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Highly *Z*- and Enantioselective Ring-Opening/Cross-Metathesis Reactions Catalyzed by Stereogenic-at-Mo Adamantylimido Complexes

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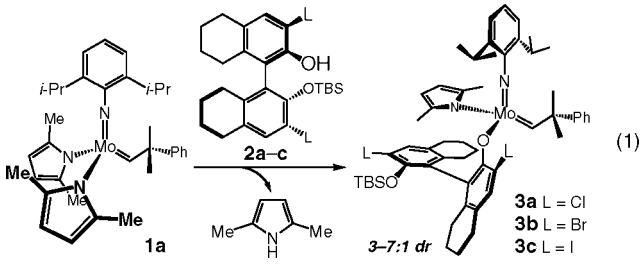
In spite of impressive advances accomplished during the past two decades, a number of unresolved issues limit the utility of catalytic olefin metathesis reactions.[1] A notable shortcoming is the lack of methods that selectively furnish *Z* alkenes.[2] Nearly all ring-opening/cross-metathesis (ROCM) reactions catalyzed by Mo or Ru complexes afford *E* olefins exclusively or predominantly.[3,4] Only when the cross partner bears an sp-hybridized substituent (acrylonitrile or an enyne) are *Z* alkenes, at times, favored.[5] Effective solutions to the above critical problem require the development of structurally distinct catalysts. Herein, we present an approach to catalytic enantioselective ROCM processes[6] that delivers *Z* olefins exclusively (>98:<2 *Z*/*E*) or with high selectivity (≥87:13 *Z*/*E*) in 50−85% yield and up to >98:<2 enantiomer ratio (er). These transformations are promoted by <2 mol % of a chiral stereogenic-at-Mo complex.

We recently introduced a class of olefin metathesis catalysts that bear a stereogenic metal center (e.g., **3a**−**c**, eq 1).[7] Mo alkylidenes are synthesized by treatment of a bispyrrolide (e.g., **1a**)[8] with a monoprotected binaphthol (**2a**−**c**).[7] In developing a *Z*-selective

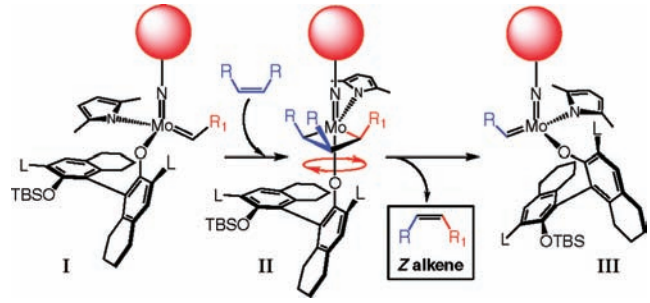


(1)

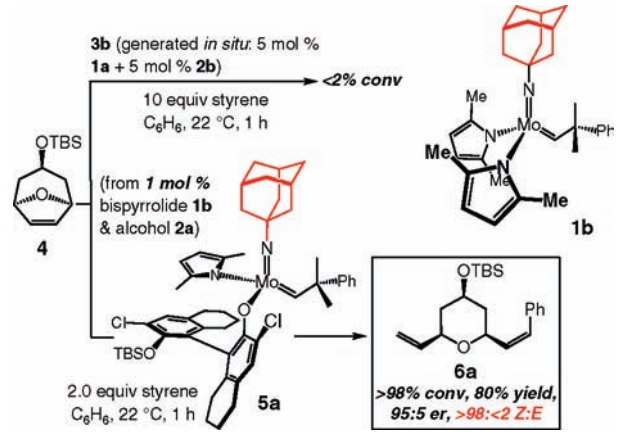
process, we reasoned that the flexibility of the Mo monoaryloxides should prove pivotal (Scheme 1). A sterically demanding but freely rotating (around the Mo−O bond) aryloxide in combination with a sufficiently smaller (vs aryloxide) imido substituent favors reaction through the *syn* alkylidene isomer (**I**, Scheme 1) and an all-*cis* metallacyclobutane (**II**, Scheme 1). Such a pathway would produce *Z* alkene products. In contrast, the hexafluoro-*t*-butoxides of an achiral Mo complex[6] or the rigidly held chiral bidentate ligands of Mo diolates (delivering >98% *E* olefins)[4a] present a less significant steric barrier; *trans*-substituted metallacyclobutanes thus become energetically accessible.

As the first step toward investigating the validity of the above hypotheses, we subjected oxabicycle **4** and styrene to chiral complex **3b**, prepared through treatment of 5 mol % **1a** with the corresponding aryl alcohol **2b**; the chiral catalyst is typically used *in situ*. As shown in Scheme 2, conversion to the desired ROCM product is not observed (<2% in 1 h; minimal benzylidene formation, as determined by 400 MHz ^{1}H NMR analysis). Such a finding led us to consider that the large arylimido in **3b**, together with the sizable aryloxide unit, might constitute a Mo complex that is too cumbersome to allow for formation of the requisite *syn* or *anti* alkylidene (cf. **I**) and subsequent cross-metathesis. We thus prepared **5a** (Scheme 2; 3.0:1 dr), an alkylidene that bears the smaller adamantylimido. Such an alteration, we reasoned, would enhance activity

Scheme 1. Size Difference between (Small) Imido and (Large) Aryloxide Ligands Can Lead to High *Z*-Selectivity



Scheme 2. Influence of the Imido Group of the Chiral Mo Complex on Efficiency and *E*/*Z*- and Enantioselectivity of ROCM



as well as promote *Z*-selectivity. When oxabicycle **4** is treated with a solution containing styrene, 1 mol % of adamantylimido bispyrrolide **1b**, and alcohol **2a**, ROCM proceeds to >98% conversion within 1 h, affording **6a** in 80% yield and 95:5 er. Most importantly, the desired product is obtained exclusively as a *Z* olefin (>98:<2 *Z*/*E*).

As the data summarized in entry 2 of Table 1 indicate, when Br-substituted chiral aryl alcohol **2b** is used to prepare the catalyst (**5b**), ROCM is catalyzed with an equally exceptional level of *Z*-selectivity but with improved enantioselectivity [98.5:1.5 er vs 95:5 er with **2a** as the aryl alcohol (entry 1)]. The product of the reaction with I-substituted **5c** is obtained in higher enantiomeric purity (>98:<2 er, entry 3), affording (*Z*)-**6a** predominantly (95:5 *Z*/*E*). The reaction efficiency is reduced with **5c** and **5d**: ROCM proceeds to ∼75% conversion, affording **6a** in 60 and 57% yield, respectively. With **5d**, catalyst synthesis is accompanied by generation of relatively inactive bisaryloxides (Table 1).[9] That is, in all of the processes described, the amount of catalytically active monoaryloxide is less than that indicated by the mole percent of bispyrrolide and alcohol used. For example, the effective catalyst loading for the transformation in entry 2 of Table 1 is ∼0.6 mol %. The lower *Z*-selectivity in the reaction with **5d** (entry 4, Table

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Table 1. *Z*- and Enantioselective ROCM of **4** with Styrene (To Afford **6a**) Catalyzed by Various Chiral Mo-Based Monoaryloxides[a]

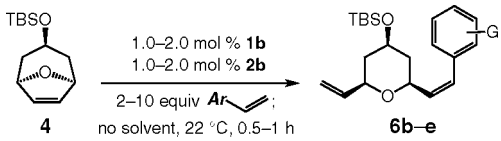
entry	chiral complex; complex dr[b]	mono/bisaryloxide/ bispyrrolide (%)	conv (%);[b] yield (%)[c]	er[d]	*Z*/*E*[e]
1	**5a** (L = Cl); 3.0:1	***56***:22:22	>98; 80	95:5	>98:<2
2	**5b** (L = Br); 2.2:1	***62***:08:30	98; 85	98.5:1.5	>98:<2
3	**5c** (L = I); 1.7:1	***67***:04:29	76; 60	>98:<2	95:5
4	**5d** (L = F); nd	***07***:47:46	75; 57	95:5	80:20

[a] Performed with 1.0 mol % bispyrrolide, 1.0 mol % enantiomerically pure (>98% ee) aryl alcohol, and 2.0 equiv of styrene in C_6H_6 (or toluene), 22 °C, 1.0 h, N_2 atmosphere. [b] Determined by analysis of 400 MHz ^{1}H NMR spectra of unpurified mixtures. nd = not determined. [c] Yield of purified products. [d] Determined by HPLC analysis (details are provided in the Supporting Information). [e] Determined by analysis of 400 MHz ^{1}H NMR spectra of unpurified mixtures in comparison with the authentic *E* olefin isomer.

1) is likely due to *E*-selective ROCM that can be promoted, albeit inefficiently, by the unreacted achiral bispyrrolide (with 5 mol % **1b**: 21% conv to **6a** in 1 h, 3:1 *E*/*Z*). The low enantiomeric purity (≤70:30 er) of the *E* isomers supports the contention that such products largely arise from reactions promoted by achiral **1b**.

Although the stereoselectivity of olefin formation can vary as a function of the electronic or steric attributes of the cross partner, *Z* alkenes remain strongly preferred (Table 2). Reaction with *p*-methoxystyrene and **5b** as the catalyst affords pyran **6b** with 94.5:5.5 *Z*/*E* selectivity (entry 1, Table 2). When *p*-trifluoromethylstyrene is used, **6c** is isolated with complete *Z*-selectivity (>98:<2 *Z*/*E*, entry 3). It is plausible that the higher activity of the electron-rich alkene allows partial reaction through the sterically less favored *anti* alkylidene. It is noteworthy that in spite of the increase in size of the aryl substituent in the reactions shown in entries 3 and 4 of Table 2, the preference for the *Z* alkene is only slightly diminished, presumably because of increased congestion in the derived all-*syn* metallacyclobutane (cf. **II**, Scheme 1).

Table 2. *Z*- and Enantioselective ROCM of **4** with Various Aryl Olefins[a]



entry	Ar; Ar-olefin equiv	mol % **1b**; mol % **2b**	time (h)	conv (%);[b] yield (%)[c]	er[d]	*Z*/*E*[e]
1	**b** *p*-OMeC$_6$H$_4$; 2	1.0; 1.0	0.5	96; 80	97:3	94.5:5.5
2	**c** *p*-CF$_3$C$_6$H$_4$; 2	1.0; 1.0	1.0	96; 67	98:2	>98:<2
3	**d** *o*-BrC$_6$H$_4$; 10	2.0; 2.0	1.0	94; 50	99:1	89:11
4	**e** *o*-MeC$_6$H$_4$; 10	2.0; 2.0	1.0	97; 54	99:1	87.5:12.5

[a–e] See footnotes *a*–*e* of Table 1.

The findings in Table 3 illustrate that Mo-catalyzed ROCM reactions proceed with a range of substrates to afford trisubstituted pyrans efficiently (75–83% yield) and with high enantio- (92:8 to 98:2 er) and *Z*-selectivity (89:11 to 96:4 *Z*/*E*).[10] The need for larger amounts of aryl olefin (10.0 equiv) and higher catalyst loadings likely results from the lower reactivity (reduced strain or intramolecular Mo chelation with the OBn group) of the bicyclic alkene diastereomers[4c] **7a–c** (vs **4**) and of the corresponding benzyl ethers **8** and **9**.

In summary, we have demonstrated that modular Mo adamantylimido complexes promote ROCM reactions with *Z*-selectivity levels that have previously been entirely out of reach. Ongoing studies are focused on related transformations with other substrate classes. The initial finding involving an alkyl-substituted cross partner, illustrated in eq 2, bodes well for future investigations.

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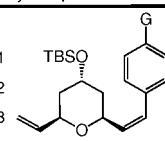
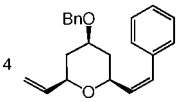
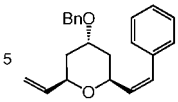
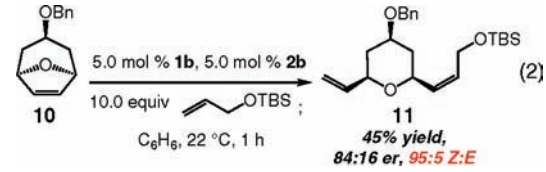
Table 3. *Z*- and Enantioselective ROCM of Oxabicycles with Aryl Olefins[a–e]

entry	product	mol % **1b** & **2b**; olefin equiv	temp (°C); time (h)	conv (%);[b] yield (%)[c]	er[d]	*Z*/*E*[e]
1	 **a** G = H	2.0; 10.0	22; 1.0	91; 83	97:3	96:4
2	**b** G = OMe	3.0; 10.0	22; 0.5	90; 80	96:4	89:11
3	**c** G = CF$_3$	2.0; 10.0	22; 1.0	97; 81	98:2	94:6
	7a–c					
4	 **8**	5.0; 10.0	60; 1.0	98; 75	92:8	95:5
5	 **9**	2.0; 10.0	22; 1.0	84; 80	92:8	91:9

[a–e] See footnotes *a*–*e* of Table 1.



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(9) Control experiments indicate that the bisaryloxides derived from **1b** and **3a–d** promote <2% conversion of **4** and styrene to **6a** within 1 h (22 °C, C_6H_6).
(10) The reactions proceed with similar efficiency and selectivity in toluene. For example, **6a** and **7a** are obtained in 84% yield, 98:2 er, 97.5:2.5 *Z*/*E* and 80% yield, 97.5:2.5 er, and 94:6 *Z*/*E*, respectively, with toluene as the solvent.

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Supporting Information Available: Experimental procedures, spectral and analytical data for all products, and crystallographic data for **7a** (CIF). This material is available free of charge via the Internet at http://pubs.acs.org.