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Enantioselective Synthesis of Cyclic Enol Ethers and All-Carbon Quaternary Stereogenic Centers Through Catalytic Asymmetric Ring-Closing Metathesis

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Abstract: The first examples of catalytic asymmetric ring-closing metathesis (ARCM) reactions of enol ethers are reported. To identify the most effective catalysts, various chiral Mo- and Ru-based catalysts were screened. Although chiral Ru catalysts (those that do not bear a phosphine ligand) promote ARCM in some cases, such transformations proceed in <10% ee. In contrast, Mo-based alkylidenes give rise to efficient ARCM and deliver the desired products in the optically enriched form. Thus, Mo-catalyzed enantioselective transformations allow access to various five- and six-membered cyclic enol ethers in up to 94% ee from readily available achiral starting materials. The first examples of catalytic ARCM that lead to the formation of all-carbon quaternary stereogenic centers are also disclosed. Mechanistic models that offer a plausible rationale for the identity of major enantiomers as well as the observed levels of enantioselectivity are provided. Representative examples demonstrate that the enol ether moiety and the unreacted alkene of the ARCM products can be discriminated with excellent site selectivity (>98%).

Introduction

Research in these laboratories has, in recent years, led to the development of an assortment of Mo-[1] and Ru-based[2] precatalysts that can be used to promote olefin metathesis reactions; several examples of such complexes are illustrated in Scheme 1. One noteworthy aspect of our programs relates to chiral complexes that give rise to efficient enantioselective transformations. Within this context, the higher oxidation state (vs Ru-based) systems have proven to be particularly effective for asymmetric ring-closing metathesis (ARCM).[1,3,4] Mo-based complexes exhibit high reactivity (1−5 mol % loading) with reactions that involve substrates bearing allylic or homoallylic ethers or amines to deliver optically enriched unsaturated heterocycles (>90% ee).[1,3]

Enol ethers, a versatile class of compounds in organic chemistry, can participate in olefin metathesis reactions.[1,2] Nonetheless, particularly for electronic reasons, the reactivity of the derived Mo-alkylidenes and Ru-based carbenes can be significantly different than those derived from allylic or homoallylic ethers.[5] Metal-catalyzed ring-closing metathesis (RCM) has been used to access small and medium ring cyclic enol ethers,[6] and such protocols have been applied to the preparation of natural products.[7] In all the studies disclosed thus far, however, optically enriched enol ethers are obtained by treatment of a nonracemic substrate with an achiral Mo- or Ru-based

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(1) For a review on achiral and chiral Mo-based complexes and their related olefin metathesis reactions, see: Schrock; R. R.; Hoveyda, A. H. *Angew. Chem., Int. Ed.* **2003**, *42*, 4592−4633.

(2) (a) Kingsbury, J. S.; Harrity, J. P. A.; Bonitatebus, P. J.; Hoveyda, A. H. *J. Am. Chem. Soc.* **1999**, *121*, 791−799. (b) Garber, S. B.; Kingsbury, J. S.; Gray, B. L.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2000**, *122*, 8168−8179. For a comprehensive review on achiral and chiral Ru-based complexes developed in these laboratories and their related olefin metathesis reactions, see: (c) Hoveyda, A. H.; Gillingham, D. G.; Van Veldhuizen, J. J.; Kataoka, O.; Garber, S. B.; Kingsbury, J. S.; Harrity, J. P. A. *Org. Biomol. Chem.* **2004**, *2*, 8−23.

(3) For examples of Mo-catalyzed ARCM, see: (a) Alexander, J. B.; La, D. S.; Cefalo, D. R.; Hoveyda, A. H.; Schrock, R. R. *J. Am. Chem. Soc.* **1998**, *120*, 4041−4042. (b) La, D. S.; Alexander, J. B.; Cefalo, D. R.; Graf, D. D.; Hoveyda, A. H.; Schrock, R. R. *J. Am. Chem. Soc.* **1998**, *120*, 9720−9721. (c) Zhu, S. S.; Cefalo, D. R.; La, D. S.; Jamieson, J. Y.; Davis, W. M.; Hoveyda, A. H.; Schrock, R. R. *J. Am. Chem. Soc.* **1999**, *121*, 8251−8259. (d) Weatherhead, G. S.; Houser, J. H.; Ford, J. G.; Jamieson, J. Y.; Schrock, R. R.; Hoveyda, A. H. *Tetrahedron Lett.* **2000**, *41*, 9553−9559. (e) Cefalo, D. R.; Keily, A. F.; Wuchrer, M.; Jamieson, J. Y.; Schrock, R. R.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2001**, *123*, 3139−3140. (f) Kiely, A. F.; Jernelius, J. A.; Schrock, R. R.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2002**, *124*, 2868−2869. (g) Dolman, S. J.; Schrock, R. R.; Hoveyda, A. H. *Org. Lett.* **2003**, *5*, 4899−4902. (h) Jernelius, J. A.; Schrock, R. R.; Hoveyda, A. H. *Tetrahedron* **2004**, *60*, 7345−7351. (i) Sattely, E. S.; Cortez, G. A.; Moebius, D. C.; Schrock, R. R.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2005**, *127*, 8526−8533.

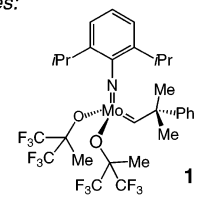
(4) For examples of Ru-catalyzed ARCM, see: (a) Seiders, T. J.; Ward, D. W.; Grubbs, R. H. *Org. Lett.* **2001**, *3*, 3225−3228. (b) Van Veldhuizen, J. J.; Kingsbury, J. S.; Garber, S. B.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2002**, *124*, 4954−4955. (c) Van Veldhuizen, J. J.; Gillingham, D. G.; Garber, S. B.; Kataoka, O.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2003**, *125*, 12502−12508. (d) Funk, T. W.; Berlin, J. M.; Grubbs, R. H. *J. Am. Chem. Soc.* **2006**, *128*, 1840−1846.

(5) Louie, J.; Grubbs, R. H. *Organometallics* **2002**, *21*, 2153−2164.

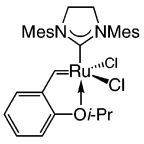
(6) For representative examples of cyclic enol ether synthesis through olefin metathesis reactions, see: (a) Fujimura, O.; Fu, G. C.; Grubbs, R. H. *J. Org. Chem.* **1994**, *59*, 4029−4031. (b) Sturino, C. F.; Wong, J. C. Y. *Tetrahedron Lett.* **1998**, *39*, 9623−9626. (c) Clark, J. S.; Kettle, J. G. *Tetrahedron* **1999**, *55*, 8231−8248. (d) Rainier, J. D.; Allwein, S. P.; Cox, J. M. *J. Org. Chem.* **2001**, *66*, 1380−1386. (e) Liu, L.; Postema, M. H. D. *J. Am. Chem. Soc.* **2001**, *123*, 8602−8603. (f) Sutton, A. E.; Seigal, B. A.; Finnegan, D. F.; Snapper, M. L. *J. Am. Chem. Soc.* **2002**, *124*, 13390−13391. (g) Hekking, K. F. W.; van Delft, F. L.; Rutjes, F. P. J. T. *Tetrahedron* **2003**, *59*, 6751−6758.

Scheme 1. Representative Achiral and Chiral Metal Complexes

Achiral complexes:

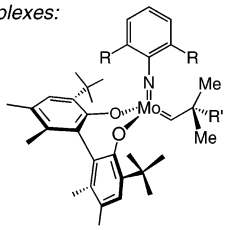


1

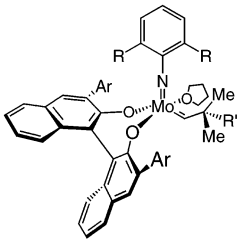


2

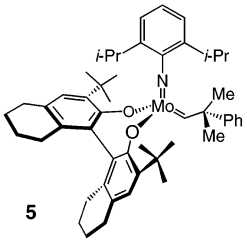
Chiral complexes:



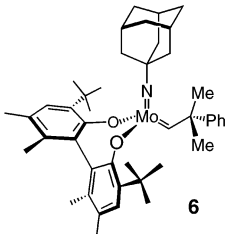
3a R = *i*-Pr R' = Ph
3b R = Me R' = Ph
3c R = Cl R' = Me



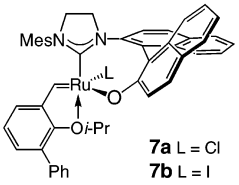
4a R = *i*-Pr R' = Ph
4b R = Me R' = Ph
4c R = Cl R' = Me



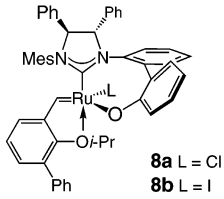
5



6



7a L = Cl
7b L = I



8a L = Cl
8b L = I

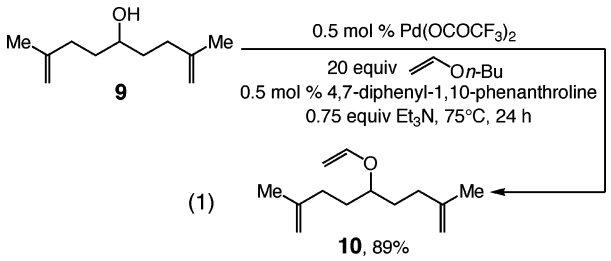
Mes = 2,4,6-$Me_3C_6H_2$, Ar = 2,4,6-(*i*-Pr)$_3C_6H_2$.

complex. A strategically unique and valuable, but thus far unexplored, alternative would be to access optically enriched cyclic enol ethers through ARCM of achiral substrates.

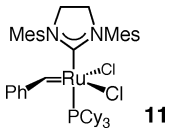
Herein, we report the first examples of catalytic enantioselective olefin metathesis reactions of enol ethers, leading to the formation of five- and six-membered ring heterocycles in up to 94% ee. The present disclosure also contains the first instances of enantioselective syntheses of all-carbon quaternary stereogenic centers[8] through olefin metathesis.

Results and Discussion

a. Synthesis of Acyclic Enol Ether Substrates. To initiate our investigations, we prepared various acyclic unsaturated enol ethers (see Tables 1−3). A representative procedure is depicted in eq 1.[9] Treatment of bis(homoallylic) alcohol **9** with 0.5 mol % of commercially available $Pd(OCOCF_3)_2$ and 4,7-diphenyl-1,10-phenanthroline in the presence of 0.75 equiv Et_3N and 20 equiv *n*-butyl vinyl ether (75 °C, 24 h) leads to the formation of the desired **10** in 89% yield after silica gel chromatography (eluted with 1% Et_3N).



b. Preliminary Screening of Achiral Mo- and Ru-Based Olefin Metathesis Catalysts. We investigated the ability of Mo- and Ru-based complexes (e.g., Scheme 1) to promote RCM. These preliminary investigations (Table 1) indicated that Ru- and Mo-based catalysts efficiently initiate the reaction; however, studies involving some of the less facile RCM (e.g., **12**) suggested that Mo alkylidenes are somewhat more effective (compare entries 1−3, Table 1) and that phosphine-free **2**[2b] promotes RCM significantly more readily than the PCy_3-bearing second-generation Grubbs complex **11**[10] (compare entries 2−5 and 8−10, Table 1). Accordingly, we included the available chiral Mo-based alkylidenes as well as phosphine-free Ru-based carbenes (Scheme 1) in our investigations of catalytic ARCM of enol ethers.



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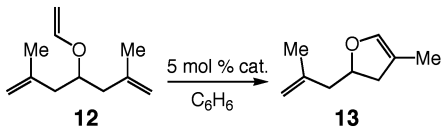
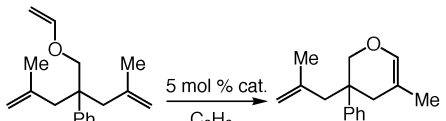
c. Mo-Catalyzed Enantioselective Synthesis of Tertiary Stereogenic Centers Through ARCM of Enol Ethers. As the data summarized in entries 1−2 of Table 2 indicate, secondary acyclic enol ethers **12** and **10**, in the presence of 5−10 mol % binaphthyl-based chiral Mo complex **4a** (see below for catalyst

Table 1. Preliminary Examination of the Reactivity of Achiral Mo- and Ru-Based Complexes[a]



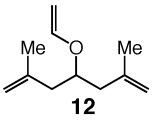
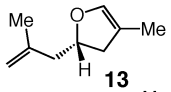
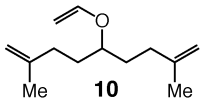
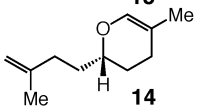
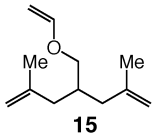
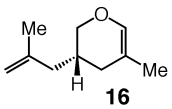
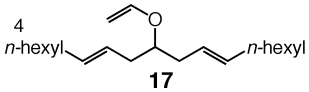
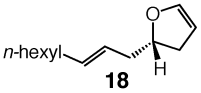
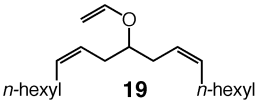
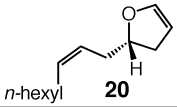


entry	catalyst	temp (°C)	time (h)	conv (%)[b]
1	**1**	22	3	>98
2	**2**	22	14	<2
3	**2**	65	1	88
4	**11**	22	14	5
5	**11**	65	1	19[c]
7	**1**	22	1	86
8	**2**	22	1	92
9	**11**	22	17	47
10	**11**	65	1	>98

[a] All reactions carried out under an atmosphere of N_2. [b] Conversions determined by 400 MHz ^{1}H NMR analysis of the unpurified product mixture. [c] 57% conv. after 4.5 h and 94% conv. after 14 h.

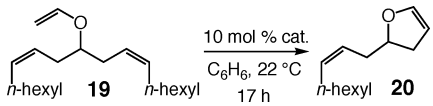
(7) For an example of enol ether RCM in natural product total synthesis, see: Oliver, S. F.; Hogenauer, K.; Simic, O.; Antonello, A.; Smith, M. D.; Ley, S. V. *Angew. Chem., Int. Ed.* **2003**, *42*, 5996−6000.
(8) For recent reviews of catalytic asymmetric methods for the formation of all-carbon quaternary stereogenic centers, see: (a) Denissova, I.; Barriault, L. *Tetrahedron* **2003**, *59*, 10105−10146. (b) Douglas, C. J.; Overman, L. E. *Proc. Natl. Acad. Sci.* **2004**, *101*, 5363−5367.
(9) Bosch, M.; Schlaf, M. *J. Org. Chem.* **2003**, *68*, 5225−5227.

Table 2. Enantioselective Synthesis of Tertiary Carbon Stereogenic Centers by Mo-Catalyzed ARCM of Enol Ethers[a]

entry	substrate	product	catalyst; mol %	solvent	time (h); temp (°C)	conv (%);[b] yield (%)[c]	ee (%)[d]
1	 **12**	 **13**	**4a**; 10	Et_2O	6; 22	90; 70[e]	90
2	 **10**	 **14**	**4a**; 5	*n*-pentane	24; 60	>98; >98	83
3	 **15**	 **16**	**4a**; 20	C_6H_6	24; 22	80; 40[e]	90
4	 **17**	 **18**	**3b**; 10	C_6H_6	20; 60[f]	86; 80	41
5	 **19**	 **20**	**3a**; 20	C_6H_6	19; 22	90; 80	62

[a] All reactions performed under N_2 atmosphere. [b] Conversions determined by analysis of the 400 MHz ^{1}H NMR spectra of unpurified mixtures. [c] Isolated yields after silica gel chromatography. [d] Enantioselectivities determined by chiral GLC analysis (see the Supporting Information for details). [e] Lower isolated yields are due to product volatility. [f] Lower conversion (68%) but identical ee is observed at 22 °C.

Table 3. Representative Data from Catalyst Screening Studies[a]



entry	catalyst	conv (%)[b]	ee (%)[c]
1	**3a**	62	56
2	**3b**	72	<10
3	**3c**	<5	nd
4	**4a**	31	22
5	**5**	29	57
6	**6**	28	58

[a] All reactions carried out under N_2 atmosphere. [b] Conversions determined by 400 MHz ^{1}H NMR analysis of the unpurified product mixture. [c] Enantioselectivities determined by chiral GLC analysis (chiraldex-GTA).

screening studies), undergo ARCM to afford dihydrofuran **13** and dihydropyran **14** in 90 and 83% ee and 70 and >98% isolated yield, respectively.[11] Mo-catalyzed ARCM of primary vinyl ether **15** (entry 3) proceeds to 80% conversion within 24 h at 22 °C to afford **16** in 90% ee.

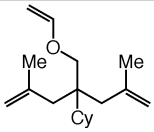
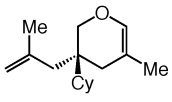
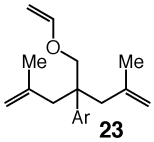
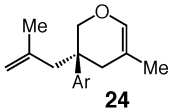
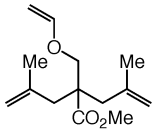
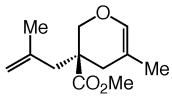
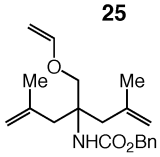
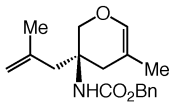
In contrast to transformations involving 1,1-disubstituted alkenes (entries 1−3), trienes **17** and **19** bearing trans- and cis-disubstituted olefins undergo catalytic ARCM to afford dihydrofurans **18** and **20** with lower asymmetric induction (41 and 62% ee, respectively). Catalytic ARCM of 1,2-disubstituted alkenes **17** and **19** proceed with diminished enantioselectivity (26 and 22% ee, respectively) when chiral alkylidene **4a**, the optimal catalyst for catalytic ARCM of 1,1-disubstituted olefins, is used.

d. Screening of Chiral Mo- and Ru-Based Catalysts. The identity of **4a** as the optimal catalyst was established by extensive screening studies involving a range of Mo- and Ru-based chiral complexes. Several points regarding these studies deserve mention. (1) Ru-based complexes **7**[4b−c] and **8**,[12] shown in Scheme 1, do not promote RCM of substrates shown in Table 2 (<2% conv at 65 °C in 18 h). (2) In the case of substrates that bear 1,1-disubstituted olefins, significant levels of catalyst activity are observed in the presence of only one chiral Mo complex (**4a**). The transformations shown in entries 1−3 of Table 1 proceed to <5% conversion in the presence of nonbinaphthyl-based Mo complexes **3a**−**c**, **5, 6** as well as Ru carbenes **7a**,**b**[4b−c] and **8a**,**b**;[12] such findings underline the significance of the availability of various structurally distinct catalyst candidates.[13] (3) As representative data in Table 3 indicate, when the substrate bears a 1,2-disubstituted olefin, appreciable levels of reactivity are detected in the presence of several chiral Mo complexes; however, product optical purity can vary significantly.

e. Enantioslective Synthesis of All-Carbon Quaternary Stereogenic Centers Through Mo-Catalyzed ARCM of Enol Ethers. With the above findings in hand, we set out to investigate whether Mo-catalyzed ARCM of enol ethers can be applied to the enantioselective synthesis of all-carbon quaternary stereogenic centers. The results of this aspect of our investigation are summarized in Table 4. As shown in entry 1 of Table 4, in the presence of 15 mol % of chiral alkylidene **4a**, catalytic ARCM of cyclohexyl-substituted triene **21** proceeds to 85% conversion (84% isolated yield) after 15 h at 22 °C to afford **22** in only 23% ee. In contrast, as illustrated in entries 2−4 of Table 4, the more synthetically versatile aryl-substituted trienes **23a**−**c** readily undergo ARCM in the presence of 15 mol % **4a** (22 °C, 18−20 h) to afford unsaturated pyrans **24a**−**c** in >90% isolated yield and in 87, 85, and 83% ee, respectively. Although Ru-based chiral complexes **7** and **8** promote RCM of substrates

(10) Scholl, M.; Ding, S.; Lee, C. W.; Grubbs, R. H. *Org. Lett.* **1999**, *1*, 953−956.
(11) The identity of major enantiomers was established through conversion and comparison with an authentic optically enriched compound. See the Supporting Information for details.
(12) Van Veldhuizen, J. J.; Campbell, J. E.; Giudici, R. E.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2005**, *127*, 6877−6882.
(13) Hoveyda, A. H.; Schrock, R. R. *Chem.−Eur. J.* **2001**, *7*, 945−950.

Table 4. Enantioselective Synthesis of Quaternary Carbon Stereogenic Centers by Mo-Catalyzed ARCM of Enol Ethers[a]

entry	substrate	product		catalyst; mol %	time (h); temp (°C)	conv (%);[b] yield (%)[c]	ee (%)[d]
1	 **21**	 **22**		**4a**; 15	15; 22	85; 84	23
2	 **23**	 **24**	**a** Ar = C_6H_5	**4a**; 15	20; 22	>98; 96	87
3			**b** Ar = *p*-$OMeC_6H_4$	**4a**; 15	19; 22	>98; 97	85
4			**c** Ar = *p*-BrC_6H_4	**4a**; 15	18; 22	91; 91	83
5	 **25**	 **26**		**4a**; 15	17; 22	>98; 94	94
6	 **27**	 **28**		**4a**; 15	19; 22	>98; 97	54

[a–c] See Table 2 (all reactions performed in C_6H_6). [d] Enantioselectivities determined by chiral GLC and HPLC analysis (see the Supporting Information for details).

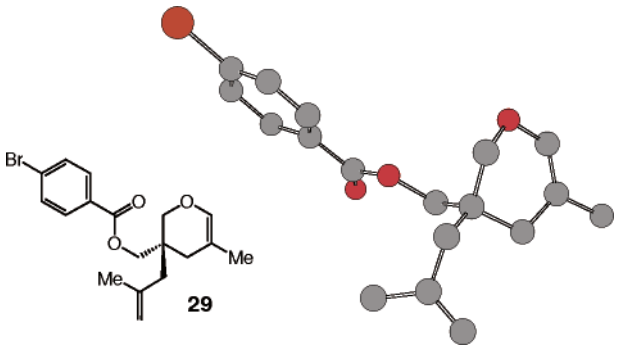


Figure 1. *p*-Bromobenzoate derivative **29** and its X-ray structure. Note: (*S*)-**29** was derivatized from (*S*)-**26** obtained through catalytic ARCM of (*R*)-**4a**; reactions in Table 4 correspond to products of reactions promoted by (*S*)-**4a**.

illustrated in Table 4 at elevated temperatures (65 °C, 4 h), these reactions afford products in <10% ee.

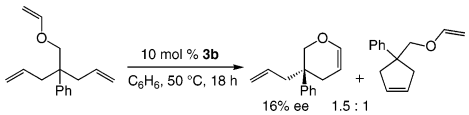
As depicted in entry 5 of Table 3, enol ether **25**, bearing a functionalizable methyl ester substituent, readily undergoes ARCM at 22 °C (21 h) to afford **26** in 94% ee and 94% isolated yield. The stereochemical identity of the major enantiomer of **26** was determined through X-ray structure analysis[14] of *p*-bromobenzoate ester **29** (Figure 1), prepared through reduction of the ester group with DIBAL-H (89% yield), followed by esterification of the resulting primary alcohol (90% yield). The assignment of the major enantiomers formed in reactions shown in Table 4 is thus by inference to the stereochemical outcome of Mo-catalyzed ARCM of **25**. To the best of our knowledge, transformations illustrated in entries 2−5 of Table 4 represent the first instances of efficient enantioselective synthesis of all-carbon quaternary stereogenic centers[8] by catalytic asymmetric olefin metathesis.

(14) See the Supporting Information for details.

The Mo-catalyzed ARCM illustrated in entry 6 of Table 4, involving carbamate **27**, proceeds to afford unsaturated pyran **28** in 97% isolated yield but in 54% ee.[15] The latter finding, as well as the difference in selectivity in reaction of **21** vs **23a−c** (entries 1−4), highlights the notable variations in selectivity that can arise, unpredictably, as a result of seemingly minor structural modifications.

f. Mechanistic Rationale for Mo-Catalyzed ARCM of Enol Ethers. The above trends in enantioselectivity can be explained through the transition state model depicted in Figure 2. The reaction is proposed to proceed via a more Lewis acidic *anti*-Mo alkylidene[16] formed by reaction of the chiral complex with the less substituted enol ether olefin; intermediacy of the cyclic complex **I** illustrated in Figure 2, where one of the enantiotopic unsaturated side chains is disposed equatorially (vs **II**), leads to the formation of the major enantiomer.[17] This mechanistic scenario is consistent with lower enantioselectivities observed in reactions of trans and cis-disubstituted olefins **17** and **19** (entries 4−5, Table 3). Thus, in the absence of the substituent (Me) of the 1,1-disubstituted olefin that is coordinated to the Mo center, reaction involving an axially situated unsaturated side chain becomes competitive with the mode of addition **I**

(15) Typically, in catalytic asymmetric desymmetrization reactions involving trienes or tetraenes, high enantioselectivities are attained if initiation (formation of the M=C bond) occurs at the central unsaturation site followed by enantioselective ring closure (e.g., reactions in Tables 2 and 4). As a result, reactions of all-terminal olefins typically proceed with low enantioselectivity. An example is illustrated below:



(16) For evidence pointing to the higher reactivity (and likely intermediacy) of antialkylidenes in Mo-catalyzed olefin metathesis reactions, see ref 1 and references therein.

(17) The corresponding pseudoboat transition structure would lead to unfavorable steric interactions between the substrate moiety and the binaphtholate unit of the chiral complex.

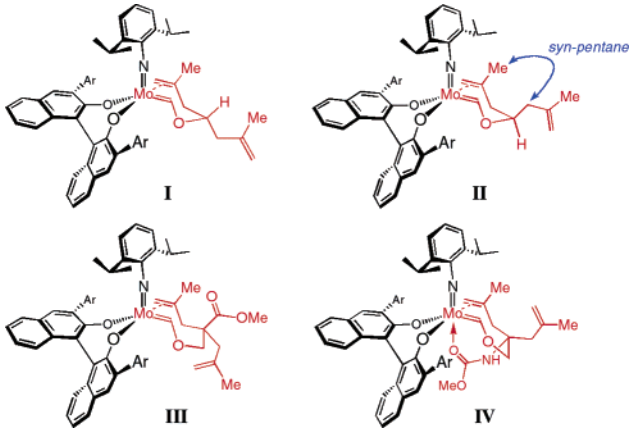


Figure 2. Proposed transition state structures for Mo-catalyzed ARCM of enol ethers.

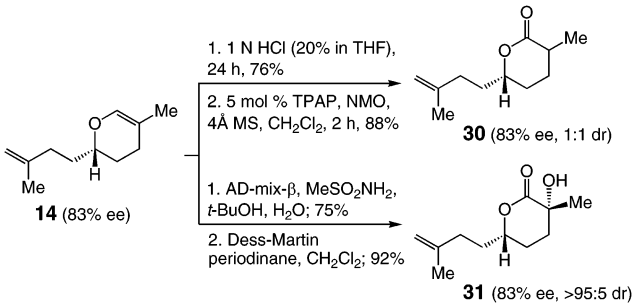
(Figure 2). The above considerations suggest that catalytic ARCM of **25** proceeds through transition state model **III** (Figure 2) to afford **26**. Unfavorable *syn*-pentane interactions are likely minimized as the substituent that bears the less sterically demanding sp^2-carbon is situated pseudoaxially (e.g., carboxylic ester or an aryl group). Such considerations account for the lower enantioselectivity observed in the reaction of Cy-substituted **21** vs aryl-substituted **23a**−**c** and carboxylic ester **25** (see Table 4), because the cycloalkane moiety of **21** likely leads to more severe steric interactions with the Me group of the Mo-bound olefin; the size difference between the unsaturated side chain and the cyclohexane unit is therefore not sufficient to lead to high asymmetric induction. The low asymmetric induction in the Mo-catalyzed ARCM of carbamate **27** (entry 6, Table 4) may be rationalized through competitive intermediacy of transition structure **IV**, whereas the Lewis basic carbamate is chelated with the transition metal center through interaction with the low energy Mo−N σ^* orbital.[18]

g. Representative Functionalization of Optically Enriched Cyclic Enol Ethers. Enantioselective desymmetrizations of trienes bearing allylic or homoallylic ethers through metal-catalyzed ARCM leads to products that bear two olefin residues that may not be easily differentiable. In contrast, in reactions involving enol ethers, the resulting optically enriched products carry olefins that are electronically distinct and can be easily functionalized site-selectively. Two representative examples are illustrated in Scheme 2. Treatment of optically enriched **14** with aqueous HCl leads to the formation of the derived cyclic hemiacetal, which can be easily oxidized to the corresponding lactone **30** in 67% overall yield (1:1 dr). Regio- and diastereoselective dihydroxylation of the cyclic enol ether with AD-mix-β,[19] followed by a Dess−Martin oxidation, delivers lactone **31** in 69% overall isolated yield and >95:5 dr.

Conclusions

We disclose the first examples of catalytic ARCM reactions involving enol ether substrates. The chiral Mo complexes

Scheme 2. Representative Functionalization of an Optically Enriched Enol Ether Obtained through Mo-Catalyzed ARCM



developed in these laboratories for the first time allow access to five- and six-membered cyclic enol ethers in up to 94% ee in a single catalytic step from achiral starting materials. Importantly, some of the products bear an all-carbon quaternary stereogenic center; to the best of our knowledge, these are the first instances of synthesis of all-carbon quaternary stereogenic centers through enantioselective olefin metathesis reactions. Our investigations illustrate that, in contrast to some Mo-based chiral complexes, the available Ru-based carbenes either do not provide significant levels of reactivity (substrates in Table 2) or promote reactions readily without inducing high asymmetric induction (substrates in Table 4). The optically enriched products obtained bear readily differentiable olefin sites that can be functionalized to access a wide range of nonracemic cyclic structures.

Enantioselectivities of the catalytic olefin metathesis reactions of enol ethers are at times <90% ee, and often 10−20 mol % catalyst loading is required for high (>80%) conversion. The results of the investigation disclosed herein thus clearly indicate that new and more effective chiral catalysts must be developed, and will be required, if the full potential of catalytic ARCM reactions of enol ethers is to be realized.

Studies directed toward the design and development of more efficient catalysts for catalytic asymmetric olefin metathesis, as well as further development of catalytic ARCM of enol ethers and demonstration of their utility in organic synthesis are in progress.

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Supporting Information Available: Experimental procedures and spectral data for substrates and products. This material is available free of charge via the Internet at http://pubs.acs.org.

JA058428R

(18) For related Mo- and W-based chelate complexes (including X-ray structure data), see: (a) Fox, H. H.; Lee, J.-K.; Park, L. Y.; Schrock, R. R. *Organometallics* **1993**, *12*, 759−768. (b) Tsang, W. C. P.; Hultzsch, K. C.; Alexander, J. B.; Bonitatebus, P. J., Jr.; Schrock, R. R.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2003**, *125*, 2652−2666.

(19) Dihydroxylation with OsO_4 leads to low levels of regioselectivity. For use of chiral dihydrtoxylation catalysts in enantioselective synthesis, see: (a) Kolb, H. C.; Van Nieuwenhze, M. S.; Sharpless, K. B. *Chem. Rev.* **1994**, *94*, 2483−2547. For catalytic dihydroxylation of enol ethers with chiral catalysts, see: (b) Curran, D. P.; Ko, S.-B. *J. Org. Chem.* **1994**, *59*, 6139−6141.