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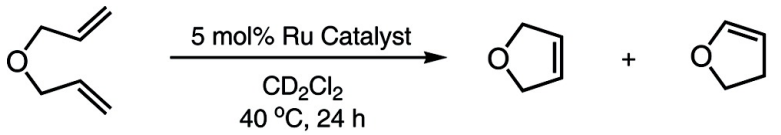

(without 1,4-Benzoquinone)	< 5%	> 95%
(***with 10 mol% of 1,4-Benzoquinone***)	> 95%	0 %

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Prevention of Undesirable Isomerization during Olefin Metathesis

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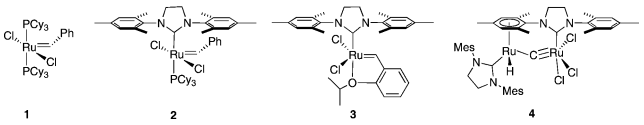
Olefin isomerization/migration is one of the side reactions in olefin metathesis that can significantly alter the product distribution and decrease the yield of the desired product, especially with ill-defined catalyst systems.[1a] Additionally, the side products resulting from unwanted isomerization are frequently difficult to remove via standard purification techniques. Well-defined ruthenium-based olefin metathesis catalysts, such as **1**, **2**, and **3**, are generally highly selective for olefin metathesis. However, there have been some reports of olefin isomerization when the catalysts are stressed by high temperatures, high dilution, and forced high turnovers.[1b−d]



1 **2** **3** **4**

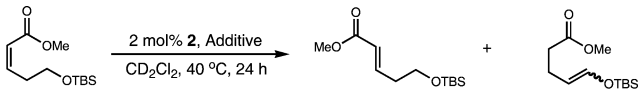
While the exact mechanism(s) responsible for this isomerization are unknown (metal-based hydride, π-allyl, or other pathways),[1,2] recent results indicate that ruthenium hydride species, such as **4**, formed from the decomposition of the ruthenium metathesis catalysts can catalyze the migration of olefins under metathesis condition.[3] This information has prompted us to develop a way to suppress the unwanted olefin isomerization reactions catalyzed by these metal hydrides.

Self-metathesis and isomerization of (*Z*)-5-*tert*-butyldimethylsilyloxy-2-pentenoate **5** to the *E*-isomer **6** and silyl enol ether **7** served as an excellent system for initially studying the effects of additives on the isomerization process.[4] Compounds **5**, **6**, and **7** all have clearly distinguishable ^{1}H NMR resonances. Through examination of the resultant *E*/*Z* ratio of the α,β-unsaturated carbonyl compounds (**6**:**5**), the effects of additives on olefin metathesis activity can be readily separated from their effect on isomerization. Upon screening additives, we found that moderate pK_a acids, such as acetic acid, or quinone-type compounds, such as 1,4-benzoquinone, work well in preventing olefin migration during olefin metathesis reactions (Table 1). Tricyclohexylphosphine oxide is an additive that has been reported to prevent isomerization of a specific substrate in a RCM reaction;[2b] however, it did not prevent the isomerization of **5** or the other substrates we tested. Acetic acid and 1,4-benzoquinone did not reduce the catalyst activity. Most metathesis reactions we tested were completed within an hour in the presence of effective additives (Tables 1−3 and Scheme 2).[5] However, we extended the reaction time to 24 h to stress the catalysts to optimize isomerization.

For the RCM of diallyl ether **8**, the metathesis product, 2,5-dihydrofuran **9**, was observed as the major product after 1 h. After extended reaction times, it is isomerized to 2,3-dihydrofuran **10**. This also suggests that decomposition products from the catalyst are responsible for the isomerization. Both acetic acid and 1,4-benzoquinone are also effective to prevent the isomerization of **9** to **10** (Table 2). Radical scavengers, such as BHT, TEMPO, phenol, and 4-methoxyphenol, were, in general, not effective in preventing isomerization (Tables 1 and 2).[6]

However, when applied to the metathetical isomerization of **11**, 1,4-benzoquinone is more effective in suppressing the undesirable isomerization than acetic acid (Table 3).

Table 1. Self-Metathesis Reaction of (*Z*)-5-*tert*-Butyldimethylsilyloxy-2-pentenoate

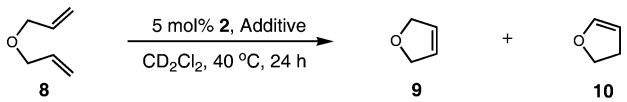


5 **6** **7**

additive	equiv (relative to **5**)	Product Distribution[a] **6**+**5**	**7**[b]
none	none	19%[c]	81%
2,2,2-trifluoroethanol	1	11%[c]	89%
hexafluoro-*tert*-butyl alcohol	1	19%[c]	81%
phenol	1	17%[c]	83%
acetic acid	0.1	>95%[c]	none
tricyclohexylphosphine oxide	0.1	22%[c]	78%
maleic anhydride	1	>95%[d]	none
1,4-benzoquinone	0.1	>95%[c]	none

[a] Determined by ^{1}H NMR. [b] *E*/*Z* ∼ 1:1. [c] *E*/*Z* ∼ 20:1. [d] *E*/*Z* ∼ 1:10.

Table 2. Ring-Closing Metathesis of Diallyl Ether

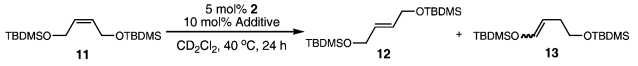


8 **9** **10**

additive	equiv (relative to **8**)	Product Distribution[a] **9**	**10**
none	none	<5%[b]	>95%[c]
acetic acid	0.1	>95%	none
1,4-benzoquinone	0.1	>95%	none
galvinoxyl	0.2	80%	20%
TEMPO	0.5	7%	93%
4-methoxyphenol	0.5	17%	83%
BHT	0.5	4%	93%

[a] Determined by ^{1}H NMR. [b] Yield ∼80%, 1 h. [c] Yield ∼20%, 1 h.

Table 3. Self-Metathesis Reaction of (*Z*)-1,4-Bis(*tert*-butyldimethylsilyloxy)-2-butene



11 **12** **13**

additive	Product Distribution[a] **12**	**13**[b]
none	none	>95%
acetic acid	none	>95%
1,4-benzoquinone	92%[c]	none

[a] Determined by ^{1}H NMR. [b] *E*/*Z* ∼ 1:1.4. [c] Due to thermodynamic equilibrium, 8% of **11** remains.

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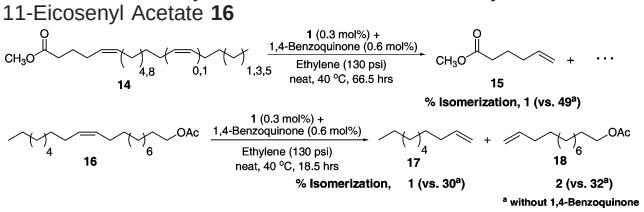
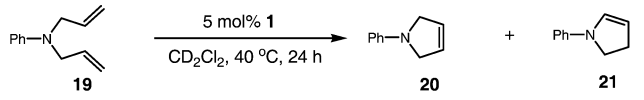
Scheme 1. Ethenolysis of Meadow Foam Oil Methyl Ester **14** and 11-Eicosenyl Acetate **16**



Scheme 2. RCM of *N*,*N*-Diallylaniline



(without additive)	16%	84%
(with 10 mol% of 1,4-Benzoquinone)	> 90%	0 %

Table 4. Effect of Benzoquinone Structure on Prevention of Olefin Isomerization

			Product Distribution[a]	
entry	additive	catalyst	**9**	**10**
1	1,4-benzoquinone	**2**	87%	13%
2	2-methylbenzoquinone	**2**	62%	38%
3	2,6-dimethyl-1,4-benzoquinone	**2**	16%	84%
4	2,6-di-*tert*-butyl-1,4-benzoquinone	**2**	<5%	>95%
5	2,5-di-*tert*-butyl-1,4-benzoquinone	**2**	<5%	>95%
6	2,6-dimethoxy-1,4-benzoquinone	**2**	22%	78%
7	2-chloro-1,4-benzoquinone	**2**	91%	9%
8	2,6-dichloro-1,4-benzoquinone	**2**	>99%	none
9	tetrafluoro-1,4-benzoquinone	**2**	>99%	none
10	none	**3**	<5%	>95%
11	1,4-benzoquinone	**3**	91%	9%
12	2,6-dichlorobenzoquinone	**3**	>99%	none

[a] Determined by ^{1}H NMR.

Ethenolysis, cross-metathesis of an olefinic compound with ethene, of seed oils and their fatty acid esters allows the synthesis of α-olefins, which have a broad range of applications.[7] However, the occurrence of olefin isomerization during this process has limited its industrial application.[7b] Again, 1,4-benzoquinone proved to be superior in suppressing olefin isomerization to other tested additives (Scheme 1),[8] and it could be readily separated from the desired products by standard techniques. Further investigations on industrial applications using this mild and inexpensive additive are in progress.

It has been reported that some allylic amines, such as *N*,*N*-diallylaniline **19**, are isomerized to enamines with catalyst **1** in toluene at 110 °C.[9a,b] In RCM of **19** under normal metathesis condition, only metathesis product **20** was observed within 30 min; however, **20** was isomerized to **21** after extended reaction times. 1,4-Benzoquinone effectively prevented this isomerization, resulting in the clean formation of the metathesis product **20** (Scheme 2). However, 1,4-benzoquinone did not prevent the isomerization of *N*,*N*-dibenzylallylamine and *N*,*N*-dimethylallylamine to enamines.[9a,b] *N*,*N*-Dialkylallylamines prevent metathesis, while less basic arylamines are active metathesis substrates.[9c]

To determine the optimal benzoquinone structure for prevention of olefin isomerization, several benzoquinone derivatives were screened in larger-scale RCM reactions of **8** (Table 4). Electron-deficient benzoquinones are more effective in preventing isomerization (entries 7−9 and 12) than the parent 1,4-benzoquinone. Conversely, electron-rich benzoquinones are less effective (entries 2, 3, and 6), and sterically hindered benzoquinones cannot prevent isomerization to any significant extent (entries 4 and 5). Benzoquinones were also effective in preventing isomerization in reactions with the phosphine-free catalyst **3** (entries 10−12).

To understand the role of benzoquinone in preventing isomerization, we studied the isomerization of allyl benzene catalyzed by complex **4** with and without 1,4-benzoquinone.[3] As expected, allyl benzene was not isomerized with 2 mol % of **4** in the presence of 10 mol % of 1,4-benzoquinone. It has been reported that quinones are reduced to the corresponding hydroquinones upon reacting with ruthenium hydrides.[10] Indeed, the formation of 1,4-hydroquinone was observed by ^{1}H NMR in this reaction (∼10%, relative to 1,4-benzoquinone). Moreover, neither the complex **4** nor any other ruthenium hydrides were observed from decomposition of $(H_2\text{-IMes})(PCy_3)(Cl)_2Ru{=}CH_2$ in benzene in the presence of 2 equiv of 1,4-benzoquinone. These results indicate that benzoquinone may prevent the formation of metal hydrides from catalyst decomposition or react rapidly with hydrides generated by decomposition. Further mechanistic investigations are currently in progress to fully understand the role of 1,4-benzoquinones (redox reactions,[10] charge-transfer complexes,[11] etc.) in preventing olefin migration and to elucidate methods to prevent olefin isomerization in substrates such as allylic alcohols and some allylic amines for which 1,4-benzoquinones are not effective.

In conclusion, 1,4-benzoquinones have been found to prevent olefin isomerization of a number of allylic ethers and long-chain aliphatic alkenes during olefin metathesis reactions with ruthenium catalysts. Electron-deficient benzoquinones are the most effective additives for the prevention of olefin migration. This mild, inexpensive, and effective method to block olefin isomerization increases the synthetic utility of olefin metathesis by improving product yield and purity.

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Supporting Information Available: Experimental details and characterization data. This material is available free of charge via the Internet at http://pubs.acs.org.

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(4) The equilibrium *E*/*Z* ratio (**6**:**5**) is greater than 20:1, and the electronics of the system disfavor product redistribution during secondary metathesis.

(5) Isomerizations also start to occur within 1 h without effective additives.

(6) Galvinoxyl is somewhat effective to prevent the isomerization, presumably due to the structural similarity with 1,4-benzoquinone (Table 2).

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(8) See Supporting Information for GC traces of these reactions.

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(11) It was reported that the catalyst **1** generates radical anions on treatment with 1,4-benzoquinones. See: (a) Amir-Ebrahimi, V.; Hamilton, J. G.; Nelson, J.; Rooney, J. J.; Thompson, J. M.; Beaumont, A. J.; Rooney, A. D.; Harding, C. J. *Chem. Commun.* **1999**, 1621−1622. (b) Amir-Ebrahimi, V.; Hamilton, J. G.; Nelson, J.; Rooney, J. J.; Rooney, A. D.; Harding, C. J. *J. Organomet. Chem.* **2000**, *606*, 84−87.

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