Catalytic and Enantioselective Route to Medium-Ring Heterocycles. Asymmetric Zirconium-Catalyzed Ethylmagnesation of Seven- and Eight-Membered Rings

Michael S. Visser, Nicola M. Heron, Mary T. Didiuk, John F. Sagal, and Amir H. Hoveyda*

Contribution from the Department of Chemistry, Merkert Chemistry Center, Boston College, Chestnut Hill, Massachusetts 02167

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Abstract: A variety of medium-ring heterocycles, prepared efficiently by the Ru-catalyzed diene metathesis method, undergo asymmetric catalytic ethylmagnesation to afford nonracemic unsaturated alcohols and amides in excellent enantiomeric purity (>98% ee). Noteworthy features of these studies are as follows: (i) Eight-membered unsaturated tosyl amides are readily prepared by transition-metal-catalyzed metathesis. (ii) With six-, seven-, and eight-membered N-containing substrates the presence of an electron-withdrawing Ts unit is required for efficient carbomagnesation (corresponding alkylamines are inert). Chiral medium-ring heterocycles are resolved by the Zr-catalyzed C−C bond-forming reaction to afford recovered starting materials in up to >99% ee. The kinetic resolution data indicate that simple steric models can reliably predict the sense of the asymmetric induction in the asymmetric carbomagnesation or kinetic resolution. However, experimental results presented herein also illustrate that the observed *levels* of enantioselectivity cannot be predicted on the basis of such paradigms.

Introduction

Stereoselective synthesis of medium-ring heterocycles constitutes an important objective in modern organic synthesis, since these structural units are commonly found within frameworks of a variety of medicinally important natural products. Of special significance, and in particular demand, are reaction technologies for the *enantioselective* preparation of various medium-ring compounds. Recent work in these laboratories has illustrated that the zirconocene-catalyzed asymmetric carbomagnesation reaction is an efficient C−C bond-forming process that allows for a convenient method for the preparation of a variety of chiral molecules in the enantiomerically pure or enriched form.[1] The ability of this catalytic transformation to promote efficient kinetic resolution of various substituted furans,[2] pyrans,[3] and cyclic ethers[4] is noteworthy, as this process provides a route for the enantioselective synthesis of a range of heterocyclic and acyclic structures. We disclose here the results of our studies on the asymmetric catalytic ethylmagnesation of various unsaturated seven- and eight-membered rings; the unsaturated alcohols or amide reaction products are obtained with high levels of enantioselection. More importantly, these transformations lead to medium-ring heterocycles with excellent enantiomeric purity through catalytic kinetic resolution. Studies outlined below provide important insights with regard to the inner workings of the catalytic process as well.

Results and Discussion

Synthesis and Carbomagnesation of Seven- and Eight-Membered Heterocycles. Instances of Tandem Catalysis. As illustrated in Scheme 1, a seven-membered heterocycle can be prepared in near quantitative yield through Ru-catalyzed metathesis of an appropriate diene ether (**1** → **2**);[5] subsequent treatment of the heterocycle with 5 equiv of EtMgCl in the presence of 10 mol % (*R*)-(EBTHI)Zr-binol[6] affords the unsaturated amide **3** in >98% ee (judged by ^{1}H NMR analysis of the derived (*R*)-MTPA ester) and 75% yield after silica gel chromatography.[7] Importantly, the unsaturated medium-ring amide—in the same reaction vessel, without recourse to isolation—may be subjected to 10 mol % of the chiral Zr catalyst and EtMgCl to afford unsaturated **3** in 81% yield after purification. The one-pot procedure thus allows for the facile synthesis of **3** in >98% ee from readily available **1**.[8] A similar tandem diene metathesis/ethylmagnesation can be carried out on ether **4**, leading to the formation of unsaturated chiral alcohol **5** in 73% yield and >99% ee (judged by GLC analysis).

[⊗] Abstract published in *Advance ACS Abstracts,* April 15, 1996.

(1) (a) Morken, J. P.; Didiuk, M. T.; Hoveyda, A. H. *J. Am. Chem. Soc.* **1993**, *115*, 6697−6698. (b) Didiuk, M. T.; Johannes, C. W.; Morken, J. P.; Hoveyda, A. H. *J. Am. Chem. Soc.* **1995**, *117*, 7097−7104 and references cited therein.

(2) Visser, M. S.; Hoveyda, A. H. *Tetrahedron* **1995**, *51*, 4383−4394.

(3) Morken, J. P.; Didiuk, M. T.; Visser, M. S.; Hoveyda, A. H. *J. Am. Chem. Soc.* **1994**, *116*, 3123−3124.

(4) Visser, M. S.; Harrity, J. P. A.; Hoveyda, A. H. *J. Am. Chem. Soc.*, in press.

(5) (a) Fu, G. C.; Nguyen, S. Y.; Grubbs, R. H. *J. Am. Chem. Soc.* **1993**, *115*, 9856−9857 and references cited therein. (b) Fujimura, O.; Fu, G. C.; Grubbs, R. H. *J. Org. Chem.* **1994**, *59*, 4029−4030. (c) Kim, S. H.; Bowden, N.; Grubbs, R. H. *J. Am. Chem. Soc.* **1994**, *116*, 10801−10802. (d) Miller, S. J.; Kim, S. H.; Chen, Z.-R.; Grubbs, R. H. *J. Am. Chem. Soc.* **1995**, *36*, 1169−1170.

(6) (a) Wild, F. R. W. P.; Waiucionek, M.; Huttner, G.; Brintzinger, H. H. *J. Organomet. Chem.* **1985**, *288*, 63−67. (b) Diamond, G. M.; Rodewald, S.; Jordan, R. F. *Organometallics* **1995**, *14*, 5−7 and references cited therein.

(7) All the Zr-catalyzed reactions described herein must be carried out with freshly prepared catalyst batches of high purity. Otherwise, sluggish reactions and/or inferior enantioselectivities will be observed.

(8) Final products of the tandem catalytic methathesis/ethylmagnesation protocol (*e.g.*, **3**) can serve as precursors to a large number of chiral nonracemic starting materials. For an example where nonracemic carbomagnesation adducts are used in natural product synthesis, see: Houri, A. F.; Xu, Z.-M.; Cogan, D. A.; Hoveyda, A. H. *J. Am. Chem. Soc.* **1995**, *117*, 2943−2944.

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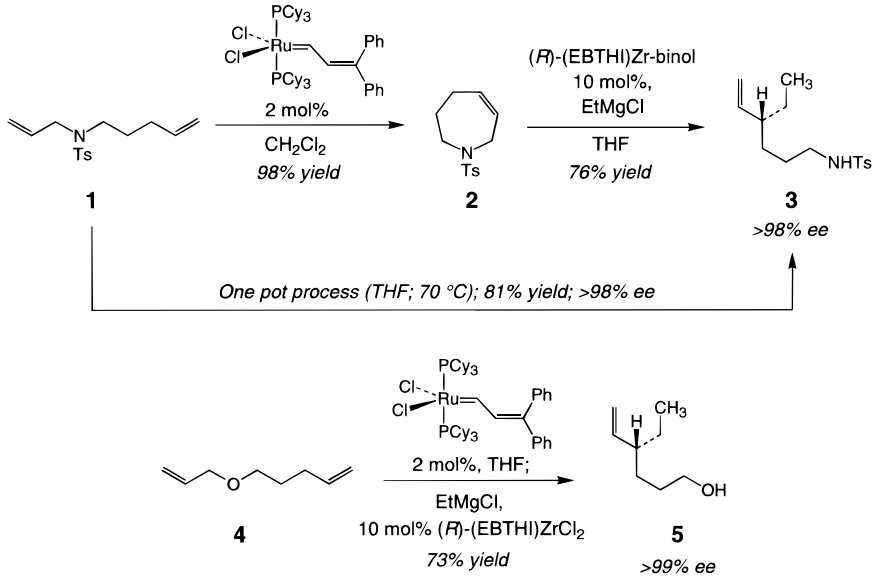
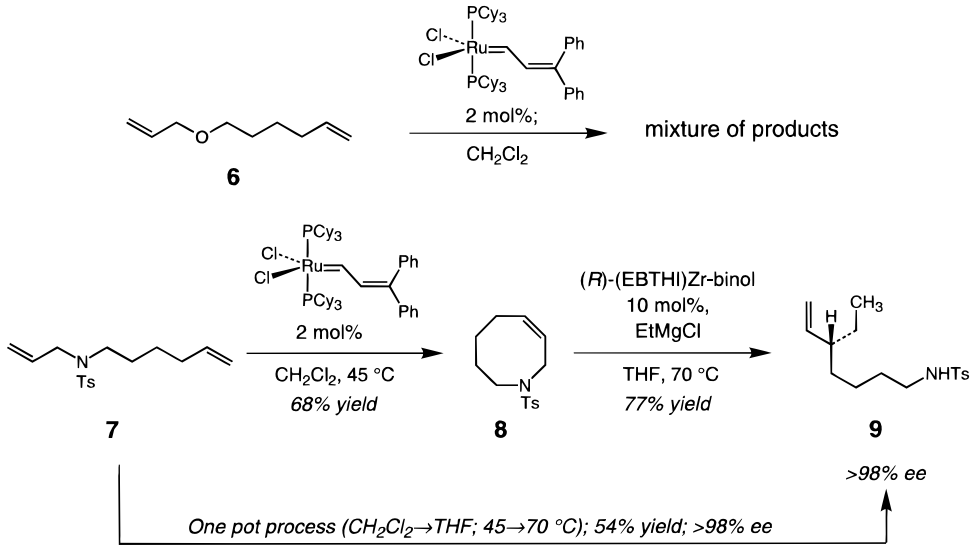
Scheme 1



Scheme 2



Data illustrated in Scheme 2 summarize the results of our studies in connection with the synthesis and carbomagnesation of the derived eight-membered heterocycles. Unlike the seven-membered-ring systems, construction of the derived eight-membered ether proceeds inefficiently, as reported previously by Grubbs and co-workers.[9] Treatment of **6** with 2 mol % of the Ru catalyst in refluxing CH_2Cl_2 leads to the formation of a variety of products (^{1}H NMR analysis). *In contrast, the related tosyl amide **7** undergoes a facile intramolecular metathesis (reaction is complete within 30 min at 45 °C), affording **8** in 68% yield after silica gel chromatography*.[10] This result is particularly worthy of note in light of recent reports that, in catalytic metathesis reactions that lead to eight-membered rings, the presence of rigid frameworks plays a critical role in the efficiency of ring formation.[8,9] It is plausible that the presence of the sterically demanding Ts group has a favorable conformational effect[11] on the diene substrate, leading to a significantly more facile catalytic cyclization. Subsequent treatment of **8** to the catalytic ethylmagnesation conditions, described above, delivers **9** in >98% ee (judged by ^{1}H NMR analysis of the derived (*R*)-MTPA ester) and 77% isolated yield. As before, metathesis and carbomagnesation of diene **7** can be carried out in the same reaction vessel (Scheme 2).

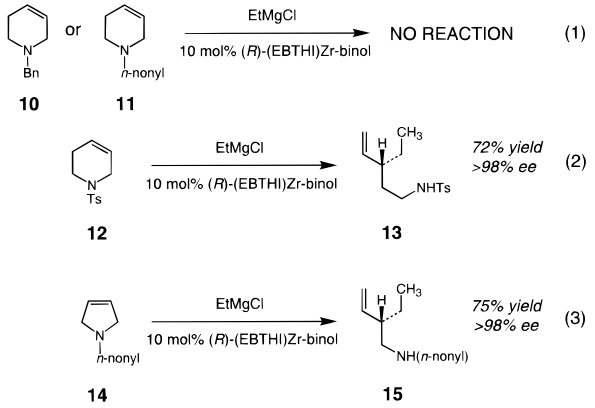
Suitability of Tosyl Amides (vs Amines) as Carbomagnesation Substrates. In connection to the Zr-catalyzed carbomagnesation of cyclic tosyl amides, a critical factor with regard to the facility of these C−C-bond-forming reactions is that the presence of the Ts unit is required. As shown in eq 1, whereas the benzylamine or *n*-alkylamine substrates are completely inert to the carbomagnesation conditions, the corresponding tosyl amide undergoes ethylmagnesation in good yield and excellent enantioselectivity: ethylmagnesation of **12** affords **13** (eq 2) in 71% yield and 98% ee (judged by chiral HPLC analysis). It merits mention that, with the more reactive five-membered-ring substrates, the presence of the Ts group is not necessary; as illustrated in eq 3, amine **14** affords **15** in 75% yield and

(9) (a) Miller, S. J.; Grubbs, R. H. *J. Am. Chem. Soc.* **1995**, *117*, 5855−5856. (b) References 5 and 8 and references cited therein.

(10) Ru-catalyzed metathesis of **7** in THF as solvent (instead of CH_2Cl_2) is notably less efficient; at 70 °C after 2 h there is only 40−50% conversion, accompanied by the formation of various byproducts.

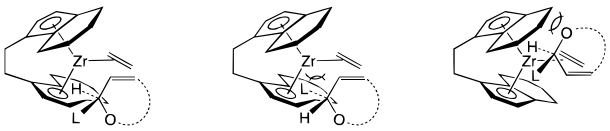
(11) For a discussion of the Thorpe−Ingold effect, see: Eliel, E. L.; Wilen, S. H.; Mander, L. N. *Stereochemistry of Organic Compounds*; Wiley-Interscience: New York, 1994; pp 682−684.

>98% ee (judged by ^{1}H NMR analysis of the derived (*S*)-MTPA ester).[12]



To determine the detailed mechanistic basis for the influence of the functionalization state of the N-substituent (*N*-Ts vs *N*-alkyl) on the efficiency of the carbomagnesation requires additional studies. However, we have established that the presence of an electron-withdrawing substituent facilitates the formation of the intermediate zirconacyclopentane. This may be because the developing electron density at the carbon of the newly formed C−Zr bond can be better stabilized (C−Zr formed preferentially α to the C−N bond). Related arguments have been used by Jordan and co-workers to explain variations in regiochemical control observed in insertions of various alkenes into $Cp_2Zr(\eta^2$-pyridyl)$(L)^+$ complexes,[13] and previously we have used similar paradigms as a predictive tool for the regiochemical outcome of the addition of zirconocene−alkene complexes with allylic alkoxides and ethers.[14] The present proposal is not in contrast to our previous mechanistic studies, where the subsequent step involving Zr−Mg ligand exchange (cleavage of the metallacycle intermediate) has been suggested to be turnover limiting: with six-membered unsaturated alkylamines (*e.g.*, **10** or **11**) the addition process may be sufficiently slow so as to emerge as the rate-determining step of the catalytic cycle. Nonetheless, although various data indicated above and the lack of reactivity of simple cyclic alkenes are conveniently rationalized by the proposed paradigm, the present available data do not unequivocally rule out the possibility that the effect of the Ts group is to facilitate the Zr−Mg ligand exchange process (lowering the activation barrier to the turnover-limiting metallacyclopentane cleavage step).

Zr-Catalyzed Kinetic Resolution of Unsaturated Medium-Ring Heterocycles.[15] The outcome of enantioselective C−C-bond formation in asymmetric carbomagnesations, such as those illustrated in Schemes 1 and 2, can be rationalized through preferential catalyst−substrate association **I**. The alternative modes **II** and **III** are expected to suffer from unfavorable steric interactions. The proposed mode of catalyst−substrate association and the observed levels of enantioselection imply tight substrate−catalyst binding. These principles would *a priori* suggest that, if formation of the intermediate zirconacyclopentane is the stereochemistry-determining event, appreciable differential rates of reaction between the two enantiomers should give rise to useful levels of kinetic resolution. Initially, it would be expected that as the size of the ligand (L) increases, more efficient levels of kinetic resolution are observed. *Data presented below will however indicate that, although structural models can, with reasonable fidelity, predict the sense of absolute asymmetric induction, they fail in allowing one to infer which substrates can be resolved more efficiently.*



As illustrated in Table 1, when racemic unsaturated seven-membered ethers **16**, **17**, and **19** (entries 1, 2, and 4) are treated with 10 mol % of (*R*)-(EBTHI)Zr-binol and 5 equiv of EtMgCl in THF, at 60% (±3%) conversion the unreacted starting material is recovered with outstanding levels of enantiomeric purity (>96% ee). However, these data indicate that, in contrast to what simple models (**I**−**III**, discussed above) would predict, certain structural modifications can lead to the diminution of enantioselectivity in the catalytic resolution. Specifically, the case in entry 3 of Table 1 illustrates that not all substitution patterns are equally suitable for the Zr-catalyzed resolution protocol. Cyclohexyl-substituted oxepin **18** is resolved less efficiently (>99% ee for **16** and **17** vs 70% ee for **18**), indicating that the presence of an α-branch in the C2 moiety can be detrimental to the success of the kinetic resolution process.

As illustrated in Table 2, in a manner similar to that observed for seven-membered heterocycles, we find that Zr-catalyzed[16] kinetic resolutions of 2-substituted dihydropyrans are sensitive to the steric bulk of the pendant alkyl group. As before, when the steric requirement of the substituent increases (*n*-Pr (**22**) → *i*-Bu (**24**) → cyclohexyl (**26**)), resolution occurs more slowly and less efficiently. Thus, unlike what simple models (**I**−**III**) would predict, with 2-substituted pyrans, as the steric requirements of the alkyl moiety increase, the rate difference between carbomagnesations of the two enantiomers is *diminished*[17] (*cf.* entries in Table 2; k_{fast}/k_{slow} = >20, 17, and 7, respectively).[18]

(12) This experiment was carried out by Dr. James P. Morken of these laboratories.

(13) Guram, A. S.; Jordan, R. F. *Organometallics* **1991**, *10*, 3470−3479.

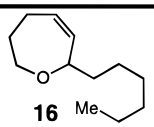
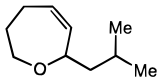
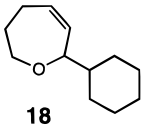
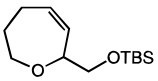
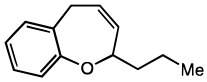
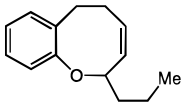
(14) Houri, A. F.; Didiuk, M. T.; Xu, Z.-M.; Horan, N. R.; Hoveyda, A. H. *J. Am. Chem. Soc.* **1993**, *115*, 6614−6624. (b) References 2 and 3.

(15) For a review of kinetic resolution, see: (a) Kagan, H. B.; Fiaud, J. C. *Top. Stereochem.* **1988**, *18*, 249−330. For recent advances in catalytic kinetic resolution, see: (b) Finn, M. G.; Sharpless, K. B. In *Asymmetric Synthesis*; Morrison, J. D., Ed.; Academic Press: New York, 1985; pp 247−308. (c) Gao, Y.; Hanson, R. M.; Klunder, J. M.; Ko, S. Y.; Masamune, H.; Sharpless, K. B. *J. Am. Chem. Soc.* **1987**, *109*, 5765−5780. (d) Hayashi, T.; Yamamoto, M. *Chem. Lett.* **1987**, 177−180. (e) Carlier, P. R.; Mungall, W. S.; Shroder, G.; Sharpless, K. B. *J. Am. Chem. Soc.* **1988**, *110*, 2978−2979. (f) Kitamura, M.; Kasahara, I.; Manabe, K.; Noyori, R.; Takaya, H. *J. Org. Chem.* **1988**, *53*, 708−710. (g) VanNieuwenhze, M. S.; Sharpless, K. B. *J. Am. Chem. Soc.* **1993**, *115*, 7864−7865. (h) Faller, J. W.; Tokunaga, M. *Tetrahedron Lett.* **1993**, *34*, 7359−7362. (i) Rein, T.; Kann, N.; Kreuder, R.; Gangloff, B.; Reiser, O. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 556−558. (j) Martin, S. F.; Spaller, M. R.; Liras, S.; Hartmann, B. *J. Am. Chem. Soc.* **1994**, *116*, 4493−4494. (k) Viso, A.; Lee, N. E.; Buchwald, S. L. *J. Am. Chem. Soc.* **1994**, *116*, 9373−9374. (l) Vander Velde, S. L.; Jacobsen, E. N. *J. Org. Chem.* **1995**, *60*, 5380−5381. (m) Noyori, R.; Tokunaga, M.; Kitamura, M. *Bull. Chem. Soc. Jpn.* **1995**, *68*, 36−56. For recent advances in noncatalytic kinetic resolution, see: (n) Naruse, Y.; Esaki, T.; Yamamoto, H. *Tetrahedron Lett.* **1988**, *29*, 1417−1420. (o) Brunner, H.; Schiessling, H. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 125−126. (p) Rein, T.; Kann, N.; Kreuder, R.; Gangloff, B.; Reiser, O. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 556−558. (q) Vedejs, E.; Chen, X. *J. Am. Chem. Soc.* **1996**, *118*, 1809−1810. (r) Rychnovsky, S. D.; McLernon, T. L.; Rajapakse, H. *J. Org. Chem.* **1996**, *61*, 1194−1195.

(16) Reactions illustrated in Table 2 and Scheme 3 were carried out with the (*R*)-(EBTHI)$ZrCl_2$ as catalyst (instead of the binol derivative used in Table 1 and Schemes 1 and 2). We have not found any notable differences in either the yield or the ee of the reaction when the two chiral complexes are used as precatalyst; however, use of the binol derivative is more convenient, as two steps in catalyst preparation are obviated (see ref 6).

(17) Molecular models indicate that reaction through **I** may require the pyran to adopt a boat conformation to avoid unfavorable substrate−catalyst propinquity. Associated torsional interactions, involving the alkyl substituent, may be exacerbated with larger moieties, disfavoring mode **I** in the latter instance.

Table 1. Zirconocene-Catalyzed Kinetic Resolution of 2-Substituted Medium Ring Ethers[a]

entry	substrate	conversion[b] (%)	time	unreacted subs.[c] config., ee (%)
1	 **16**	58	40 min	*R*, **>99**
2	 **17**	58	30 min	*R*, **>99**
3	 **18**	60	90 min	*R*, **70**
4	 **19**	63	100 min	*R*, **96**
5	 **20**	60	8 hr	*R*, **60**
6	 **21**	63	11 hr	*R*, **79**

[a] Conditions: 10 mol % of (*R*)-(EBTHI)Zr-binol, 5.0 equiv of EtMgCl, THF, 70 °C. [b] Conversions determined by GLC analysis in comparison with an internal standard, by analysis of ^{1}H NMR spectrum of the reaction mixture, and through isolation (silica gel chromatography). [c] Enantiomeric excess of recovered starting materials determined by GLC through comparison with authentic materials (entries 1−4, BETA-DEX 120 chiral column by Supelco; **19** was first converted to its derived alcohol; entries 5 and 6, CHIRALDEX-GTA chiral column by Alltech).

In connection with this trend, in reactions represented in Table 2, with larger substituents, the carbometalation product is formed with *lower* levels of enantioselection.[19] These observations are mechanistically informative, as they suggest that with (EBTHI)-Zr as catalyst, slow enantiomers of (*R*)-**22**−**26** react increasingly through addition mode **III**, not **II**. This is because, although zirconacyclopentanes resulting from addition routes **I** and **II** are diastereomeric, after elimination of the metal alkoxide and formation of the product disubstituted alkene, the final carbomagnesation products are identical (both enantiomers afford the *trans*-alkene product exclusively).[20]

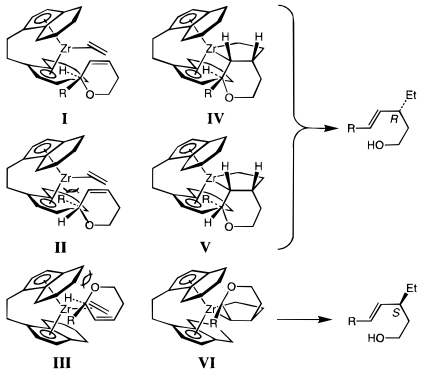
Pathways for catalyst−substrate association represented by **I**−**III** imply that as the size of the alkyl substituent increases, reaction of the matched enantiomer through **I** should remain unaffected. However, experimental data summarized in Scheme 3 indicate that this is not the case: bulkier substituents do not necessarily allow for greater differential rates of carbomagnesation, since not only is the rate of reaction of the mismatched enantiomer retarded (compare reaction of (*R*)-**28** with (*R*)-**26** in Scheme 3), but the matched isomer reacts more sluggishly as well (compare reaction of (*S*)-**26** with reaction of (*S*)-**28**).

It may be proposed that, as suggested by the mechanistic studies on related systems,[1b] it is the cleavage of the intermediate metallacyclopentane that is the product-determining step: metallacyclopentane formation may well be highly reversible, rendering the addition events represented by **I**−**III** unimportant. In such a case, the metallacycle derived from mode **III**, although less favored, could undergo cleavage significantly faster than that originated from **I** (rate difference dependent on the C2 substituent), presumably because a more significant amount of

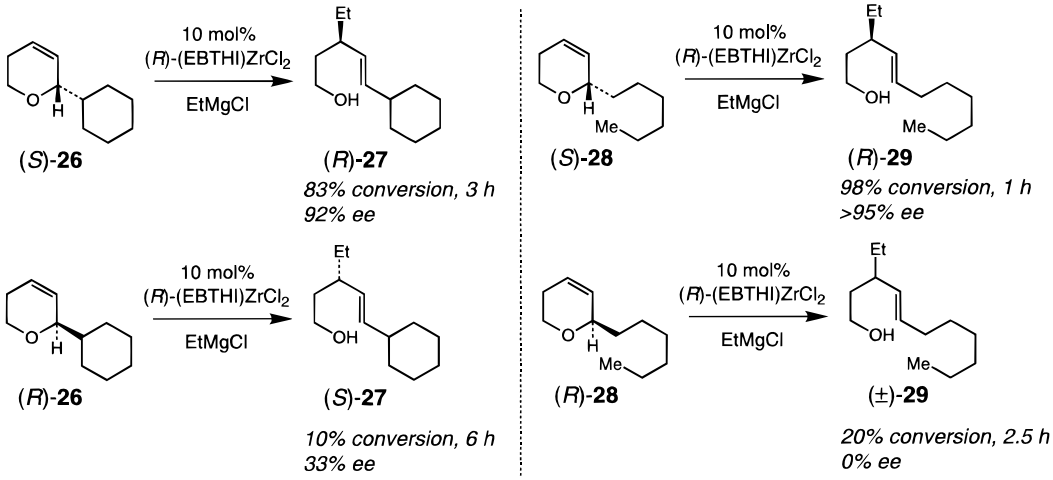
(18) Relative rates were calculated by an equation reported previously. See refs 15a,b.

(19) Control experiments indicate that in the absence of (EBTHI)$ZrCl_2$ (at 70 °C) there is little reaction and there is <5% decomposition of the starting materials. Thus, the observed products (cf. Table 2) are derived solely from the metal-catalyzed carbomagnesation reactions of **22**−**26**.

(20) As illustrated below, modes of addition **I** and **II** eventually afford the same product enantiomer, whereas reaction through **III** leads to the formation of the opposite antipode. Thus, the product ee is a direct indication of the extent to which asymmetric carbomagnesation proceeds through **III**. The fact that both substrate enantiomers afford trans olefin isomers indicates that (i) the zirconacyclopentane does not simultaneously undergo β-metal alkoxide elimination (otherwise **V** would afford the cis product) and (ii) the intermediate β-alkoxymagnesium (product of Zr−Mg ligand exchange) undergoes rapid inversion prior to elimination.



Scheme 3



steric strain would be relieved through cleavage of a metallacyclopentane that originates from mode of addition **III**. Regardless of such mechanistic intricacies, the enantioselectivity trends obtained in these studies underline a major pathway through which the slow heterocycle enantiomer evades complete recovery. These data offer critical insight with regard to possible alteration of catalyst ligand structure, so that with substrates such as **26**, which have bulky substituents, more effective kinetic resolution can be achieved. Specifically, with substrates that bear a bulky group at C2, ligand structure must be modified to disallow entirely mode of addition **III**. Only two competing reaction pathways involving **I** and **II** would then be operative, where, as our data indicate, there should be a significant preference for **I**.[21]

Several other issues with regard to the data presented in Table 1 merit additional comment:

(1) Although silyl ether **19** is a suitable substrate for the zirconocene-catalyzed resolution, the corresponding alcohol (or magnesium alkoxide) or benzyl ether derivatives are not. This is because both of the aforementioned substrates react with EtMgCl to afford the carbomagnesation product in the absence of the transition-metal catalyst. For example, the primary alcohol precursor to **19** reacts with EtMgCl to afford the corresponding alkylation product in 86% yield after silica gel chromatography. Whether the presence of the primary hydroxy group directs the addition of the alkylmagnesium halide or chelation of the side chain alkoxide and the ring oxygen with Mg salts leads to activation of the resident alkene toward nucleophilic attack is unclear and must await future studies.

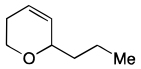
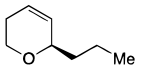
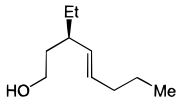
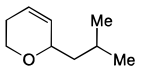
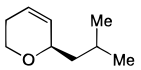
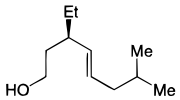
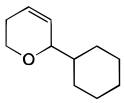
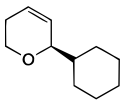
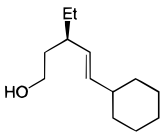
(2) Comparison of the data shown in entries 1 and 5 of Table 1 indicates that the presence of an aromatic substituent can have an adverse influence on the outcome of the catalytic resolution. That the eight-membered-ring substrate **21** is resolved more efficiently may imply that the origin of the adverse influence is due more to conformational preferences of the heterocycle than to the attendant electronic factors (a phenoxy group is a better leaving group that an alkoxy unit).

Conclusions

Studies reported herein demonstrate that asymmetric catalytic ethylmagnesation of seven- and eight-membered-ring oxygen-containing heterocycles may be used as a convenient and efficient route to a variety of nonracemic unsaturated alcohols and heterocycles. As detailed in the Experimental Section (*e.g.*, tandem metathesis/carbomagnesation of **1** → **3**), these transformations can be readily carried out on a synthetically useful (grams) scale. Importantly, data derived from asymmetric carbomagnesation of a range of heterocycle substrates indicate that enantioselectivity in the C−C bond-forming process depends on subtle structural variations: simple steric arguments alone may not account for the observed selectivity patterns. Further studies in the area of asymmetric catalytic carbomagnesation continue in these laboratories.

(21) If reaction through **II** were mainly responsible for inefficient resolution, product ee's would not suffer as observed. Particularly with larger alkyl units at C2, addition through mode **II** represents the minor pathway (Scheme 3).

Table 2. Zirconocene-Catalyzed Kinetic Resolution and Enantioselective Ethylmagnesation of Unsaturated Pyrans[a]

substrate	recovered substrate[b]	ee (%)[c]	product[b]	ee (%)[c]
 (±)-**22**	 (*R*)-**22**	>99	 (*R*)-**23**	94
 (±)-**24**	 (*R*)-**24**	96	 (*R*)-**25**	87
 (±)-**26**	 (*R*)-**26**	78	 (*R*)-**27**	74

[a] Conditions as reported for Table 1, except that (*R*)-(EBTHI)$ZrCl_2$ was used as precatalyst. All data obtained at 60% (±2%) conversion; mass recovery >90% in all cases. [b] Conversions and identity of recovered starting materials and products determined as described in Table 1. [c] Enantiomeric excesses for recovered substrates and products determined by chiral GLC (BETA-DEX 120 column by Supelco) in comparison with an authentic enantiomer and racemic material; ee of **24** was determined by analysis of its derived epoxide; ee of **27** was established by analysis of the derived (*S*)-MTPA ester.

Experimental Section

General. Infrared (IR) spectra were recorded on a Perkin-Elmer 781 spectrophotometer, ν_{max} in cm^{-1}. Bands are characterized as broad (br), strong (s), medium (m), and weak (w). ^1H NMR spectra were recorded on a Varian Unity 300 (300 MHz) or Varian GN-400 (400 MHz). Chemical shifts are reported in parts per million 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 on a Varian Unity 300 (75 MHz) or Varian GN-400 (100 MHz) with complete proton decoupling. Chemical shifts are reported in parts per million from tetramethylsilane with the solvent as the internal reference ($CDCl_3$: δ 77.0 ppm). An Alltech Associates DB-1 capillary column (30 m × 0.32 mm) was used to determine conversions. Enantiomer ratios were determined by GLC with either a BETA-DEX 120 (30 m × 0.25 mm) chiral column by Supelco or a CHIRALDEX GTA (20 × 0.25 mm) chiral column by Alltech Assoc., Inc. Microanalyses were performed by Robertson Microlit Laboratories (Madison, NJ).

All reactions were conducted in oven-dried (135 °C) and flame-dried glassware under an inert atmosphere of dry argon. Tetrahydrofuran was distilled from sodium metal/benzophenone ketyl. Ethylmagnesium chloride was prepared from ethyl chloride and Mg (turnings), which were purchased from Aldrich and used without further purification. (*R*)-(EBTHI)Zr-binol was prepared and resolved by the published methods.[6] Nonracemic (EBTHI)$ZrCl_2$ and (EBTHI)Zr-binol were stored under argon in a glovebox. $(PCy_3)_2Cl_2Ru{=}CHCH{=}CPh_2$ was prepared by the method of Grubbs.[5]

Representative Experimental Procedure for the Zirconium-Catalyzed Kinetic Resolution. A 5.0 mL flame-dried flask with side-arm Teflon stopcock was charged with 100.0 mg (0.55 mmol) of **16**, 30.0 mg of tetradecane (internal standard), 1.03 mL of THF, and 1.72 mL of freshly prepared EtMgCl (1.60 mmol). A 50.0 μL t_0 aliquot was subsequently removed and quenched with moist Et_2O (the mixture was diluted with water and washed with two 1.0 mL portions of Et_2O). Filtration of the aliquot through a small plug (~300 mg) of silica gel followed by washing of the silica with a 0.5 mL portion of Et_2O provided a sample suitable for GLC analysis. The precatalyst (*R*)-(EBTHI)Zr-binol was added (35.2 mg, 5.5×10^{-2} mmol). The flask was first equipped with a flame-dried reflux condenser, which was lowered into a 70 °C oil bath. The reaction mixture was stirred at 70 °C for approximately 30 min, at which time GLC 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 2.0 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 with 200:1 hexanes/EtOAc afforded 42.8 mg (0.23 mmol) of recovered **16** (96% yield based on % converion; 50% is maximum yield in a resolution).

***N*-Tosyl-1,5,6,7-tetrahydro-2*H*-azepine (2).** IR (KBr): 3023 (m), 2927 (s), 2838 (m), 1592 (s), 1442 (s), 1323 (s), 1156 (s) cm^{-1}. ^1H NMR: δ 7.67 (2H, d, J = 8.3 Hz, aromatic CH), 7.28 (2H, d, J = 8.1 Hz, aromatic CH), 5.76 (1H, dtt, J = 10.9, 5.4, 1.3 Hz, vinyl CH), 5.65 (1H, dtt, J = 10.9, 5.0, 1.6 Hz, vinyl CH), 3.82 (2H, m, CH_2CH_2-NTs), 3.38 (2H, dd (apparent t), J = 6.1 Hz, C=CHCH_2NTs), 2.45 (3H, s, $ArCH_3$), 2.18 (2H, m, HC=CHCH_2), 1.79 (2H, m, HC=CHCH_2CH_2). ^{13}C NMR: δ 143.6, 137.2, 137.1, 133.5, 130.2, 127.9, 127.3, 50.3, 47.1, 27.5, 22.1. Anal. Calcd for $C_{13}H_{17}NO_2S$: C, 62.12; H, 6.81. Found: C, 62.31; H, 6.86.

(*R*)-4-Ethyl-*N*-tosyl-5-hexene-1-sulfonamide (3). Procedure for One-Pot Tandem Metathesis/Carbomagnesation. Diene **1** (1.05 g, 3.76 mmol) was dissolved in 19.0 mL of anhydrous THF, and 69.0 mg (0.07 mmol) of $(PCy_3)_2Cl_2Ru{=}CHCH{=}CPh_2$ was added to the solution as a single portion. The reaction flask was submerged in an oil bath heated to 70 °C; the reaction mixture was stirred at this temperature for approximately 90 min, at which time TLC analysis indicated complete consumption of the starting material (3:1 hexanes/EtOAc; R_f(**1**) = 0.62, R_f(**2**) = 0.52). The mixture was then cooled to 22 °C and charged with EtMgCl (18.8 mmol) and (*R*)-(EBTHI)Zr-binol (241 mg, 0.37 mmol). The resulting red solution was stirred at 70 °C for 2 h, after which the mixture was chilled to 0 °C and the reaction was quenched upon addition of 20.0 mL of water and 40.0 mL of a saturated solution of NH_4Cl. Aqueous extraction (Et_2O), drying of the organic layers over anhydrous $MgSO_4$, and removal of solvent under reduced pressure left behind a brown-black oil. Silica gel chromatography (15:1 followed by 9:1 hexanes/EtOAc) afforded 709 mg (2.52 mmol) of **3** (67% yield). Comparison (400 MHz ^1H NMR) of the derived (*R*)-MTPA ester to that from the racemic mixture and the authentic material, prepared by the procedure shown below, indicated >98% enantiomeric excess (minor enantiomer could not be detected). IR (KBr): 3265 (br), 2925 (s), 2850 (s), 1591 (s), 1459 (m), 1418 (m), 1326 (s), 1159 (s), 1095 (m) cm^{-1}. ^1H NMR: δ 7.75 (2H, d, J = 8.3 Hz, aromatic CH), 7.31 (2H, d, J = 8.0 Hz, aromatic CH), 5.44−5.35 (1H, ddd, J = 17.1, 10.3, 8.9 Hz, vinyl CH), 4.96−4.92 (1H, dd, J = 10.2, 2 Hz, vinyl CH), 4.90−4.85 (1H, dd, J = 17.1, 2 Hz, vinyl CH), 4.34 (1H, t, J = 6.0 Hz, NH), 2.95−2.88 (2H, ddd, J = 13.3, 6.6, 1.6 Hz, C=CCH_2NTs), 2.40 (3H, s, $ArCH_3$), 1.79−1.70 (1H, m, aliphatic CH), 1.48−1.11 (6H, m, aliphatic CH_2), 0.81 (3H, t, J = 7.4 Hz, CH_2CH_3). ^{13}C NMR: δ 144.0, 143.0, 137.8, 130.3, 127.8, 115.5, 46.1, 44.0, 32.1, 28.4, 28.0, 22.2, 12.2. Anal. Calcd for $C_{15}H_{23}NO_2S$: C, 64.02; H, 8.23. Found: C, 64.20; H, 8.37.

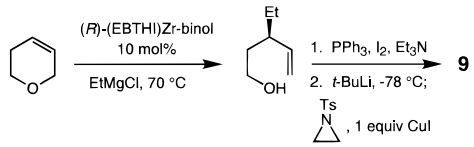
(*R*)-4-Ethyl-5-hexen-1-ol (5). IR (KBr): 3357 (br, s), 3076 (m), 2975 (s), 2892 (s), 1640 (m), 1461 (s), 1455 (w), 1420 (m), 1059 (s), 910 (s) cm^{-1}. ^1H NMR: δ 5.50 (1H, dt, J = 16.9, 8.9, vinyl CH), 4.96 (1H, m, vinyl CH_2), 3.63 (1H, s, O*H*), 3.61 (2H, t, J = 6.2 Hz, CH_2CH_2OH), 1.85 (1H, m, allylic CH), 1.68−1.20 (6H, m, aliphatic CH), 0.84 (3H, t, J = 7.4 Hz, CH_2CH_3). ^{13}C NMR: δ 142.8, 114.5, 63.1, 45.6, 30.6, 30.5, 27.7, 11.5. Anal. Calcd for $C_8H_{16}O$: C, 74.94; H, 12.58. Found: C, 74.63; H, 12.29.

(*R*)-*N*-Tosyl-1,2,5,6,7,8-hexahydroazocine (8). Procedure for Ru-Catalyzed Diene Metathesis. Diene **7** (300 mg, 1.02 mmol) was dissolved in 102 mL of anhydrous CH_2Cl_2 (under Ar atmosphere), and to this mixture was added in one portion 56 mg (0.06 mmol) of $(PCy_3)_2Cl_2Ru{=}CHCH{=}CPh_2$. The reaction mixture was stirred at 45 °C for 30 min, after which solvent was removed *in vacuo*. Purification of the resulting dark brown oil by silica gel chromatography (9:1 hexanes/EtOAc) afforded **8** (183 mg, 0.69 mmol; 68% yield) as a colorless crystalline solid. IR (KBr): 3008 (br), 2920 (s), 2855 (s), 1598 (w), 1434 (br), 1328 (s) cm^{-1}. ^1H NMR: δ 7.66 (2H, d, J = 8.3 Hz, aromatic H), 7.29 (2H, d, J = 8.4 Hz, aromatic CH), 5.78 (1H, dt, J = 11.1, 8.2 Hz, vinyl CH), 5.40 (1H, dt, J = 11.1, 5.6 Hz, vinyl CH), 3.80 (2H, d, J = 5.7 Hz, C=CHCH_2NTs), 3.28 (2H, t, J = 5.3 Hz, CH_2NTs), 2.42 (3H, s, $ArCH_3$), 2.38 (2H, m, C=CHCH_2), 1.67 (2H, m, aliphatic CH_2), 1.55 (2H, aliphatic CH_2). ^{13}C NMR: 143.7, 143.4, 132.8, 130.3, 127.8, 125.5, 48.5, 46.5, 27.3, 26.3, 25.3, 22.2. Anal. Calcd for $C_{14}H_{19}NO_2S$: C, 63.36; H, 7.21; N, 5.28. Found: C, 63.87; H, 7.25; N, 5.02.

(*R*)-5-Ethyl-*N*-tosyl-6-heptene-1-sulfonamide (9). Procedure for One-Pot Tandem Metathesis/Carbomagnesation with Two Different Solvent Systems. Diene **7** (100 mg, 0.34 mmol) was dissolved in 34.0 mL of anhydrous CH_2Cl_2 (under Ar atmosphere), and 19.0 mg (0.02 mmol) of $(PCy_3)_2Cl_2Ru{=}CHCH{=}CPh_2$ was added to this solution (one portion). The reaction vessel was placed in an oil bath heated to 45 °C, and the mixture was stirred at this temperature for 30 min. At this point TLC analysis (5:1 hexanes/EtOAc; R_f(sm) = 0.66, R_f(prod) = 0.53) indicated complete consumption of the diene. The reaction mixture was allowed to cool to 22 °C, and solvent was removed *in vacuo*. The dark brown residue was then dissolved in 0.70 mL of THF. Subsequently, EtMgCl (1.70 mmol) and (*R*)-(EBTHI)Zr-binol (21.0 mg, 0.03 mmol) were added and the reaction mixture was placed in an oil bath maintained at 70 °C. The mixture was stirred for 3 h, after which the reaction mixture was cooled to 22 °C and the reaction was quenched by addition of water (0.20 mL) and 10.0 mL of a saturated solution of NH_4Cl. Aqueous extraction (Et_2O), drying of the organic layers over anhydrous $MgSO_4$, and removal of solvent under reduced pressure left behind a brown oil. Silica gel chromatography (9:1 hexanes/EtOAc) afforded 54.0 mg (0.18 mmol) of **9** (54% yield). Comparison (400 MHz ^1H NMR) of the derived (*R*)-MTPA ester to that from the racemic mixture and the authentic material, prepared by the procedure shown below, indicated >98% enantiomeric excess (minor enantiomer could not be detected). IR (KBr): 3281 (br), 2957 (m), 2924 (s), 2857 (d), 1597 (w), 1458 (m), 1419 (m), 1324 (s), 1157 (s), 1095 (s) cm^{-1}. ^1H NMR: δ 7.75 (2H, d, J = 8.3 Hz, aromatic CH), 7.31 (2H, d, J = 8.4 Hz, aromatic CH), 5.45 (1H, ddd, J = 17.1, 10.2, 8.9 Hz, vinyl CH), 4.94 (1H, dd, J = 17.2, 1.9 Hz, vinyl CH), 4.86 (1H, dd, J = 10.2, 2.0 Hz, vinyl CH), 4.43 (1H, t, J = 6.0 Hz, NH), 2.94−2.88 (2H, q, J =

6.8 Hz, C=CCH_2NTs), 2.42 (3H, s, ArCH_3), 1.82−1.11 (8H, m, aliphatic CH_2), 0.82 (3H, t, J = 7.4 Hz, CH$_2$CH_3). ^{13}C NMR: δ 143.9, 143.4, 137.8, 130.3, 127.8, 115.1, 46.3, 43.9, 34.6, 30.3, 28.3, 24.8, 22.2, 12.2. Anal. Calcd for $C_{16}H_{25}NO_2S$: C, 65.04; H, 8.53; N, 4.74. Found: C, 65.25; H, 8.37; N, 4.47.

Synthesis of authentic material

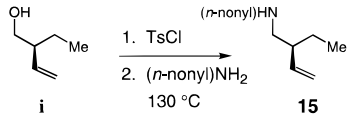


(*R*)-3-Ethyl-*N*-tosyl-4-pentene-1-sulfonamide (13). IR (KBr): 3283 (br), 3072 (w), 2965 (s), 2925 (s), 2874 (s), 1602 (m), 1423 (m), 1324 (w), 1156 (s) cm^{-1}. ^{1}H NMR: δ 7.73 (2H, m, aromatic CH), 7.28 (2H, m, aromatic CH), 5.39 (1H, ddd, J = 17.1, 10.0, 9.0 Hz, vinylic CH), 4.87 (1H, m, vinylic CH$_2$), 2.95 (2H, m, CH$_2$NHTs), 2.45 (3H, s, benzylic CH$_3$), 1.86 (1H, m, allylic CH), 1.60−1.10 (4H, m, aliphatic CH), 0.77 (3H, t, J = 7.3 Hz, CH$_2$CH$_3$). Anal. Calcd for $C_{14}H_{21}O_2NS$: C, 62.89; H, 7.92; N, 5.24. Found: C, 63.10; H, 8.01, N, 5.13.

((*R*)-2-Ethyl-3-buten-1-yl)-*n*-nonylamine (15). IR (KBr): 2960 (s, br), 1640 (w) cm^{-1}; ^{1}H NMR: δ 5.48 (1H, dt, J = 18.0, 10.9 Hz, vinyl CH), 5.03 (2H, m, vinyl CH$_2$), 2.95 (4H, m, CH_2N), 2.08 (1H, m, CHCH$_2$N), 1.45−1.18 (21H, m, *n*-alkyl CH and CH_2CH$_3$), 0.84 (6H, t, J = 7.1 Hz, CHCH$_2$CH_3 and (CH$_2$)$_8$CH_3). ^{13}C NMR: δ 141.4, 116.0, 53.8, 50.4, 46.2, 31.8, 30.1, 29.6, 29.2, 27.4, 25.7, 24.0, 22.6, 14.0, 11.5. HR CIMS $C_{15}H_{31}N$ + 1 requires 226.2535, found 226.2547.

Proof of Absolute Stereochemistry. The stereochemical identity of secondary amine **15** was proved by conversion of enantiomerically pure **i** (prepared according to ref 15b) to this amine, in the manner shown below.

Synthesis of authentic material



(*R*)-2-Hexyl-2,5,6,7-tetrahydrooxepin (16). IR (KBr): 3021 (w), 2968 (w), 2932 (s), 2871 (m), 1453 (m), 1146 (m), 1108 (m) cm^{-1}. ^{1}H NMR: δ 5.80 (1H, ddt, J = 11.2, 5.4, 2.2 Hz, vinyl CH), 5.54 (1H, m, vinyl CH), 4.03 (2H, m, CH$_2$CH_2OCH), 3.67 (1H, m, CH$_2$CH$_2$OCH), 2.35 (1H, m, allylic CH), 2.22 (1H, m, allylic CH), 1.80 (2H, m, CH_2-CH$_2$OCH), 1.61−1.26 (10H, m, aliphatic CH), 0.88 (3H, t, J = 6.8 Hz, CH$_2$CH_3). ^{13}C NMR: δ 135.2, 131.8, 78.3, 71.6, 36.7, 32.1, 29.6, 29.5, 27.2, 25.8, 22.9, 14.3. Anal. Calcd for $C_{12}H_{22}O$: C, 79.06; H, 12.16. Found: C, 78.78; H, 12.06.

Proof of Absolute Stereochemistry for Recovered 16. An authentic sample of the nonracemic **15** was synthesized by the Ru-catalyzed diene metathesis of the requisite diene, which was prepared from the corresponding optically enriched allylic alcohol. A similar procedure was carried out for **18**, **29**, and **21** (Table 1).

(*R*)-2-Isobutyl-2,5,6,7-tetrahydrooxepin (17). IR (KBr): 3018 (m), 2952 (s), 2929 (s), 2868 (m), 2841 (m), 1467 (m), 1139 (s), 1113 (s) cm^{-1}. ^{1}H NMR: δ 5.81 (1H, ddt, J = 11.1, 5.5, 2.3 Hz, vinyl CH), 5.52 (1H, m, vinyl CH), 4.06 (2H, m, CH$_2$CH_2OCH), 3.69 (1H, m, CH$_2$CH$_2$OCH), 2.35 (1H, m, allylic CH), 2.23 (1H, m, allylic CH), 1.86−1.55 (4H, m, aliphatic CH), 1.26 (1H, m, CH$_3$CHCH$_3$), 0.92 (3H, d, J = 3.2 Hz, CH$_2$CH_3), 0.90 (3H, d, J = 3.0 Hz, CH$_3$). ^{13}C NMR: δ 135.2, 131.6, 76.0, 71.4, 45.4, 29.2, 26.9, 24.5, 23.2, 22.0. Anal. Calcd for $C_{10}H_{18}O$: C, 77.87; H, 11.76. Found: C, 78.10; H, 12.01.

(*R*)-2-Cyclohexyl-2,5,6,7-tetrahydrooxepin (18). IR (KBr): 3017 (w), 2929 (s), 2851 (s), 1450 (m), 1177 (s), 1144 (s) cm^{-1}. ^{1}H NMR: δ 5.86 (1H, ddt, J = 11.2, 5.4, 2.2 Hz, vinyl CH), 5.61 (1H, ddt, J = 11.3, 2.9, 1.5 Hz, vinyl CH), 4.04 (1H, dt, J = 11.7, 6.1 Hz, CH$_2$CH_2-OCH), 3.79 (1H, m, CH$_2$CH_2OCH), 3.64 (1H, m, CH$_2$CH$_2$OCH), 2.39 (1H, m, allylic CH), 2.18 (1H, m, allylic CH), 1.85−0.98 (13H, m, aliphatic CH). ^{13}C NMR: δ 133.1, 131.8, 82.4, 71.2, 43.3, 29.0, 28.9, 28.0, 26.6, 26.5, 26.3. HRMS requires 180.1514, found 180.1512.

(*R*)-2-((*tert*-Butyldimethylsiloxy)methyl)-2,5,6,7-tetrahydrooxepin (19). IR (KBr): 3007 (w), 2923 (m), 2845 (s), 1465 (m), 1250 (s), 1118 (s), 801 (s), 778 (s) cm^{-1}. ^{1}H NMR: δ 5.90−5.83 (1H, ddd, J = 11.2, 5.4, 2.4 Hz, vinylic CH), 5.67−6.62 (1H, ddt, J = 11.3, 2.9, 1.4 Hz, vinyl CH), 4.15−4.00 (2H, m, (CH$_3$)$_2$SiCH_2CHO), 3.75−3.67 (2H, m, CH$_2$CH_2O), 3.55 (1H, dd, J = 10.2 Hz, CH$_2$CHOCH$_2$), 2.43−2.32 (1H, m, allylic CH), 2.25−2.15 (1H, m, allylic CH), 1.92−1.72 (2H, m, aliphatic CH$_2$), 0.84 (9H, s, (CH_3)$_3$CSi(CH$_3$)$_2$), 0.07 (6H, s, (CH$_3$)$_3$CSi(CH_3)$_2$). ^{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.

(*R*)-2-Propyl-2,5-dihydro-1-benzoxepin (20). IR (KBr): 3052 (w), 2959 (s), 2932 (m), 2872 (m), 1488 (s), 1455 (m), 1237 (s) cm^{-1}. ^{1}H NMR: δ 7.17−6.96 (4H, m, aromatic), 5.81 (1H, m, vinyl CH), 5.38 (1H, dt, J = 11.7, 2.0 Hz, vinyl CH), 4.40 (1H, m, OCH(CH$_2$)$_2$CH$_3$), 3.78 (1H, dd, J = 16.8, 2.9 Hz, benzylic CH), 3.10 (1H, dd, J = 16.9, 7.3 Hz, benzylic CH), 1.79−1.54 (4H, m, aliphatic CH), 0.97 (3H, t, J = 7.1 Hz, CH$_3$). ^{13}C NMR: δ 157.8, 136.0, 131.5, 128.6, 127.6, 125.8, 123.7, 121.9, 80.1, 38.2, 31.7, 18.9, 13.9. Anal. Calcd for $C_{13}H_{16}O$: C, 82.94; H, 8.57. Found: C, 82.72; H, 8.32.

(*R*)-2-Propyl-5,6-dihydro-2*H*-1-benzoxocin (21). IR (KBr): 3052 (w), 2952 (s), 2922 (s), 2861 (w), 1577.7 (w), 1491 (s), 1446 (m), 1213 (s), 1097 (s) cm^{-1}. ^{1}H NMR: δ 7.20−6.90 (4H, m, aromatic CH), 5.69 (1H, dt, J = 11.0, 7.8 Hz, vinyl CH), 5.35 (1H, ddd, J = 10.9, 3.5, 1.1 Hz, vinylic CH), 4.5 (1H, dt, J = 7.6, 5.0 Hz, CH=CHCH(*n*-Pr)OAr), 3.28 (1H, m, benzylic CH), 3.13 (1H, ddd, J = 16.2, 6.1, 3.4 Hz, benzylic CH), 2.81 (1H, m, allylic CH), 2.25 (1H, m, allylic CH), 1.94−1.5 (4H, m, aliphatic CH), 0.98 (3H, t, J = 7.0 Hz, CH$_3$). ^{13}C NMR: δ 158.1, 134.1, 131.6, 131.4, 130.7, 127.8, 124.4, 123.8, 85.1, 38.7, 33.2, 27.2, 19.9, 14.7. Anal. Calcd for $C_{14}H_{18}O$: C, 83.12; H, 8.97. Found: C, 83.05; H, 9.14.

(*R*)-2-Propyl-5,6-dihydro-2*H*-pyran (22). IR (KBr): 3032 (w), 2959 (s), 2932 (s), 2973 (s), 2850 (m), 1710 (w), 1465 (m), 1185 (m), 1086 (s) cm^{-1}. ^{1}H NMR: δ 5.79 (1H, m, vinylic CH), 5.60 (1H, m, vinylic CH), 4.04 (1H, br m, CH$_2$CHOCH$_2$), 3.94 (1H, ddd, J = 11.2, 7.1, 5.6 Hz, CH$_2$CH$_2$OCH), 3.62 (1H, dt, J = 9.8, 3.7 Hz, CH$_2$CH_2-OCH), 2.22 (1H, m, CH_2OCH), 1.9 (1H, m, CH_2OCH), 1.4 (4H, br m, CH$_3$CH_2CH_2CH), 0.90 (3H, t, J = 7.1 Hz, CH_3). ^{13}C NMR: δ 130.5, 124.4, 73.6, 63.4, 37.5, 25.3, 18.4, 14.1. Anal. Calcd for $C_8H_{14}O$: C, 76.14; H, 11.18. Found: C, 76.25; H, 11.07.

Proof of Absolute Stereochemistry for Recovered 22. An authentic sample of the nonracemic starting material was prepared by converting the requisite enantiomerically enriched (1:2) allylic alcohol (prepared by Sharpless's kinetic resolution procedure[15b]) to the corresponding diene. Subsequent diene metathesis was performed according to the procedure reported by Grubbs.[5] A similar procedure was carried out for **24** and **26** (Table 2).

(*R*)-3-Ethyl-*trans*-4-octen-1-ol (23).[22] IR (KBr): 3341 (br, s), 2956 (s), 2935 (s), 2873 (s), 1463 (s), 1378 (s), 1059 (s), 1021 (s), 969 (s) cm^{-1}. ^{1}H NMR: δ 5.40 (1H, dt, J = 15.1, 6.6 Hz, vinylic CHCH$_2$), 5.12 (1H, ddt, J = 15.1, 9.0, 1.2 Hz, vinylic CHCH), 3.63 (2H, m, CH_2OH), 1.96 (3H, m, allylic CH and allylic CH_2), 1.2−1.7 (6H, br m, CH$_3$CH_2CH_2 and CH$_3$CH_2CH), 0.88 (3H, t, J = 7.3 Hz, CH_3), 0.84 (3H, t, J = 7.3 Hz, CH_3). ^{13}C NMR: δ 134.2, 131.0, 61.5, 41.7, 40.0, 34.6, 28.4, 22.7, 13.6, 11.6. Anal. Calcd for $C_{10}H_{20}O$: C, 76.86; H, 12.90. Found: C, 76.81; H, 12.87.

(*R*)-2-Isobutyl-5,6-dihydro-2*H*-pyran (24). IR (KBr): 2958 (s), 2924 (s), 2869 (m), 2360 (s), 2342 (m), 1088 (m) cm^{-1}. ^{1}H NMR: δ 5.82 (1H, ddt, J = 10.2, 4.9, 2.0 Hz, vinylic CHCHO), 5.62 (1H, dt, J = 10.2 Hz, 1.7 Hz, vinylic CHCH$_2$), 4.13 (1H, m, allylic CHO), 3.97 (1H, ddd, J = 10.5, 4.9, 2.0 Hz, CH$_2$CH_2O), 3.67 (1H, ddd, J = 11.2, 9.8, 4.2 Hz, CH$_2$CH_2O), 2.30 (1H, m, allylic CH_2CH$_2$O), 1.85 (2H, m, allylic CH_2CH$_2$O and CH$_3$CHCH$_3$), 1.50 (1H, m, CHCH_2CH), 1.25 (1H, m, CHCH_2CH), 0.94 (3H, d, J = 1.2 Hz, CH_3), 0.92 (3H, d, J = 1.2 Hz, CH_3). ^{13}C NMR: δ 131.0, 124.2, 72.0, 63.3, 44.4, 31.6, 25.4, 24.4, 23.4, 22.7, 22.1, 14.1. Anal. Calcd for $C_9H_{16}O$: C, 77.09; H, 11.50. Found: C, 77.18, H, 11.24.

(*R*)-3-Ethyl-7-methyl-*trans*-4-octen-1-ol (25). IR (KBr): 3330 (br, m), 2957 (s), 2928 (s), 1463 (m), 1061 (m), 970 (m) cm^{-1}. ^{1}H NMR: δ 5.38 (1H, dt, J = 15.0, 7.1 Hz, vinylic CHCH$_2$), 5.10 (1H, ddt, J =

(22) For proof of stereochemistry of **22**−**25**, see the supporting information for ref 1a.

15.0, 9.0, 1.2 Hz, vinylic C*H*CH), 3.62 (2H, br dt, J = 6.0, 6.0 Hz, CH_2OH), 1.95 (1H, m, allylic C*H*), 1.88 (2H, dd, J = 6.5, 6.5 Hz, allylic CH_2), 1.2−1.7 (5H, br m, CH_2CH$_2$OH, CH$_3$CH_2, and CH$_3$C*H*CH$_3$), 0.87 (3H, d, J = 6.8 Hz, CH_3), 0.84 (3H, d, J = 7.3 Hz, CH_3). ^{13}C NMR: δ 135.2, 130.0, 61.4, 42.0, 41.7, 38.0, 28.5, 22.3, 22.2, 11.7. Anal. Calcd for $C_{11}H_{22}O$: C, 77.58; H, 13.02. Found: C, 77.64; H, 12.70.

(*S*)-2-Cyclohexyl-5,6-dihydro-2*H*-pyran (26). IR (KBr): 2924 (s), 2851 (s), 1450 (m), 1089 (s), cm^{-1}. ^{1}H NMR: δ 5.85 (1H, m, vinyl C*H*CH$_2$), 5.66 (1H, ddt, J = 10.5, 2.7, 1.0 Hz, vinylic C*H*CHO), 3.96 (1H, br dd, J = 11.0, 4.6 Hz, allylic C*H*O), 3.86 (1H, m, CH_2O), 3.62 (1H, dt, J = 10.5, 3.7 Hz, CH_2O), 2.26 (2H, m, allylic CH_2), 1.9−1.0 (10H, br m, aliphatic). ^{13}C NMR: δ 129.0, 125.1, 78.2, 63.7, 42.7, 28.7, 28.1, 26.6, 26.3 (2C), 25.5. Anal. Calcd for $C_{11}H_{18}O$: C, 79.46; H, 10.92. Found: C, 79.46; H, 10.57.

((*R*)-3-Ethyl-5-hydroxy-*trans*-1-pentene-1-yl)cyclohexane (27). IR (KBr): 3330 (br), 2924 (s), 2852 (s), 1449 (m), 1057 (m), 968 (m) cm^{-1}. ^{1}H NMR: δ 5.37 (1H, dd, J = 15.4, 6.8 Hz, vinyl CH), 3.63 (2H, dt, J = 10.3, 5.6 Hz, CH$_2$OH), 1.9 (2H, m, allylic CH and C*H*CH$_2$-CH$_3$), 1.8−1.0 (14H, m, aliphatic), 0.83 (3H, t, J = 7.3 Hz, CH$_2$CH_3). ^{13}C NMR: δ 137.4, 131.5, 61.7, 41.9, 40.7, 38.0, 33.3, 28.5, 26.2, 26.0, 11.6. Anal. Calcd for $C_{13}H_{24}O$: C, 79.53; H, 12.32. Found: C, 79.35; H, 12.09.

(*R*)-2-*n*-Hexyl-5,6-dihydro-2*H*-pyran (28). ^{1}H NMR: δ 5.81 (1H, m, vinyl CH), 5.64 (1H, m, vinylic CH), 4.03 (1H, m, CHC*H*O), 3.96 (1H, ddd, J = 11.2, 5.6, 3.2 Hz, CH$_2$CH_2OCH), 3.67 (1H, m, CH$_2$CH_2-OCH), 2.27 (1H, m, allylic CH), 1.90 (1H, m, allylic CH), 1.58−1.21 (10H, m, aliphatic CH), 0.87 (3H, t, J = 6.6 Hz, CH$_3$). ^{13}C NMR: δ 130.6, 124.4, 73.9, 63.5, 35.4, 31.8, 29.7, 29.4, 25.4, 22.6, 14.1. Anal. Calcd for $C_{11}H_{20}O$: C, 78.51; H, 11.98. Found: C, 78.50; H, 11.88.

(*R*)-3-Ethyl-*trans*-4-undecen-1-ol (29). IR (KBr): 3326 (br, s), 2957 (m), 2925 (s), 2872 (m), 2854 (m), 1460 (m), 1375 (w), 1059 (s) 1016 (w), 968 (s) cm^{-1}. ^{1}H NMR: δ 5.41 (1H, dt, J = 15.4, 6.6 Hz, vinyl CH), 5.13 (1H, ddt, J = 15.1, 10.2, 1.2 Hz, vinyl CH), 3.64 (2H, m, CH$_2$CH_2OH), 1.97 (3H, m, allylic CH), 1.21−1.70 (12H, m, aliphatic CH), 0.88 (3H, t, J = 5.13 Hz, CH$_3$), 0.84 (3H, t, J = 7.3 Hz, CH$_2$CH_3); ^{13}C NMR: δ 134.0, 131.3, 61.6, 41.8, 38.0, 32.5, 31.7, 29.6, 28.9, 28.5, 22.6, 14.0, 11.6. Anal. Calcd for $C_{13}H_{26}O$: C, 78.72; H, 13.21. Found: C, 78.76; H, 13.12.

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Supporting Information Available: Representative GLC, ^{1}H NMR, and spectral data for products or recovered starting materials (9 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, can be ordered from the ACS, and can be downloaded from the Internet; see any current masthead page for ordering information and Internet access instructions.

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