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

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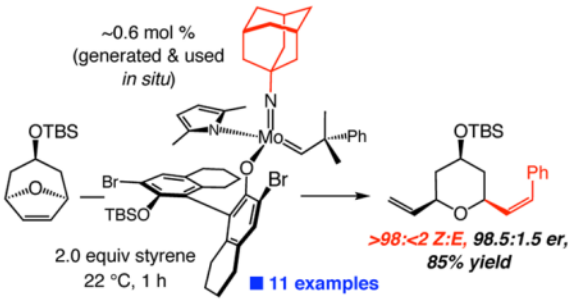
Abstract

The first highly *Z*- and enantioselective class of ring-opening/cross-metathesis (ROCM) reactions is presented. Transformations are promoted in the presence of <2 mol % of chiral stereogenic-at-Mo monoaryloxide complexes, which bear an adamantylimido ligand and are prepared and used *in situ*. Reactions involve *meso* oxabicyclic substrates and afford the desired pyrans in 50–85% yield and in up to >98:<2 enantiomer ratio (er). Importantly, the desired chiral pyrans are thus obtained bearing a *Z* olefin either exclusively (>98:<2 *Z:E*) or predominantly (≥87:13 *Z:E*).



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, at times, *Z*-alkenes 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). Transformations are promoted by <2 mol % of a chiral stereogenic-at-Mo complex.

We recently introduced a class of olefin metathesis catalysts, which bear a stereogenic metal center (e.g., **3a**–**c**, eq 1).[7] Mo alkylidenes are synthesized by treatment of a bispyrrolide (e.g.,

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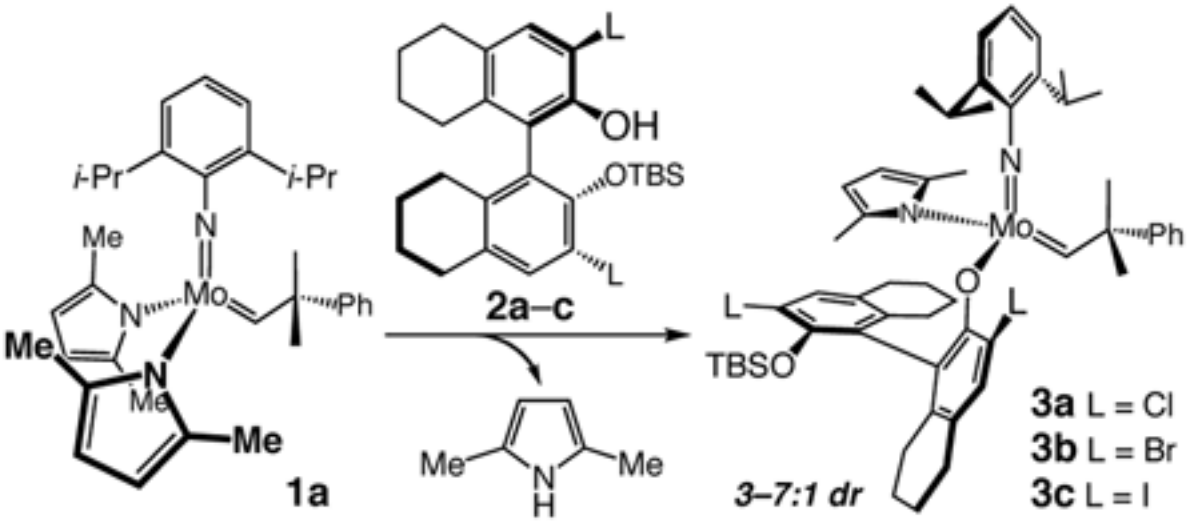
Supporting Information Available: Experimental procedures and spectral, analytical data for all products (PDF). This material is available on the web: http://www.pubs.acs.org

1a)[8] with a mono-protected binaphthol (**2a**–**c**).[7] In developing a *Z*-selective process, we reasoned that the flexibility of the Mo monoaryloxides should prove pivotal (Scheme 1). A sterically demanding but freely rotating aryloxide (around the Mo–O bond) in combination with a sufficiently smaller imido substituent (vs aryloxide) favors reaction through the *syn* alkylidene isomer (**I**, Scheme 1) and an all-*cis* metallacyclobutane (**II**, Scheme 1). Such pathways 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.



(1)

As the first step towards 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 by 400 MHz ^{1}H NMR analysis). Such a finding led us to consider that the large arylimido unit in **3b**, together with the sizeable 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 unit. Such an alteration, we reasoned, would enhance activity 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 one hour, 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*).

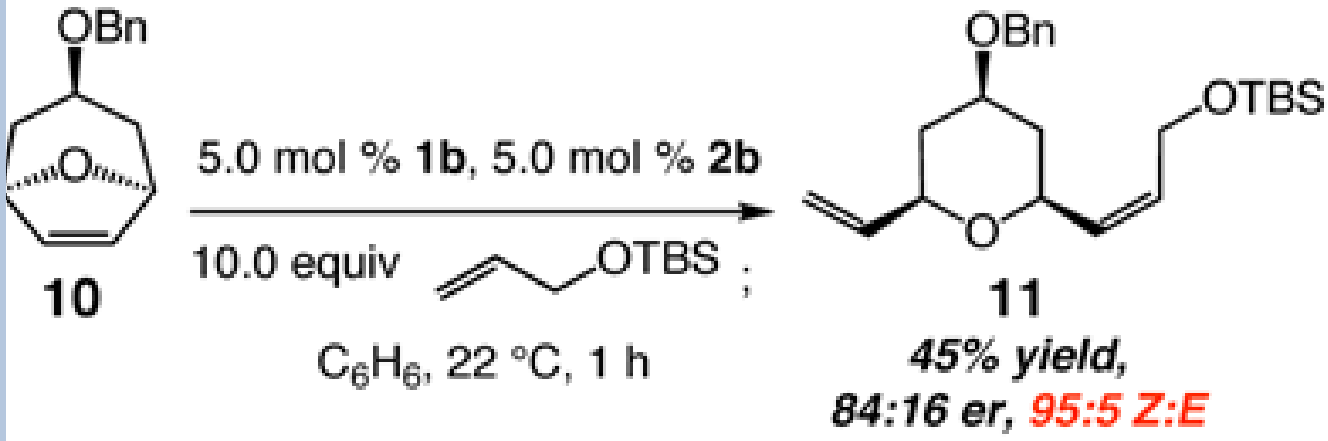
As the data summarized in entry 2 of Table 1 indicate, when Br-substituted chiral aryl alcohol **2b** is used to prepare the catalyst (**5b**), ROCM is catalyzed with an equally exceptional level of *Z*-selectivity but with improved enantioselectivity (98.5:1.5 er vs 95:5 er with **2a** as aryl alcohol in entry 1). Product from reaction with I-substituted **5c** is obtained in higher enantiomeric purity (>98:<2 er, entry 3), affording *Z*-**6a** predominantly (95:5 *Z:E*). Reaction efficiency is reduced with **5c**-**d**: 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 processes described, the amount of

catalytically active monoaryloxide is less than that indicated by the mol % 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 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 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*-methoxy styrene and **5b** as the catalyst affords pyran **6b** with 94.5:5.5 *Z:E* selectivity (entry 1, Table 2). When *p*-trifluoromethyl styrene 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 3–4 of Table 2, preference for the *Z*-alkene is only slightly diminished, presumably due to increased congestion in the derived all-*syn* metallacyclobutane (cf. **II**, Scheme 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- (92:8–98:2 er) and *Z*-selectivity (89:11–96:4 *Z:E*).[10] The need for larger amounts of aryl olefin (10.0 equiv) and the higher catalyst loadings is likely because of the lower reactivity (reduced strain or intramolecular Mo chelation with OBn group) of bicyclic alkene diastereomers[4c] **7a**–**c** (vs **4**) and that of the corresponding benzyl ethers **8**–**9**.

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



(2)

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgements

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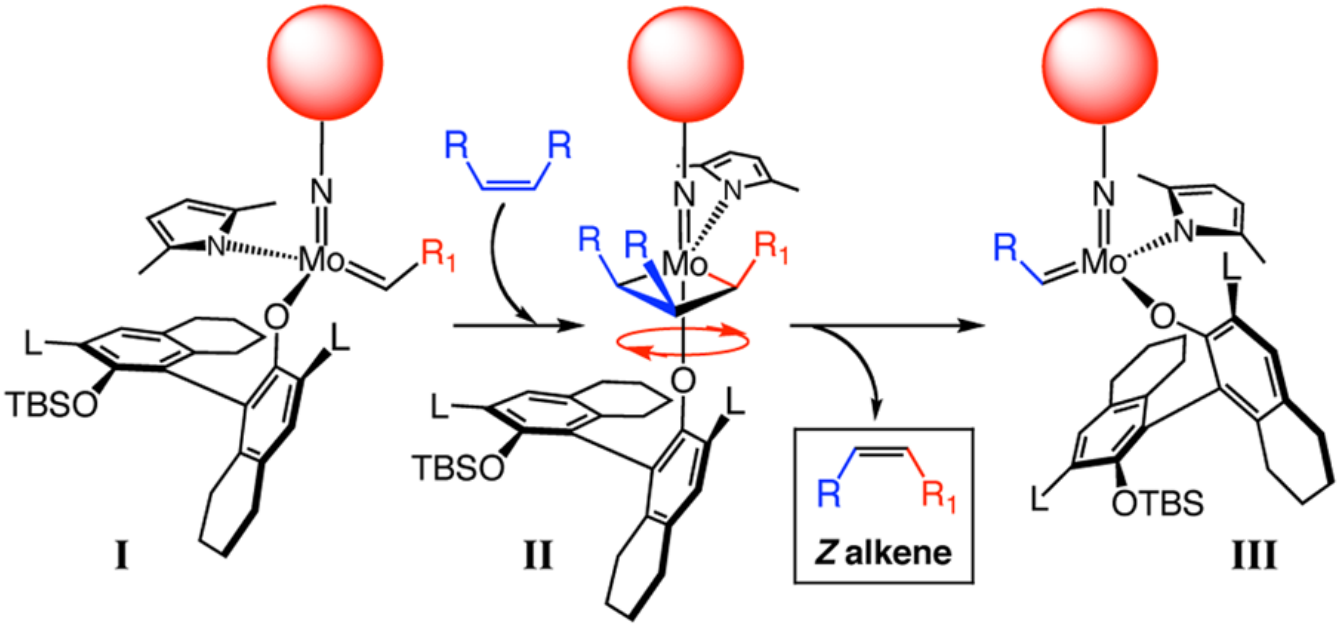
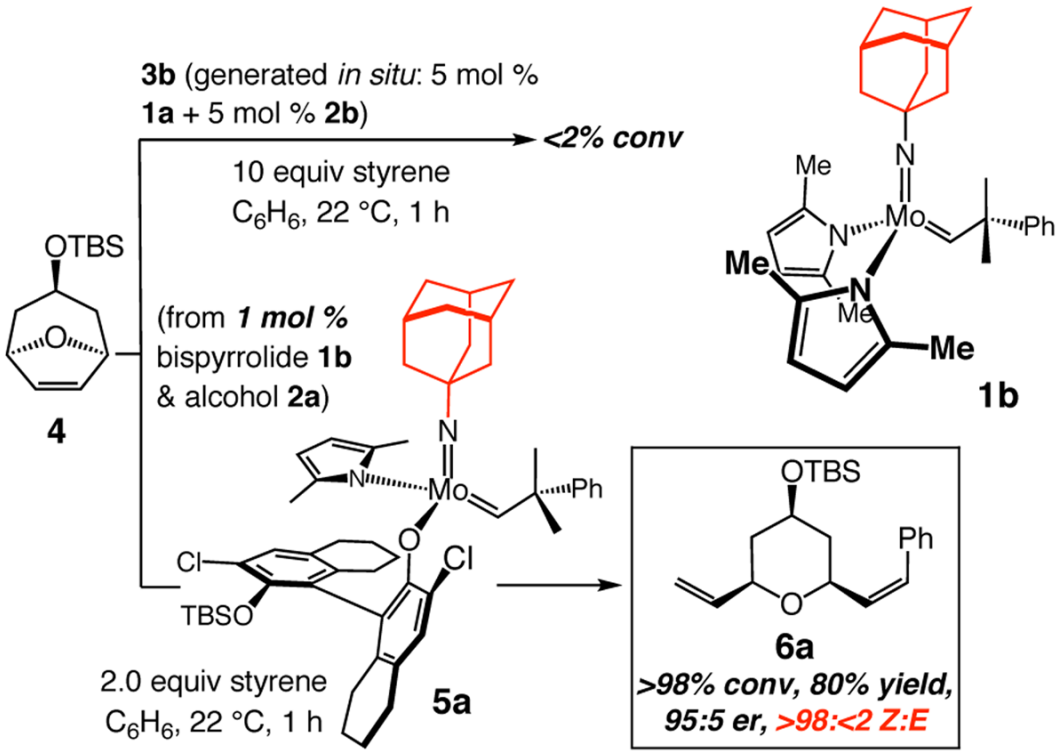
9. Control experiments indicate that bisaryloxides derived from 1b and 3a–d promote <2% conv of 4 and styrene to 6a within 1 h (22 °C, C6H6).
10. Reactions proceed with similar efficiency and selectivity in toluene. For example, 6a and 9 are obtained in 84% yield, 98:2 er, 97.5:2.5 *Z:E* and 80% yield, 92:8 er and 91:9 *Z:E*, respectively, with toluene as the solvent.



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



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

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=CI); 3.0:1	***56***:22:22	>98; 80	95:5	>98:<2
2	**5b**(L = Br); 2.2:1	***62***:8:30	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 and 1.0 mol % enantiomerically pure (>98% ee) aryl alcohol, 2.0 equiv styrene in C_6H_6 (or toluene), 22 °C, 1.0 h, N_2 atm.

[b] Determined by analysis of 400 MHz ^{1}H NMR spectra of unpurified mixtures.

[c] Yield of purified products.

[d] Determined by HPLC analysis (details in the Supporting Information).

[e] Determined by analysis of 400 MHz ^{1}H NMR spectra of unpurified mixtures in comparison with authentic *E*-olefin isomer. nd = not determined.

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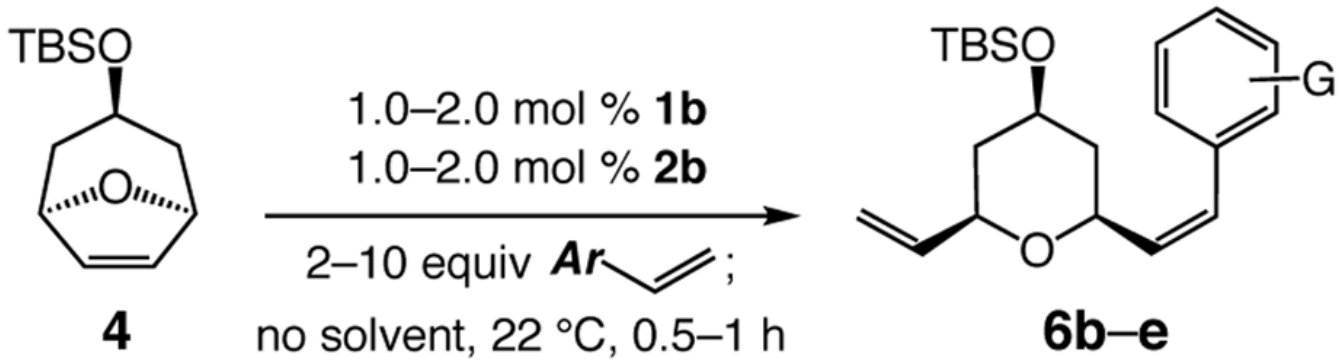
Table 2

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_6H_4; 2	1.0; 1.0	0.5	96; 80	97:3	94.5:5.5
2	**c** *p*-$CF_3C_6H_4$; 2	1.0; 1.0	1.0	96; 67	98:2	>98:<2
3	**d** *o*-BrC_6H_4; 10	2.0; 2.0	1.0	94; 50	99:1	89:11
4	**e** *o*-MeC_6H_4;10	2.0; 2.0	1.0	97; 54	99:1	87.5:12.5

[a] Performed with 1.0 mol % bispyrrolide and 1.0 mol % enantiomerically pure (>98% ee) aryl alcohol, 2.0 equiv styrene in C_6H_6 (or toluene), 22 °C, 1.0 h, N_2 atm.

[b] Determined by analysis of 400 MHz ^{1}H NMR spectra of unpurified mixtures.

[c] Yield of purified products.

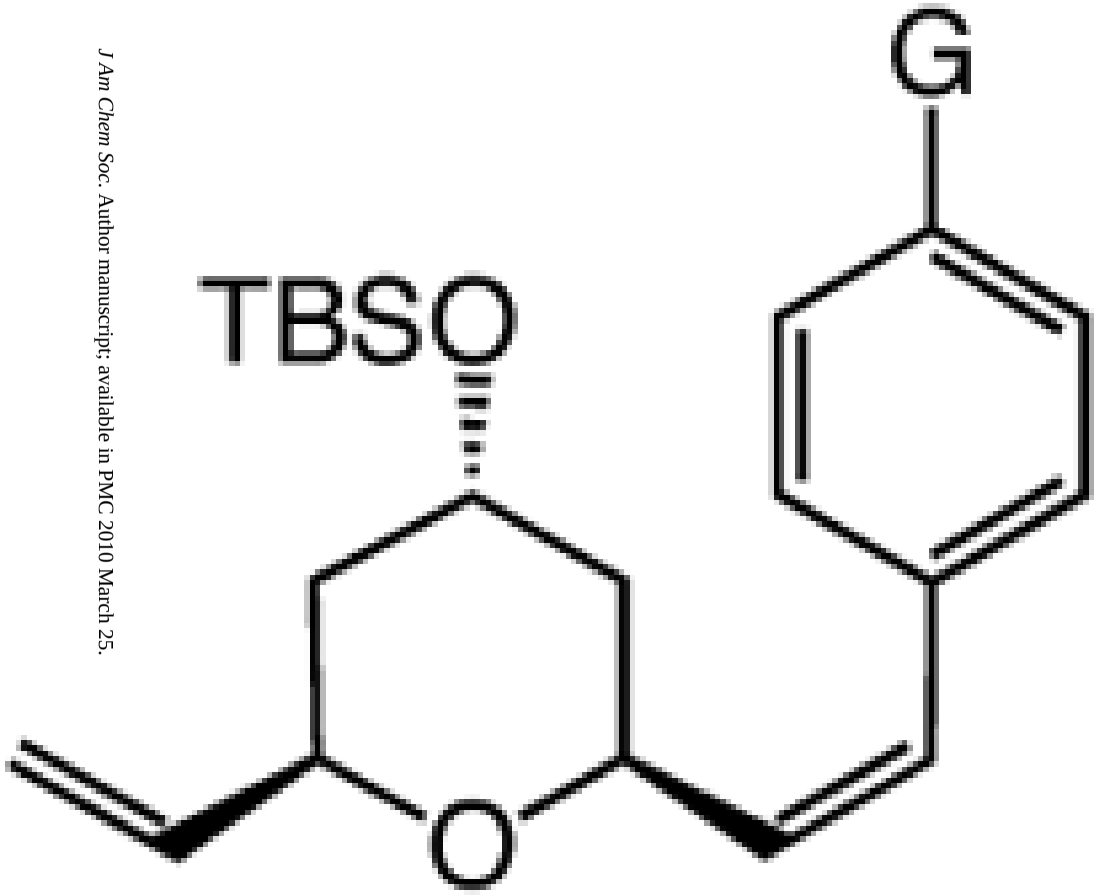
[d] Determined by HPLC analysis (details in the Supporting Information).

[e] Determined by analysis of 400 MHz ^{1}H NMR spectra of unpurified mixtures in comparison with authentic *E*-olefin isomer.

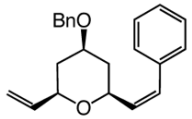
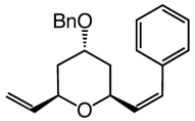
Table 3

Z

- and Enantioselective ROCM of Oxabicycles with Aryl Olefins[a]

product		mol% 1b & 2b; olefin equiv	temp (°C); time (h)	conv (%);[b] yield (%)[c]	er[d]	*Z*:*E*[e]
	**a** G = H	2.0; 10.0	22; 1.0	91; 83	97:3	96:4
	b G = OMe	3.0; 10.0	22; 0.5	90; 80	96:4	89:11
	c G = CF_3	2.0; 10.0	22; 1.0	97; 81	98:2	94:6

7a–c

product	mol% 1b & 2b; olefin equiv	temp (°C); time (h)	conv (%);[b] yield (%)[c]	er[d]	Z:E[e]
 **8**	5.0; 10.0	60; 1.0	98; 75	92:8	95:5
 **9**	2.0; 10.0	22; 1.0	84; 80	92:8	91:9

ed with 1.0 mol % bisprrolide and 1.0 mol % enantiomerically pure (>98% ee) aryl alcohol, 2.0 equiv styrene in C_6H_6 (or toluene), 22 °C, 1.0 h, N_2 atm.

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