Asymmetric Ring-Closing Metathesis Catalyzed by Chiral Molybdenum Alkylidene Complexes

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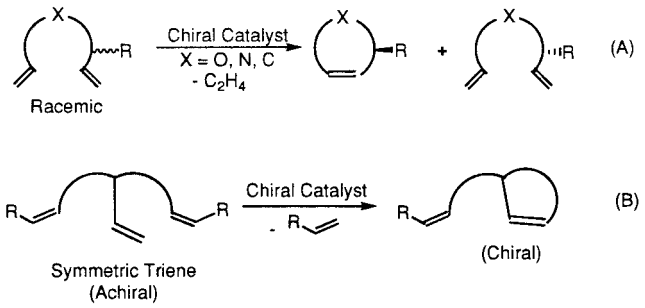
Kinetic resolution was observed in ring-closing metathesis of racemic dienes catalyzed by the newly developed chiral molybdenum alkylidene complexes (*R*,*R*)-Mo(CHCMe$_2$Ph)(NAr)(TBEC) **1** (Ar = 2,6-*i*-Pr$_2$C$_6$H$_3$, TBEC = 2′,2′,2″,2″-tetrakis(trifluoromethyl)-1,2-bis(2′-hydroxyethyl)cyclopentane) and (*R*,*R*)-Mo(CHCMe$_2$Ph)(NAr)(TBEH) **2** (Ar = 2,6-*i*-Pr$_2$C$_6$H$_3$, TBEH = 2′,2′,2″,2″-tetrakis(trifluoromethyl)-1,2-bis(2′-hydroxyethyl)cyclohexane). In the case of a prochiral symmetric triene substrate, optically active cyclized product was formed by catalytic ring-closing metathesis with **1**, which opens the possibility of a new version of two-directional synthesis. Although the observed enantiomeric excesses were modest to low, this data demonstrates the feasibility of asymmetric induction by chiral alkylidene catalysts in ring-closing metathesis.

Introduction

Olefin metathesis reactions catalyzed by well-defined group VI metal alkylidene complexes have made significant progress in recent years.[2] These processes are widely used in polymer synthesis such as ring-opening metathesis polymerization (ROMP)[3] and acyclic diene metathesis polymerization (ADMET).[4] For organic synthesis, ring-closing metathesis (RCM) has become a new powerful strategy for constructing various cyclic structures.[5] Though detailed studies on these reactions have been carried out, an asymmetric version of this reaction remains a significant challenge.[6] The kinetic resolution of racemic dienes (A in Scheme 1) and the asymmetric cyclization of symmetric prochiral trienes (B in Scheme 1) represent two approaches to asymmetric ring-closing metathesis. We have recently reported the first example of the kinetic resolution of racemic dienes catalyzed by new chiral molybdenum alkylidene complex (*R*,*R*)-Mo(CHCMe$_2$Ph)(NAr)(TBEC) (**1**, Ar = 2,6-*i*-Pr$_2$C$_6$H$_3$, TBEC = 2′,2′,2″, 2″-tetrakis(trifluoromethyl)-1,2-bis(2′-hydroxyethyl)cyclopentane).[7] This proved the principle that chiral catalysts could differentiate the rate of cyclization of the enantiomers. In this paper we present a full account of our studies of this system as well as several other results in this new area of asymmetric RCM.

Scheme 1



(1) Present address: Ube Laboratory, Ube Industries, Ltd., 1978-5 Kogushi, Ube, Yamaguchi 755, Japan.

(2) Molybdenum: (a) Schrock, R. R.; Murdzek, J. S.; Bazan, G. C.; Robbins, J.; DiMare, M.; O'Regan, M. *J. Am. Chem. Soc.* **1990**, *112*, 3875−3886. (b) Bazan, G. C.; Oskam, J. H.; Cho, H.-N.; Park, L. Y.; Schrock, R. R. *J. Am. Chem. Soc.* **1991**, *113*, 6899−6907. (c) Bazan, G. C.; Schrock, R. R.; Cho, H.-N.; Gibson, V. C. *Macromolecules* **1991**, *24*, 4495−4502. (d) Fox, H. H.; Yap, K. B.; Robbins, J.; Cai, S.; Schrock, R. R. *Inorg. Chem.* **1992**, *31*, 2287−2289. (e) Schrock, R. R. *Strem Chemiker* **1992**, *14*, 1−6. Tungsten: (f) Schrock, R. R.; DePue, R. T.; Feldman, J.; Schaverien, C. J.; Dewan, J. C.; Liu, A. H. *J. Am. Chem. Soc.* **1988**, *110*, 1423−1435. (g) Schrock, R. R.; DePue, R. T.; Feldman, J.; Yap, K. B.; Yang, D. C.; Davis, W. M.; Park, L.; DiMare, M.; Schofield, M.; Anhaus, J.; Walborsky, E.; Evitt, E.; Kruger, C.; Betz, P. *Organometallics*, **1990**, *9*, 2262−2275. (h) Aguero, A.; Kress, J.; Osborn, J. A. *J. Chem. Soc., Chem. Commun.* **1985**, 793−794. (i) Couturier, J.; Paillet, C.; Leconte, M.; Basset, J. M.; Weiss, K. *Angew. Chem., Int. Ed. Engl.* **1992**, *31*, 628−631. (j) Johnson, L. K.; Grubbs, R. H.; Ziller, J. W. *J. Am. Chem. Soc.* **1993**, *115*, 8130−8145. (k) Van der Schaaf, P. A.; Abbenhuis, R. A.; Van der Noort, W. P. A.; De Graaf, R.; Grove, D. M.; Smeets, W. J. J.; Spek, A. L.; Van Koten, G. *Organometallics* **1994**, *13*, 1433−1444.

(3) For leading references, see: (a) Breslow, D. S. *Prog. Polym. Sci.* **1993**, *18*, 1141−1195. (b) Ivin, K. J. *Olefin Metathesis*; Academic Press: London, 1983. (c) Grubbs, R. H.; Tumas, W. *Science* **1989**, *243*, 907−915. (d) Grubbs, R. H. In *Comprehensive Organic Synthesis*; Trost, B. M., Ed.; Pergamon: New York, 1991; Vol. 8, pp 499−551.

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(6) Applications of chiral metathesis catalysts are found only in the stereoregulation of ring-opening metathesis polymerization: (a) McConville, D. H.; Wolf, J. R.; Schrock, R. R. *J. Am. Chem. Soc.* **1993**, *115*, 4413−4414. (b) O'Dell, R.; McConville, D. H.; Hofmeister, G. H.; Schrock R. R. *J. Am. Chem. Soc.* **1994**, *116*, 3414−3423.

(7) Fujimura, O.; Grubbs, R. H., *J. Am. Chem. Soc.* **1996**, *118*, 2499−2500.

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(10) For the example of intramolecular ring-closing reaction of *cis*-1,2-bis(iodomethyl)cyclohexane by tBuLi to form cis-fused bicyclo-[4.2.0]octane, see: Bailey, W. F.; Gagnier, R. P. *Tetrahedron Lett.* **1982**, *23*, 5123.

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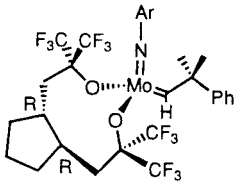
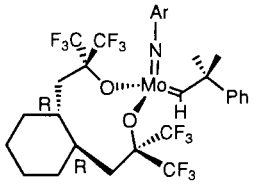
Results and Discussion

Ligands and Catalysts Synthesis. In addition to the previously reported (*R*,*R*)-MoTBEC **1**,[7,8] we synthesized a new chiral molybdenum alkylidene complex (*R*,*R*)-MoTBEH **2**.

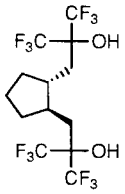


1, (R,R)-MoTBEC

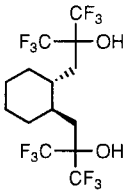


2, (R,R)-MoTBEH

(Ar=2,6-*i*-$Pr_2C_6H_3$)



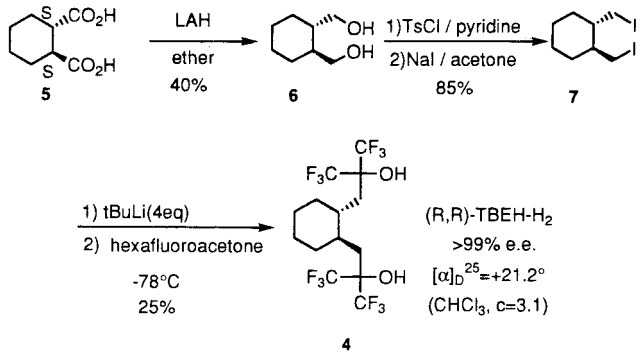
3, (R,R)-TBEC-H_2



4, (R,R)-TBEH-H_2

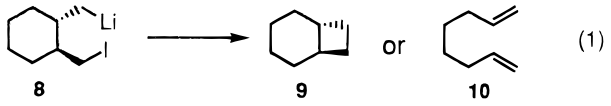
The new ligand (1*R*,2*R*)-2′,2′,2″,2″-tetrakis(trifluoromethyl)-1,2-bis(2′-hydroxyethyl)cyclohexane (**4**, TBEH-H_2) is a cyclohexane analogue of TBEC-H_2 **3** and was synthesized from readily available optically pure (1*S*,2*S*)-cyclohexanedicarboxylic acid **5**[9] by the conventional transformations shown in Scheme 2. Optically pure (1*R*,2*R*)-TBEH-H_2 was thus obtained.

Scheme 2



5 **6** **7** **4**

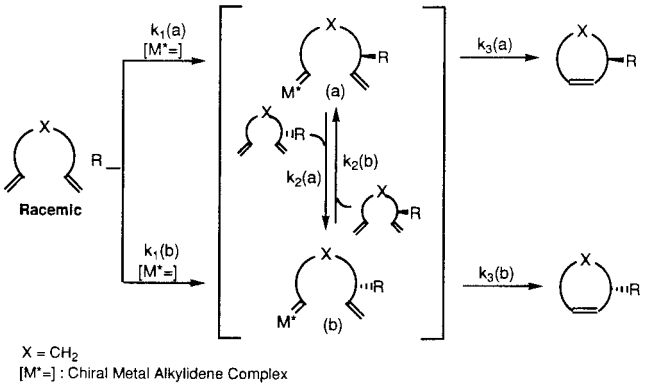
The low yield for the last step is probably due to intramolecular cyclization of the intermediate **8** to form bicyclo[4.2.0]octane **9** (mw = 110) (eq 1).[10] GC-MS analysis of the crude reaction of the last step showed the existence of a compound which has a molecular weight of 110. This bicyclic compound is strained and might rearrange to 1,7-octadiene **10** (mw = 110).[11]

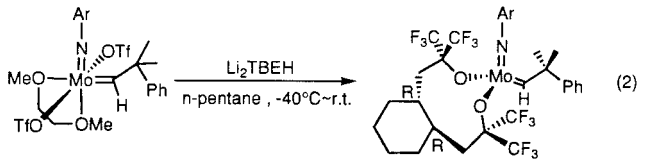


8 **9** or **10** (1)

The corresponding chiral molybdenum alkylidene complex (*R*,*R*)-Mo(CHCMe$_2$Ph)(NAr)(TBEH) **2** was synthesized in good yield by the reaction of the dilithium alkoxide of TBEH-H_2 and Mo(CHCMe$_2$Ph)(NAr)(OTf)$_2$dme (**11**, Ar = 2,6-(*i*-Pr)$_2$C$_6$H$_3$)[12] in ether at −40 °C. The complex was isolated as a brown, yellow solid in 92% yield (eq 2).

Scheme 3





11 **2** (2)

Complex **2** can be stored under N_2 at low temperature (−10 °C) for several months without any decomposition. Even in benzene solution at ambient temperature, **2** is stable for more than one month suggesting stabilization by the chelating diol ligands.

The two methyl groups of the neophylidene are inequivalent in **2**. The ^{13}C NMR chemical shift of these methyl groups are δ = 31.4 and 30.5, respectively. This implies differentiation of the two faces of the metal−carbon double bond by the chiral ligand.

Kinetic Resolution of Racemic Dienes. (1) Five-Membered Ring Formation. As shown in Scheme 3, RCM consists of three steps. The first step is assumed to be irreversible due to evaporative loss of the volatile olefins. The second step is interconversion of the intermediates a and b, and the third is cyclization. We presumed the third step (ring-closing step) to be suitable for asymmetric induction, as this step involves diastereomeric cyclic transition states that would likely be of different energies. Thus, if k_3(a) and k_3(b) are sufficiently different and slower than k_2(a) and k_2(b), kinetic resolution could be observed.

For the substrates, we chose dienes which contain a trisubstituted olefin moiety to slow the cyclization step as well as to control the site of first metathesis.[13] The results are shown in Table 1.

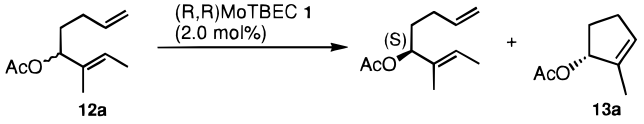
When racemic (6*E*)-5-acetoxy-6-methyl-1,6-octadiene (**12a**) was treated with 2.0 mol % of **1** at 25 °C in benzene, ring-closing metathesis reaction was observed and gave a cyclized product **13a** (Table 1, entry 1). The reaction was quenched after 20 min at which time 90% of **12a** was consumed. The unreacted **12a** (10%) was recovered,

(11) *Advanced Organic Chemistry*; March, J., Ed.; Wiley: New York, 1985; Chapter 18, p 1039 and references cited there in.

(12) Oskam, J. H.; Fox, H. H.; Yap, K. B.; McConville, D. H.; O'Dell, R.; Lichtenstein, B. J.; Schrock, R. R. *J. Organomet. Chem.* **1993**, *459*, 185−198.

(13) The first metathesis occurs in the following order: (1) monosubstituted olefin, (2) disubstituted olefin, (3) trisubstituted olefin, see ref 5f.

Table 1. Kinetic Resolution of 12a Catalyzed by (*R*,*R*)-MoTBEC 1



entry	solvent	temp (°C)	time (min)	conversion of **12a** (%)[a,b]	ee of recvd **12a**[14] (%)	config[15] of recvd **12a**
1	benzene	rt	20	90	84	*S*
2	THF	rt	60	51	34	*S*
3	toluene	0	3	21	19	*S*
4		0	10	46	29	*S*
5		0	20	59	34	*S*
6		0	90	62	40	*S*
7		0	480	90	78	*S*

[a] Mass balance (yield of **13a** + recovery of **12a**), 85−95%. [b] Determined by ^{1}H NMR.

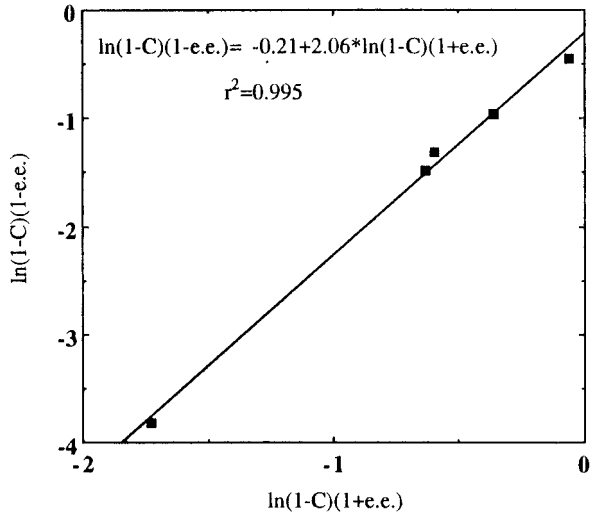


Figure 1. Plot of the ln(1 − *C*)(1 − ee) vs ln(1 − *C*)(1 + ee), taken from Table 1, entries 3−7.

and the enantiomer excess was determined to be 84%.[14] The configuration was determined to be the *S* isomer.[15] The reaction rate was slower with the coordinating solvent THF, but the efficiency of the kinetic resolution remained at the same level (Table 1, entry 2).

The progress of the reaction can be followed by lowering the reaction temperature by using toluene as solvent (entries 3−7). From these results, the relative rate k_{rel} = k_3(fast)/k_3(slow) was calculated to be 2.06 according to the following equation (eq 3),

$$k_{rel} = \frac{\ln(1 - C)(1 - ee)}{\ln(1 - C)(1 + ee)} \qquad (3)$$

where C = conversion of starting material, and ee is the enantiomeric excess of the remaining starting material (Figure 1).[16]

Next, we studied the effect of the substitution pattern of the double bond of the substrate. The results are shown in Table 2. As we expected, removing one methyl group (i.e. change the trisubstituted double bond of **12a** to disubstituted double bond **12b**,**c**) resulted in complete loss of asymmetric induction.

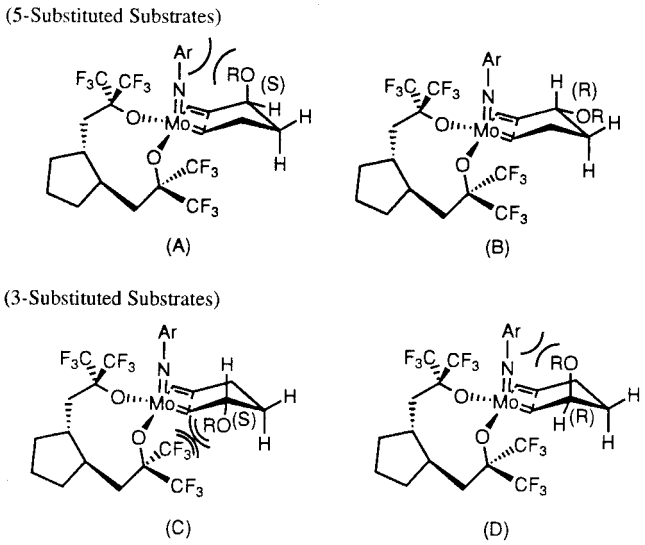


Figure 2. Proposed models for five-membered ring formation.

In Scheme 3, we believe the first and second steps are nonstereoselective steps and the third cyclization step is the key to the asymmetric induction.[17] Kinetic resolution could be realized in the case where the cyclization step is slower than the interconversion of intermediates a and b (k_2(a,b) > k_3(a,b)) but not in the case where the cyclization step becomes faster than the interconversion (k_2(a,b) < k_3(a,b)). By changing the substitution, the rates for the ring-closing step could become much faster in **12b**,**c** than in **12a**. We assume in **12a**, k_2(a,b) are greater than k_3(a,b) and kinetic resolution was observed. On the other hand, in **12b**,**c**, kinetic resolution was not observed since k_3(a,b) are greater than or equal to k_2(a,b).

Table 3 shows the effect of changing the protecting group and the location of the stereocenter of the substrates. Changing the protecting group to a noncoordinating triethylsilyl group resulted in an acceleration of the reaction. At 0 °C, **12d** completely cyclized in 90 min to give **13d** quantitatively (Table 3, entry 2). The kinetic resolution of **12d** could be carried out at −20 °C, but efficiency and configuration remained same as the acetate-protected substrate **12a** (Table 3, entry 3). By changing the position of the triethylsiloxy group from the 5- to the 3-position, the reaction rate decreased significantly at −20 °C (Table 3, entry 4), so the kinetic resolution of **12e** was carried out at 0 °C (Table 3, entry 5), and a slight decrease of the efficiency of the resolution was observed relative to the result for **12a** at same level of conversion (46% conversion, 29% ee, Table 1, entry 4). In the case of **12f**, the reaction did not proceed due to the stable six-membered intramolecular chelation of the acetate carbonyl to the molybdenum metal center of the intermediate complex produced by the first metathesis.[5b]

Taking these results into consideration, our working models for five-membered ring formation are shown in

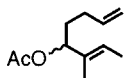
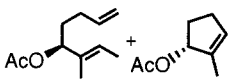
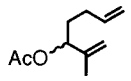
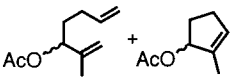
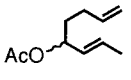
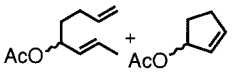
(14) **12a** and **13a** could not be separated by column chromatography. After determination of the ratio of **12a** and **13a** of the reaction mixture by ^{1}H NMR, these compounds were hydrolyzed, separated, and converted to the Mosher ester to determine the ee. See Experimental Section for details.

(15) The absolute configuration of recovered **12a** was determined after derivatization to the Mosher ester and comparison to a sample of known absolute configuration (synthesized by the Sharpless kinetic resolution). See experimental section for details.

(16) Balavoine, G.; Moradpour, A.; Kagan, H. B. *J. Am. Chem. Soc.* **1974**, *96*, 5152−5158. See also ref 23.

(17) There is a possibility for asymmetric induction in these steps. However these metathesis are occurring at the monosubstituted olefin of the substrates (see ref 13) and in this case, the asymmetric centers of the substrates are located too far from the catalyst to cause asymmetric induction.

Table 2. The Effect of the Double Bond Substitution Pattern of the Substrates[a,b]

entry	substrate	products	solvent	temp /time(min)	conversion of **12** (%)[c]	unreacted subst. config.[d], e.e.(%)[e]
1	 **12a**	 **13a**	toluene	0°C / 10	46	S, 29
2	 **12b**	 **13a**	toluene	0°C / 10	52	racemic
3	 **12c**	 **13c**	toluene	0°C / 10	54	racemic

[a] 2.0 mol% (R,R)-MoTBEC was used.
[b] Mass balance (yield of cyclic product+recovery of substrate), >90% Determined by ^{1}H NMR
[d] Determined by synthesis of enantiomerically enriched allyl alcohol by the Sharpless kinetic resolution and derivatization to the Mosher ester.
[e] Determined by ^{1}H NMR of Mosher ester derivatized after deprotection.

Figure 2.[18] In the case of the substrates which have a stereocenter at 5-position, the (*S*)-isomer has a steric interaction between the pseudoaxial 5-substituent and the bulky imido ligand (A). On the other hand, the (*R*)-isomer does not have such an interaction (B). Therefore the (*R*)-isomer is consumed faster than the (*S*)-isomer, resulting in (*S*)-enriched unreacted substrate.

Applying the same model to the substrates which have stereocenter at the 3-position, the (*R*)-isomer has steric interaction between the pseudoaxial 3-substituent and the bulky imido ligand (D), but the (*S*)-isomer appears to have more severe steric repulsion between the pseudoequatorial 3-substituent and the TBEC ligand (C). Thus, kinetic resolution can be realized due to the relatively faster consumption of the (*R*)-isomer (i.e. recovery of (*S*)-enriched substrate). This also explains the observed differences in the kinetic resolution of the 3-substituted substrates (i.e. slow conversion and lower degree of asymmetric induction relative to the corresponding 5-substituted substrate).

(2) Six-Membered Ring Formation. Kinetic resolution was also observed for the substrates which ring-close to form six-membered ring cyclized products. The results are shown in Table 4.

Presumably due to the slower rate of ring closure for six-membered ring relative to the analogous five-membered rings, [19] kinetic resolution was observed in **12g**, a substrate which possesses a disubstituted olefin instead of trisubstituted olefin (entry 1). Interestingly, the enantioselectivity was opposite to that of the analogous five-membered ring case. For six-membered ring formation, the (*R*)-*enriched* unreacted substrates were recovered (entries 1, 2). Figure 3 shows proposed models for six-membered ring-closure. The (*S*)-isomer has its 6-substituent in a pseudoequatorial position in its chairlike transition state (A), whereas the (*R*)-isomer has the substituent in a pseudoaxial position which causes steric destabilization. Thus the (*S*)-isomer was consumed faster and the (*R*)-enriched substrate was recovered.

(3) The Results of Ligand Variation. Kinetic resolution was also observed in the ring-closing metathesis of **12a** catalyzed by the newly developed chiral molybdenum alkylidene complex (*R,R*)-MoTBEH **2**. The results are shown in Table 5.

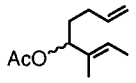
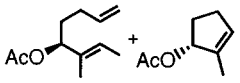
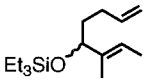
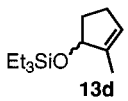
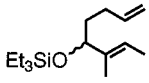
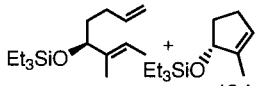
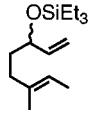
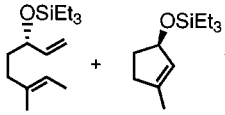
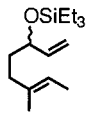
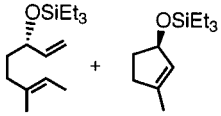
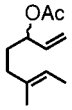
Both catalysts showed the same trend in stereoselectivity, but **2** was much less reactive when compared to **1**. It is notable that the slight change in the ligand structure affected the efficiency of the kinetic resolution. At the same level of the substrate conversion, **2** shows a far lower degree of kinetic resolution than **1**. The reason for the reactivity difference is not clear, but it is obvious that the reactivity and efficiency of the asymmetric induction can be altered by subtle changes in ligand design.

Asymmetric Cyclization of a Prochiral Triene. Asymmetric cyclization of prochiral symmetric trienes (B in Scheme 1) are a variation of two-directional chain synthesis.[20]

For the preliminary study, we designed the substrate triene **14** with the following considerations in mind. (1) Two disubstituted olefins were chosen for the symmetric chains to ensure that the first metathesis is with the desired central olefin. (2) According to the previous results, a disubstituted double bond provides sufficient steric bulk to ensure the asymmetric induction in six-membered ring closure. (3) The disubstituted double bonds will prevent secondary metathesis (more complicated analysis) after cyclization to give **15** since the dimerization of **15** will form a tetrasubstituted olefin which is unlikely (Scheme 4).[21]

(18) Similar conformational models are proposed in intramolecular Ziegler−Natta alkene insertion reactions. See: (a) Young, J. R.; Stille, J. R. *Organometallics* **1990**, *9*, 3022−3025. (b) *Idem. J. Am. Chem. Soc.* **1992**, *114*, 4936−4937. (c) Barta, N. S.; Kirk, B. A.; Stille, J. R. *J. Am. Chem. Soc.* **1994**, *116*, 8912−8919.
(19) Fujimura, O.; Grubbs, R. H., unpublished results.
(20) Poss, C. S.; Schreiber, S. L. *Acc. Chem. Res.* **1994**, *27*, 9−17.
(21) The synthesis of tetrasubstituted olefins by metathesis is much slower than the formation of less substituted double bonds in acyclic cross metathesis. Grubbs, R. H., unpublished results.

Table 3. The Effect of Protecting Group and Position of Stereocenter[a,b]

entry	substrate	products	solvent	temp /time(min)	conversion of **12** (%)[c]	unreacted subst. config.[d], e.e.(%)[e]
1	 **12a**	 **13a**	toluene	0°C / 90	62	S, 40
2	 **12d**	 **13d**	toluene	0°C / 90	100	NA
3	 **12d**	 **13d**	toluene	-20°C / 660	72	S, 48
4	 **12e**	 **13e**	toluene	-20°C / 600	10	ND[f]
5	 **12e**	 **13e**	toluene	0°C/ 20	46	S, 22
6	 **12f**		toluene	0°C/ 20	No Reaction	ND[f]

[a] 2.0 mol% (R,R)-MoTBEC was used.
[b] Mass balance (yield of cyclic product+recovery of substrate), >90% .
[c] Determined by ^{1}H NMR.
[d] Determined by synthesis of enantiomerically enriched allyl alcohol by the Sharpless kinetic resolution and derivatization to the Mosher ester.
[e] Determined by ^{1}H NMR of Mosher ester derivatized after deprotection.
[f] Not determined.

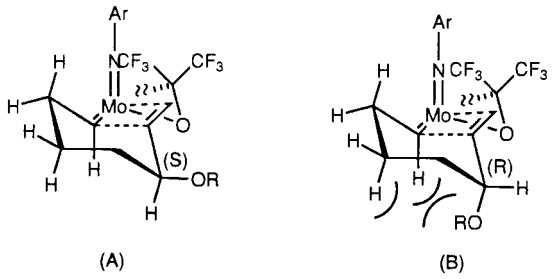


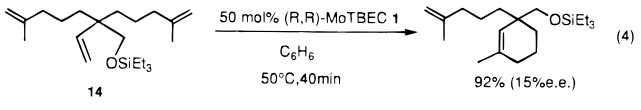
Figure 3. Partial structures of proposed reaction models for six-membered ring formation.

The triene **14** was synthesized by the procedure shown in Scheme 5.

The iodide **17** was synthesized in two steps from the corresponding alcohol **16**, synthesized according to the method of Ganem.[22] The double alkylation of the dienolate generated from ethyl crotonate by **17** gave the α,α-dialkylated ester which was successively transformed into the alcohol **18**. Protection of **18** by the triethylsilyl group afford the desired triene **14**.

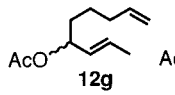
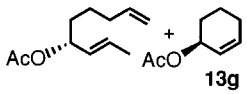
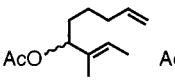
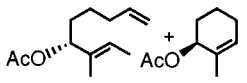
At first, to establish the reaction conditions, **14** was cyclized with catalytic amounts of Mo(CHCMe$_2$Ph)(NAr)-(OCMe(CF$_3$)$_2$)$_2$ (**19**, Ar = *i*Pr$_2$C$_6$H$_3$).[2a,5a–c] The reaction was extremely slow when carried out at rt (less than 1% conversion in 60 min). When heated to 50 °C, the reaction proceeded to afford the cyclized product **15** as the sole product. No dimeric product was formed. Due to the high reaction temperature, large amounts of the catalyst (50 mol %) were required to complete the reaction.

Next **14** was treated with 50 mol % of (*R,R*)-MoTBEC **1** at 50 °C. The reaction proceeded cleanly to give **15** in 92% isolated yield (eq 4). Again, no dimeric product was observed. The isolated **15** was deprotected and converted to the Mosher ester in quantitative yield which had an enantiomer excess of 15%.



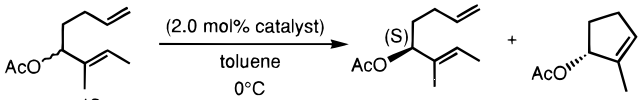
(22) Eis, M. J.; Wrobel, J. E.; Ganem, B. *J. Am. Chem. Soc.* **1984**, *106*, 3693–3694.

Table 4. (*R,R*)-MoTBEC-Catalyzed Kinetic Resolution in Six-Membered Ring Formation[a,b]

entry	substrate	products	solvent	temp /time(min)	conversion of **3** (%)[c]	unreacted subst. config.[d], e.e.(%)[e]
1	 **12g**	 **13g**	toluene	0°C/ 90	67	R, 22
2	 **12h**	 **13h**	toluene	0°C/ 120	64	R, 26

[a] 7.0 mol% (R,R)-MoTBEC was used.
[b] Mass balance (yield of cyclic product+recovery of substrate), >90% .
[c] Determined by ^{1}H NMR.
[d] Determined by synthesis of enantiomerically enriched allyl alcohol by the Sharpless kinetic resolution and derivatization to the Mosher ester.
[e] Determined by ^{1}H NMR of Mosher ester derivatized after deprotection.

Table 5. The Effect of the Ligand



entry	catalyst	time (min)	conversion of **12a** (%)[a,b]	ee of recvd **12a**[c] (%)	config[d] of recvd **12a**
1	**1**	3	21	19	*S*
2	**2**	10	20	6	*S*
3	**1**	10	46	29	*S*
4	**2**	90	33	10	*S*
5	**1**	90	62	40	*S*
6	**2**	510	65	24	*S*

[a] Mass balance (yield of **13a** + recovery of **12a**), 85−95%. [b] Determined by ^{1}H NMR. [c] Determined by ^{1}H NMR of Mosher ester derivatized as follows. Hydrolysis of **12a**, then formation of Mosher ester. [d] Determined by synthesis of enantiomerically enriched allyl alchol by Sharpless kinetic resolution and derivatization to Mosher ester.

The observed enantiomeric excess demonstrated the possibility of asymmetric RCM (desymmetrization) of trienes.

Conclusion

The chiral molybdenum alkylidene complexes (*R,R*)-MoTBEC **1** and (*R,R*)-MoTBEH **2** catalyzed asymmetric ring-closing metathesis. When racemic dienes are treated with these catalysts, the kinetic resolution was observed both in five- and six-membered ring formation. The prochiral triene was also asymmetrically cyclized by the (*R,R*)-MoTBEC **1**. Although the degree of asymmetric induction about these reactions were still low, these findings demonstrate the potential of asymmetric ring-closing metathesis by chiral alkylidene catalysts. Improvements in the efficiency of asymmetric induction will require the design and the development of new chiral ligands and catalysts.

Experimental Section

General Methods. Standard techniques were used for spectroscopic analysis and solvent purification.[8] Ethyl crotonate and hexamethylphosporamide were both dried over CaH_2 and distilled, respectively. (*R,R*)-TBEC-H_2 and (*R,R*)-MoTBEC were prepared according to the reference.[8]

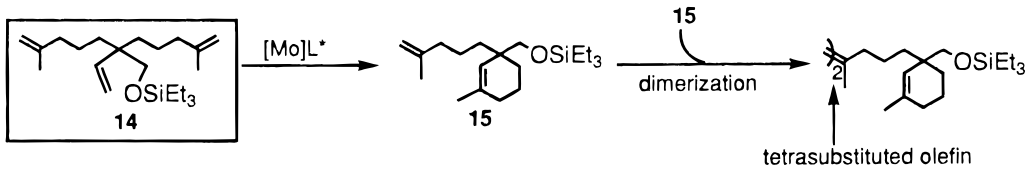
(1*S*,2*S*)-1,2-Bis{hydroxymethyl}cyclohexane (6). (1*S*,2*S*)-cyclohexanedicarboxylic acid **5** [9] (5.8 g, 33 mmol) in dry ether (100 mL) was added dropwise to lithium aluminum hydride (2.5 g, 67 mmol) suspended in dry ether (200 mL) (under argon), over a 1 h period. After stirring for 2 h at ambient temperature, the reaction mixture was cooled to 0 °C, and water (2.5 mL) was added carefully, followed by the addition of 15% NaOH aq (2.5 mL) and water (7.5 mL). The reaction mixture was then heated to reflux for 5 min and cooled to room temperature. The white precipitate was filtered, and the filtrate was concentrated in vacuo. Flash chromatography (EM reagents silica gel 60, 230−400 mesh, hexane/EtOAc = 1/1 to EtOAc) yielded 2.0 g (40%) of **6** as white solid.

(1*S*,2*S*)-1,2-Bis(hydroxymethyl)cyclohexane (6): IR (thin film) 3318, 2926, 2853, 1447, 1382, 1269, 1209, 1092, 1007, 988, 967, 713 cm^{-1}; ^{1}H NMR (300 MHz, C_6D_6) δ 4.79 (s, 2H), 3.60−3.49 (m, 4H), 67−1.54 (m, 2H), 1.54−1.43 (m, 2H), 1.33−1.28 (m, 2H), 1.27−1.02 (m, 2H), 1.01−0.82 (m, 2H); ^{13}C NMR (75 MHz, C_6D_6) δ 67.7, 44.9, 30.1, 26.4; $[\alpha]^{25}_D = -20.8°$ (c = 1.3, $CHCl_3$); mass spectrum (CI, NH_3) m/z (relative intensity): 162 (M + NH_4^+, 20), 145 (100), 127 (15), 109 (30), 95 (28), 81 (20), 67 (14), 54 (8); HRMS, m/z calcd for $C_8H_{17}O_2$ (M + H^+): 145.1229, found: 145.1226.

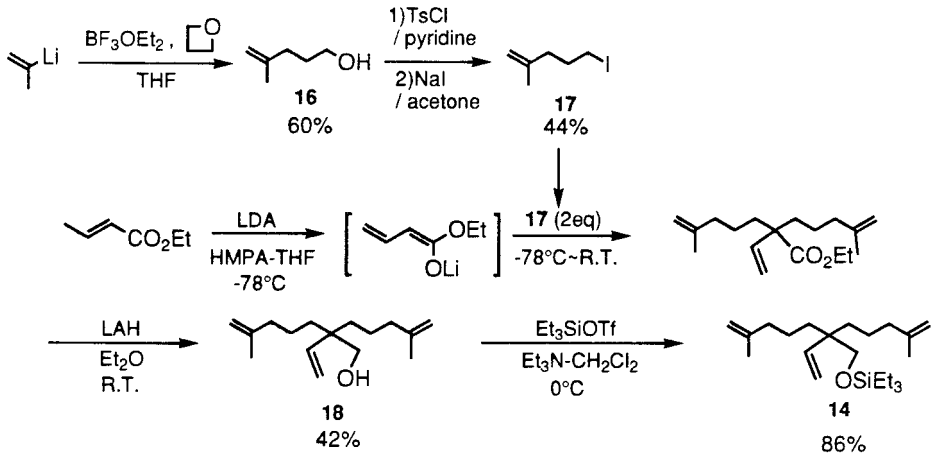
(1*S*,2*S*)-1,2-Bis(iodomethyl)cyclohexane (7). To **6** (1.8 g, 13 mmol) in pyridine (36 mL) was added tosyl chloride (6.5 g, 34 mmol) portionwise at 0 °C. The reaction mixture was warmed to room temperature and stirred for 18 h. Water was added (300 mL), and the mixture was extracted with AcOEt (100 mL × 3). The extracts were combined, washed with saturated aqueous $CuSO_4$, dried over $MgSO_4$, and concentrated in vacuo. The solid thus obtained (5.0 g) was dissolved in acetone (70 mL), NaI (10.0 g, 67 mmol) was added, and the mixture was heated to reflux. The reaction mixture was stirred at the same temperature for 18 h and then cooled to room temperature. Water (500 mL) was added, and the mixture was extracted with *n*-hexane (150 mL × 3). The *n*-hexane extracts were washed with saturated aqueous $Na_2S_2O_3$ solution, dried over $MgSO_4$, and concentrated in vacuo. Flash chromatography (EM reagents silica gel 60, 230−400 mesh, hexane) yielded 3.8 g (85%) of **7** as white solid.

(1*S*,2*S*)-1,2-Bis(iodomethyl)cyclohexane (7): IR (thin film) 2922, 2852, 1446, 1418, 1291, 1240, 1173, 1058, 850 cm^{-1}; ^{1}H NMR (300 MHz, C_6D_6) δ 2.83 (dd, J = 10.3, 4.5, 2H), 2.71 (dd, J = 10.3, 1.7, 2H), 1.50−1.44 (m, 2H), 1.41−1.20 (m, 2H), 1.17−0.90 (m, 4H,), 0.56−0.42 (m, 2H); ^{13}C NMR (75 MHz, C_6D_6) δ 41.2, 32.4, 25.6, 15.4; $[\alpha]^{25}_D = +53.8°$ (c = 2.7, $CHCl_3$); mass spectrum (EI) m/z (relative intensity): 364 (M^+, 16), 237

Scheme 4



Scheme 5



(86), 127 (31), 109 (100), 81 (25), 67 (54), 55 (29); HRMS, *m*/*z* calcd for $C_8H_{14}I_2$ (M^+): 363.9185, found: 363.9195.

(1*R*,2*R*)-2′,2′,2″,2″-Tetrakis(trifluoromethyl)-1,2-bis(2′-hydroxyethyl)cyclohexane [(*R*,*R*)-TBEH-H$_2$] (4). To diiodide **7** (3.3 g, 9.0 mmol) in dry ether (180 mL) was added a solution of *tert*-butyllithium in pentane (1.7 M, 21 mL, 36 mmol) dropwise at −78 °C under argon and stirred for 5 min. To the stirring reaction mixture was introduced excess hexafluoroacetone via a long hypodermic needle which penetrated the liquid surface. The reaction mixture turned a pale yellow color and was then allowed to warm to room temperature. To the reaction mixture was added 1 M aqueous hydrochloric acid solution (300 mL), and the mixture was extracted with ether (150 mL × 3). The ether extracts were dried over $MgSO_4$ and concentrated in vacuo. Flash chromatography (EM reagents silica gel 60, 230−400 mesh, hexane/EtOAc = 10/1) yielded 0.98 g (25%) of **4** as white crystal. The enantio excess were determined as >99% ee (no other enantiomer observed) by GLC with a CHIRASIL-VAL (25 m × 0.25 mm) chiral column by Alltech Assoc., Inc. (At column temperature 110 °C, retention time for (1*R*,2*R*)-**4** was 56 min and (1*S*,2*S*)-**4** was 54 min.)

(1*R*,2*R*)-2′,2′,2″,2″-Tetrakis(trifluoromethyl)-1,2-bis(2′-hydroxyethyl)cyclohexane [(*R*,*R*)-TBEH-H$_2$] (1*R*,2*R*)-4: IR (neat) 3604, 3443 (br), 2936, 2863, 1714, 1454, 1210, 1044, 957, 719, 670 cm^{-1}; ^{1}H NMR (300 MHz, C_6D_6) δ 2.64 (s, 2H,), 2.09 (d, J = 14.8, 2H), 1.68 (dd, J = 14.8, 2.3, 2H), 1.60−1.49 (m, 4H), 1.28−1.12 (m, 2H), 1.08−0.90 (m, 2H), 0.89−0.67 (m, 2H); ^{13}C NMR (75 MHz, C_6D_6) δ 123.8 (q, J_{CF} = 288.4), 76.6 (sept, J_{CCF} = 28.6), 35.1, 33.1, 32.6, 24.3; $[\alpha]^{25}_D$ = +21.2° (c = 3.1, $CHCl_3$); mass spectrum (EI) *m*/*z* (relative intensity): 444 (M^+, 5), 406 (25), 263 (100), 249 (12), 236 (20), 221 (31), 207 (50), 69 (59); HRMS, *m*/*z* calcd for $C_{14}H_{16}O_2F_{12}$ (M^+): 444.0959, found: 444.0967.

Preparation of Dilithium Alkoxide of (*R*,*R*)-TBEC-H$_2$. A solution of *n*-butyllithium in hexane (1.6 M, 2.24 mL, 3.4 mmol) was added dropwise to a stirred *n*-pentane (15 mL) solution of (1*R*,2*R*)-**4** (750 mg, 1.7 mmol) at 0 °C under argon. The reaction mixture was stirred for 3 h, and the solvent was removed to yield 720 mg (93%) of a white solid. The dilithium alkoxide is pure (^{1}H NMR spectra). No residual n-BuLi nor free OH was observed.

(*R*,*R*)-TBEH-Li$_2$: ^{1}H NMR (300 MHz, THF-d_8) δ 2.15−1.60 (m, 6H), 1.60−1.35 (m, 2H), 1.35−1.00 (m, 4H), 1.00−0.80 (m, 2H).

(*R*,*R*)-Mo(CHCMe$_2$Ph)(NAr)TBEH (Ar = 2,6-(*i*-Pr)$_2$C$_6$H$_3$) (2). Mo(CHCMe$_2$Ph)(NAr)(OTf)$_2$dme (**11**, Ar = 2,6-(*i*-Pr)$_2$C$_6$H$_3$)[12] (1.32 g, 1.67 mmol) was suspended in dry *n*-pentane (40 mL). To this heterogeneous mixture was added (*R*,*R*)-TBEH-Li$_2$ (760 mg, 1.67 mmol) in dry *n*-pentane (30 mL) at −40 °C. The reaction was allowed to warm to room temperature and stirred for 3 h. The lithium triflate precipitated was removed by filtration through Celite, and the filtrate was evaporated to dryness in vacuo to give a orange yellow solid 1.30 g (92%). The solid thus obtained was virtually pure according to ^{1}H, ^{13}C NMR spectra and elemental analysis.

(*R*,*R*)-Mo(CHCMe$_2$Ph)(NAr)TBEC [Ar = 2,6-(*i*-Pr)$_2$C$_6$H$_3$)]-2: ^{1}H NMR (300 MHz, C_6D_6) δ 12.38 (s, 1H, C*H*CMe$_2$Ph), 7.26 (d, J = 8.3, 2H, arom), 7.12 (dd, J = 7.8, 7.8, 2H, arom), 7.02−6.93 (m, 4H, arom), 3.68 (septet, J = 6.8, 2H), 2.25−1.88 (m, 6H), 1.73 (s, 3H), 1.59 (s, 3H), 1.35−1.10 (m, 4H), 1.25 (d, J = 6.8, 12H), 0.95−0.75 (m, 4H); ^{13}C NMR (75 MHz, C_6D_6) δ 291.5, 154.7, 148.4, 147.8, 129.4, 128.5, 126.5, 126.2, 123.4, 85.4 (sept, J_{CCF} = 27.6, 83.1 (sept, J_{CCF} = 28.0), 56.5, 35.0, 34.2, 36.6, 32.0, 31.4, 30.5, 29.3, 29.0, 26.7, 26.4, 23.6, 21.3, 21.0. Anal. Calcd for $C_{36}H_{43}O_2NF_{12}Mo$: C, 51.13; H, 5.13; N, 1.66. Found: C, 51.71; H, 5.30; N, 1.73.

A Typical Experimental Procedure for Chiral Molybdenum Alkylidene Complex Catalyzed Kinetic Resolution. (6*E*)-5-Acetoxy-6-methyl-1,6-octadiene (**12a**) (53 mg, 0.29 mmol) in 1.5 mL of dry toluene was cooled to 0 °C and then added to a homogeneous yellow solution of **1** (5 mg, 0.006 mmol) in 1.5 mL of dry toluene under argon at 0 °C. The resulting mixture was stirred at 0 °C for 90 min. The reaction was then quenched by exposure to air with simultaneous addition of methanol (0.2 mL). The reaction mixture was stirred for 15 min prior to concentration. Flash chromatography (EM reagents silica gel 60, 230−400 mesh, hexane/EtOAc = 100/0∼20/1) yielded 42 mg of the mixture containing 23 mg of cyclized product **13a** and 19 mg of unreacted **12a** (determined by ^{1}H NMR). Mass balance 92%, conversion of **12a** 62% (unreacted **12a**:**13a** = 38:62). Unreacted **12a** was determined to be (*S*)-enriched and 40% ee. (The methods of ee and configuration determination are described below.)

Determination of ee of the Recovered Substrates. (a) 12a−c,g,h. In the cases of acetoxy-substituted substrates **12a−c**,**g**,**h**, unreacted substrates and their cyclized products could not be separated by column chromatography. After determination of the ratio of unreacted substrates and cyclized products by ^{1}H NMR of reaction mixture, these compounds

were hydrolyzed (K_2CO_3 (10 equiv)/MeOH-H_2O (2:1), rt, 12 h) and separated. The dienols were converted to their Mosher esters to determine the ee ((*S*)-(+)-MTPACl (1.4 equiv), pyridine, rt 16 h). In both hydrolysis and Mosher ester formation, reaction completion was confirmed by thin-layer chromatography prior to workup.

(b) 12d,e. In the cases of triethylsiloxy-substituted substrates **12d**,**e**, unreacted substrates and their cyclized products were separated by column chromatography. Unreacted **13d**,**e** were deprotected (^{n}Bu$_4$NF (1.0 equiv)/THF, rt, 1 h) and the resulting dienols were derived to Mosher esters to determine the ee ((*S*)-(+)-MTPACl (1.4 equiv), pyridine, rt, 16 h). In both deprotection and Mosher ester formation, reaction completion was confirmed by thin-layer chromatography prior to workup.

Determination of Stereocenter Configuration. (*R*)-Enriched dienols were prepared according to the kinetic resolution procedure of Sharpless.[23] These alcohols were converted to the Mosher esters ((*S*)-(+)-MTPACl (1.4 equiv), pyridine, rt, 16 h) and compared with the Mosher ester derived from recovered **12** by ^{1}H NMR.

Hydrolyzed Product from Recovered 12a. (*S*)-(6*E*)-6-Methyl-1,6-octadien-5-ol: IR (neat) 3353 (br), 2936, 1671, 1641, 1445, 1381, 1303, 1056, 1004, 910, 829 cm^{-1}; ^{1}H NMR (300 MHz, C_6D_6) δ 5.79 (ddt, J = 17.1, 10.3, 6.6, 1H), 5.34 (qq, J = 6.6, 1.1, 1H), 5.04 (ddt, J = 17.1, 2.0, 2.0, 1H), 4.96 (ddt, J = 10.3, 2.0, 1.3, 1H), 3.87 (t, J = 6.6, 1H), 2.15 (s, 1H), 2.20−1.94 (m, 2H), 1.72−1.48 (m, 2H), 1.51 (dd, J = 1.1, 1.1, 3H), 1.49 (d, J = 6.6, 3H); ^{13}C NMR (75 MHz, C_6D_6) δ 138.9, 138.6, 120.1, 114.6, 77.2, 34.5, 30.6, 13.0, 11.0; mass spectrum (CI, NH_3) *m*/*z* (relative intensity): 158 (MNH_4^+, 3), 140 (82), 123 (100), 98 (2), 81 (4); HRMS, *m*/*z* calcd for $C_9H_{20}NO$ (MNH_4^+): 158.1545, found: 158.1543.

Hydrolyzed Product from Cyclized Product 13a. 2-Methyl-2-cyclopenten-1-ol: IR (neat) 3333 (br), 2938, 2855, 1660, 1454, 1315, 1164, 1054, 1031, 973, 824 cm^{-1}; ^{1}H NMR (300 MHz, C_6D_6) δ 5.29 (m, 1H), 4.33 (m, 1H), 2.24−2.11 (m, 1H), 2.10−1.89 (m, 2H), 1.66 (s, 3H), 1.57−1.48 (m, 1H), 0.85 (s, 1H); ^{13}C NMR (75 MHz, C_6D_6) δ 142.5, 127.3, 79.6, 34.4, 29.9, 13.7; mass spectrum (EI) *m*/*z* (relative intensity): 98 (M^+, 60), 83 (100), 80 (40), 69 (30), 55 (50), 41 (57); HRMS, *m*/*z* calcd for $C_6H_{10}O$ (M^+): 98.0732, found: 98.0729.

Recovered 12d. (*S*)-(6*E*)-6-Methyl-5-(triethylsiloxy)-1,6-octadiene (12d): IR (neat) 2954, 2877, 1671, 1642, 1456, 1415, 1239, 1073, 1005, 910, 742 cm^{-1}; ^{1}H NMR (300 MHz, C_6D_6) δ 5.82 (ddt, J = 17.0, 10.3, 6.6, 1H), 5.37 (qq, J = 6.6, 0.8, 1H), 5.07 (ddt, J = 17.0, 1.9, 1.9, 1H), 4.98 (ddt, J = 10.3, 1.9, 1.2, 1H), 4.02 (t, J = 6.6, 1H), 2.20−1.96 (m, 2H), 1.81−1.69 (m, 1H), 1.65−1.55 (m, 1H), 1.58 (dd, J = 1.1, 1.1, 3H), 1.49 (dd, J = 6.7, 0.9, 3H), 1.01 (t, J = 7.9, 9H,), 0.62 (q, J = 7.9, 6H, ^{13}C NMR (75 MHz, C_6D_6) δ 139.0, 138.6, 120.0, 114.6, 78.3, 35.9, 30.5, 13.0, 10.8, 7.2, 5.3; mass spectrum (CI, CH_4) *m*/*z* (relative intensity): 253 ($M-H^+$, 10), 225 (100), 199 (65), 123 (65), 103 (17), 81 (9); HRMS, *m*/*z* calcd for $C_{15}H_{29}OSi$ ($M - H^+$): 253.1988, found: 253.1990.

Cyclized Product 13d. 1-Methyl-5-(triethylsiloxy)cyclopentene (13d): IR (neat) 2956, 2877, 1456, 1353, 1239, 1086, 1004, 994, 743 cm^{-1}; ^{1}H NMR (300 MHz, C_6D_6) δ 5.36 (m, 1H), 4.54−4.50 (m, 1H), 2.36−2.22 (m, 1H), 2.14−1.95 (m, 2H), 1.75 (s, 3H), 1.75−1.69 (m, 1H), 1.01 (t, J = 7.9, 9H), 0.61 (q, J = 7.9, 6H); ^{13}C NMR (75 MHz, C_6D_6) δ 142.7, 126.5, 79.9, 35.0, 30.0, 14.0, 7.2, 5.3; mass spectrum (CI, CH_4) *m*/*z* (relative intensity): 211 ($M - H^+$, 20), 183 (100), 161 (5), 115 (15), 103 (62), 81 (92); HRMS, *m*/*z* calcd for $C_{12}H_{23}OSi$ ($M - H^+$): 211.1518, found: 211.1512.

Recovered 12e. (*S*)-(6*E*)-6-Methyl-3-(triethylsiloxy)-1,6-octadiene (12e): IR (neat) 2954, 2877, 1671, 1645, 1456, 1416, 1239, 1089, 1007, 920, 743 cm^{-1}; ^{1}H NMR (300 MHz, C_6D_6) δ 5.81 (ddd, J = 16.7, 10.3, 6.1, 1H), 5.34−5.23 (m, 1H), 5.15 (ddd, J = 16.7, 1.1, 0.6, 1H), 4.96 (ddd, J = 10.3, 0.6, 0.6, 1H), 4.07 (dt, J = 6.1, 6.1, 1H), 2.21−2.01 (m, 2H), 1.79−1.57 (m, 2H), 1.55 (s, 3H), 1.54 (d, J = 6.3, 3H), 1.02 (t, J = 7.9, 9H), 0.62 (q, J = 7.9, 6H); ^{13}C NMR (75 MHz, C_6D_6) δ 142.2, 135.7, 118.6, 113.7, 73.9, 37.1, 35.6, 15.8, 13.5, 7.2, 5.4; mass spectrum (CI, CH_4) *m*/*z* (relative intensity): 253 ($M - H^+$, 7), 225 (100), 213 (2), 185 (5), 171 (12), 123 (90), 103 (14), 81 (15); HRMS, *m*/*z* calcd for $C_{15}H_{29}OSi$ ($M - H^+$): 253.1988, found: 253.1985.

Cyclized Product 13e. 1-Methyl-3-(triethylsiloxy)cyclopentene (13e): IR (neat) 2955, 2876, 1660, 1456, 1359, 1238, 1156, 1058, 1007, 899, 840, 743 cm^{-1}; ^{1}H NMR (300 MHz, C_6D_6) δ 5.45 (dq, J = 1.6, 1.6, 1H), 4.87−4.84 (m, 1H), 2.31−2.19 (m, 1H), 2.19−2.07 (m, 1H), 1.97−1.79 (m, 2H), 1.57 (s, 3H), 1.03 (t, J = 7.9, 9H), 0.63 (q, J = 7.9, 6H); ^{13}C NMR (75 MHz, C_6D_6) δ 143.4, 128.9, 78.3, 35.3, 35.2, 16.7, 7.2, 5.4; mass spectrum (CI, CH_4) *m*/*z* (relative intensity): 213 (MH^+, 5), 183 (92), 161 (1), 133 (3), 103 (45), 81 (100); HRMS, *m*/*z* calcd for $C_{12}H_{25}OSi$ (MH^+): 213.1675, found: 211.1677.

Hydrolyzed Product from Recovered 12g. (*R*)-(7*E*)-1,7-nonadien-6-ol: IR (neat) 3353 (br), 2934, 2859, 1673, 1641, 1440, 1064, 994, 966, 910 cm^{-1}; ^{1}H NMR (300 MHz, C_6D_6) δ 5.76 (ddt, J = 17.1, 10.2, 6.7, 1H), 5.55−5.37 (m, 2H), 5.00 (ddt, J = 17.1, 1.7, 1.7, 1H), 4.95 (ddt, J = 10.2, 1.7, 0.9, 1H), 4.00−3.85 (m, 1H), 2.70 (s, 1H), 1.98 (dt, J = 6.7, 6.7, 2H), 1.54 (d, J = 5.6, 3H), 1.54−1.30 (m, 4H); ^{13}C NMR (75 MHz, C_6D_6) δ 139.0, 135.4, 125.5, 114.7, 72.7, 37.2, 34.1, 25.2, 17.1; mass spectrum (CI, NH_3) *m*/*z* (relative intensity): 140 (M^+, 100), 123 (75), 98 (2), 81 (10); HRMS, *m*/*z* calcd for $C_9H_{16}O$ (M^+): 140.1201, found: 140.1207.

Hydrolyzed Product from Cyclized Product 13g. 2-Cyclohexen-1-ol: ^{1}H NMR (300 MHz, C_6D_6) δ 5.70−5.62 (m, 1H), 5.61−5.54 (m, 1H), 4.02−3.92 (m, 1H), 1.81−1.39 (m, 5H), 1.38−1.20 (m, 1H), 0.89 (s, 1H). Identical with the authentic sample.

Hydrolyzed Product from Recovered 12h. (*R*)-(7*E*)-7-Methyl-1,7-nonadien-6-ol: IR (neat) 3353 (br), 2932, 2861, 1671, 1641, 1443, 1380, 1317, 995, 909, 829 cm^{-1}; ^{1}H NMR (300 MHz, C_6D_6) δ 5.76 (ddt, J = 17.0, 10.2, 6.7, 1H), 5.36 (q, J = 6.6, 1H), 5.01 (ddt, J = 17.0, 1.6, 1.6, 1H), 4.96 (ddt, J = 10.2, 1.6, 0.8, 1H), 3.87 (dd, J = 6.7, 5.5, 1H), 2.50 (s, 1H), 1.99 (td, J = 7.0, 6.7, 2H), 1.60−1.25 (m, 4H), 1.54 (s, 3H), 1.50 (d, J = 6.6, 3H); ^{13}C NMR (75 MHz, C_6D_6) δ 139.1, 138.8, 119.9, 114.7, 77.7, 34.8, 34.1, 25.6, 13.1, 11.0; mass spectrum (CI, NH_3) *m*/*z* (relative intensity): 155 (MH^+, 2), 137 (100), 111 (2), 95 (7), 81 (12), 69 (2); HRMS, *m*/*z* calcd for $C_{10}H_{19}O$ (MH^+): 155.1436, found: 155.1438.

Hydrolyzed Product from Cyclized Product 13h. 2-Methyl-2-cyclohexen-1-ol: IR (neat) 3354 (br), 2934, 1454, 1434, 1286, 1051, 960, 727 cm^{-1}; ^{1}H NMR (300 MHz, C_6D_6) δ 5.34 (s, 1H), 3.74 (m, 1H), 1.89−1.64 (m, 2H), 1.71 (s, 3H), 1.60−1.40 (m, 3H), 1.38−1.25 (m, 1H), 0.84 (s, 1H); ^{13}C NMR (75 MHz, C_6D_6) δ 136.1, 124.7, 68.2, 32.7, 25.7, 20.8, 18.7; mass spectrum (EI) *m*/*z* (relative intensity): 112 (M^+, 70), 97 (100), 84 (55), 83 (50), 69 (67), 55 (57), 43 (50), 41 (60); HRMS, *m*/*z* calcd for $C_7H_{12}O$ (M^+): 112.0888, found: 112.0890.

4-Methyl-4-penten-1-ol (16). To a solution of (1-methylvinyl)lithium[24] in ether (0.83 M, 100 mL, 83 mmol), was aded oxetane (4.6 g, 80 mmol) at −78 °C under argon. To the stirring reaction mixture was added BF_3OEt_2 (11.8 g, 83 mmol) dropwise. The reaction was exothermic. The reaction mixture was stirred for 5 min, and then saturated $NaHCO_3$ aqueous solution was added to quench the reaction. After addition of aqueous hydrochloric acid to the reaction mixture, it was extracted with ether (150 mL × 3). The ether extracts were dried over $MgSO_4$ and concentrated in vacuo. Flash chromatography (EM reagents silica gel 60, 230−400 mesh, hexane to hexane/EtOAc = 5/1) yielded 4.8 g (60%) of **16** as colorless oil.

4-Methyl-4-penten-1-ol (16): ^{1}H NMR (300 MHz, C_6D_6) d 4.80 (s, 2H), 3.75 (t, 2H, J = 6.8), 1.95 (t, J = 6.7, 2H), 1.65 (s, 3H), 1.50 (tt, J = 6.8, 6.7, 2H), 1.15 (br s, 1H).

5-Iodo-2-methyl-1-pentane (17). To **16** (3.6 g, 36 mmol) in pyridine (80 mL), was added tosyl chloride (15 g, 79 mmol)

(23) (a) Martin, V. S.; Woodard, S. S.; Katsuki, T.; Yamada, Y.; Ikeda, M.; Sharpless, K. B. *J. Am. Chem. Soc.* **1981**, *103*, 6237−6240. (b) *Catalytic Asymmetric Synthesis*; Ojima, I., Ed.; VCH: New York, 1993; chapter 4.1.

(24) Prepared from 2-bromopropene and lithium dispersion. See Bates, G. S.; Masamune S. *Org. Synth. 55*, 103−113.

portionwise at 0 °C. The reaction mixture was warmed to room temperature and stirred for 9 h. To the reaction mixture was added water (400 mL), and the mixture was extracted with AcOEt (120 mL × 3). The extracts were combined, washed with saturated aqueous $CuSO_4$, dried over $MgSO_4$, and concentrated in vacuo. The solid tosylate thus obtained was dissolved in acetone (200 mL), NaI (9.0 g, 60 mmol) was added, and the mixture was heated to reflux. The reaction mixture was stirred at the same temperature for 30 min and then cooled to room temperature. Water (500 mL) was added, and the mixture was extracted with *n*-hexane (150 mL × 3). The *n*-hexane extracts were washed with saturated aqueous $Na_2S_2O_3$ solution, dried over $MgSO_4$, and concentrated in vacuo. Flash chromatography (EM reagents silica gel 60, 230−400 mesh, hexane) yielded 3.3 g (44%) of **17** as a colorless oil.

5-Iodo-2-methyl-1-pentane (17): ^{1}H NMR (300 MHz, C_6D_6) δ 4.73 (s, 1H,), 4.66 (s, 1H), 2.66 (t, J= 7.0, 2H), 1.80 (t, J = 6.9, 2H), 1.55 (tt, J = 7.0, 6.9, 2H), 1.45 (s, 3H).

2, 2-Bis(4′-methyl-4′-pentenyl)-3-buten-1-ol (18). To a THF solution of LDA (0.26 M, 45 mL, 12 mmol) cooled to −78 °C was added hexamethylphosporamide (2.0 mL, 11.6 mmol), and the mixture was stirred for 5 min. To the reaction mixture was added ethyl crotonate (0.66 g, 5.8 mmol) dropwise, and the solution was stirred at −78 °C for additional 60 min. The iodide **17** (2.4 g, 11.6 mmol) in THF (15 mL) was added to the reaction mixture which was allowed to warm to room temperature and stir for 15 h. To the reaction mixture was added saturated aqueous NH_4Cl solution, and the mixture was extracted with ether (50 mL × 3). The ether extracts were combined and dried over $MgSO_4$ and concentrated in vacuo. The crude product was dissolved in ether (15 mL) and added dropwise to an $LiAlH_4$ (0.4 g, 10 mmol) suspension in ether (35 mL). After stirring for 1 h at ambient temperature, the reaction mixture was cooled to 0 °C, and water 0.4 mL was added carefully, followed by the addition of 15% NaOH aq (0.4 mL) and water (1.2 mL). The white precipitate was filtered, and the filtrate was concentrated in vacuo. Flash chromatography (EM reagents silica gel 60, 230−400 mesh, hexane to hexane/EtOAc = 10/1) yielded 580 mg (42%) of **18** as colorless oil.

2,2-Bis(4′-methyl-4′-pentenyl)-3-buten-1-ol (18): ^{1}H NMR (300 MHz, C_6D_6) δ 5.48 (dd, J = 17.1, 11.1, 1H), 5.01 (dd, J = 11.1, 1.3, 1H), 4.88 (dd, J = 17.8, 1.3, 1H), 4.81 (s, 2H), 4.80 (s, 2H), 3.25 (d, J = 5.8, 2H), 1.94 (t, J = 6.2, 4H), 1.64 (s, 6H), 1.45−1.20 (m, 8H), 0.75 (t, J = 5.8, 1H).

3,3-Bis(4′-methyl-4′-pentenyl)-4-(triethylsiloxy)-1-butene (14). To alcohol **18** (580 mg, 2.4 mmol) in dichloromethane (10 mL) was added triethylamine (0.54 g, 5.3 mmol), and the solution was cooled to 0 °C. Triethylsilyl triflate (0.70 g, 2.6 mmol) was added dropwise to the reaction mixture and stirred for 30 min at 0 °C. To the reaction mixture was added saturated aqueous NH_4Cl solution (50 mL), and the mixture was extracted with *n*-hexane (30 mL × 3). The *n*-hexane extracts were combined, dried over $MgSO_4$, and concentrated in vacuo. Flash chromatography (EM reagents silica gel 60, 230−400 mesh, hexane) yielded 722 mg (86%) of **14** as colorless oil.

3,3-Bis(4′-methyl-4′-pentenyl)-4-(triethylsiloxy)-1-butene (14): IR (neat) 3075, 2940, 2877, 1651, 1456, 1416, 1374, 1239, 1097, 1006, 886, 821, 741 cm^{-1}; ^{1}H NMR (300 MHz, C_6D_6) δ 5.68 (dd, J = 17.9, 11.2, 1H), 5.08 (dd, J = 11.2, 1.4, 1H), 4.95 (dd, J = 17.9, 1.4, 1H), 4.84 (s, 2H), 4.82 (s, 2H), 3.51 (s, 2H), 2.00 (t, J = 6.4, 4H), 1.68 (s, 6H), 1.52−1.38 (m, 8H), 1.01 (t, J = 7.9, 9H), 0.59 (q, J = 7.9, 6H); ^{13}C NMR (75 MHz, C_6D_6) δ 145.8, 144.5, 113.1, 110.5, 66.8, 44.3, 38.9, 34.7, 22.4, 21.9, 7.1, 4.8; mass spectrum (EI) *m*/*z* (relative intensity): 350 (M^+, 2), 321 (20), 211 (20), 171 (20), 149 (20), 135 (25), 117 (100), 103 (68), 93 (15), 81 (16); HRMS, *m*/*z* calcd for $C_{22}H_{42}OSi$ (M^+): 350.3005, found: 350.3012.

Asymmetric Ring-Closing Metathesis of 14 Catalyzed by 1. 1 (24 mg, 0.029 mmol) was dissolved in dry benzene (0.4 mL). Triene **14** (20 mg, 0.057 mmol) in dry benzene (0.4 mL) was added to the catalyst solution. The reaction mixture was stirred at 50 °C for 40 min. The reaction was quenched by the addition of MeOH (0.2 mL) and concentrated in vacuo. Flash chromatography (EM reagents silica gel 60, 230−400 mesh, hexane) yielded 17 mg (92%) of 1-methyl-3-(4′-methyl-4′-pentenyl)-3-[(triethylsiloxy)methyl]cyclohexene (**15**) as a colorless oil. The enantiomeric excess of **15** was determined to be 15% after deprotection (^{n}Bu$_4$NF (1.0 equiv)/ THF, rt, 1 h) and formation of Mosher ester ((*S*)-(+)-MTPACl (1.4 equiv), pyridine, rt 16 h). In both deprotection and Mosher ester formation, reaction completion was confirmed by thin-layer chromatography prior to workup.

1-Methyl-3-(4′-methyl-4′-pentenyl)-3-[(triethylsiloxy)methyl]cyclohexene (15): IR (neat) 3074, 2937, 2876, 1651, 1456, 1415, 1375, 1238, 1089, 1007, 886, 814, 741 cm^{-1}; ^{1}H NMR (300 MHz, C_6D_6) δ 5.29 (s, 1H), 4.85 (s, 1H), 4.82 (s, 1H), 3.46 (d, J = 9.5, 1H), 3.39 (d, J = 9.5, 1H), 2.10−1.98 (m, 2H), 1.82−1.75 (m, 2H), 1.68 (s, 3H), 1.63 (s, 3H), 1.70−1.30 (m, 8H), 1.02 (t, J = 8.0, 9H), 0.61 (q, J = 8.0, 6H); ^{13}C NMR (75 MHz, C_6D_6) δ 146.0, 135.0, 127.2, 110.3, 68.9, 39.8, 39.1, 37.5, 30.6, 29.7, 24.3, 22.4, 22.3, 19.8, 7.1, 4.8; mass spectrum (CI, NH_3) *m*/*z* (relative intensity): 323 ($M + H^+$, 2), 293 (3), 267 (3), 239 (4), 205 (9), 191 (90), 177 (27), 135 (15), 121 (100), 109 (18), 95 (39), 84 (49); HRMS, *m*/*z* calcd for $C_{20}H_{39}OSi$ ($M + H^+$): 323.2770, found: 323.2773.

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Supporting Information Available: The proof of the absolute stereo configurations of the products and asymmetric induction in product **15** (23 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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