2.14 (1H, m), 1.90−1.75 (4H, m); ^{13}C NMR: δ 133.7, 132.2, 78.4, 71.5, 61.1, 37.9, 28.9, 26.8. Anal. Calcd for $C_8H_{14}O_2$: C, 67.57; H, 9.92. Found: C, 67.28; H, 10.20.

(*S*)-(*E*)-1-Hydroxy-5-butyloct-3-en-8-ol ((*S*)-15). IR (KBr): 3339 (br), 2961 (s), 2930 (s), 2860(s), 1652 (w) cm^{-1}; ^1H NMR: δ 5.37−5.30 (1H, dt, J = 15.6, 6.4 Hz), 5.28−5.22 (1H, dd, J = 15.2, 8.4 Hz), 3.63−3.59 (4H, m), 2.29−2.24 (2H, dt, J = 6.4, 6.0 Hz), 1.96−1.89 (1H, m), 1.60−1.16 (10H, m),

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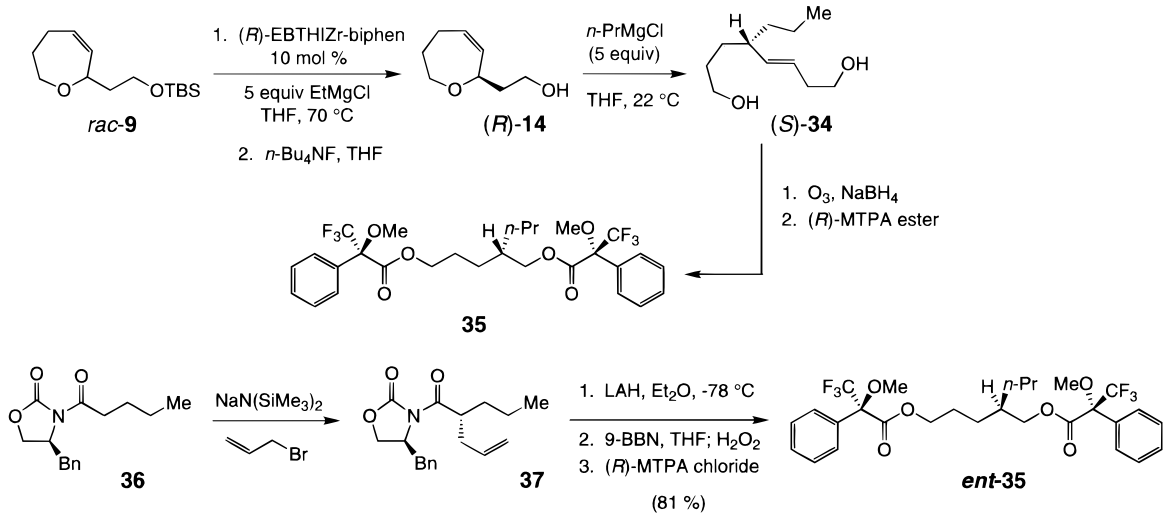
(15) Schwab, P.; Grubbs, R. H.; Ziller, J. W. *J. Am. Chem. Soc.* **1996**, *118*, 100−110.

Scheme 6



0.86 (3H, t, J = 7.2 Hz, CH_3); ^{13}C NMR: δ 138.4, 125.9, 63.0, 62.1, 42.8, 36.0, 35.1, 31.2, 30.5, 29.5, 22.7, 14.1. HRMS calcd $C_{12}H_{24}O_2$ (M+1) requires 201.1854, found 201.1855.

(*R*)-*E*-1-Hydroxy-5-isobutyloct-3-en-8-ol ((*S*)-16). IR (KBr): 3320 (br), 2948 (s), 2923 (s), 2867(s), 1652 (w) cm^{-1}; ^{1}H NMR: δ 5.38−5.31 (1H, dt, J = 15.2, 6.8 Hz), 5.26−5.20 (1H, dd, J = 15.2, 8.8 Hz), 3.64−3.60 (4H, m), 2.29−2.25 (2H, dt, J = 6.8, 6.4 Hz), 2.09−2.00 (1H, m), 1.60−1.10 (8H, m), 0.87−0.85 (3H, d, J = 6.8 Hz), 0.84−0.82 (3H, d, J = 6.8 Hz); ^{13}C NMR: δ 138.8, 126.6, 63.5, 62.7, 45.5, 41.2, 36.6, 32.2, 31.0, 25.9, 24.2, 22.4. HRMS calcd $C_{12}H_{24}O_2$ (M + 1) requires 201.1854, found 201.1860.

Proof of Absolute Stereochemistry for Alkylation of (*R*)-14 with *n*-PrMgCl (not shown in Table 1). The stereochemical identity of the product of addition of *n*-PrMgCl to (*R*)-**14** was determined as illustrated in Scheme 6. Analysis of the 400 MHz ^{19}F NMR of the derived (*R*)-MTPA esters supports the correlation.

(*R*)-2-[(Benzyloxy)ethyl]-2,5,6,7-tetrahydrooxepin ((*R*)-17). IR (KBr): 3005 (br), 2936 (s), 2835 (s), 1658 (w), 1507 (m) cm^{-1}; ^{1}H NMR: δ 7.35−7.27 (5H, m), 5.84−5.78 (1H, m), 5.57−5.54 (1H, m), 4.55−4.48 (2H, dd, J = 16.1, 12.0 Hz), 4.23 (1H, m), 4.04−3.98 (1H, m), 3.68−3.54 (3H, m), 2.41−2.30 (1H, m), 2.26−2.15 (1H, m), 1.88−1.70 (4H, m); ^{13}C NMR: δ 134.5, 132.1, 128.3, 127.6, 127.5, 126.7, 74.6, 72.9, 71.5, 66.9, 36.5, 29.1, 26.9. Anal. Calcd for $C_{15}H_{20}O_2$: C, 77.55; H,8.68. Found: C, 77.68; H, 8.89.

(*S*)-(*E*)-1-(Benzyloxy)-5-butyloct-3-en-8-ol (acetate of (*S*)-18). IR (KBr): 2961 (m), 2923 (m), 2854 (w), 1765 (s) cm^{-1}; ^{1}H NMR: δ 7.34−7.26 (5H, m), 5.41−5.34 (1H, dt, J = 15.2, 6.4), 5.21−5.15 (1H, dd, J = 15.6, 8.8 Hz), 4.51 (2H, s), 4.03−3.99 (2H, t, J = 6.4 Hz), 3.51−3.47 (2H, t, J = 6.8 Hz), 2.35−2.30 (2H, app. q, J = 6.8 Hz), 2.03 (3H, s), 1.90−1.86 (1H, m), 1.63−1.13 (10H, m), 0.88−0.84 (3H, t, J = 7.2 Hz, CH_2CH_3); ^{13}C NMR: δ 171.9, 139.2, 137.2, 129.0, 128.3, 128.2, 127.3, 73.5, 71.5, 71.0, 43.3, 35.8, 33.8, 32.1, 30.1, 27.1, 23.4, 21.7, 14.8.

2-(Hydroxypropyl)-2,5,6,7-tetrahydrooxepin (19a). IR (KBr): 3389 (br), 3024 (w), 2923 (m), 2860 (m), 1652 (w) cm^{-1}; ^{1}H NMR: δ 5.83−5.77 (1H, m), 5.53−5.50 (1H, m), 4.08−4.02 (2H, m), 3.70−3.62 (3H, m), 2.53 (1H, br s, OH), 2.40−2.10 (2H, m), 1.85−1.67 (4H, m); ^{13}C NMR: δ 134.1, 131.9, 77.9, 71.3, 62.7, 33.1, 28.9, 26.8, 76.7. Anal. Calcd for $C_9H_{16}O_2$: C, 69.19; H,10.32. Found: C, 68.84; H, 10.57.

2-[(Benzyloxy)propyl]-2,5,6,7-tetrahydrooxepin (19b). IR (KBr): 3024 (br), 2930 (m), 2867 (m), 1652 (w) cm^{-1}; ^{1}H NMR: δ 7.35−7.27 (5H, m), 5.83−5.77 (1H, m), 5.56−5.52 (1H, m), 4.50 (2H, s), 4.07−4.00 (2H, m), 3.68−3.62 (1H, ddd, J = 11.6, 7.2, 4.4 Hz), 3.52−3.47 (2H, m), 2.38−2.16 (2H, m), 1.84−1.60 (6H, m); ^{13}C NMR: δ 138.6, 134.6, 131.8, 128.3, 127.6, 127.4, 77.6, 72.3, 71.3, 70.2, 32.9, 29.1, 26.9, 25.8. Anal. Calcd for $C_{16}H_{22}O_2$: C, 78.01; H, 9.00. Found: C, 78.00; H, 8.85.

2-[(*p*-Methoxybenzyloxy)ethyl]-2,5,6,7-tetrahydrooxepin (20). IR (KBr): 3024 (br), 2942 (s), 2841 (s), 1620 (m) cm^{-1}; ^{1}H NMR: δ 7.27−7.25 (2H, d, J = 8.8 Hz), 6.88−6.86 (2H, d, J = 8.8 Hz), 5.85−5.79 (1H, ddt, J = 11.2, 2.8, 1.6 Hz), 5.69−5.65 (1H, m), 4.27−4.21 (1H, d, J = 11.2 Hz), 4.40−4.36 (1H, d, J = 11.6 Hz), 4.24−4.17 (1H, m), 4.04−3.98 (1H, ddd, J = 12, 7.2, 5.2 Hz), 3.79 (3H, s), 3.68−3.51 (3H, m), 2.40−2.12 (2H, m), 1.86−1.75 (4H, m); ^{13}C NMR: δ 159.8, 135.2, 132.7, 131.4, 129.9, 114.4, 75.3, 73.3, 72.1, 67.2, 55.9, 37.1, 29.8, 27.6. Anal. Calcd for $C_{11}H_{18}O_2$: C, 72.96; H, 8.74. Found: C, 73.08; H, 8.72. HRMS calcd $C_{16}H_{23}O_3$ requires 263.1647, found 263.1648.

2-[(*tert*-Butyldimethylsiloxy)methyl]-2,3,4,7-tetrahydrooxepin (21a). IR (KBr): 3018 (w), 2930 (br), 2854 (s), 1658 (w) cm^{-1}; ^{1}H NMR: δ 5.84−5.78 (1H, m), 5.67−5.62 (1H, m), 4.34−4.02 (2H, m), 3.69−3.60 (2H, m), 3.52−3.47 (1H, m), 2.42−2.09 (2H, m), 1.97−1.60 (2H, m), 0.89 (9H, s), 0.05 (6H, s); ^{13}C NMR: δ 132.4, 130.5, 82.2, 68.2, 66.5, 30.9, 26.6, 26.3, 19.1, −4.5, −4.6. HRMS calcd $C_{11}H_{22}O_2$ (M + 1) requires 243.1780, found 243.1770.

2-(Hydroxymethyl)-2,3,4,7-tetrahydrooxepin (21b). IR (KBr): 3420 (br), 2930 (s), 2854 (s), 1658 (w), 1463 (m) cm^{-1}; ^{1}H NMR: δ 5.86−5.80 (1H, m), 5.70−5.65 (1H, m), 4.39−4.34 (1H, dd, J = 15.6, 4.8 Hz), 4.12−4.06 (1H, m), 3.71−3.65 (1H, m), 3.57−3.48 (2H, m), 2.45−4.10 (2H, m), 1.57−1.48 (2H, m); ^{13}C NMR: δ 132.4, 130.3, 82.5, 68.6, 66.4, 30.9, 26.5. HRMS calcd $C_7H_{12}O_2$ requires 128.0837, found 128.0838.

2-[(Benzyloxy)methyl]-2,3,4,7-tetrahydrooxepin (21c). IR (KBr): 3383 (br), 3024 (s), 2930 (m), 2854 (m), 1671 (w) cm^{-1}; ^{1}H NMR: δ 7.35−7.26 (5H, m), 5.86−5.78 (1H, m), 5.70−5.63 (1H, m), 4.64−4.52 (2H, dd, J = 28.8, 16.4 Hz), 4.39−4.32 (1H, dd, J = 21.6, 6.4 Hz), 4.14−4.07 (1H, m), 3.88−3.80 (1H, m), 3.59−3.38 (2H, m), 2.42−2.10 (2H, m), 1.97−1.60 (2H, m); ^{13}C NMR: δ 138.9, 132.3, 130.5, 129.0, 128.4, 128.2, 80.5, 74.0, 73.7, 68.2, 31.4, 26.3; HRMS calcd $C_{14}H_{18}O_2$ requires 218.1306, found 218.1307.

(*Z*)-5-Undecene-1,2-diol (23b). IR (KBr): 3376 (m), 2962 (m), 2920 (s), 2860 (m), 1655 (w) cm^{-1}; ^{1}H NMR: δ 5.48−5.33 (2H, m), 3.75−3.69 (2H, m), 3.66−3.62 (1H, m), 2.19−1.95 (4H, m), 1.49−1.24 (8H, m), 0.89−0.85 (3H, t, J = 6.8 Hz); ^{13}C NMR: δ 131.7, 129.3, 72.6, 67.5, 33.7, 32.2, 30.0, 29.3, 27.9, 24.0, 14.8. Anal. Calcd for the diacylated derivative: requires $C_{15}H_{26}O_4$: C, 66.62; H, 9.70. Found: C, 66.68; H, 9.53.

(*Z*)-1-(Benzyloxy)-5-undecen-2-ol (23c). IR (KBr): 3446 (m), 2923 (s), 2860 (m), 1652 (w) cm^{-1}; ^{1}H NMR: δ 7.36−7.30 (5H, m), 5.42−5.30 (2H, m), 4.55 (2H, s), 3.86−3.80 (1H, m), 3.52−3.49 (1H, dd, J = 9.6, 3.2 Hz), 3.36−3.32 (1H, dd, J = 9.6, 8.0 Hz), 2.35 (1H, m, OH), 2.19−2.11 (2H, m), 2.05−1.99 (2H, dt, J = 13.6, 6.8 Hz), 0.89−0.86 (3H, t, J = 6.4 Hz); ^{13}C NMR: δ 138.7, 131.4, 129.5, 129.1, 128.4, 75.2, 73.9, 70.6, 33.7, 32.1, 30.0, 27.8, 23.9, 23.2, 14.8; HRMS calcd $C_{18}H_{28}O_2$ ($-H_2O$) requires 258.1983, found 258.1980.

2-(Hydroxyethyl)-2,3,4,7-tetrahydrooxepin (24a). IR (KBr): 3389 (br), 2942 (s), 1665 (w) cm^{-1}; ^1H NMR: δ 5.87−5.81 (1H, m), 5.70−5.64 (1H, m), 4.31−4.26 (1H, dd, J = 16.0, 5.2 Hz), 4.10−4.03 (1H, m), 3.88−3.74 (3H, m,), 2.40−2.10 (2H, m), 1.91−1.81 (2H, m), 1.67−1.59 (2H, m); ^{13}C NMR: δ 132.9, 130.3, 82.6, 67.7, 62.3, 38.6, 34.9, 26.5; Anal. Calcd for $C_8H_{14}O_2$: C, 67.57; H, 9.92. Found: C, 67.24; H, 9.98; HRMS calcd $C_8H_{14}O_2$ requires 142.0994, found 142.0993.

2-[(*p*-Methoxybenzyloxy)ethyl]-2,3,4,7-tetrahydrooxepin (24b). IR (KBr): 3024 (m), 2942 (br), 2841 (m), 1620 (m) cm^{-1}; ^1H NMR: δ 7.27−7.25 (2H, d, J = 8.8 Hz), 6.89−6.86 (2H, d, J = 8.8 Hz), 5.85−5.79 (1H, m), 5.69−5.65 (1H, m), 4.40 (2H, s), 4.27−4.21 (1H, dd, J = 16.0, 4.0 Hz), 4.03−3.97 (1H, m), 3.80 (3H, s, OMe), 3.78−3.76 (1H, m), 3.62−3.47 (2H, m), 2.40−2.10 (2H, m), 1.92−1.54 (4H, m); ^{13}C NMR: δ 159.7, 132.4, 131.3, 130.7, 129.9, 114.3, 78.7, 73.3, 67.6, 67.5, 55.9, 36.9, 34.9, 26.5; HRMS calcd $C_{16}H_{22}O_3$ (M − H) requires 261.1491, found 261.1493.

(*Z*)-6-Dodecene-1,3-diol (26a). IR (KBr): 3346 (br), 2932 (m), 2857 (m), 1651 (w) cm^{-1}; ^1H NMR: δ 5.41−5.33 (2H, m, 3.91−3.79 (3H, m), 2.19−2.09 (2H, m), 2.05−2.00 (2H, m), 1.71−1.35 (10H, m), 0.89−0.86 (3H, t, J = 6.8 Hz); ^{13}C NMR: δ 131.6, 129.5, 72.8, 62.5, 38.9, 38.3, 32.2, 30.0, 27.9, 24.1, 23.2, 14.7. Anal. Calcd for the diacylated derivative: $C_{16}H_{28}O_4$: C, 67.57; H, 9.92. Found C, 67.65; H, 9.70.

4-(Hydroxymethyl)-2,5,6,7-tetrahydrooxepin (27a). IR (KBr): 3408 (br), 2930 (s), 2860 (s), 1658 (w) cm^{-1}; ^1H NMR: δ 5.78−5.73 (1H, dtd, J = 11.6, 4.0, 2.4 Hz), 5.70−5.67 (1H, d, J = 11.4 Hz), 4.18−4.14 (1H, m), 4.03−3.97 (1H, dt, J = 12.4, 5.6 Hz), 3.78−3.74 (1H, dd, J = 8.8, 4.4 Hz), 3.75−3.71 (1H, dd, J = 8.8, 4.8 Hz), 3.67−3.59 (2H, m), 1.97−1.90 (1H, m), 1.84−1.75 (1H, m); ^{13}C NMR: δ 133.5, 131.5, 70.8, 68.9, 67.0, 41.6, 32.7; HRMS calcd $C_7H_{12}O_2$ (M − H) requires 127.0378 found 127.0755.

4-[(*p*-Methoxybenzyloxy)methyl]-2,5,6,7-tetrahydrooxepin (27b). IR (KBr): 3011 (w), 2930 (m), 2848 (s), 1608 (m) cm^{-1}; ^1H NMR: δ 7.27−7.25 (2H, d, J = 8.8 Hz), 6.89−6.87 (2H, d, J = 8.4 Hz), 5.73−5.65 (2H, m, vinylic CH), 4.64 (2H, s), 4.15−4.13 (2H, m), 3.99−3.94 (1H, dt, J = 11.6, 4.8 Hz), 3.80 (3H, s, OMe), 3.75−3.69 (1H, ddd, J = 11.6, 9.2, 4.0 Hz), 3.45−3.36 (2H, m), 2.78−2.76 (1H, m), 1.91−1.85 (1H, m), 1.81−1.72 (1H, m); ^{13}C NMR: δ 159.8, 134.4, 131.1, 130.9, 129.9, 114.4, 74.2, 73.4, 71.2, 68.9, 55.9, 39.4, 32.9. Anal. Calcd for $C_{15}H_{20}O_3$: C, 72.54; H, 8.12. Found: C, 72.69; H, 8.14. HRMS calcd $C_{15}H_{20}O_3$ requires 248.1412, found 248.1407.

(*S*)-2-[(But-2-enyloxy)methyl]-2,5,6,7-tetrahydrooxepin (28). IR (KBr): 3024 (m), 2930 (s), 2854 (s), 1677 (w), 1652 (w) cm^{-1}; ^1H NMR: δ 5.85−5.79 (1H, m), 5.69−5.49 (3H, m), 4.20−4.18 (1H, m), 4.08−4.02 (1H, m), 3.96−3.86 (1H, m), 3.70−3.64 (2H, m), 3.49−3.33 (2H, m), 2.39−2.24 (1H, m), 2.10−2.04 (1H, m, allylic CH), 1.81−1.62 (2H, m), 1.65−1.64 (3H, d, J = 6.4 Hz), 1.61−1.59 (3H, d, J = 6.8 Hz); ^{13}C NMR: δ 133.9, 131.7, 130.5, 128.2, 77.4, 73.4, 72.8, 72.4, 29.7, 27.8, 18.5. Anal. Calcd for $C_{11}H_{18}O_2$: C, 72.48; H, 9.96. Found: C, 72.62; H, 10.01.

(*R*)-(*E*)-1-(But-2-enyloxy)-4-isobutylhep-2-en-7-ol (29a). IR (KBr): 3389 (br), 3011 (w), 2955 (s), 2867 (m), 1671 (w) cm^{-1}; ^1H NMR: δ 5.74−5.63 (1H, m), 5.61−5.56 (1H, m), 5.53−5.46 (1H, m), 5.40−5.33 (1H, m), 3.91−3.90 (2H, d, J = 6.4 Hz), 3.88−3.86 (2H, d, J = 6.0 Hz), 3.59 (2H, t, J = 6.4 Hz), 2.11−2.02 (1H, m), 1.70 (3H, d, J = 6.4 Hz), 1.66−1.18 (8H, m), 0.84 (3H, d, J = 6.4 Hz), 0.82 (3H, d, J = 6.4 Hz); ^{13}C NMR: δ 138.5, 129.5, 127.6, 126.5, 70.6, 70.5, 63.1, 44.6, 40.1, 31.5, 30.5, 25.3, 23.5, 21.8, 17.7; HRMS $C_{15}H_{28}O_2$ (M + H) requires 241.2167, found 241.2163. Anal. Calcd for $C_{15}H_{28}O_2$: C, 74.95; H, 11.74. Found: C, 75.28; H, 12.04.

(*S*)-(*E*)-1-(But-2-enyloxy)-4-(3-pentynyl)hep-2-ene 7-(*tert*-Butyldimethylsilyl ether) (29b). IR (KBr): 3408 (br), 3024 (w), 2923 (s), 2854 (s), 1677 (w) cm^{-1}; ^1H NMR: δ 5.73−5.50 (3H, m), 5.40−5.32 (1H, m), 3.92−3.91 (2H, d, J = 6.0 Hz), 3.88−3.86 (2H, d, J = 6.4 Hz), 3.58−3.55 (2H, t, J = 6.4 Hz), 2.11−2.00 (3H, m), 3.59 (2H, t, J = 6.4 Hz), 2.11−2.02 (1H, m), 1.77−1.75 (3H, t, J = 2.4 Hz), 1.71−1.70 (2H, d, J = 6.4 Hz), 1.56−1.24 (6H, m), 0.88 (9H, s), 0.03 (6H, s); ^{13}C NMR: δ 137.4, 137.3, 129.4, 127.6, 127.4, 79.1, 75.4, 70.6, 70.5, 70.4, 64.9, 63.2, 41.4, 34.3, 30.9, 30.4, 25.9, 18.3, 17.7, 16.6, 3.4, −5.3; HRMS $C_{22}H_{40}SiO_2$ (M + H) requires 365.2875, found 365.2877.

(*S*)-(*E*)-1-(But-2-enyloxy)-4-*n*-butylhep-2-en-7-ol (30). IR (KBr): 3389 (br), 2923 (s), 2860 (s), 1665 (w) cm^{-1}; ^1H NMR: δ 5.73−5.62 (1H, m), 5.61−5.54 (1H, m), 5.53−5.43 (1H, m), 5.43−5.36 (1H, m), 3.91−3.90 (2H, d, J = 6.0 Hz), 3.88−3.86 (2H, d, J = 6.0 Hz), 3.59 (2H, t, J = 6.4 Hz), 1.96 (1H, m), 1.70 (3H, d, J = 6.4 Hz), 1.65−1.17 (10H, m), 0.86 (3H, t, J = 6.8 Hz); ^{13}C NMR: δ 138.5, 129.5, 127.6, 126.5, 70.6, 70.4, 63.1, 42.3, 34.8, 31.1, 30.5, 29.4, 22.7, 17.7, 14.1; HRMS $C_{15}H_{28}O_2$ (M + H) requires 241.2167, found 241.2168. Anal. Calcd for $C_{15}H_{28}O_2$: C, 74.95; H, 11.74. Found: C, 74.92; H, 12.04.

Representative Procedure for the Mo-Catalyzed Removal of the Chelating Group. A 5.0 mL flame-dried flask was taken into the glovebox and charged with 2 mg of the Mo catalyst **31** (2.6×10^{-3} mmol). To this was added a solution of diene (*S*)-**30** in benzene (8.5 mg, 0.025 mmol, 0.05 M). The mixture was removed from the glovebox, sealed under an atmosphere of ethylene, and stirred at 22 °C for 3 h. Reaction was quenched by the addition of anhydrous MeOH (0.5 mL), volatiles were removed in vacuo, and the remaining dark brown residue purified by silica gel chromatography (hexanes) to afford 6.1 mg of (*S*)-**32** (2.2×10^{-4} mmol, 89% yield).

(*S*)-4-Ethenyloctan-1-ol (32). IR (KBr): 2930 (s), 2860 (s), 1652 (w) cm^{-1}; ^1H NMR: δ 5.56−5.47 (1H, ddd, J = 19.2, 10.4, 8.8 Hz), 4.97−4.90 (2H, m), 3.59−3.56 (2H, t, J = 6.4 Hz), 1.93−1.91 (1H, m), 1.65−1.17 (10H, m), 0.88 (12H, m), 0.04 (6H, s); ^{13}C NMR: δ 144.1, 114.7, 64.1, 44.5, 35.4, 31.7, 31.2, 30.1, 26.7, 23.5, 20.8, 14.8, −4.6; HRMS $C_{16}H_{34}O_{Si}$ (M − H) requires 269.2301, found 269.2309.

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Supporting Information Available: Spectral data for determination of product enantiopurities (4 pages). This material is available free of charge via the Internet at http://pubs.acs.org.

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