Catalytic Asymmetric Ring-Opening Metathesis/Cross Metathesis (AROM/CM) Reactions. Mechanism and Application to Enantioselective Synthesis of Functionalized Cyclopentanes

Daniel S. La,[†] Elizabeth S. Sattely,[†] J. Gair Ford,[†] Richard R. Schrock,[‡] and Amir H. Hoveyda*,[†]

Contribution from the Departments of Chemistry, Merkert Chemistry Center, Boston College, Chestnut Hill, Massachusetts 02467, and Massachusetts Institute of Technology, Cambridge, Massachusetts 02139

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Abstract: Studies regarding the first examples of catalytic asymmetric ring-opening metathesis (AROM) reactions are detailed. This enantioselective cleavage of norbornyl alkenes is followed by an intermolecular cross metathesis with a terminal olefin partner; judicious selection of olefin is required so that oligomerization and dimerization side products are avoided. Results outlined herein suggest that the presence of suitably positioned heteroatom substituents may be critical to reaction efficiency. Mo-catalyzed tandem AROM/CM affords functionalized cyclopentyl dienes in >98% ee and >98% trans olefin selectivity; both secondary and tertiary ether products can be obtained. The examples provided include the catalytic synthesis of an optically pure cyclopentyl epoxide and dimethyl acetal. Mechanistic studies suggest that it is the more substituted benzylidene or silylated alkylidenes that are involved in the catalytic process (vs the corresponding Mo-methylidenes). Although electron rich benzylidenes react more efficiently, the derived electron poor Mo complexes promote AROM/CM transformations as well; alkylidenes that bear a boron substituent are unreactive.

Introduction

Metal-catalyzed ring-opening metathesis (ROM) represents a class of C−C bond-forming transformations that has notable potential in organic synthesis but has received less attention than the related ring-closing metathesis (RCM).[1] Since catalytic ROM processes generate a new metal-alkylidene complex, they can be followed by a subsequent metathesis step. A tandem catalytic ring-opening metathesis/cross metathesis (ROM/CM) protocol may therefore be envisioned.[2−5] Such transformations allow for synthetically useful skeletal reorganizations to be effected that are unique to olefin metathesis. In the context of asymmetric catalysis and the synthesis of optically pure materials,[6] a wider range of such tandem catalytic transformations realize their full potential if efficient and functional group tolerant *chiral nonracemic* metathesis catalysts are available. Easily accessible achiral substrates can then be directly converted into optically enriched and highly functionalized compounds (e.g., **5** in Scheme 1). To access the products obtained in this study by the more commonly adopted strategy, namely, the utilization of achiral catalysts to effect metatheses of optically enriched starting materials,[7] would be less practical; this is largely because the preparation of the requisite nonracemic starting materials would require significantly longer routes.

[†] Boston College.

[‡] Massachusetts Institute of Technology.

(1) For reviews on catalytic olefin metathesis, see: (a) Grubbs, R. H.; Miller, S. J.; Fu, G. C. *Acc. Chem. Res.* **1995**, *28*, 446−452. (b) Schmalz, H.-G. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 1833−1836. (c) Schuster, M.; Blechert, S. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 2036−2056. (d) Ivin, K. J.; Mol, J. C. *Olefin Metathesis and Metathesis Polymerization*; Academic Press: San Diego, 1997. (e) Furstner, A. *Top. Catal.* **1997**, *4*, 285−299. (f) Schrock, R. R. In *Alkene Metathesis in Organic Synthesis*; Furstner, A., Ed.; Springer: Berlin 1998; pp 1−36. (g) Armstrong, S. K. *J. Chem. Soc., Perkin Trans. 1* **1998**, 371−388. (h) Grubbs, R. H.; Chang, S. *Tetrahedron* **1998**, *54*, 4413−4450. (i) Randall, M. L.; Snapper, M. L. *The Strem Chemiker* **1998**, *17*, 1−9. (j) Phillips, A. J.; Abell, A. D. *Aldrichchim. Acta* **1999**, *32*, 75−89. (k) Wright, D. L. *Curr. Org. Chem.* **1999**, *3*, 211−240. (l) Furstner, A. *Angew. Chem., Int. Ed.* **2000**, *39*, 3012−3043.

(2) For studies on metal-catalyzed nonasymmetric tandem ROM/CM processes, see: (a) Randall, M. L.; Tallarico, J. A.; Snapper, M. L. *J. Am. Chem. Soc.* **1995**, *117*, 9610−9611. (b) Snapper, M. L.; Tallarico, J. A.; Randall, M. L. *J. Am. Chem. Soc.* **1997**, *119*, 1478−1479. (c) Schneider, M. F.; Lucas, N.; Velder, J.; Blechert, S. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 257−259. (d) Cuny, G. D.; Cao, J.; Hauske, J. R. *Tetrahedron Lett.* **1997**, *38*, 5237−5240. (e) Cao, J.; Cuny, G. D.; Hauske, J. R. *Mol. Divers.* **1998**, *3*, 173−179. (f) Michaut, M.; Parrain, J.-L.; Santelli, M. *Chem. Commun.* **1998**, 2567−2568. (g) Katayama, H.; Urushima, H.; Nishioka, T.; Wada, C.; Nagao, M.; Ozawa, F. *Angew. Chem., Int. Ed.* **2000**, *39*, 4513−4515.

(3) For studies on metal-catalyzed nonasymmetric ROM/RCM reactions, see: (a) Zuercher, W. J.; Hashimoto, M.; Grubbs, R. H. *J. Am. Chem. Soc.* **1996**, *118*, 6634−6640. (b) Harrity, J. P. A.; Visser, M. S.; Gleason, J. D.; Hoveyda, A. H. *J. Am. Chem. Soc.* **1997**, *119*, 1488−1489. (c) Harrity, J. P. A.; La, D. S.; Cefalo, D. R.; Visser, M. S.; Hoveyda, A. H. *J. Am. Chem. Soc.* **1998**, *120*, 2343−2351. (d) Burke, S. D.; Quinn, K. J.; Chen, V. J. *J. Org. Chem.* **1998**, *63*, 8626−8627. Related application to target-oriented synthesis: (e) Johannes, C. W.; Visser, M. S.; Weatherhead, G. S.; Hoveyda, A. H. *J. Am. Chem. Soc.* **1998**, *120*, 8340−8347. (f) Adams, J. A.; Ford, J. G.; Stamatos, P. J.; Hoveyda, A. H. *J. Org. Chem.* **1999**, *64*, 9690−9696. (g) Stragies, R.; Blechert, S. *J. Am. Chem. Soc.* **2000**, *122*, 9584−9591. (h) Voigtmann, U.; Blechert, S. *Org. Lett.* **2000**, *2*, 3971−3974.

(4) For recent examples of tandem CM/RCM and applications to target-oriented synthesis, see: (a) Smith, A. B.; Adams, C. M.; Kozmin, S. A. *J. Am. Chem. Soc.* **2001**, *123*, 990−991 and references therein. (b) Furstner, A.; Thiel, O. R.; Ackermann, L. *Org. Lett.* **2001**, *3*, 449−451.

(5) For recent reviews on catalytic ring-opening/cross metathesis, see: (a) Gibson, S. E.; Keen, S. P. In *Alkene Metathesis in Organic Synthesis*; Furstner, A., Ed.; Springer: Berlin, 1998; pp 172−179. (b) Arjona, O.; Csaky, A. G.; Plumet, J. *Synthesis* **2000**, *6*, 857−861.

(6) For a brief overview of catalytic enantioselective olefin metathesis, see: Hoveyda, A. H.; Schrock, R. R. *Chem.−Eur. J.* **2001**, *7*, 945−950.

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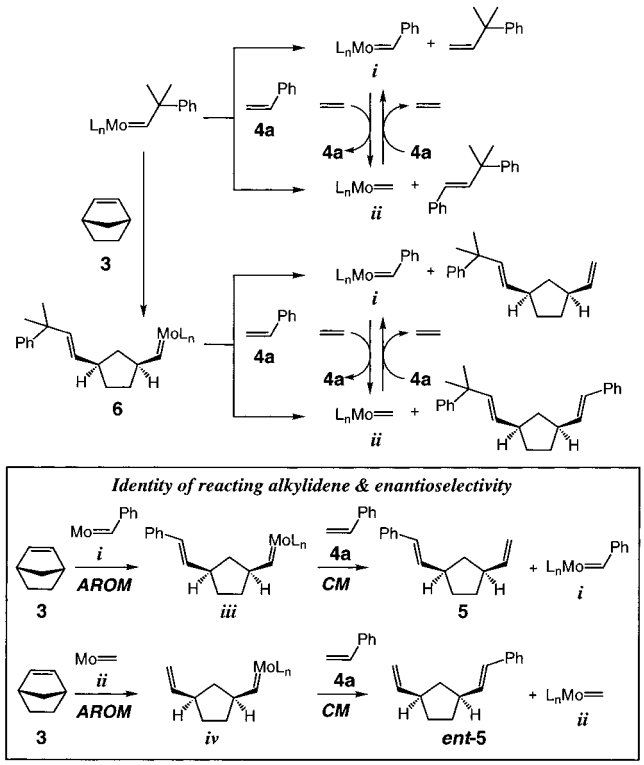
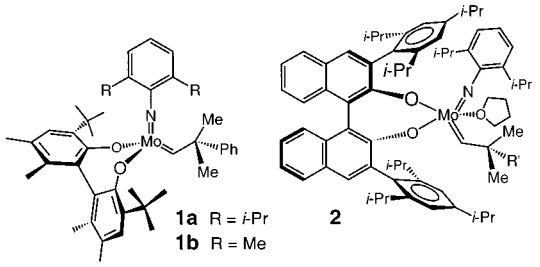
Scheme 1



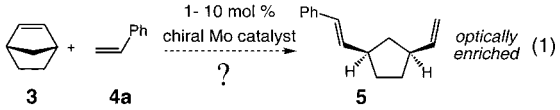
The above considerations, together with the efficiency with which chiral Mo-based complexes **1**[8] and **2**[9] (Chart 1) have been used in these laboratories in catalytic asymmetric ring-closing metathesis (ARCM), led us to establish a program toward developing the Mo-catalyzed tandem asymmetric ring-opening metathesis/cross metathesis (AROM/CM).[10] Our studies have led us to carry out the first examples of catalytic tandem AROM/CM transformations with meso norbornenes in conjunction with a range of terminal alkenes. The results of this study are detailed herein.[11]

Chart 1



Results and Discussion

1. Initial Mechanistic Considerations. Catalytic AROM/CM processes involve the intermolecular reactions of two different alkene substrates that could also react to afford a variety of side products in addition to the desired chiral compounds. That is, alkene substrates can (i) catalytically dimerize or self-oligomerize and (ii) react with the transition metal catalyst to afford various metal-alkylidenes that promote the formation of different products (see below for details). Thus, the effectiveness of catalytic tandem asymmetric ring-opening metathesis/cross metathesis (AROM/CM) is directly and strongly related to myriad mechanistic issues that must first be considered in the context of reaction design. Conditions must be carefully selected to minimize other competitive metathesis reactions that yield a multitude of undesired compounds and may give rise to low enantioselectivity. Some of these issues become more apparent when a specific catalytic AROM/CM reaction, such as that involving norbornene (**3**) and styrene (**4a**) to afford chiral cyclopentyl adduct **5**, is considered (eq 1). Related questions and their implications will be briefly discussed first, since an awareness of mechanistic principles is imperative for a better understanding of various subtleties implied by the data disclosed below.



One of the most critical issues vis-à-vis the mechanism of catalytic AROM/CM reactions relates to the identity of the reacting Mo-alkylidene (Scheme 1).[12] The chiral Mo-based catalyst (the initial Mo neophylidene in Scheme 1), through direct reaction with styrene (**4a**) or by initial reaction with norbornene (**6** via **3**) may be transformed to benzylidene ***i*** or methylidene ***ii***, which are readily interconvertible. Reaction of ***ii*** with **4a** affords ethylene in addition to ***i***, which can then react with ethylene to regenerate ***ii***. Importantly, as illustrated in Scheme 1 (box), if reaction of **3** with ***i*** delivers **5** via ***iii***, reaction through methylidene ***ii*** with the *same* enantiofacial selectivity would afford ***ent*-5** via ***iv***. Thus, *whereas in a nonasymmetric process either* ***i*** *or* ***ii*** *may deliver the desired product, in a catalytic enantioselective variant reaction through the Mo-benzylidene or the Mo-methylidene can result in the formation of opposite enantiomers and reduced enantioselection*.

Highly reactive olefinic substrates, such as norbornene (**3**), allow for two strategic advantages in the design of catalytic

(7) For examples of enantioselective total syntheses, where a chiral nonracemic intermediate has been subjected to catalytic metathesis (in addition to refs 3−4), see: (a) Xu, Z.; Johannes, C. W.; Houri, A. F.; La, D. S.; Cogan, D. A.; Hofilena, G. E.; Hoveyda, A. H. *J. Am. Chem. Soc.* **1997**, *119*, 10302−10316. (b) Meng, D.; Su, D. S.; Balog, A.; Bertinato, P.; Sorensen, E. J.; Danishefsky, S. J.; Zheng, Y.-H.; Chou, T.-C.; He, L.; Horwitz, S. B. *J. Am. Chem. Soc.* **1997**, *119*, 2733−2734. (c) Nicolaou, K. C.; Winssinger, N.; Pastor, J.; Ninkovic, S.; Sarabia, F.; He, Y.; Vourloumis, D.; Yang, Z.; Li, T.; Giannakakou, P.; Hamel, E. *Nature* **1997**, *387*, 268−272. (d) Johannes, C. W.; Visser, M. S.; Weatherhead, G. S.; Hoveyda, A. H. *J. Am. Chem. Soc.* **1998**, *120*, 8340−8347. (e) Delgado, M.; Martin, J. D. *J. Org. Chem.* **1999**, *64*, 4798−4816. (f) Lee, D.; Sello, J. K.; Schreiber, S. L. *J. Am. Chem. Soc.* **1999**, *121*, 10648−10649. (g) Furstner, A.; Thiel, O. R. *J. Org. Chem.* **2000**, *65*, 1738−1742. (h) Limanto, J.; Snapper, M. L. *J. Am. Chem. Soc.* **2000**, *122*, 8071−8072. (i) Smith, A. B.; Kozmin, S. A.; Adams, C. M.; Paone, D. V. *J. Am. Chem. Soc.* **2000**, *122*, 4984−4985. (j) Wu, Y.; Esser, L.; De Brabander, J. K. *Angew. Chem., Int. Ed.* **2000**, *39*, 4308−4310.

(8) (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) Weatherhead, G. S.; Houser, J. H.; Ford, J. G.; Jamieson, J. Y.; Schrock, R. R.; Hoveyda, A. H. *Tetrahedron Lett.* **2000**, *41*, 9553−9559. (d) Aeilts, S. L.; Cefalo, D. R.; Bonitatebus, P. J., Jr.; Houser, J. H.; Hoveyda, A. H.; Schrock, R. R. *Angew. Chem., Int. Ed.* **2001**, *40*, 1452−1456. For application of catalytic ARCM in target-oriented synthesis: (e) Burke, S. D.; Muller, N.; Beudry, C. M. *Org. Lett.* **1999**, *1*, 1827−1829.

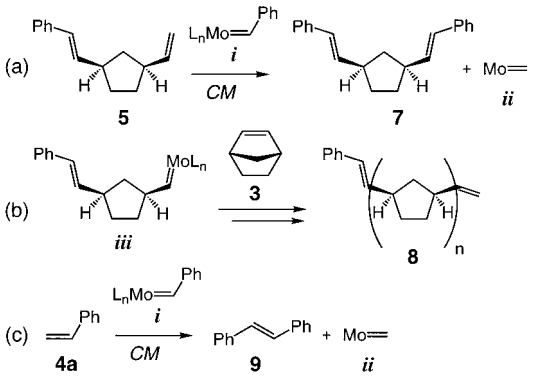
(9) Zhu, S.; Cefalo, D. R.; La, D. S.; Jamieson, J. Y.; Davis, W. M.; Hoveyda, A. H.; Schrock, R. R. *J. Am. Chem. Soc.* **1999**, *121*, 8251−8259.

(10) For the initial communication regarding this work, see: La, D. S.; Ford, J. G.; Sattely, E. S.; Bonitatebus, P. J.; Schrock, R. R.; Hoveyda, A. H. *J. Am. Chem. Soc.* **1999**, *121*, 11603−11604.

(11) For related catalytic tandem AROM/RCM reactions, see: (a) Weatherhead, G. S.; Ford, J. G.; Alexanian, E. J.; Schrock, R. R.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2000**, *122*, 1828−1829. (b) Cefalo, D. R.; Kiely, A. F.; Wuchrer, M.; Jamieson, J. Y.; Schrock, R. R.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2001**, *123*, 3139−3140.

(12) (a) Schrock, R. R. *Polyhedron* **1995**, *14*, 3177−3195. (b) Feldman, J.; Schrock, R. R. *Prog. Inorg. Chem.* **1991**, *39*, 1−74. (c) Reference 1f.

Scheme 2. Representative Potential Side Reactions in Catalytic AROM/CM

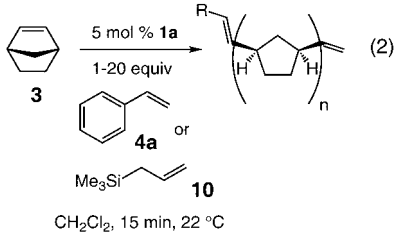


AROM/CM: (1) Strained olefins more likely possess the reactivity to ensure that catalytic AROM/CM is appropriately efficient. Otherwise, with slower reacting disubstituted alkene partners, longer reaction times will be required and, as shown in Scheme 2 (a), further CM of **5** with styrene (**4a**) effectively competes to contaminate the desired reaction product with meso **7**. (2) ROM is likely irreversible due to the release of ring strain. Ring cleavage (e.g., **3** → ***iii***, box in Scheme 1) therefore becomes the likely stereochemistry-determining step (kinetic control of enantioselectivity), allowing various substrate−catalyst association models to serve as reasonably reliable elements in understanding the origins of stereochemical control. Strained olefins should however not be too reactive, as the initial metal-alkylidene intermediates ***iii*** or ***iv*** (cf. Scheme 1) may then react with another molecule of the strained alkene to cause oligomerization (see (b), Scheme 2).

Various considerations need to be applied to the terminal olefin partner as well: it must be sufficiently reactive not to allow the metal-alkylidene intermediate ***iii*** or ***iv*** to initiate the previously mentioned oligomerization. Yet, the same terminal alkene, if too reactive, may be prematurely consumed through homodimerization (see (c), Scheme 2) and not be available to react with the alkylidene that results from ROM (e.g., ***iii***, Scheme 2).

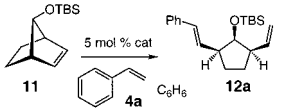
With the above mechanistic issues in mind, we set out to examine the possibility of Mo-catalyzed tandem AROM/CM reactions involving various meso norbornyl substrates and terminal alkenes. In the discussion outlined below, first the results of the methodological studies on catalytic AROM/CM of several norbornyl substrates and terminal olefins are presented. Subsequently, various mechanistic issues and the related additional data are disclosed.

2. Mo-Catalyzed AROM/CM with Norbornyl Substrates. (a) Initial Attempts with Norbornene 3. We began our investigation by examining the reaction of norbornene **3** in the presence of varying amounts of styrene **4a** and 5 mol % of the chiral Mo complex **1a**. As illustrated in eq 2, these conditions



(at 22 °C, CH_2Cl_2 or C_6H_6) lead to the rapid formation of oligomeric substances (15 min). Larger equivalents of styrene

Scheme 3



1) Catalyst optimization
(10 equiv **4a**, C_6H_6, 7 h)

catalyst, temp (°C)	conv (%), ee (%)
1a, *22*	39, 98
1b, 22	51, 79
2, 22	18, 86
2, 50	29, 81

2) Styrene equivalent optimization
(5 mol % **1a**, C_6H_6, 22 °C)

styrene (**4a**) equiv	conv (%), ee (%)
10	39, 98
5	52, 97
2	77, 96

do little to increase the amount of the desired AROM/CM product; even in the presence of 10 equiv of styrene, <5% of the nonoligomeric adducts is detected (400 MHz ^{1}H NMR analysis of the unpurified reaction mixture). Similarly discouraging results were obtained with allylsilane **10** (eq 2). Slow addition of **3** to a CH_2Cl_2 solution of 10 equiv of **10** leads to <5% of the desired AROM/CM adduct (as judged by analysis of the 400 MHz ^{1}H NMR spectrum).

(b) Initial Investigation with 7-Norbornyl TBS Ether 11. To address the above complications in connection to norbornene oligomerization, we decided to reduce the reactivity of the strained disubstituted olefin through incorporation of some steric bulk in the vicinity of the reacting alkene, but without jeopardizing the meso character of the substrate. Toward this end, we prepared 7-siloxynorbornene **11**[13] (Scheme 3) since we surmised that the Mo-alkylidene likely approaches the norbornyl alkene from the exo face; this conjecture finds support in X-ray crystal structures of various norbornyl molybdacyclobutanes reported previously.[12b,14]

As illustrated in Scheme 3 (catalyst optimization section), when **11** is subjected to 5 mol % of chiral Mo complexes **1a**, **1b**, or **2** in the presence of 10 equiv of styrene (**4a**) at 22 °C, the desired AROM/CM product **12a** is formed in appreciable amounts (reaction progress was monitored by 400 MHz ^{1}H NMR). The most promising level of enantioselectivity is that obtained from the reaction of **1a** (>98% ee; chiral HPLC analysis), although the sterically less demanding dimethylimido complex **1b** delivers the best reactivity (51% conversion in 7 h).[15]

Next, we turned our attention to improving the efficiency of the catalytic process without imposing any adverse effects on enantioselectivity. Within this context, we were surprised to find that, contrary to our initial expectation, *lowering the amount of styrene leads to higher levels of conversion* (see Scheme 3, styrene optimization section). Furthermore, as the data in Scheme 3 indicate, variations in styrene concentration result in little or no change in the optical purity of **12a**.

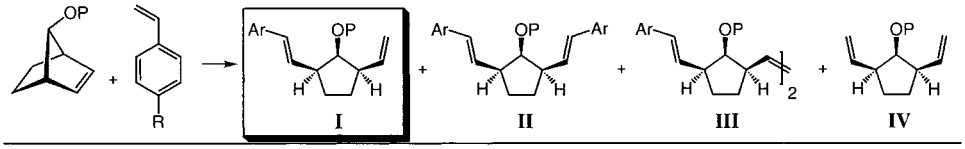
A plausible rationale regarding the lower rate of AROM/CM product formation with higher equivalents of **4a** may involve nonproductive or degenerate reaction of the chiral Mo-ben-

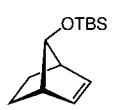
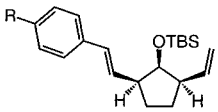
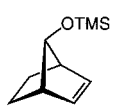
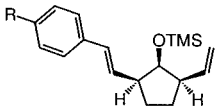
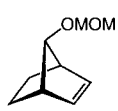
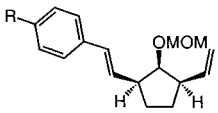
(13) Gerteisen, T. J.; Kleinfelter, D. C. *J. Org. Chem.* **1971**, *36*, 3255−3259.

(14) (a) Bazan, G. C.; Khosravi, E.; Schrock, R. R.; Feast, W. J.; Gibson, V. C.; O'Reagan, M. B.; Thomas, J. K.; Davis, W. M. *J. Am. Chem. Soc.* **1990**, *112*, 8378−8387. (b) Bazan, G. C.; Oskam, J. H.; Cho, H.; Park, L. Y.; Schrock, R. R. *J. Am. Chem. Soc.* **1991**, *113*, 6899−6907.

(15) At the time these studies were carried out, only complexes **1** and **2** were available. Additional chiral Mo complexes are now in hand (see refs 6 and 8).

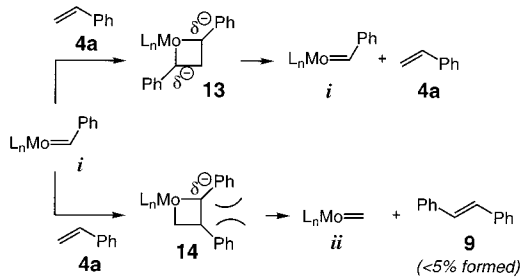
Table 1. Tandem Mo-Catalyzed AROM/CM Reactions with Norbornyl Secondary Ethers and Various Styrenes[a]



entry	substrate	terminal alkene	AROM / CM product	time (h)	conv (%) I : II : III : IV[b]	trans[c] (%)	ee[d] (%)	yield[e] (%)
1		**a** R = H		7	61 : 8 : 0 : 8	>98	96	57
2		**b** R = OMe		7	75 : 8 : 0 : 7	>98	91	64
3		**c** R = CF_3		20	<10	>98	--	--
	11	**4**	**12**					
4		**a** R = H		1	97 : 0 : 0 : 3	>98	>98	85
5		**b** R = OMe		1	>98 : 0 : 0 : 0	>98	>98	92
6		**c** R = CF_3		4.5	67 : 9 : 0 : 11	>98	>98	48
	15	**4**	**16**					
7		**a** R = H		0.3	96 : 3 : 1 : 0	>98	>98	96
8		**b** R = OMe		0.1	95 : 3 : 2 : 0	>98	>98	88
9		**c** R = CF_3		0.4	83 : 9 : 8 : 0	>98	>98	80
	17	**4**	**18**					

[a] Conditions: 5 mol % **1a**, 2 equiv **4**, Ar atm 22 °C, C_6H_6. [b] Percent product determined by 400 MHz ^{1}H NMR analysis. [c] Determined by 400 MHz ^{1}H NMR analysis. [d] Determined by chiral HPLC (Chiralcel OD for entries 1,2, 4−7 and AD chiralpak for entries 8−9), in comparison with authentic racemic materials. Analysis of products in entries 1, 4, 6, and 7 was performed on the derived acetates. [e] Isolated yield of purified products by silica gel chromatography.

Scheme 4



zylidene (***i***) or methylidene (***ii***) with excess styrene.[16] Thus, as illustrated in Scheme 4, reaction of benzylidene ***i*** with **4a** may lead to the formation of metallacyclobutanes **13** or **14**. Intermediate **13** can only decompose to re-deliver styrene and benzylidene ***i***, whereas molybdacycle **14** could lead to the formation of stilbene (**9**). Analysis of the unpurified reaction mixtures does not indicate a substantial amount of stilbene generation (<5% **9** with 10 equiv of **4a**). Formation of metallacycle **13** may be favored due to the following: (i) Accumulation of electron density at both carbons of the two C−Mo bonds is stabilized by an adjacent phenyl group (cf. Scheme 4). (ii) Metallacyclobutane **14** might suffer from more severe steric interactions than the alternative **13** (steric interaction between Ph and MoL_n is offset by the longer C−Mo bond). Excess styrene can thus preoccupy the active chiral catalyst and cause diminution of reaction rates through formation of the more favored and relatively stable **13**. Similar arguments may be put forth involving the Mo-methylidene complex ***ii***; the metallacyclobutane from addition of styrene to ***ii*** can undergo fragmentation to regenerate ***ii*** and styrene or ethylene and benzylidene complex ***i*** (see below for discussions related to evidence favoring the intermediacy of Mo-benzylidene ***i***).

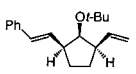
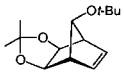
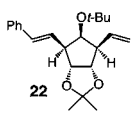
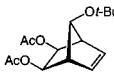
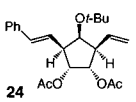
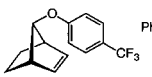
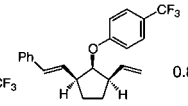
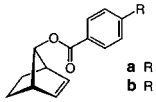
(c) Catalytic AROM/CM Reaction of Secondary Norbornyl Ethers. With the first successful example of a catalytic AROM/CM in hand, we next set out to examine in detail the following critical issues: (i) The influence of the size and nature of the norbornyl alkoxy substituent. (ii) The effect of the electronic attributes of the styrenes. (iii) The identity and extent of side products that may be formed as a function of various pathways, some of which are mentioned earlier. As illustrated at the heading of Table 1, in addition to the expected catalytic AROM/CM product represented by **I**, potential side products include meso diene **II**, homometathesis adduct **III**, and meso terminal diene **IV**.

The results in entries 1 and 2 of Table 1 indicate that with the sterically demanding TBS ether reaction with the electron rich *p*-OMe-styrene **4b** is more efficient in delivering the derived AROM/CM product (**12**) than styrene **4a**. In contrast, when the electron deficient *p*-CF_3-styrene **4c** is used, <10% reaction is observed after 10 h (see below for discussion of rate difference). Although the transformation with **4a** (96% ee) is somewhat more enantioselective than that with **4b** (91% ee), both processes generate exclusively trans products (>98%) and nearly equal amounts of side products corresponding to meso dienes **II** and **IV**; <2% homometathesis product (i.e., **III**) is detected in both instances (analysis of 400 MHz ^{1}H NMR spectrum of the unpurified reaction mixture).

With TMS ether **15** as the substrate (Table 1, entries 4−6), catalytic AROM/CM reactions occur smoothly, affording the desired products **16a**−**c** in >98% ee and >98% trans selectivity. Catalytic metathesis of **4a** or **4b** with the more reactive TMS ether (vs **11**) generates lower amounts of byproducts (compare entries 4−5 with entries 1−2), indicating that with a faster reacting substrate (1 h for **15** vs 7 h for **11**), the desired pathway can more effectively compete with unwanted side reactions (see

(16) For a study of degenerate exchanges in a catalytic cross metathesis reaction, see: McGinnis, J.; Katz, T. J.; Hurwitz, S. *J. Am. Chem. Soc.* **1976**, *98*, 605−606.

Table 2. Tandem Mo-Catalyzed AROM/CM Reactions with Functionalized Norbornyl Secondary Ethers, Secondary Esters and Styrene[a]

entry	substrate	product	time (h)	conv (%); [b] conv to prod (%)	trans [c] (%)	ee [d] (%)	yield [e] (%)
1	 **19**	 **20**	1.0	>98; >98	>98	>98	92
2	 **21**	 **22**	2.0	>98; >98	>98	>98	94
3	 **23**	 **24**	5.0	>98; >98	>98	>98	94
4	 **25**	 **26**	0.8	>98; 77	>98	>98	74
5	 **27**	**a** R = OMe **b** R = CF_3	4.5 11	NO REACTION			

[a] Conditions: 5 mol % of **1a**, 2 equiv of **4a**, Ar atm, 22 °C, C_6H_6. [b] Percent product determined by 400 MHz ^{1}H NMR analysis. [c] Determined by 400 MHz ^{1}H NMR analysis. [d] Determined by chiral HPLC (OJ Chiralpak for entry 1, AD Chiralpak for entry 2, and Chiralcel OD for entries 3−4), in comparison with authentic racemic materials. [e] Isolated yield of purified products by silica gel chromatography.

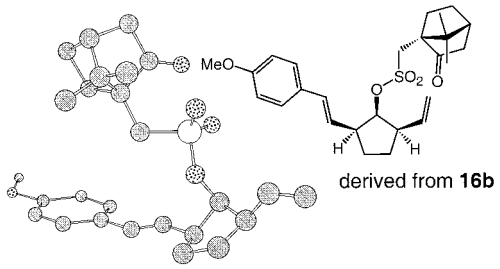


Figure 1. Chem 3D rendition of the crystal structure of the camphor sulfonate derivative obtained from **16b**.

below for further details). It is important to note that when the less sterically demanding TMS ether **15** is used (vs TBS ether **11**), catalytic reactions proceed to completion with all three styrene substrates (**4a**−**4c**). Thus, the less reactive *p*-CF_3 styrene undergoes efficient metathesis with **15**, albeit at a rate slower than **4a** and **4b**, to afford **16c** in 48% isolated yield and >98% ee (>98% trans). Another noteworthy difference between reaction of **15** with **4a,b** and that with the less reactive **4c** is that in the latter case similar to transformations with the sterically more encumbered norbornyl alkene in **11**, significant amounts of byproducts corresponding to **II** and **IV** are generated.

The stereochemical identity of the reaction products in Table 1 is based on the X-ray crystal structure of the camphor sulfonate derivative (Figure 1) obtained from AROM/CM product **16b** (Table 1, entry 5). Deprotection of **12b** and **18b** affords the same parent alcohol enantiomer as that obtained from desilylation of **16b**. The remainder of the stereochemical assignments, including results in Tables 2 and 3 are by inference.

The catalytic AROM/CM reactions of the MOM ether **17** are illustrated in entries 7−9 of Table 1. As before, all reactions afford the expected Mo-catalyzed AROM/CM products **18a**−**c** in >98% ee and >80% isolated yield with >98% trans olefin

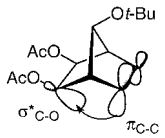


Figure 2.

selectivity. The trend in relative rates of various styrenes (**4b** > **4a** > **4c**), similar to that observed with **11** (entries 1−3) and **15** (entries 4−6), is recorded here. With this sterically less demanding substrate (vs **11** and **15**), reactions proceed to >98% conversion in less than an hour even with the least reactive **4c**; but compounds from further functionalization of the initial AROM/CM product are also formed before all the substrate is consumed. In the case of the reaction of **17** with **4a** (entry 7), 4% of the meso adduct corresponding to **II** and 1% product represented by **III** are observed; nearly an identical mixture is obtained from the reaction of **17** with **4b** (entry 8). Longer reaction times lead to an increase in the amount of **II**−**IV**.

Additional data in connection to Mo-catalyzed AROM/CM reactions of secondary norbornyl ethers are illustrated in Table 2. All transformations were carried out with styrene (**4a**) as the terminal alkene partner. The enantioselective metathesis of the sterically demanding *t*-Bu ether **19**[17] proceeds to deliver **20** within 1 h in the optically pure form with <2% byproduct formation (see **II**−**IV**, Table 1), >98% trans selectivity, and in 92% yield after silica gel chromatography. The highly functionalized chiral cyclopentyl adducts **22**[18] (entry 2, Table 2) and **24** (entry 3) are generated catalytically with similarly high levels of selectivity and efficiency. The relative rates with which substrates **19** (fastest, 1 h), **21**, and **23** (slowest, 5 h) undergo reaction is likely, at least in part, due to the reduced Lewis basicity of the reactive alkene caused by the interaction of the C−C π electrons with the properly aligned low-lying σ^* orbitals at C5 and C6 (Figure 2). Thus, the rate of AROM/CM is slowest with the more electron withdrawing (lowest energy C−O σ^*) acetate substituents.[19] The absence of byproducts (corresponding to **II** and **III**, Table 1) derived from further reaction of the terminal alkene in **20**, **22**, and **24** likely arises from the steric bulk of the O-*t*-Bu group which renders reaction at the olefinic site sterically prohibitive.

Similar to substrates in Table 1 and the alkyl ethers **19**, **21**, and **23** in Table 2, aryl ether **25**[20] undergoes catalytic AROM/CM readily to afford **26** in >98% ee and >98% trans selectivity (Table 2, entry 4). The reaction mixture is however contaminated with previously mentioned byproducts (>98% conversion, 77% conversion to **26**). As illustrated in entry 5 (Table 2), the derived electron rich and electron deficient esters **27a** and **27b** afford <2% reaction product even after several hours (>95% recovery

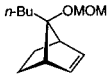
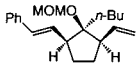
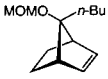
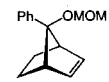
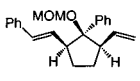
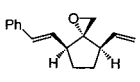
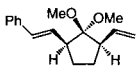
(17) Micheli, R. A.; Hajos, Z. G.; Cohen, N.; Parrish, D. R.; Portland, L. A.; Sciamanna, W.; Scott, M. A.; Wehrli, P. A. *J. Org. Chem.* **1975**, *40*, 675−681.

(18) Cheikh, A. B.; Craine, L. E.; Recher, S. G.; Zemlicka, J. *J. Org. Chem.* **1988**, *53*, 928−936. (b) Story, P. R.; Hahrenholtz, S. R. *Organic Syntheses*; Wiley: New York, 1973; Collect. Vol. 5, pp 151−154.

(19) For examples of studies relating to the effect of stereoelectronics on the reactivity and selectivity of reactions with rigid polycyclic substrates, see: (a) Winstein, S.; Shatavsky, M. *J. Am. Chem. Soc.* **1955**, *78*, 592−597. (b) Lambert, J. B.; Holcomb, A. G. *J. Am. Chem. Soc.* **1971**, *93*, 2994−3001. (c) Cristol, S. J.; Beimborn, D. A. *J. Am. Chem. Soc.* **1973**, *95*, 3651−3654. (d) Goering, H. L.; Chang, C.-H. *J. Am. Chem. Soc.* **1977**, *99*, 1547−1550. (e) Srivastava, S.; le Noble, W. J. *J. Am. Chem. Soc.* **1987**, *109*, 5874−5875. (f) Lin, M.-H.; Cheung, C. K.; le Noble, W. J. *J. Am. Chem. Soc.* **1988**, *110*, 6562−6563. (g) Hahn, J. M.; le Noble, W. J. *J. Am. Chem. Soc.* **1992**, *114*, 1916−1917. (h) Mehta, G.; Khan, F. A. *Tetrahedron Lett.* **1992**, *33*, 3065−3068. (i) Pudzianowski, A. T.; Barrish, J. C.; Spergel, S. H. *Tetrahedron Lett.* **1992**, *33*, 293−296.

(20) Substrate **25** was prepared by treatment of the corresponding C7-potassium alkoxide (KH at 0 °C) with 1-iodo-4-trifluoromethylbenzene (1 equiv).

Table 3. Tandem Mo-Catalyzed AROM/CM Reactions with Norbonyl Tertiary Ethers and Styrene[a]

entry	substrate	product	time (h)	conv (%);[b] conv to prod (%)	trans[c] (%)	ee[d] (%)	yield[e] (%)
1	 **28**	 **29**	0.8	>98; >98	>98	>98	85[f]
2	 **30**		12	—— NO REACTION ——			
3	 **31**	 **32**	14	94; 94	>98	98	84
4	 **33**	 **34**	1.2	>98; >98	>98	>98	84
5	 **35**	 **36**	0.5	>98; >98	>98	>98	32

[a] Conditions: 5 mol % of **1a**, 2 equiv of **4a**, Ar atm, 22 °C, C_6H_6. [b] Percent product determined by 400 MHz ^{1}H NMR analysis. [c] Determined by 400 MHz ^{1}H NMR analysis. [d] Determined by chiral HPLC (AD Chiralpak for entries 1 (on the deprotected alcohol) and 4 and Chiralcel OD for entries 3 and 5), in comparison with authentic racemic materials. [e] Isolated yield of purified products by silica gel chromatography. [f] Overall yield of deprotected alcohol.

of unreacted starting material). Addition of diallyl ether to the reaction mixture leads to rapid and complete RCM to afford 2,5-dihydrofuran. Therefore, the lack of reactivity is not due to irreversible binding of the catalyst to the Lewis basic ester moiety, leading to its sequestration and inactivation. It is possible however that association of the ester carbonyl with the Lewis acidic Mo center preempts reaction with the strained olefin. The observed catalyst inhibition may be due to the following: (i) The Mo center becomes significantly less Lewis acidic due to chelation with the ester group and thus does not bind to an olefin unless it is dissociated from the substrate (reassociation with alkene may rapidly lead to re-coordination with the ester). (ii) Geometric contraints do not allow Mo-olefin association once the transition metal is bound to the ester unit (either intramolecular Mo transfer from ester to alkene or two-point binding of Mo with alkene and ester is inhibited).

(d) Catalytic AROM/CM Reaction of Tertiary Norbornyl Ethers. The catalytic transformations illustrated above provide a unique, efficient, and highly enantioselective entry to the preparation of functionalized cyclopentanes that bear a secondary C−O bond and easily differentiable olefin moieties. Next, we extended this strategy to the catalytic asymmetric preparation of adducts that bear tertiary ether units. Considering the scarcity of effective methods for enantioselective alkylation of ketones,[21] we judged that, if successful, the Mo-catalyzed AROM/CM protocol would provide a valuable tool that can be used in enantioselective synthesis. The results of our study regarding catalytic metatheses of tertiary norbornyl ethers are summarized in Table 3.

As illustrated in entry 1 of Table 3, treatment of tertiary MOM ether **28**[22] with 5 mol % of **1a** in the presence of 2 equiv of styrene (**4a**) leads to the rapid formation of optically pure (>98% ee) diene **29** (85% yield of the derived alcohol after silica gel chromatography). Olefin stereocontrol is complete (>98% trans isomer) and there are <2% byproducts detected in the 400 MHz ^{1}H NMR spectrum of the unpurified reaction mixture (cf. **II**−**IV**, Table 1). *Whereas catalytic AROM/CM of **28** is complete in less than 1 h, when diastereomeric MOM ether **30** (entry 2) is subjected to the same reaction conditions, even after 12 h there is no detectable product formation* (<2% by 400 MHz ^{1}H NMR). Tertiary ether **31** reacts with **4a** to deliver optically pure **32** in 14 h (entry 3, Table 3). The conclusion may thus be drawn that the heteroatom substituent must be disposed such that it is proximal to the reacting olefin (see below for discussions on mechanism). Nonetheless, the high reactivity of the epoxide diastereomer **33**,[23] shown in entry 4 of Table 3, suggests that with less hindered C7 alkyl substituents catalytic AROM/CM may proceed efficiently. The cyclic nature of the epoxide ring is expected to impose less steric hindrance toward the approaching Mo complex (vs an *n*-Bu group). (See below for further discussion of the influence of resident heteroatoms on reactivity.)

Mechanistic implications notwithstanding, the epoxycyclopentane **34**, a compound that should readily serve as a versatile optically pure synthon, is obtained in >98% ee, >98% trans selectivity, and in 84% yield after silica gel chromatography. Entry 5 of Table 3 depicts a related example that involves the efficient catalytic enantioselective preparation of optically pure acetal **36**.[24]

(e) Range of Terminal Olefin Partners. The experiments outlined above involve various styrene substrates. This class of terminal alkenes includes attractive reaction partners that may be used in Mo-catalyzed AROM/CM reactions, since the related homodimerization process is relatively slow (<2% stilbene and related derivatives observed in all experiments). As depicted in Scheme 5, the suitability of other terminal olefin systems for effective participation in the catalytic AROM/CM processes was examined as well.[25] When (vinyl)trimethylsilane is used with norbornyl MOM ether **17**, functionalized cyclopentyl ether **37** is obtained in >98% ee and 62% isolated yield (Scheme 5). (Vinyl)trimethoxysilane can also be used effectively with the added advantage that the derived product can be directly subjected to Pd-catalyzed cross-coupling[26] to afford other optically pure cyclopentyl dienes (e.g., **38**). It must be noted that catalytic transformations with (vinyl)trimethylsilanes and (vinyl)trimethoxysilane are significantly slower than those of styrenes **4**. This difference in reactivity is likely partly attributable to the steric bulk of the silyl moiety. Hyperconjugative effects of the silylated anti Mo-alkylidenes **A** and **B** and chelation in **B**,[27] shown in Scheme 4, could not only lead to diminished transition metal Lewis acidity and result in lower reaction rates but also cause reduced availability of the syn alkylidene isomer. Slower catalytic metatheses would therefore

(21) (a) Dosa, P. I.; Fu, G. C. *J. Am. Chem. Soc.* **1998**, *120*, 445−446. (b) Casolari, S.; D'Addario, D.; Tagliavini, E. *Org. Lett.* **1999**, *1*, 1061−1063.

(22) For synthesis of the ketone used to prepare substrates **28**, **30**, and **31** in Table 3, see: Gassman, P. G.; Pape, P. G. *J. Org. Chem.* **1964**, *29*, 160−163.

(23) For preparation of substrate **33**, see: Bly, R. K.; Bly, R. S. *J. Org. Chem.* **1963**, *28*, 3165−3172.

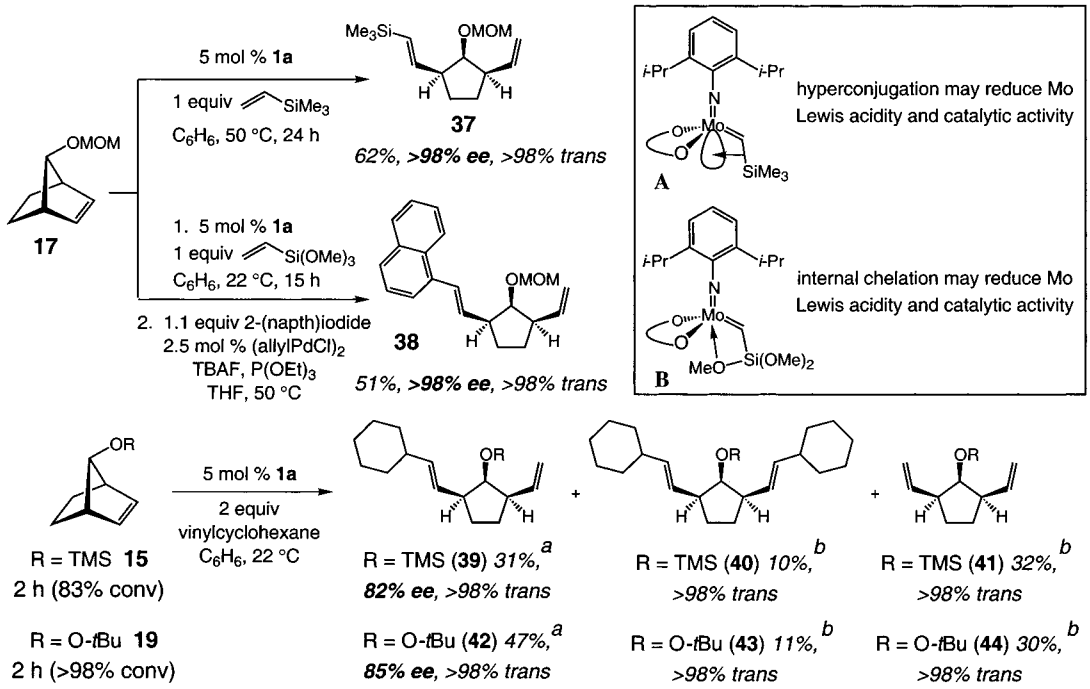
(24) The ^{1}H NMR spectrum of the unpurified reaction mixture for catalytic AROM/CM of **35** indicates the presence of the desired **36** only with <2% byproduct formation. The low isolated yield is due to the instability of the acetal product to silica gel.

(25) For Mo-catalyzed cross metatheses reactions involving allylsilanes, see: Crowe, W. E.; Goldberg, D. R.; Zhang, Z. J. *Tetrahedron Lett.* **1996**, *37*, 2117−2120.

(26) Tamao, K.; Kobayashi, K.; Ito, Y. *Tetrahedron Lett.* **1989**, *30*, 6051−6054.

(27) For a previous report, where Mo−O coordination is proposed to lead to the stabilization of the anti Mo-alkylidene isomer, see: Schrock, R. R.; Crowe, W. E.; Guillermo, C.; DiMare, M.; O'Regan, M. B.; Schofield, M. H. *Organometallics* **1991**, *10*, 1832−1843.

Scheme 5. Mo-Catalyzed AROM/CM with Non-Styrenyl Alkenes



[a] Isolated yield after deprotection of the TMS and *t*-Bu group (overall for two steps); 41% conversion for **39**, 59% conversion for **42**. [b] Percent conversion based on analysis of the 400 MHz ^{1}H NMR spectrum of the unpurified reaction mixture.

be observed regardless of whether it is the syn or the anti alkylidene isomer that is the active complex. There is spectroscopic evidence in support of the hyperconjugation illustrated in **A** (Scheme 5): the ^{1}H NMR spectrum of silylated Mo-alkylidene generated from reaction of **1a** and vinyltrimethylsilane exhibits an equal mixture of syn and anti isomers, whereas that of styrene (**1a**) shows a 3:1 ratio.[28]

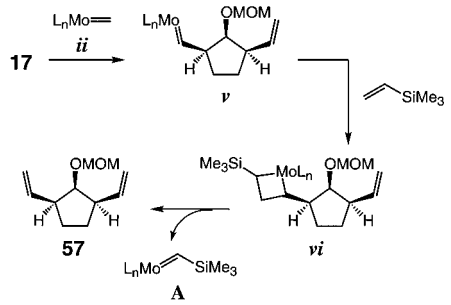
Three additional issues regarding the proposed intermediacy of substituted Mo-alkylidenes represented by **A** and **B** merit mention: (i) If the above catalytic AROM/CM reactions involved the intermediacy of the Mo-methylidene ***ii*** (vs alkylidenes represented by **A** and **B**), little rate difference would be expected between reactions with styrenes and vinylsilanes (more on the identity of the active Mo-alkylidene, below).[29] (ii) The lower reactivity of the silylated alkylidenes may be partially tied to delocalization of the electron density at the carbon atom of the Mo=C moiety into the available empty d orbitals of the adjacent Si atom (see below for further discussion). (iii) Another rationale for the lower reactivity of vinylsilanes is that the derived metal alkylidene (**A**) may be converted to an α,α'-disubstituted metallacycle that can undergo a β-hydride rearrangement to deliver a reduced and inactive Mo(IV) complex.[30]

The catalytic transformation of TMS ether **15** with aliphatic vinylcyclohexane (→ **39**, Scheme 5) is hampered by substantial formation of homometathesis products from the terminal olefin substrate in addition to dienes **40** and **41** (Scheme 4). Diene **40** is the result of further CM of the initial AROM/CM product **39**. The deprotected alcohol corresponding to chiral nonracemic cyclopentane **39** is obtained in 31% isolated yield and 82% ee (>98% trans); the unpurified mixture contains ~40% **40** and **41**. The reaction of *tert*-butoxy ether **19** proceeds to deliver **42** with similar levels of enantioselectivity (85% ee vs 82% ee with **15**). Under identical conditions, AROM/CM product **42** is generated more efficiently than **39** (59% vs 41% conversion by ^{1}H NMR analysis). If these transformations were allowed to proceed further, larger amounts of the disubstituted meso products **40** and **43** would be isolated. In support of the above contention, unlike styrenes, which are relatively resistant toward homometathesis, when vinylcyclohexane is treated with 5 mol % of **1a** (22 °C, C_6D_6), 30% of the corresponding homometathesis product is formed within 90 min. Additional studies are required for the identification of catalysts and conditions that allow catalytic AROM/CM reactions with aliphatic terminal alkenes to deliver outcomes competitive with that of styrenyl substrates.

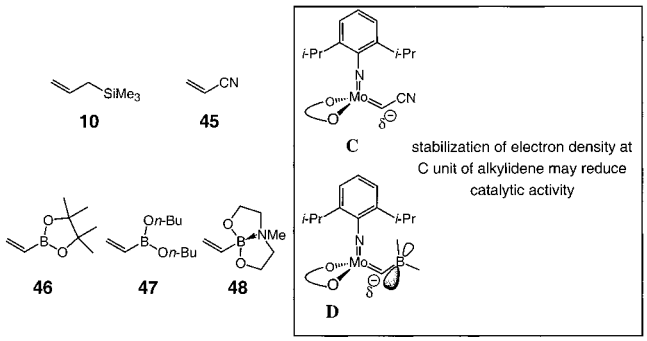
As illustrated in Scheme 6, a number of other terminal alkenes were examined as partners in Mo-catalyzed AROM/CM processes. Catalytic transformations of norbornyl TMS ether **15** with allylsilane **10** affords a complex mixture of products including homometathesis adduct of **10** and meso dienes represented by **II** and **IV** in Table 1. When the reaction is stopped before complete consumption of the starting material,

(28) Alexander, J. B.; Schrock, R. R.; Davis, W. M.; Hultzsch, K. C.; Hoveyda, A. H.; Houser, J. H. *Organometallics* **2000**, *19*, 3700−3715.

(29) It may be suggested that the Mo-alkylidene (***ii***) is the active catalyst (vs alkylidenes **A** or **B**) and the slower rate of reactions of vinylsilanes is due to conversion of the corresponding AROM intermediate, shown below, with a sterically more bulky terminal alkene (vs styrene). As will be discussed later, the alkylidene intermediate ***v*** would likely afford meso diene **57** (via metallacyclobutene ***vi***) instead of chiral diene **37**. Moreover, as will be described later it is unlikely that **57** is converted to chiral nonracemic **37** through a subsequent asymmetric CM (cf. eq 3 and Scheme 8).



Scheme 6. Ineffective Terminal Alkenes in Catalytic AROM/CM



substantial amounts of undesired products can be observed in the 400 MHz ^{1}H NMR spectrum of the unpurified reaction mixture, indicating that alternative pathways are competitive with the formation of the desired chiral AROM/CM adduct.

Mo-catalyzed reactions with acrylonitrile **45** and vinyl boranes **46** and **47**[31] result in <5% reaction after 12 h (5 mol % of **1a**, 22 °C). A plausible rationale for this lack of reactivity may involve the intermediacy of chiral Mo alkylidenes **C** and **D**, where the electron density at the carbon of the Mo=C is stabilized by the electron-withdrawing CN and Lewis acidic boron-containing groups, respectively.[32] Such charge delocalization may thus lead to stabilization of the Mo-alkylidenes, reducing the rate of formation of the intermediate metallacyclobutane. It must be noted that the above interactions do not necessarily lead to higher Lewis acidity of the Mo center, in turn enhancing initial catalyst−olefin association and catalytic activity. This is because the nonbonding electrons of the N atom of the imido ligand or diolate oxygens can donate into the Mo d orbitals and compensate for diminished electron density at the alkylidene carbon.[33] To minimize the Lewis acidity of the boron atoms in vinyl boranes, vinyl boronate **48** was prepared and examined. Despite the significant occupation of the boron p orbital by its heteroatom substituents, the terminal olefin in **48** proves to be an ineffective reaction partner as well.

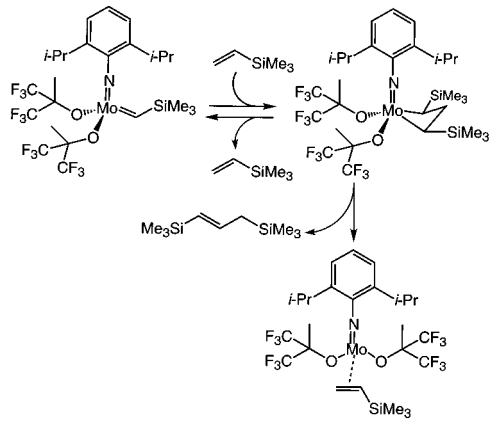
(f) The Identity of the Reacting Mo-alkylidene: Benzylidene vs Methylidene Complex. The arguments put forth above, in relation to the lack of reactivity of acrylonitrile **45** and vinyl boranes **46**−**48**, may also be extended to the faster rate of catalytic AROM/CM reactions with *p*-OMe styrene **4b** vs those of *p*-CF_3 styrene **4c**. With the more electron rich terminal alkene, the corresponding Mo-alkylidene might be more reactive, due to increased electron density at the alkylidene carbon. In contrast, similar to complex **C** (cf. Scheme 6), the electron-withdrawing CF_3 group stabilizes the alkylidene and diminishes its catalytic activity. Such rate differences are thus more easily rationalized if the intermediacy of Mo-benzylidene ***i*** is proposed instead of Mo-methylidene complex ***ii***. Similar logic was provided in relation to the lower reactivity of vinyl silanes vs styrenes (see Scheme 5).

To gain further insight regarding the identity of the Mo-alkylidene that is responsible for the above catalytic reactions (see box in Scheme 1), we monitored the progress of the reaction of chiral Mo complex **1a** with styrene by 400 MHz ^{1}H NMR spectroscopy. Treatment of **1a** with 40 equiv of styrene **4a** (to emulate catalytic conditions) in C_6D_6 at 22 °C leads to immediate release of cumyl ethylene olefin **51** (see Scheme 7) and generation of Mo-benzylidene ***i*** (L_n = 2,2′-di-*t*-Bu-4,5-dimethylbiphen). As illustrated in Scheme 7, the dd signal at δ 5.92 corresponds to the vinylic CH of **51** and the singlet at 11.50 represents the Mo-alkylidene CH of the syn isomer of the transition metal complex. Also illustrated in Scheme 7 is the expansion of the downfield region of the ^{1}H NMR spectrum; the minor singlet at δ 13.05 corresponds to the Mo=CH of the anti isomer (3:1 syn:anti).[34] We appreciate that the above observations do not bear testimony to the identity of the more active Mo complex. Rather, it is the indirect observations, such as the relative reactivity of various styrenes, that are perhaps more informative in that regard. The ^{1}H NMR experiments presented here simply indicate that formation of the Mo-benzylidene complex is rapid and highly favored, providing support for the paradigm that involves the participation of such complexes.

Additional indirect evidence favoring the preferential involvement of Mo-benzylidenes is illustrated in Scheme 8. If Mo-methylidene ***ii*** were an active catalyst, intermediate **49** would likely react with styrenes (e.g., **4a**) to afford meso diene **41** via molybdacyclobutane **50**. The alternative mode of addition, involving the intermediacy of metallacycle **52**, would be less favored (→ AROM/CM product **16a**). In the 2,4-disubstituted molybdacyclobutane **50**, the longer Mo−C bonds give rise to less steric repulsion between the aryl and alkyl groups; furthermore, the charge density at C of the C−Mo bond is better stabilized by the phenyl substituent. Thus, whereas addition by the Mo-benzylidenes and the related substituted alkylidenes affords the catalytic AROM/CM products shown in Tables 1−3, the meso diene byproducts **IV** (e.g., **41**; see also Table 1) are likely formed as a result of competitive reaction by Mo-methylidene ***ii***.

It may be argued that Mo-methylidene (***ii***) might be an active catalyst and meso dienes such as **41** may well be intermediates

(30) (a) Robbins, J.; Bazan, G. C.; Murdzek, J. S.; O'Regan, M. B.; Schrock, R. R. *Organometallics* **1991**, *10*, 2902−2907. (b) Schrock, R. R.; Murdzek, J. S.; Bazan, G. C.; Robbins, J.; DiMare, M.; O'Regan, M. *J. Am. Chem. Soc.* **1990**, *112*, 3875−3886.



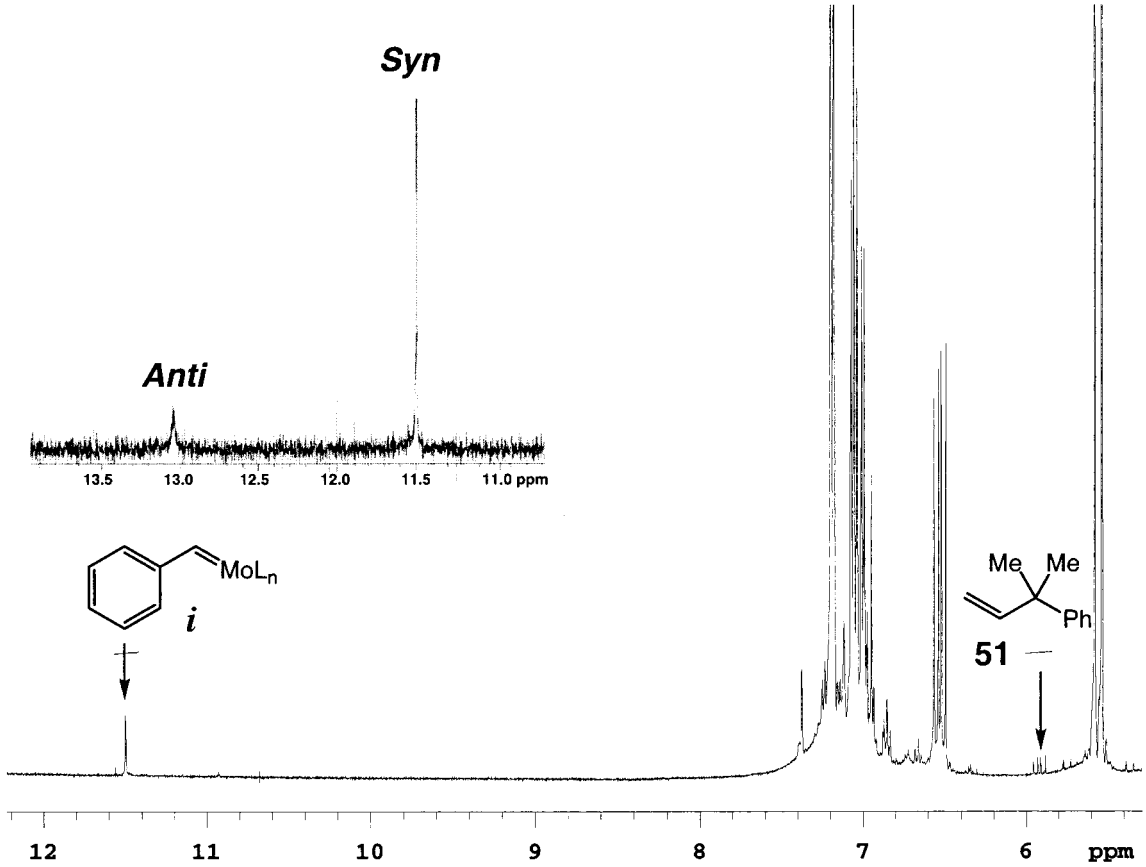
(31) Vinylboranes **46**−**48** were prepared according to published procedures: Matteson, D. S. *J. Am. Chem. Soc.* **1960**, *82*, 4228−4233.

(32) For Ru-catalyzed olefin metathesis reactions involving vinylboranes, see: Renaud, J.; Ouellet, S. G. *J. Am. Chem. Soc.* **1998**, *120*, 7995−7996.

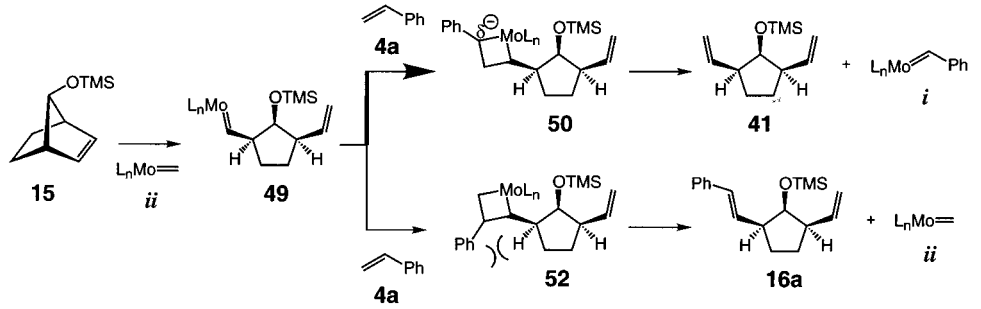
(33) Consistent with this rationale, positioning of electron-withdrawing groups (e.g., CF_3 or halogens) at the C_2 and/or C_6 positions of the imido ligand leads to enhanced catalytic activity. This is because reduction of electron density at the Mo-centered LUMO is concomitant with lowering of imido N Lewis basicity; Jamieson, J. Y.; Kiely, A.; Hoveyda, A. H.; Schrock, R. R. Unpublished results. See also: Weatherhead, G. S.; Houser, J. H.; Ford, J. G.; Jamieson, J. Y.; Schrock, R. R.; Hoveyda, A. H. *Tetrahedron Lett.* **2000**, *41*, 9553−9559.

(34) The assignment for syn and anti Mo-alkylidene protons is based on values previously reported for biaryl-Mo systems (vs bis(alkoxides)Mo complexes). See: (a) Totland, K. M.; Boyd, T. J.; Lavoie, G. G.; Davis, W. M.; Schrock, R. R. *Macromolecules* **1996**, *29*, 6114−6125. (b) O'Dell, R.; McConville, D. H.; Hofneister, G. E.; Schrock, R. R. *J. Am. Chem. Soc.* **1994**, *116*, 3414−3423.

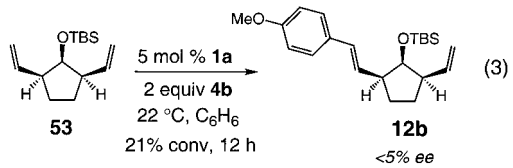
Scheme 7



Scheme 8



in the AROM/CM catalytic cycle. This paradigm would then involve, as illustrated in eq 3, catalytic *inter*molecular desymmetrization of such meso dienes through an asymmetric cross-metathesis (ACM) transformation. To address this possibility, authentic diene **53** was prepared and treated with 5 mol % of **1a** in the presence of 2 equiv of *p*-OMe styrene **4b** to deliver the expected AROM/CM product in the racemic form (<5% ee). Thus, the catalytic enantioselective transformation shown above involves an AROM rather than an asymmetric cross metathesis.



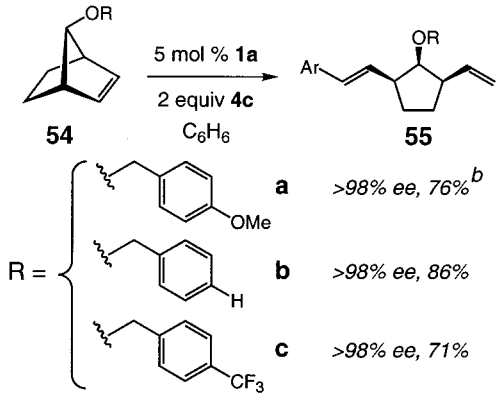
(g) The Effect of Substrate Lewis Basic Sites on Reactivity. To investigate the unexpected effect of the stereochemistry of the neighboring heteroatom on reactivity (see entry 2, Table 3), we prepared benzyl ethers **54a**−**c** shown in Scheme 9. We reasoned that the above-mentioned reactivity difference may involve, in part, simultaneous association of the transition metal with the Lewis basic heteroatom and the norbornyl olefin.[35] If such a scenario is operative, subtle electronic variations, such as those that exist in **54a**−**c**, would manifest themselves in terms of differential reaction rates.

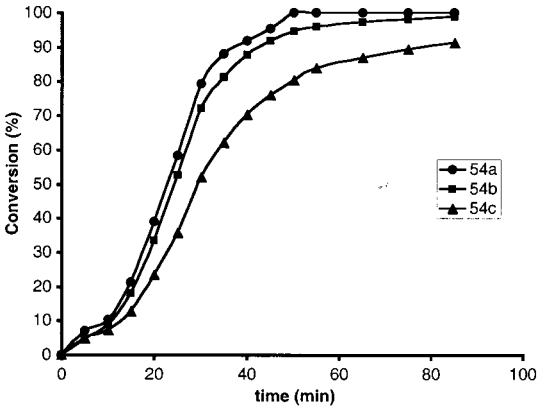
As illustrated in Scheme 9, when all three benzyl ethers are allowed to undergo asymmetric metathesis in the same vessel, AROM/CM products are obtained in >98% ee and 71−86% yield (>98% trans). Importantly, however, *p*-CF_3-benzyl ether **54c** reacts noticeably slower than *p*-OMe-benzyl ether **54a** (22 °C). *The rate differences observed are notable, particularly in light of the fact that the aryl groups of the benzyl ethers are separated from the C7 oxygen by a methylene unit.*[36]

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

(36) Our attempts to prepare the corresponding phenyl ethers were successful only in the case of *p*-CF_3-phenyl ether **25** (see entry 4, Table 2).

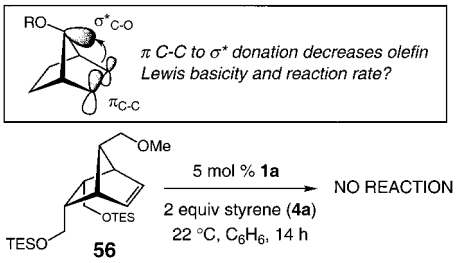
Scheme 9[a]





[a] Yields of reactions run individually (not as mixture of 54a−c). [b] >98% trans in all cases.

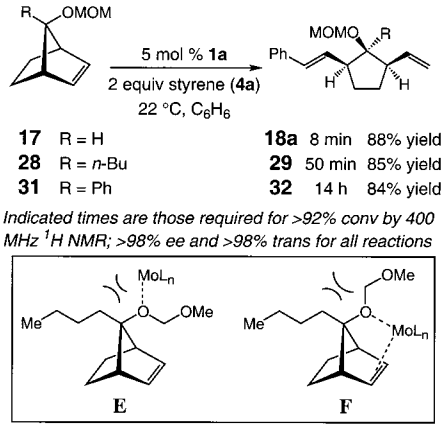
Scheme 10



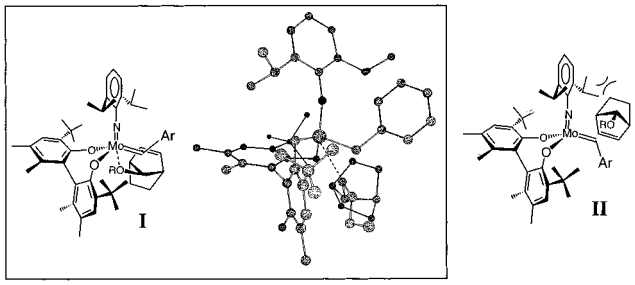
The above data do not preclude other factors that lead to the rate difference observed and may be less relevant in the case of sterically congested C7 silyl ethers. For example, it is tenable that anti norbornyl ethers such as **30** (see Table 3) may be rendered *unreactive* by a specific electronic factor (vs activation of syn norbornenyl diastereomer by chelation). As illustrated in Scheme 10, one such scenario could involve diminution of olefin Lewis basicity as a result of donation of π electrons to σ^* C−O at C7.[37] Efficient catalytic metathesis of epoxide **33** and acetal **35** (entries 4−5, Table 3) and the lack reactivity of **56**[38] (Scheme 10) suggest, however, that the latter issues may not be significant and it may well be the positioning of the heteroatom vis-à-vis the reacting olefin that is the critical factor to reactivity. The unfavorable hyperconjugative effects shown in Scheme 10 can reduce reactivity, but they are likely not the predominant reason as to why most anti tertiary ether norbornenes are completely resistant to catalytic AROM/CM.

Examination of the data presented in Tables 1−3 reveals reactivity trends that may shed further light on factors related to substrate−catalyst interaction. As the results in Scheme 11 illustrate, whereas secondary ether **17** is completely consumed in 8 min to afford optically pure **18a**, catalytic AROM/CM with tertiary ether **28** requires 50 min to proceed to completion (→ optically pure **29**) and that of tertiary ether **31** proceeds to 94% conversion after 14 h (→ optically pure **32**). One plausible explanation for the observed rate differences may involve requisite Mo-oxygen association, as shown in **E** and **F** (Scheme 11). It may be argued, however, that approach of the sterically demanding Mo complex from the exo face of the norbornyl alkene would cause steric strain due to enforced propinquity between the OMOM and the C7 alkyl groups (**F**, Scheme 11).

Scheme 11



Scheme 12



Regardless of the exact origin of the rate variations depicted in Scheme 11, these data illustrate that the steric bulk of substituents that are seemingly remote from the reactive alkene site may have a notable influence on the facility of the catalytic AROM/CM reaction.

(h) The Origin of Stereochemical Induction in Mo-Catalyzed AROM/CM. A transition state model, consistent with the stereochemical outcome of the above catalytic transformations, is proposed in Scheme 12 (complex **I**). The approach of the alkene occurs from the face of the transition metal complex so that the olefin can attain maximum overlap with the Mo-based LUMO,[39] and the addition of the syn Mo complex takes place from the exo face of norbornyl ethers. The alternative mode of addition (**II**), with the anti isomer of the Mo-benzylidene complex, would suffer from unfavorable steric strain between the substrate and the *i*-Pr units at the C2 and C6 position of the imido ligand. Thus, the lower sense of enantioselectivity observed in the reaction of TBS ether **11** and styrene with the corresponding dimethyl catalyst **1b** is consistent with

(37) Winstein, S.; Shatavsky, M.; Norton, C.; Woodward, R. B. *J. Am. Chem. Soc.* **1955**, *77*, 4183−4184.

(38) Substrate **56** was prepared according to a previously reported procedure. See: Corey, E. J.; Ravindranathan, T.; Terashima, S. *J. Am. Chem. Soc.* **1971**, *93*, 4326−4327.

the suggested paradigm (79% ee vs 98% ee with catalyst **1a**). The steric repulsion between the Ar group of the alkylidene and the imido ligand substituents is minimized by the large Mo=C−C angle caused by agostic interaction between the alkylidene C−H and Mo−N σ^* orbital (Mo−C has significant triple bond character). The latter hyperconjugative association implies reduced Lewis acidity of the Mo center. The driving force behind the preference for **I** over the more Lewis acidic **II** may thus be largely steric in nature. Approach of the alkene toward the Mo complex is consistent with the orientation of the complex's LUMO (front approach is blocked by the protruding *t*-Bu group). The approach of the norbornene substrate, as shown in **I**, allows interaction of the C7 heteroatom with the Mo−N σ^*, an antibonding orbital that is believed to be the next ranking LUMO.[40] Such an association accounts for the observed rate differences in reactions of various benzyl ethers (Scheme 9) and the substantial rate differences shown in entries 1−2 of Table 3.

Conclusions

We have disclosed the details of our studies regarding the first examples of catalytic asymmetric ring-opening metathesis (AROM) reactions. The catalytic enantioselective C−C bond cleavage (ring-opening) is followed by a C−C bond-forming cross metathesis reaction to afford efficiently a wide range of functionalized cyclopentanes in the optically pure form (>98% ee) with complete control of olefin stereochemistry (>98% trans). Products may bear either a secondary or a tertiary ether stereogenic center, in addition to a terminal and a trans disubstituted alkene. Considering the paucity of methods available for enantioselective synthesis of tertiary ethers and because olefinic moieties can be further functionalized in a variety of manners, the present protocol offers a unique catalytic approach to optically pure materials that should serve as building blocks for enantioselective complex molecule synthesis.

Future work includes the development of efficient catalytic AROM/CM reactions involving other alkene substrates (instead of norbornenes), catalytic processes that allow utilization of vinyl boranes, and applications to complex molecule total synthesis.

Experimental Section[41]

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 Varian Gemini 2000 (400 MHz) and Varian INOVA 500 (500 MHz) spectrometers. Chemical shifts are reported in ppm from tetramethylsilane with the solvent resonance as the internal standard ($CDCl_3$: δ 7.26). Data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, br = broad, m = multiplet), coupling constants (hertz), integration. ^{13}C NMR spectra were recorded on Varian Gemini 2000 (100 MHz) and Varian NOVA (125 MHz) spectrometers with complete proton decoupling. Chemical shifts are reported in ppm from tetramethylsilane with the solvent as the internal reference ($CDCl_3$: δ 77.70 ppm). Enantiomer ratios were determined by chiral HPLC analysis (Chiral Technologies Chiralcel OD, Chiralpak OJ, and Chiralpak AD (0.46 cm × 25 cm) in comparison with authentic racemic materials. Microanalyses were performed by Robertson Microlit Laboratories (Madison, NJ). High-resolution mass spectrometry was performed at the University of Illinois Mass Spectrometry Laboratories (Urbana-Champaign, IL).

All reactions were conducted in oven- (135 °C) and flame-dried glassware under an inert atmosphere of dry argon. All metathesis substrates were vigorously dried by repeated (3 times) azeotropic distillation of water (benzene) under high vacuum. Handling of Mo catalyst was done in a drybox. Benzene was distilled from sodium metal/benzophenone ketal. CH_2Cl_2 was distilled from CaH_2 under an atmosphere of Ar. Mo(NAr)($CHCMe_2Ph$)$(OTf)_2$·DME,[30b] Mo(N-2,6-(i-Pr)$_2C_6H_3$)($CHCMe_2Ph$)((*S*)-(−)-*tert*-Bu_2Me_4(biphen)),[8a] and (*R*)-(+)-Mo(N-2,6-(i-Pr)$_2C_6H_3$)($CHMe_2Ph$)(3,3′-bis(2,4,6-triisopropylphenyl)-2,2′-dihydroxy-1,1′-dinaphthyl)·THF[9] were synthesized based on previously reported procedures.

Representative Procedure for Mo-Catalyzed Asymmetric Ring-Opening Metathesis/Cross Metathesis. In a drybox, substrate **15** (163 mg, 0.891 mmol) was dissolved in benzene (4.46 mL). A 1.0 M solution of **4b** in benzene (1.78 mL) was then added to the vessel followed by the addition of optically pure catalyst **1a** (6.77 mg, 9.00×10^{-3} mmol) in one portion. A Teflon cap was secured to the vessel and the reaction was allowed to stir at 22 °C. After 5 h, the reaction was exposed to air and the volatiles were removed in vacuo. The dark brown residue was purified by silica gel chromatography (60:1 hexanes:Et_2O). Organic solvents were removed to afford **16b** as a colorless oil (259 mg, 92%).

(1*S*,2*S*,5*R*)-1-*tert*-Butoxy-2-styryl-5-vinylcyclopentane (20). IR (NaCl): 3074 (w), 2968 (s), 1634 (w), 1369 (m), 1193 (m), 1092 (m) cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ 7.38 (d, J = 7.5 Hz, 2H), 7.32 (t (br), J = 7.5 Hz, 2H), 7.20 (t, J = 7.0 Hz, 1H), 6.37 (dd, J = 16.5, 7.5 Hz, 1H), 6.33 (d, J = 16.0 Hz, 1H), 5.97 (ddd, J = 17.5, 10.5, 9.0 Hz, 1H), 5.03−4.96 (m, 2H), 4.01 (t, J = 4.0 Hz, 1H), 2.69 (ddd, J = 13.5, 5.0, 5.0 Hz, 1H), 2.57 (ddd, J = 13.5, 4.0, 4.0 Hz, 1H), 1.85−1.75 (m, 4H), 1.17 (s, 9H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 141.4, 138.3, 133.7, 128.9, 128.7, 126.9, 126.2, 113.8, 79.1, 73.5, 50.7, 49.9, 29.9, 29.6, 29.3. HRMS calcd for $C_{19}H_{26}O$: 270.1984. Found: 270.1993. Anal. Calcd for $C_{19}H_{26}O$: C, 84.39; H, 9.69. Found: C, 84.18; H, 9.48.

(1*S*,2*R*,3*R*,4*S*,5*S*)-4-*tert*-Butoxy-1,2-*O*-isopropylidene-3-styryl-5-vinylcyclopentane (22). IR (NaCl): 3069 (w), 2980 (s), 2936 (m), 1646 (w), 1401 (m), 1212 (s), 1086 (s) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.36 (d, J = 7.2 Hz, 2H), 7.30 (t (br), J = 7.2, 2H), 7.20 (t (br), J = 7.2 Hz, 1H), 6.48 (d, J = 16.0 Hz, 1H), 6.33 (dd, J = 16.0, 8.8 Hz, 1 H), 5.97 (ddd, J = 17.2, 10.0, 8.8 Hz, 1H), 5.17 (dd, J = 17.6, 0.4 Hz, 1H), 5.13 (ddd, J = 10.4, 2.0, 0.8 Hz, 1H), 4.67−4.60 (m, 2H), 4.27 (t, J = 4.6 Hz, 1H), 2.81 (ddd, J = 9.2, 4.8, 4.8 Hz, 1H), 2.68 (ddd, J = 9.2, 4.8, 4.8 Hz, 1H), 1.53 (s, 3H), 1.33 (s, 3H), 1.11 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 138.0, 137.7, 129.8, 129.0, 127.6, 126.6, 116.9, 113.0, 84.9, 84.5, 81.1, 74.7, 56.5, 55.7, 29.6, 28.1, 25.5. HRMS calcd for $C_{22}H_{30}O_3$: 342.2195. Found: 342.2200. Anal. Calcd for $C_{22}H_{30}O_3$: C, 77.16; H, 8.83. Found: C, 76.88; H, 8.58.

(1*S*,2*R*,3*R*,4*S*,5*S*)-4-*tert*-Butoxy-1,2-diacetoxy-3-styryl-5-vinylcyclopentane (24). IR (NaCl): 2980 (m), 1759 (s), 1388 (m), 1250 (s), 1086 (m) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.36 (dd, J = 7.6, 1.2 Hz, 2H), 7.31 (dd, J = 7.2, 7.2 Hz, 2H), 7.21 (ddd, J = 8.0, 8.0, 1.2 Hz, 1H), 6.41 (d, J = 16.0 Hz, 1H), 6.27 (dd, J = 16.0, 9.2 Hz, 1H), 5.92 (ddd, J = 17.6, 9.2, 9.2 Hz, 1H), 5.36−5.32 (m, 2H), 5.13−5.09 (m, 2H), 4.16 (t, J = 5.6 Hz, 1H), 2.92−2.74 (m, 2H), 2.04 (s, 3H), 2.02 (s, 3H), 1.09 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.9, 138.2, 137.3, 132.8, 129.6, 129.2, 128.3, 127.2, 118.1, 76.2, 75.9, 75.5, 55.0, 54.1, 30.0, 22.0. HRMS calcd for $C_{23}H_{30}O_5$: 386.2093. Found: 386.2091. Anal. Calcd for $C_{23}H_{30}O_5$: C, 71.48; H, 7.82. Found: C, 71.55; H, 7.57.

(1*S*,2*S*,5*R*)-1-(4-Trifluoromethylphenoxy)-2-styryl-5-vinylcyclopentane (26). IR (NaCl): 3037 (w), 2968 (m), 1627 (m), 1527 (m), 1331 (s), 1256 (s), 1124 (s) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.48 (d, J = 6.8 Hz, 2H), 7.28−7.18 (m, 5H), 7.01 (d, J = 6.8 Hz, 2H), 6.45 (d, J = 12.8 Hz, 1H), 6.17 (dd, J = 12.8, 6.8 Hz, 1H), 5.89 (ddd, J = 14.0, 8.4, 6.8 Hz, 1H), 5.13 (dd, J = 14.0, 0.8 Hz, 1H), 5.01 (dd, J = 8.0, 1.2 Hz, 1H), 4.75 (t, J = 2.8 Hz, 1H), 2.99−2.84 (m, 2H), 2.06−1.95 (m, 4H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 162.7, 138.6,

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(41) The spectral and analytical data for products in Table 1 and the X-ray data for the crystal structure in Figure 1 may be found in the Supporting Information section of ref 10.

137.9, 131.2, 130.6, 129.0, 127.7, 127.3, 123.7, 123.0, 116.6, 116.4, 87.1, 50.8, 50.3, 30.2, 29.7. HRMS calcd for $C_{22}H_{21}F_3O$: 358.1544. Found: 358.1536. Anal. Calcd for $C_{22}H_{21}F_3O$: C, 73.73; H, 5.91. Found: C, 73.62; H, 5.73.

(1*S*,2*S*,5*R*)-1-Butyl-2-styryl-5-vinylcyclopentanol (Alcohol Derived from 29). To a solution of **29** (9.90 mg, 3.15×10^{-2} mmol in 0.222 mL CH_2Cl_2) was added an activated 4 Å molecular sieve and the mixture was cooled to −30 °C in a dry ice/acetone bath (monitored by external thermometer). TMSBr (16.6 μL) was then added dropwise to the stirring solution over 1 min. The vessel was then transferred to an ice bath and warmed to 0 °C. The reaction was stirred for 8 h and then poured into 5 mL of a saturated solution of sodium bicarbonate. This mixture was then washed three times with 10 mL of CH_2Cl_2. The organic layers were combined, dried over $MgSO_4$, filtered, and concentrated by rotary evaporation. The crude product was purified by silica gel chromatography (12:1 hexanes:diethyl ether). The organic solvent was removed to provide (1*S*,2*S*,5*R*)-1-butyl-2-styryl-5-vinylcyclopentanol as a colorless oil (8.49 mg, 99%). IR (NaCl): 3484 (m), 2943 (s), 2873 (m), 1659 (m), 1470 (m) cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ 7.42−7.39 (m, 2H), 7.32 (ddd, J = 8.0, 8.0, 2.0 Hz, 2H), 7.23 (tt, J = 7.5, 1.5 Hz, 1H), 6.45 (d, J = 16.0 Hz, 1H), 6.31 (dd, J = 15.5, 8.0 Hz, 1H), 5.18 (ddd, J = 10.5, 2.0, 0.5 Hz, 1H), 5.13 (ddd, J = 17.0, 2.0, 1.0 Hz, 1H), 2.65 (dd, J = 18.0, 9.0 Hz, 1H), 2.55 (dd, J = 17.0, 9.0 Hz, 1H), 1.93−1.82 (m, 4H), 1.57−1.28 (m, 6H), 0.92 (t (br), J = 6.5 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 138.3, 138.0, 132.1, 130.4, 129.0, 127.6, 126.7, 117.3, 84.1, 51.7, 51.5, 37.9, 29.1, 28.3, 27.1, 24.1, 14.9. HRMS calcd for $C_{19}H_{26}O$: 270.1984. Found: 270.1982. Anal. Calcd for $C_{19}H_{26}O$: C, 84.39; H, 9.69. Found: C, 84.60; H, 9.76.

(1*S*,2*S*,5*R*)-1-Methoxymethoxy-1-phenyl-2-styryl-5-vinylcyclopentane (32). IR (NaCl): 3059 (m), 3025 (m), 2946 (s), 2905 (m), 2876 (m), 2829 (m), 2792 (w), 1652 (m), 1621 (m), 1494 (m), 1446 (m), 1306 (m), 1218 (m), 1159 (m), 1061 (s), 1023 (s), 929 (s) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.48−7.45 (m, 2H), 7.36−7.24 (m, 7H), 7.19 (tt, J = 6.8, 1.6 Hz, 1H), 6.50 (dd, J = 16.0, 8.4 Hz, 1H), 6.25 (d, J = 16.4 Hz, 1H), 6.10 (ddd, J = 18.0, 10.8, 8.0 Hz, 1H), 5.04 (d, J = 10.4 Hz, 1H), 4.96 (d, J = 18.0 Hz, 1H,), 4.59 (dd, J = 10.0, 6.4 Hz, 2H), 3.47 (s, 3H), 3.05 (dd, J = 16.8, 8.4 Hz, 2H), 2.94 (dd, J = 7.2, 8.4 Hz, 2H), 2.14−1.99 (m, 2H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 141.1, 138.5, 138.3, 131.9, 130.4, 129.1, 128.6, 127.9, 127.7, 127.6, 126.8, 117.0, 94.1, 92.4, 56.2, 55.9, 55.2, 28.8, 28.4. HRMS calcd for $C_{23}H_{26}O_2$: 334.1933. Found: 334.1931. Anal. Calcd for $C_{23}H_{26}O_2$: C, 82.60; H, 7.84. Found: C, 82.36; H, 7.62.

(3*R*,4*S*,7*R*)-4-Styryl-7-vinyl-1-oxaspiro[2.4]heptane (34). IR (NaCl): 3075 (w), 3028 (m), 2966 (s), 2929 (s), 2872 (m), 1647 (w), 1459 (m), 974 (m), 928 (m) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.34−7.28 (m, 4H), 7.21 (tt, J = 7.3, 1.5 Hz, 1H), 6.33 (d, J = 16.1 Hz, 1H), 6.02 (dd, J = 15.6, 8.8 Hz, 1H), 5.72−5.65 (m, 1H), 5.03 (dt, J = 4.9, 1.5 Hz, 1H), 5.00 (d, J = 1.0 Hz, 1H), 2.83 (dd, J = 15.1, 8.3 Hz, 1H), 2.75 (dd, J = 6.8, 4.9 Hz, 2H), 2.70 (dd, J = 14.6, 8.3 Hz, 1H), 2.18−2.08 (m, 2H), 1.80−1.70 (m, 2H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 138.6, 137.9, 131.6, 130.3, 129.2, 128.0, 126.8, 116.4, 70.4, 49.8, 48.4, 47.8, 30.8, 30.4.

(2*S*,5*R*)-1,1-Dimethoxy-2-styryl-5-vinylcyclopentane (36). IR (NaCl): 3027 (m), 2937 (s), 2848 (m), 1703 (s), 1635 (s), 1596 (m), 1492 (m), 1449 (s), 1360 (s), 1287 (s), 1230 (s), 1155 (m), 1070 (s), 964 (s), 918 (m) cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ 7.37−7.36 (m, 2H), 7.30 (dd, J = 7.8, 7.8 Hz, 2H), 7.20 (tt, J = 6.8, 1.2 Hz, 1H), 6.38 (d, J = 15.6, 1H), 6.34 (dd, J = 15.6, 6.8, 1H), 6.01 (ddd, J = 17.6, 10.7, 8.3 Hz, 1H), 5.09−5.04 (m, 2H), 3.27 (s, 3H), 3.26 (s, 3H), 2.91 (ddd, J = 7.3, 7.3, 4.4 Hz, 1H), 2.80 (ddd, J = 8.3, 8.3, 4.9 Hz, 1H), 2.02−1.91 (m, 2H), 1.75−1.67 (m, 2H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 139.7, 138.5, 131.6, 130.6, 129.2, 127.7, 126.8, 115.4, 112.3, 51.4, 50.8, 50.6, 49.8, 30.2, 30.0. HRMS calcd for $C_{17}H_{22}O_2$: 258.1620. Found: 258.1616. Anal. Calcd for $C_{17}H_{22}O_2$: C, 79.03; H, 8.58. Found: C, 78.80; H, 8.48.

(1*S*,2*S*,5*R*)-2-(2-Cyclohexylvinyl)-5-vinylcyclopentanol (Alcohol Derived from 39 and 42). A modified procedure for deprotection of is **42** based on literature precedent.[42] An unpurified mixture of three products (0.50 mmol total) obtained from reaction of **19** (84 mg, 0.50 mmol) with 5 mol % of **1a** was combined with 2.5 mL of CH_2Cl_2 in a 5 mL round-bottom flask. TMSI (93 μL, 0.65 mmol) was added dropwise, and the reaction was allowed to stir for 45 min. At this time, all starting material was consumed as indicated by TLC. The reaction was then diluted with 2.5 mL of CH_2Cl_2 and subsequently quenched by addition of 2 mL of ethanol. After addition of 3 mL of water, the resulting aqueous layer was washed three times with 3 mL portions CH_2Cl_2. Organic layers were combined and washed with 10 mL of a saturated solution of sodium bicarbonate, then dried over $MgSO_4$, filtered, and concentrated by rotary evaporation. ^1H NMR analysis of the unpurified mixture revealed successful deprotection of all three metathesis products. The desired product **(1*S*,2*S*,5*R*)-2-(2-cyclohexylvinyl)-5-vinylcyclopentanol** was isolated by silica gel chromatography (20:1 pentane:Et_2O) in 47% yield (52 mg, 0.24 mmol) over two steps from **19**. IR (NaCl): 3452 (m), 3075 (w), 2924 (s), 2848 (m), 1445 (w), 1073 (w), 973 (w), 910 (w) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 6.03−5.49 (m, 1H), 5.50−5.49 (m, 2H), 5.13 (d, J = 1.47 Hz, 1H), 5.10 (ddd, J = 5.5, 1.8, 1.5 Hz, 1H), 3.94−3.92 (m, 1H), 2.64−2.54 (m, 2H), 1.99−1.92 (m, 1H), 1.83−1.02 (m, 14H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 139.6, 139.1, 127.0, 116.4, 78.6, 50.1, 49.2, 41.6, 33.9, 28.2, 27.8, 26.8, 26.7. HRMS calcd for $C_{15}H_{24}O$: 220.1827. Found: 220.1833. Anal. Calcd for $C_{15}H_{24}O$: C, 81.76; H, 10.98. Found: C, 81.70; H, 10.87.

(1*S*,2*S*,5*R*)-1-(4-Methoxybenzyloxy)-2-styryl-5-vinylcyclopentane (55a). ^1H NMR (400 MHz, $CDCl_3$): δ 7.36−7.20 (m, 7H), 6.83 (d, J = 8.8 Hz, 2H), 6.42 (d, J = 15.6 Hz, 1H), 6.37 (dd, J = 16.0, 6.8 Hz, 1H), 6.05 (ddd, J = 17.6, 10.0, 8.4 Hz, 1H), 5.10 (dd, J = 17.2, 0.8 Hz, 1H), 4.53 (d, J = 11.2 Hz, 1H), 4.46 (d, J = 11.2 Hz, 1H), 3.83 (t, J = 4.0 Hz, 1H), 3.78 (s, 3H), 2.79−2.60 (m, 2H), 1.91−1.82 (m, 4H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.4, 140.0, 138.3, 132.2, 131.6, 130.2, 129.9, 129.0, 127.4, 115.3, 114.1, 87.7, 74.0, 55.9, 50.8, 50.0, 30.0, 29.6. HRMS calcd for $C_{23}H_{26}O_2$: 334.1933. Found: 334.1925. Anal. Calcd for $C_{23}H_{26}O_2$: C, 82.60; H, 7.84. Found: C, 82.49; H, 8.07.

(1*S*,2*S*,5*R*)-1-(4-Benzyloxy)-2-styryl-5-vinylcyclopentane (55b). IR (NaCl): 3609 (m), 2949 (s), 2873 (s), 1344 (m), 1099 (s) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.35−7.19 (m, 10H), 6.44 (d, J = 16.0 Hz, 1H), 6.39 (dd, J = 16.4, 6.8 Hz, 1H), 6.06 (ddd, J = 17.2, 10.0, 8.8 Hz, 1H), 5.12 (dd, J = 17.2, 1.2 Hz, 1H), 5.05 (d, J = 10.4 Hz, 1H), 4.60 (d, J = 11.6 Hz, 1H), 4.55 (d, J = 12.0 Hz, 1H), 3.85 (t, J = 4.4 Hz, 1H), 2.86−2.62 (m, 2H), 1.94−1.83 (m, 4H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 139.9, 139.1, 138.3, 132.1, 130.3, 129.0, 128.8, 128.3, 127.9, 127.4, 126.6, 115.4, 88.1, 74.4, 50.9, 50.1, 30.0, 29.7. Anal. Calcd for $C_{22}H_{24}O$: C, 86.80; H, 7.95. Found: C, 86.76; H, 8.03.

(1*S*,2*S*,5*R*)-1-(4-Trifluoromethylbenzyloxy)-2-styryl-5-vinylcyclopentane (55c). IR (NaCl): 2962 (w), 1331 (s), 1162 (m), 1136 (s) cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ 7.55 (d, J = 7.5 Hz, 2H), 7.44 (d, J = 8.5 Hz, 2H), 7.37−7.23 (m, 5H), 6.45 (d, J = 15.5 Hz, 1H), 6.35 (dd, J = 16.0, 8.5 Hz, 1H), 6.04 (ddd, J = 17.0, 10.0, 7.5 Hz, 1H), 5.14 (ddd, J = 17.0, 2.0, 1.0 Hz, 1H), 5.07 (dd, J = 10.5, 2.0 Hz, 1H), 4.66 (d, J = 12.0, 1H), 4.60 (d, J = 12.5 Hz, 1H), 3.86 (t, J = 4.0 Hz, 1H), 2.48−2.67 (m, 2H), 1.96−1.85 (m, 4H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 143.7, 139.7, 138.3, 131.8, 130.7, 129.2, 128.2, 127.7, 126.7, 125.8, 115.8, 88.7, 73.5, 50.7, 49.9, 29.8, 29.5. HRMS calcd for $C_{23}H_{23}F_3O$: 372.1701. Found: 372.1705. Anal. Calcd for $C_{23}H_{23}F_3O$: C, 74.18; H, 6.22. Found: C, 74.05; H, 6.44.

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Supporting Information Available: Experimental procedures and spectral and analytical data for starting materials (except for those in Table 1, which are found in the Supporting Information of ref 10). This material is available free of charge via the Internet at http//:www.acs.pubs.org.

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