CHAPTER 4

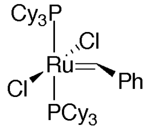
Effect of Water on the Stability and Initiation of Olefin Metathesis Catalysts Containing an *N*-Heterocyclic Carbene Ligand

Abstract

To aid the development of a water-soluble, ruthenium-based olefin metathesis catalyst containing an *N*-heterocyclic-carbene ligand, the decomposition of $(H_2IMes)(PCy_3)(Cl)_2Ru{=}CHPh$ (H_2IMes = 1,3-dimesityl-imidazolidine-2-ylidine, PCy_3 = tricyclohexylphosphine) and its methylidene and ethylidene analogs are examined in water/THF solvent mixtures. While the benzylidene is quite stable towards water, the ethylidene and methylidene analogs are much less stable. The methylidene analog decomposes the most rapidly of the three complexes examined, and this decomposition is only mildly affected by the presence of added chloride ion or PCy_3. The initiation of both the benzylidene and methylidene complexes is more rapid in water, which yields higher concentrations of the reactive fourteen-electron species and may contribute to the increased decomposition rates. Furthermore, methylidene analog decomposition occurs through multiple pathways, though most pathways involve the generation of tricyclohexyl(methyl)phosphonium chloride salt. The decomposition behavior of both the methylidene and ethylidene analogs in the presence of water indicate a direct interaction between water and the ruthenium complex. Finally, two interesting characteristics of ethylidene decomposition are observed.

Introduction

Up to this point, the focus of aqueous metathesis has been modifying the ligand scaffold of catalysts **1**–**3** to increase their solubility in water. The results of this research are water-soluble catalysts **4**–**6**.[1-6] While catalysts **4**–**6** all perform olefin metathesis in water, they are insufficiently stable to mediate the full range of metathesis processes. As described in Chapters 2 and 3, the goal of this thesis is the production of water-soluble catalysts containing an *N*-heterocyclic carbene (NHC) ligand. For reasons explained in Chapter 3, water-soluble analogs of catalyst **2** are of particular interest. To assist the design of such catalysts that are stable and soluble in water, the effect of water on the decomposition of parent catalyst **2** is of interest.



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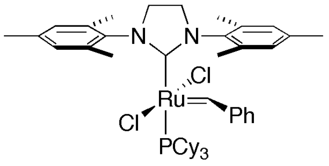

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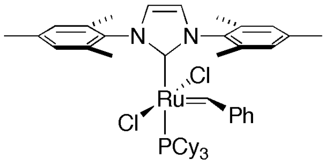

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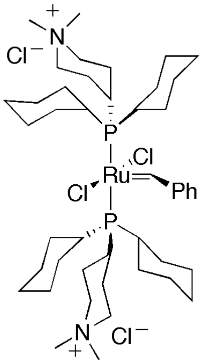

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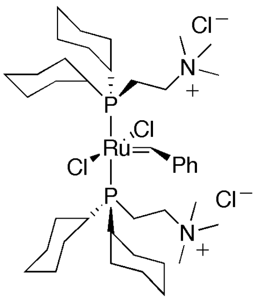

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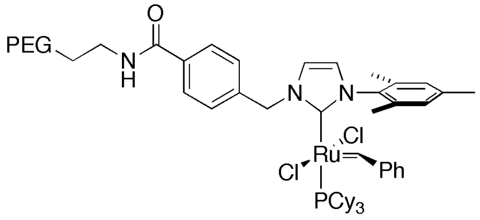

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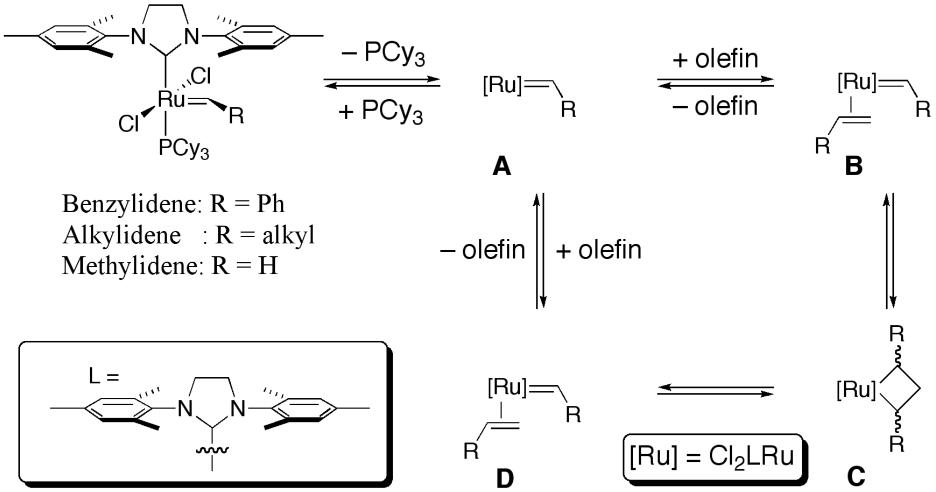
Scheme 4.1 illustrates the accepted mechanism of ruthenium-based olefin metathesis.[7] Every step of this mechanism is fully reversible. The catalytic cycle is initiated by the dissociation of the phosphine ligand to yield the fourteen-electron species

A. The interaction of **A** with a substrate molecule forms olefin-bound complex **B**, which further reacts to generate metalocyclobutane **C**. Fragmentation of the metalocyclobutane and dissociation of the product olefin from complex **D** completes the catalytic cycle. In olefin metathesis reactions, the initial ruthenium-benzylidene complex (R = Ph, benzyl carbene) reacts with substrate to form either an alkylidene (R = alkyl, alkyl carbene) or methylidene (R = H, methylidene carbene) complex. In productive metathesis, the alkylidene complex reacts with a second substrate molecule to generate product and a propagating ruthenium alkylidene or methylidene complex when the second substrate's olefin is internal or terminal respectively. Therefore, to fully understand catalyst stability, the relative stabilities of the ruthenium benzylidene and its alkylidene and methylidene analogs must be examined. This prompts the study of the decomposition of catalyst **2** and the alkylidene/ethylidene (**7**) and methylidene (**8**) analogs of **2** in the presence of water.

Scheme 4.1.

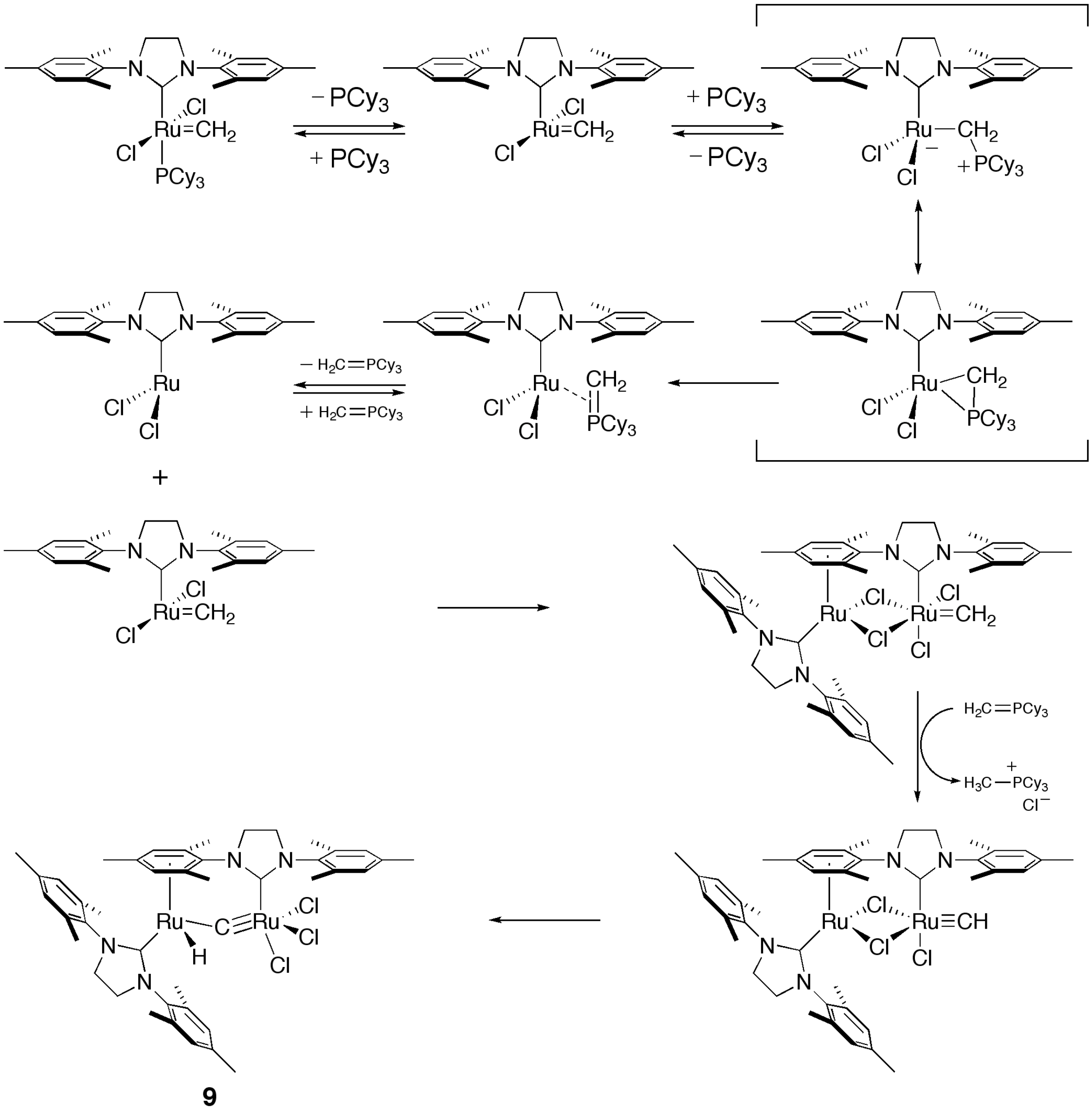


Earlier research reveals a few aspects regarding the decomposition of ruthenium-based olefin metathesis catalysts.[8-14] Ulman and Grubbs report that the bis(phosphine) methylidene complex decomposes by a very different mechanism than alkylidene complexes.[8,9] The rate of bis(phosphine) methylidene decomposition is clearly first order in the methylidene complex. In contrast, alkylidene complexes decompose by bimetallic mechanisms as revealed by the formation of 3-hexene during the decomposition of the bis(phosphine) propylidene complex.[8] The results of this research indicate that the order of complex stability is benzylidene > alkylidene > methylidene.[9]

More recent studies examine the decomposition of ruthenium catalysts containing NHC ligands.[10-14] The available research suggests that, like the bis(phosphine) complexes, the order of complex stability for catalysts containing an NHC ligand is benzylidene > alkylidene > methylidene.[10] However, in general, the stabilities of catalysts containing an NHC ligand are one or two orders of magnitude higher than their bis(phosphine) analogs.[11,12] Furthermore, research by Hong and Grubbs illuminates the decomposition of ruthenium methylidene complex **8** in organic solvents.[13,14] They show that the free tricyclochexylphosphine (PCy_3) generated upon complex initiation can nucleophilically attack the carbon double-bonded to the ruthenium center, the methylidene carbon.[13,14] This is the first step along a decomposition pathway that produces the bimetallic ruthenium hydride complex, **9**, as shown in Scheme 4.2. The rate of this decomposition is independent of the concentration of free PCy_3.[13]

Methylidene complex, **8**, is a crucial intermediate formed during the metathesis of terminal olefins with catalyst **2**.[9-11,15] However, as described above, **8** is the least stable ruthenium complex produced during olefin metathesis.[10,13,14] Moreover, methylidene complexes are particularly unstable in aqueous environments.[5,6] Therefore, this research, which pursues the production of stable, water-soluble metathesis catalysts, will focus on understanding the effect of water on the decomposition of methylidene complex **8**, though the decomposition of benzylidene **2** and alkylidene/ethylidene **7** will also be examined.

Scheme 4.2.



Results and Discussion

Experimental approach. The decomposition rates were determined using ^{1}H NMR spectroscopy by following the diminution of the integral of the ruthenium complex's alkylidene-hydrogen resonance over time.[16] Water/THF solvent mixtures were the chosen media for these studies due to the high solubility of water in THF. This solubility allowed for the measurement of decomposition in solutions with water concentrations as high as 8 M. Poor catalyst solubility in THF solutions with water concentrations ≥10 M prevented the examination of decomposition in the presence of higher water concentrations.[17] Protio water was utilized in these experiments to avoid any proton/deuterium exchange of the alkylidene hydrogen, as has been previously observed for other ruthenium alkylidene complexes in this solvent environment.[18] Therefore, to attain adequate solute signal to noise, at water concentrations >4 M, solvent suppression was used to minimize the proton resonance due to water. All samples were freshly prepared prior to each experiment. Limited stability of the examined compounds in THF prohibited the use of stock solutions.

Decomposition of ruthenium benzylidene complex 2 in the presence of water. Previous research showed that ruthenium benzylidene complex **2** is quite stable in organic solvents, even in the presence of trace water.[7,11] Consistent with this data, following the decomposition of **2** at ambient temperature in 4 M water/THF yields a half-life of roughly 6 days. Moreover, **2** can be observed for hours at 50 °C in 8 M water/THF without noticeable decomposition. These data suggest that ruthenium benzylidene complexes that contain an NHC ligand are reasonably persistent in an aqueous environment. Therefore, it is believed that their stability is likely sufficient for a water-soluble analog of catalyst **2**.

Decomposition of methylidene complex 8 in the presence of water. In contrast with complex **2**, ruthenium methylidene complex, **8**, fully decomposes in less than 10 minutes at 50 °C in the presence of just 20 equivalents (0.46 M) of water in THF. However, at 25 °C, its rate of decomposition is sufficiently slow to allow for its measurement at water concentrations as high as 8 M. Representative plots for the observed sample decomposition over time are provided in Figure 4.1. Additionally, the measured decomposition rate constants for complex **8** at 25 °C and multiple water concentrations are listed in Table 4.1.

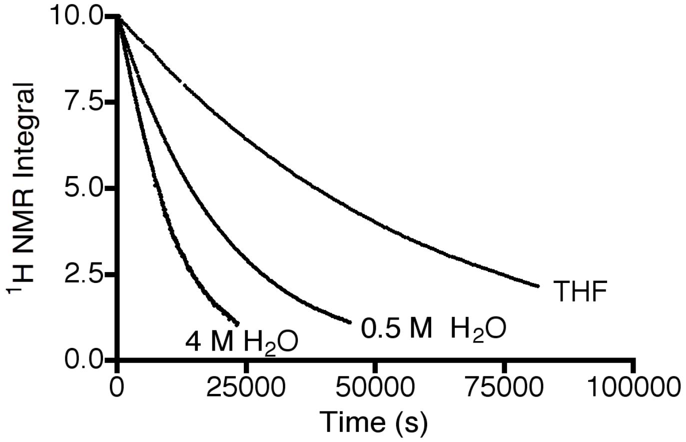


Figure 4.1. The decomposition rate of ruthenium methylidene complex **8** increases with increasing water concentrations.

Table 4.1. Effect of water on the decomposition rate of 0.023 M ruthenium methylidene complex **8** at 25 °C

Solvent	**k_{obs} (s^{-1})**	**$t_{1/2}$ (h)**
THF	$(1.78 \pm 0.01) \times 10^{-5}$	10.79 ± 0.09
0.5 M H_2O/THF	$(5.03 \pm 0.01) \times 10^{-5}$	3.83 ± 0.01
1 M H_2O/THF	$(6.59 \pm 0.02) \times 10^{-5}$	2.93 ± 0.01
2 M H_2O/THF	$(7.92 \pm 0.05) \times 10^{-5}$	2.43 ± 0.02
3 M H_2O/THF	$(8.78 \pm 0.05) \times 10^{-5}$	2.19 ± 0.01
4 M H_2O/THF	$(9.33 \pm 0.09) \times 10^{-5}$	2.07 ± 0.02
8 M H_2O/THF	$(15.7 \pm 0.1) \times 10^{-5}$	1.30 ± 0.01

As shown in Table 4.1, the rate constants for the decomposition of **8** rapidly increase from $(1.78 \pm 0.01) \times 10^{-5}$ s^{-1} in the absence of water to $(6.59 \pm 0.02) \times 10^{-5}$ s^{-1} in 1 M water/THF. Interestingly, the acceleration of the decomposition rate greatly diminishes at water concentrations greater than 1 M. The observed behavior is consistent with an exponential decay of this acceleration with respect to water concentration. Indeed, a plot of the measured half-lives versus water concentration, Figure 4.2, can be readily fit to a two-phase exponential decay with an R^2 value of 0.9998. From this fit, the extrapolated half-life of methylidene complex **8** in pure water, 55.5 M, is 143 s with a standard error of 4400 s. Despite the large error due to extensive extrapolation, these data clearly indicate that the decomposition of **8** in water is quite rapid at 25 °C. From these data, the order of water in the decomposition kinetics of complex **8** is unclear. However, as will be discussed later, this effect of water on the decomposition of **8** may be indicative of a direct interaction between water and complex **8**.

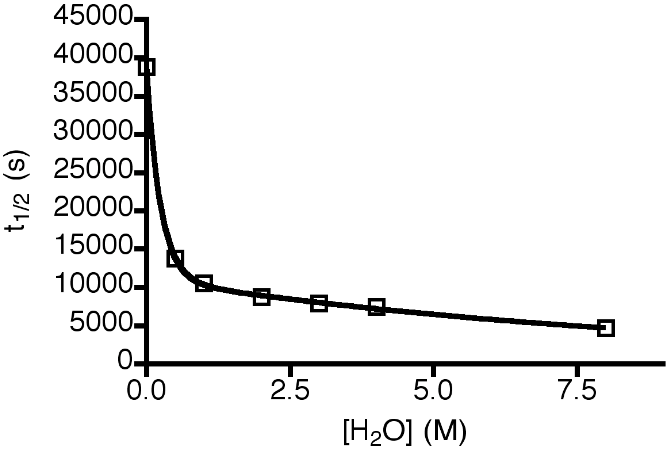


Figure 4.2. A plot of the decomposition half-life versus water concentration for 0.023 M of ruthenium methylidene complex **8** at 25 °C is nonlinear. The acceleration of **8**'s decomposition due to increasing water concentration can be fit to a two-phase exponential decay ($R^2 = 0.9998$).

As demonstrated in Figure 4.3, a plot of ln[**8**]$_0$ – ln[**8**] versus time yields straight lines for the decomposition of **8** in pure THF and 0.5 and 4 M aqueous THF. These data are consistent with decomposition being first order in methylidene complex **8**. Measuring the decomposition of samples containing twice the initial concentration of **8** in 4 M water/THF readily confirms this kinetic order. Such samples do decompose twice as fast to yield a rate constant of $(1.16 \pm 0.01) \times 10^{-4}$ s^{-1} (initial rate = ~5.3×10^{-6} $M{\bullet}s^{-1}$) which is in reasonable agreement with the $(9.33 \pm 0.09) \times 10^{-5}$ s^{-1} rate constant (initial rate = ~2.1×10^{-6} $M{\bullet}s^{-1}$) obtained from earlier samples with lower initial concentrations of complex **8**.

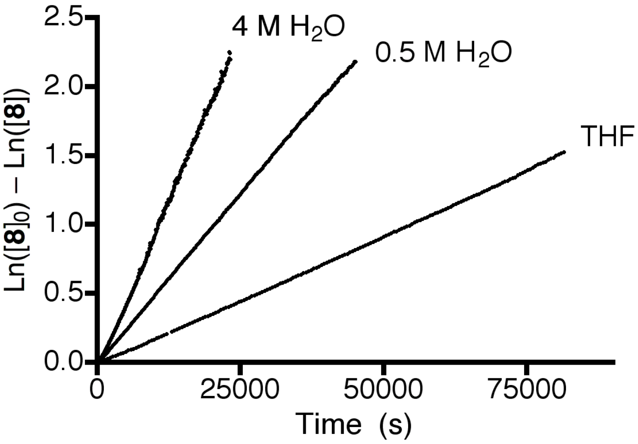
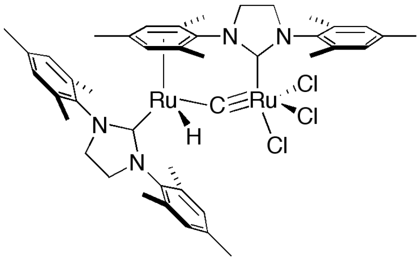


Figure 4.3. Plotting ln([**8**]$_0$ – ln([**8**]) versus time reveals that the decomposition of **8** is first order in itself in both the presence and absence of water.

The decomposition of **8** in THF and water/THF solvent mixtures produces black, opaque solutions. Spectroscopic examination of these solutions reveals that decomposition occurs through a variety of pathways. After decomposition in 0.5 M water, 7 peaks can be observed in the hydride region of the ^{1}H NMR spectrum between 0 and –30 ppm while only 4 of these peaks can be observed after decomposition in 4 M water. Peaks are not observed between 0 and –30 ppm in the ^{1}H NMR spectrum after decomposition in 8 M water.

One of the observed resonances in the ^{1}H NMR spectra is a doublet centered at –25.3 ppm. Removing the volatiles from a decomposed sample *in vacuo* and obtaining its ^{1}H and ^{31}P NMR spectra in deuterated dichloromethane reveals that this resonance is consistent with ruthenium hydride **10**.[19,20] This hydride is also observed for the decomposition of benzylidene compound **2** in the presence of methanol or other aliphatic alcohols.[19]



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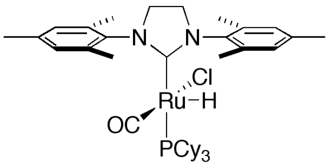

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At this time, the other six resonances in the hydride region of the ^{1}H NMR spectra have not been identified, although a singlet at –8.6 ppm is speculated to be the bimetallic hydride **9** as observed in the decomposition of **8** in benzene.[13] Regardless, all of these high-field resonances are actually minor peaks in the ^{1}H NMR spectra and represent relatively small amounts of material. Therefore, while ^{1}H NMR spectroscopy does not reveal any single dominant, ruthenium-based decomposition product, it does indicate the existence of a branch-point in the mechanism of **8**'s decomposition, which allows for the generation of the multiple products observed.

In contrast with the ^{1}H NMR spectra, the ^{31}P NMR spectra of solutions of decomposed **8** clearly show the presence of one dominant phosphorus-containing decomposition product at 34.8 ppm in all samples containing added water. In the absence of water, this peak is still the major phosphorus resonance, but other significant resonances are also observed. Suspecting the peak at 34.8 ppm to correspond to tricyclohexyl(methyl)phosphonium chloride salt (Cy_3PMeCl),[13] mild purification of multiple decomposed samples was accomplished by precipitation into ether to attain a black solid. High-resolution mass spectroscopy of this solid reveals the presence of the salt (calc: 295.2555, measured: 295.2552). Moreover, ^{1}H NMR and ^{1}H/^{31}P HMQC NMR spectroscopy confirm the assignment of the 34.8 ppm phosphorus resonance as

Cy_3PMeCl.[21] Therefore, while ^1H NMR reveals the presence of many decomposition pathways, ^{31}P NMR shows that pathways yielding Cy_3PMeCl tend to dominate the decomposition of ruthenium methylidene complex **8**.

Effect of additives on the decomposition of methylidene compound 8 in water. To develop a water-soluble analog of catalyst **2**, this issue of methylidene complex stability must be addressed. Therefore, experiments were designed to obtain information regarding the decomposition of methylidene complex **8** in the presence of water. Two components of **8** were identified as likely sources of complex instability—the ruthenium-chloride bonds and the fourteen-electron species generated upon phosphine dissociation (Scheme 4.1).

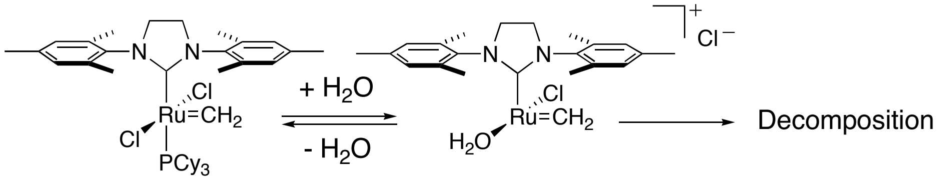
That the chloride ligands in complex **2** can be readily displaced by a variety of nucleophiles is well documented. Carboxylic acids,[22-24] various alcohols,[11,25,26] sulfonates,[23] and other halides[7] are all reported to displace the chloride ligands. Furthermore, research studying the formation and isomerization behavior of ruthenium hydrides generated by treating catalysts **1** and **2** with various protic solvents reveal a rate enhancement of ruthenium hydride formation upon the addition of base.[19,27] Therefore, these authors propose chloride displacement to generate hydrogen chloride as an early step in hydride formation. Furthermore, water is proposed to displace a chloride during deuterium exchange with the alkylidene hydrogen of bis(phosphine) complex **5** in deuterium oxide.[18] Given these observations, displacement of a chloride ligand of methylidene complex **8** by water is considered a potential step in catalyst decomposition (Table 4.2).

Measuring the effect of tetrabutylammonium chloride ($^{n}Bu_4NCl$) on the rate of **8**'s decomposition in 4M water/THF allows for the examination of potential chlorine displacement by water. By the common ion effect, the added chloride ions should inhibit or preclude the displacement of a chloride ligand by water. This should decrease the rate of complex decomposition assuming that chlorine displacement by water is an initial step in decomposition. However, the measured rate constant of $(8.7 \pm 0.2) \times 10^{-5}$ s^{-1} in the presence of 10 equivalents of excess chloride is only mildly slower than the rate constant of decomposition measured in the absence of the additive ($(9.33 \pm 0.09) \times 10^{-5}$ s^{-1}). Thus, displacement of the chloride ligand by water either does not occur under these conditions, is not involved in a major decomposition pathway or is a relatively rapid process occurring after the rate-determining step in the decomposition of ruthenium methylidene complex **8**.

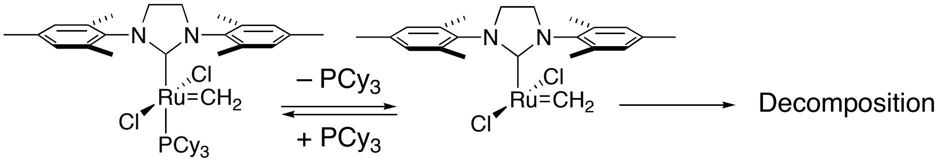
Another aspect of complex **8** that may play a role in its decomposition is the stability of the fourteen-electron species generated upon phosphine dissociation. This dissociation serves as a catalyst initiation step within the context of the metathesis reaction[7,28] and is known to play a major role in the decomposition of some metathesis-active ruthenium bis(phosphine) complexes.[8] Along with freeing a ruthenium coordination site, phosphine dissociation greatly reduces the steric shielding around the methylidene carbon of **8**. Rates for decomposition pathways that require coordination to this newly available site and/or nucleophilic attack at the methylidene carbon should be greatly affected by the concentration of the fourteen-electron species.

As phosphine dissociation is a reversible process for ruthenium-based metathesis catalysts,[7,28] the presence of excess free phosphine will lower the concentration of the fourteen-electron species. Hence, the effect of excess phosphine on the rate of methylidene complex **8**'s decomposition should illuminate the possible role of the fourteen-electron species in this decomposition. An examination of **8**'s decomposition in 4 M water/THF in the presence of 10 equivalents of PCy_3 yields an observed rate constant of (7.63 ± 0.01) × 10^{-5} s^{-1}, which is moderately slower than decomposition in the absence of excess phosphine ((9.33 ± 0.09) × 10^{-5} s^{-1}). Increasing the amount of PCy_3 to 20 equivalents has a similar effect on the rate of complex **8**'s decomposition as compared to adding 10 equivalents of PCy_3 (Table 4.2).

Table 4.2. Effect of additives on the decomposition rate of 0.023 M ruthenium methylidene complex **8** in 4 M H_2O/THF at 25 °C

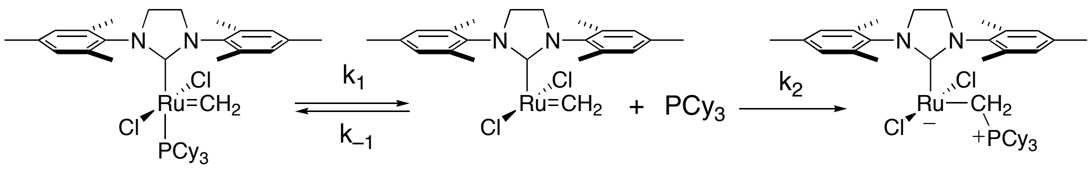


Additive (amount)	k (s^{-1})	$t_{1/2}$ (h)
None	(9.33 ± 0.09) × 10^{-5}	2.07 ± 0.02
$^{n}Bu_4NCl$ (10 equiv)	(8.7 ± 0.2) × 10^{-5}	2.22 ± 0.04



Additive (amount)	k (s^{-1})	$t_{1/2}$ (h)
PCy_3 (10 equiv)	(7.63 ± 0.01) × 10^{-5}	2.545 ± 0.005
PCy_3 (20 equiv)	(7.16 ± 0.02) × 10^{-5}	2.690 ± 0.007

As previously described, recent research examining the decomposition of ruthenium methylidene complex **8** in benzene demonstrated that PCy_3 plays an active role during decomposition by reacting with the methylidene carbon to form Cy_3PMeCl.[13,14] This salt may be the result of phosphine migration from the ruthenium atom in complex **8** to its methylidene carbon or caused by nucleophilic attack on the methylidene carbon of the fourteen-electron species by PCy_3. Later steps are then responsible for the cleavage of the ruthenium-carbon bond and protonation to form the phosphonium salt. Consistent with this earlier research, the formation of Cy_3PMeCl is observed for the decomposition of **8** in THF in both the presence and absence of water.



8 **11** **12**

$$\frac{d[\mathbf{12}]}{dt} = k_2[\mathbf{11}][PCy_3] \tag{4.1}$$

$$[\mathbf{11}][PCy_3] = \frac{k_1[\mathbf{8}]}{k_{-1} + k_2} \qquad \text{(steady - state approximation)} \tag{4.2}$$

$$\frac{d[\mathbf{12}]}{dt} = \frac{k_2 k_1[\mathbf{8}]}{k_{-1} + k_2} \tag{4.3}$$

The rate of complex **8**’s decomposition should be independent of phosphine concentration in the case of phosphine migration as the process is unimolecular. Assuming the steady-state approximation, decomposition by the nucleophilic attack of PCy_3 at the methylidene carbon is also expected to proceed with a rate independent of phosphine concentration as illustrated in eqs 4.1–4.3. Increasing the concentration of free phosphine has a moderate effect on the rate complex **8**’s decomposition. This effect can be understood as a mild breakdown of the steady-state approximation within the context of nucleophilic attack by free PCy_3 on complex **8**'s fourteen-electron species' methylidene carbon.

Effect of water on complex initiation. Assuming that the described nucleophilic attack by free PCy_3 plays a prominent role in methylidene complex **8**'s decomposition, one explanation for water's effect on this decomposition is that water increases the rate of phosphine dissociation. Research shows that phosphine-containing, ruthenium-based metathesis catalysts initiate more rapidly in solvents with higher dielectric constants (Table 4.3, first three entries).[7] Moreover, the observed data indicates that initiation may occur through solvent-assisted pathways in coordinating solvents though a solvent coordinated complex is not observed.[7] Therefore, in the context of the current study, added water may be largely serving to increase the rate of phosphine dissociation by increasing the solution's dielectric and/or by participating in a solvent-assisted dissociation mechanism as exemplified in Scheme 4.3. To examine this possibility, ethyl vinyl ether-based kinetics were performed on compounds **2** and **8** in the presence and absence of water in THF at 25 °C.

Scheme 4.3.

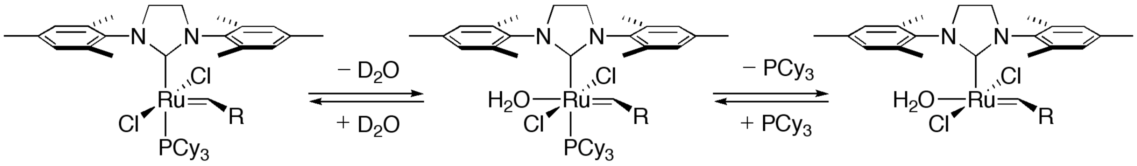
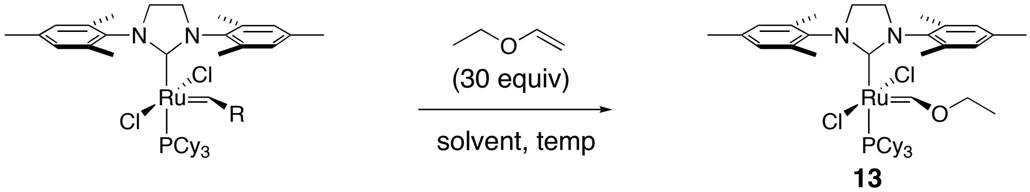


Table 4.3. ^{1}H NMR initiation kinetics for 0.017 M ruthenium complex and 0.5 M ethyl vinyl ether at the listed temperature and solvent



Solvent	R	Temp (°C)	Dielectric Constant	k (s^{-1})	$t_{1/2}$ (min)
toluene[a]	Ph	35	2.38	$(4.6 \pm 0.4) \times 10^{-4}$	25 ± 2
Dichloromethane[a]	Ph	35	8.9	$(6.1 \pm 0.2) \times 10^{-4}$	18.9 ± 0.6
THF[a]	Ph	35	7.32	$(1.0 \pm 0.1) \times 10^{-3}$	12 ± 1
THF	Ph	25	7.32	$(2.377 \pm 0.004) \times 10^{-4}$	48.60 ± 0.08
4 M H_2O/THF	Ph	25	–	$(3.923 \pm 0.008) \times 10^{-4}$	29.45 ± 0.06
THF	H	25	7.32	7.0×10^{-5}	152
4 M H_2O/THF	H	25	–	1.7×10^{-4}	70

[a]These results are reported in reference 7. [b]These results are qualitative.

Ethyl vinyl ether reacts with complexes **2** and **8** to form the Fischer carbene, **13**.[29] In the presence of a large excess of the ether, this reaction was used by Grubbs and co-workers to measure the initiation activities of a variety of ruthenium-based metathesis catalysts (Table 4.3, first three entries).[7] Furthermore, the kinetics of this reaction were shown to equal the rate of phosphine exchange for these complexes as phosphine dissociation is the rate-determining step of catalyst initiation.[7] In this manner, ethyl vinyl ether is used in this study to examine the effect of water on the initiation/phosphine dissociation rates of complexes **2** and **8**.

Mixing ruthenium complex **2** or **8** with 30 equivalents of ethyl vinyl ether in the presence and absence of water in THF yields the initiation rate constants shown in Table 4.3 as measured by ^{1}H NMR spectroscopy. In 4 M water/THF, ruthenium benzylidene complex **2** initiates ~1.7 times faster than in water's absence. Water has the same effect on ruthenium methylidene complex **8**, which appears to initiate ~2 times faster in the presence of water. However, the results for complex **8**'s initiation should be treated as qualitative. While >90% of **8** is observed to form Fischer carbene **13**, significant decomposition is also observed prohibiting the quantitative measurement of complex **8**'s initiation. While **8**'s initiation appears to roughly double in the presence of 4 M water, its rate of decomposition increases by a factor of ~5. Therefore, although water does increase the rate of phosphine dissociation and such likely contributes to complex **8**'s increased rate of decomposition, water appears to serve a more extensive role in **8**'s decomposition.

Mechanism of the decomposition of methylidene complex 8 in the presence of water. The decomposition mechanism of ruthenium methylidene complex **8** is complicated, as the observed decomposition products indicate multiple decomposition pathways. However, the decomposition of **8** is first order in itself, and most decomposition pathways involve the formation of Cy_3PMeCl. Therefore, many of the decomposition pathways likely share a single initiation step. From the effect of excess PCy_3 on complex **8**'s decomposition and the effect of water on complex initiation, this step is proposed to be phosphine dissociation. Nucleophilic attack on the the methylidene carbon of **8**'s fourteen-electron species by PCy_3 followed by fragmentation then yields the observed phosphonium salt (Scheme 4.4). These steps are already proposed to be part of the dominant pathway for the decomposition of **8** in anhydrous benzene.[13,14] In the same way, nucleophilic attack on the methylidene carbon of **8**'s fourteen-electron species by water may be an initial step in the formation of the observed ruthenium carbonyl hydride, **10**.

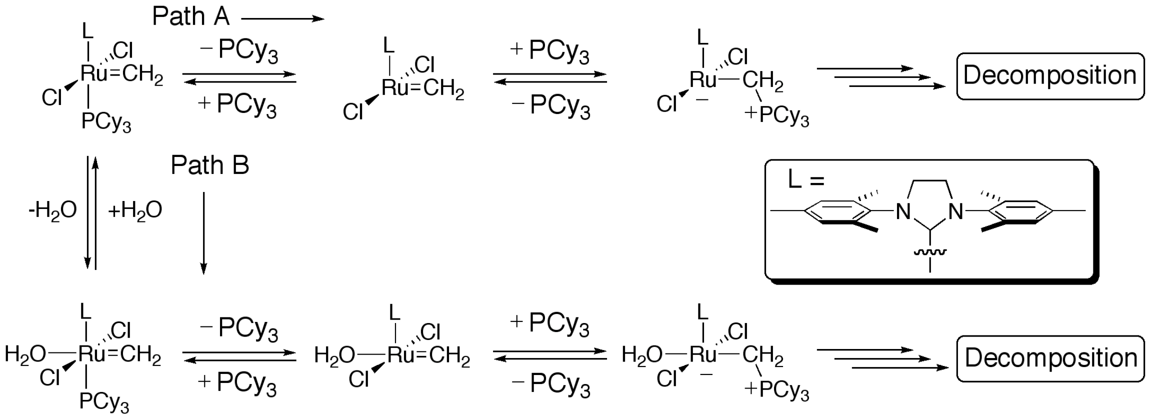
The effect of water on the decomposition of **8** can be considered as the aggregate result of two distinct causes. First, the addition of water changes the chemical environment (i.e., dielectric constant). Clearly such changes should effect the rate of decomposition. Additionally, water may directly interact with **8** by coordinating to the metal center or a variety of other mechanisms.[30]

If water's impact on decomposition rates can be attributed entirely to its effect on the chemical environment, the effect of increasing the water concentration on decomposition rates should be approximately linear since environmental properties will be changing roughly linearly with increasing water concentration.[31-34] However, Figure 4.2 clearly shows that the relationship between increasing water concentration and the decomposition rate is nonlinear. Indeed, while increasing the water concentration from 0 to 1 M increases the decomposition rate constant by a factor of ~3.7, further increasing the water concentration to 4 M corresponds to a rate constant increase of only ~1.4.

The observed decomposition behavior appears indicative of a direct interaction between methylidene complex **8** and water under these conditions. However, the inability to directly observe such an interaction makes this proposition speculative, and a decomposition mechanism where water simply effects the chemical environment cannot be discounted at this time.

The current hypothesis regarding the speculated water/**8** interaction is that water may be reversibly coordinating to the ruthenium center to form a hexacoordinate complex, which may then decompose as illustrated in Scheme 4.4. The examined water concentrations are too high to determine the order of water in complex decomposition.[35] However, the proposed coordination is reasonable as other sigma-donating ligands, such as pyridines, are known to coordinate to ruthenium at that position,[36] and the negligible effect of chloride concentration on complex decomposition precludes the reversible displacement of the chloride ligands by water before the rate-determining step. Unfortunately, evidence for water coordination cannot be directly observed by UV-Vis, NMR spectroscopy nor crystallography, which prevents a stronger endorsement for this conjecture. Even so, this is currently the favored explanation for the experimental results since an irreversible interaction should not cause the observed decrease in the acceleration of the decomposition rate of complex **8** at increased water concentrations (Figure 4.2).

Scheme 4.4.



Assuming a reversible coordination of water, the decomposition kinetics of ruthenium methylidene complex **8** can be interpreted as arising from the relative contributions of two competing decomposition pathways, A and B (Scheme 4.4). Pathway A involves decomposition of complex **8** absent any direct interaction between **8** and water during the initial decomposition steps while pathway B involves the coordination of water (Scheme 4.4). The relative contribution of pathway A to the total decomposition rate is then greater at lower water concentrations and diminishes at higher water concentrations as more of the water-coordinated species is formed. At sufficiently high water concentrations, all decomposition occurs through pathway B involving the coordination of water to **8**'s ruthenium atom (Scheme 4.4). From Figure 4.2, the decomposition rate of **8** rapidly increases with increasing water concentration up to 1 M water. At these concentrations of water, both decomposition pathways A and B operate, and the large acceleration of decomposition is primarily due to the shunting of greater amounts of complex **8** through pathway B which is hypothesized to be more rapid. At water concentrations greater than 1 M, all decomposition occurs through pathway B and the slower rate of acceleration solely reflects the effect of the increasingly polar protic environment on pathway B's rate of decomposition.

At this point, it should be noted that PCy_3 is a good base, and it may deprotonate water to form hydroxide which is known to decompose ruthenium methathesis catalysts.[4] However, acid-base reactions always favor the formation of the weaker acid, and water (pKa = 15.7) is a weaker acid by several orders of magnitude than protonated PCy_3 (pka ~9.7).[37] Therefore, this process should be negligible. Even so, PCy_3 may be involved in other base-mediated decomposition pathways such as the deprotonation of ruthenium-coordinated water molecules.

Decomposition of ethylidene compex 7 in the presence of water. The observed data indicate that ruthenium methylidene complex **8** is not sufficiently stable toward water for productive aqueous metathesis. Also, an examination of the effect of additives on the decomposition rate does not yield immediate insights toward structural changes that may address this instability. Another approach to productive aqueous metathesis is to avoid ruthenium methylidene complex formation entirely by the appropriate choice of substrate. Obviously, internal olefins containing terminal phenyl groups make for ideal substrates since they yield the relatively stable ruthenium benzylidene complex **2** during productive metathesis (Scheme 4.1). A second strategy is to employ substrates that contain internal olefins with terminal methyl groups. Such substrates have the advantage of being more synthetically available than their phenyl analogs. Productive metathesis reactions with these substrates produce ruthenium ethylidene complex **7** (Scheme 4.1). Therefore, examination of the decomposition of **7** in the presence of water should demonstrate the feasibility of this strategy. Additionally, as all productive metathesis reactions involve ruthenium alkylidene intermediates (Scheme 4.1), examination of ethylidene complex **7**'s decomposition can serve as a model for the general stability of ruthenium alkylidenes toward water.

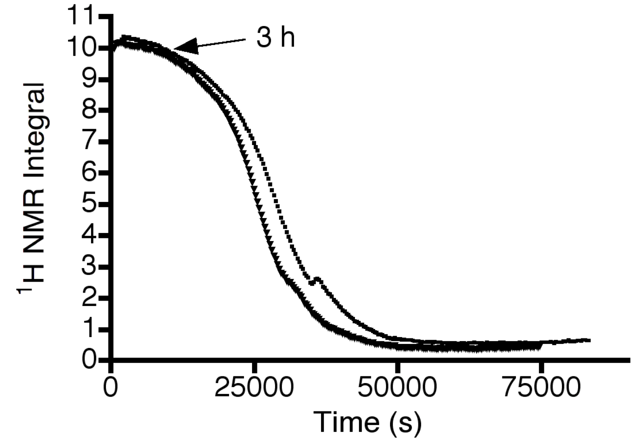


Figure 4.4. The decomposition of 0.023 M ruthenium ethylidene complex **7** in 4 M H_2O/THF at 25 °C occurs with ~3 hours of slow decomposition followed by rapid decomposition and with an observed half-life of ~7.5 hours. The two plots represent two separate trials.

Ruthenium ethylidene complex **7** can be readily synthesized by the reaction of **2** with *cis*-2-butene.[38] An examination of its decomposition in 4 M water/THF at 25 °C reveals the interesting decomposition behavior shown in Figure 4.4. There appears to be a

~3 hour period of slow decomposition followed by more rapid decomposition. Unfortunately, this behavior prohibits simple fitting of the data to an exponential decay to extract rate constants. However, ~6 hours are required for 75% decomposition of complex **8** in 4 M water/THF while ~11 hours are required to reach 75% decomposition for complex **7**. Therefore, ethylidene complex **7** is more stable toward water than methylidene complex **8**.

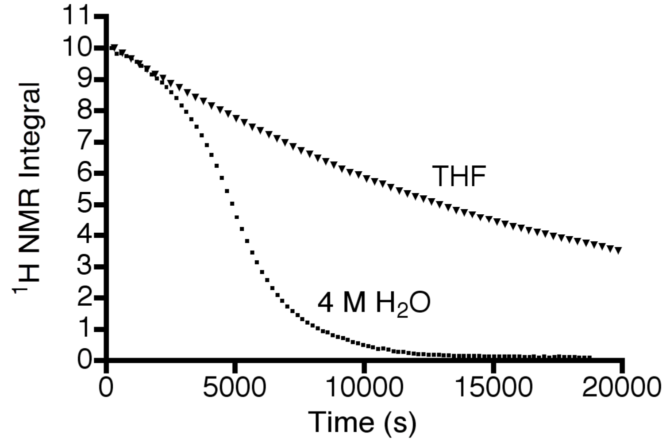


Figure 4.5. These plots represent the decomposition of 0.023 M ruthenium ethylidene complex **7** at 35 °C in the presence and absence of water.

Recently published work by Wagener and co-workers briefly examines the decomposition of complex **7** in benzene at 55 °C.[38] The published decomposition curves show far different behavior than that demonstrated in Figure 4.4. Therefore, the observed manner of decomposition may be due to the presence of water. To explore this possibility, the decomposition of **7** in THF and in 4 M water/THF was examined at 35 °C. As illustrated in Figure 4.5, in the absence of added water, complex **7** decomposes through a typical exponential decay ($k_{obs} = (5.87 \pm 0.03) \times 10^{-5}\ s^{-1}$ at 0.023 M). However, in the presence of 4 M water, curvature is observed at the beginning of the collected decay, which is further evidence that water directly interacts with the ruthenium complex. Observation of **7**'s decomposition at 35 °C yielded two further interesting results.

As already described, ruthenium alkylidene and methylidene derivatives of bis(phosphine) complex **1** are known to decompose by very different mechanisms.[8] This is also believed to be true for metathesis catalysts containing NHC ligands.[7] The decomposition of ruthenium methylidene complexes, such as complex **8**, is known to be first order in the ruthenium methylidene complex.[8,13] However, the decomposition of ruthenium benzylidene and alkylidene complexes, such as complexes **2** and **7** respectively, is believed to be second order in the phosphine-dissociated fourteen-electron ruthenium complex.[8] To determine the kinetic order of ruthenium complex **7** in its decomposition under these conditions, the effect of doubling the concentration of **7** on its decomposition rate can be examined in both the presence and absence of 4 M water in THF (Figure 4.6).

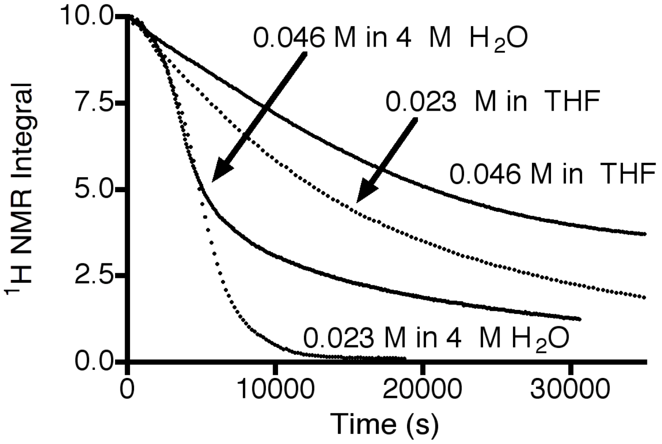
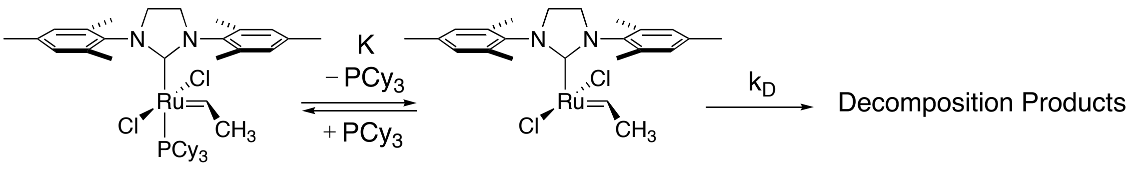


Figure 4.6. Doubling the initial concentration of ruthenium ethylidene complex **7** has a very different effect on its decomposition rate in the presence of water than in water's absence.



7 **14**

$$[\mathbf{14}] = \frac{K[\mathbf{7}]_t}{n([\mathbf{7}]_0 - [\mathbf{7}]_t)} \quad \text{(preequilibrium)} \tag{4.4}$$

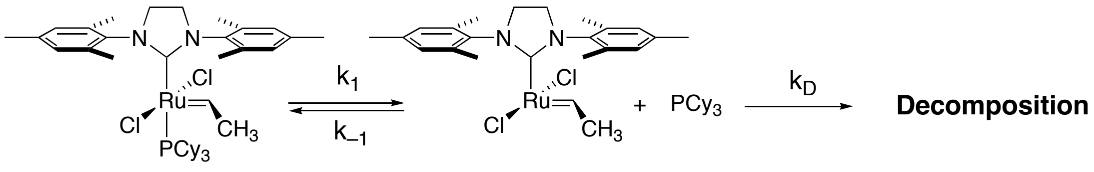
$$\text{Decomposition\_Rate} = k_D\left[\frac{K[\mathbf{7}]_t}{n([\mathbf{7}]_0 - [\mathbf{7}]_t)}\right]^x \tag{4.5}$$

$$\text{Decomposition\_Rate}_y = k_D\left[\frac{K(1-y)[\mathbf{7}]_0}{n([\mathbf{7}]_0 - (1-y)[\mathbf{7}]_0)}\right]^x \quad \text{(rate at y percent decomposition)} \tag{4.6}$$

$$\text{Decomposition\_Rate}_y = k_D\left[\frac{K(1-y)}{ny}\right]^x \quad \text{(simplification)} \tag{4.7}$$

In the absence of water, the decomposition of ethylidene complex **7** is less than first order in **7** itself (Figure 4.6). This behavior is actually consistent with a decomposition pathway analogous to that proposed for the decomposition of the propylidene derivative of ruthenium bis(phosphine) **1**.[8] This mechanism involves a preequilibrium of the bis(phosphine) complex with its phosphine-dissociated fourteen-electron species followed by bimolecular decomposition. Assuming **7** similarly equilibrates with its fourteen-electron species, **14**, its decomposition can be represented by eqs 4.4 and 4.5. For these equations, $[\mathbf{7}]_t$ is the concentration of **7** at time "t." $[\mathbf{7}]_0$ Is the initial concentration of **7**. The variable "n" represents the fraction of PCy_3 actually present relative to the amount potentially present, and "x" is the fourteen-election species' decomposition kinetic order. Equations 4.6 and 4.7 demonstrate that given any percentage of decomposition, "y," the rate of **7**'s decomposition (Decomposition_Rate$_y$) is independent of the concentration of **7**. Consistent with this analysis, with an initial concentration of 0.023 M in THF, the decomposition rate is ~1.0 × 10^{-5} M•s^{-1} at 10% decomposition of **7** while this rate is ~1.1 × 10^{-5} M•s^{-1} when the initial concentration is 0.046 M.

Doubling the initial concentration of complex **7** in the presence of 4 M water in THF has a very different effect on its rate of decomposition than in water's absence. Up to 50% decomposition, complex **7** appears to decompose twice as fast when the initial concentration is doubled, which is consistent with the decomposition being first order in **7**. Beyond 50% decomposition, the decomposition rate drastically reduces when **7**'s initial concentration is doubled (Figure 4.6).



7 **14**

$$\frac{d[\mathbf{Decomposition}]}{dt} = k_D[\mathbf{14}]^x \tag{4.8}$$

$$[\mathbf{14}] = \frac{k_1[\mathbf{7}]}{k_{-1}[PCy_3] + k_D} \qquad \text{(steady - state approximation)} \tag{4.9}$$

$$\frac{d[\mathbf{Decomposition}]}{dt} = k_D\left[\frac{k_1[\mathbf{7}]}{k_{-1}[PCy_3] + k_D}\right]^x \tag{4.10}$$

$$[PCy_3] = n([\mathbf{7}]_0 - [\mathbf{7}]_t) \tag{4.11}$$

A cursory examination of the plots for the decomposition of ethylidene compound **7** in the presence of 4 M water indicates that it decomposes by a different mechanism in aqueous THF than in water's absence. Assuming that decomposition primarily involves the fourteen-electron species, **14**, and that PCy_3 is not immediately involved in **14**'s decomposition, the decomposition of **7** can be modeled with eqs 4.8–4.10. Equation 4.11 accounts for the processes that adsorb PCy_3 in later decomposition steps. The variables "n" and "x" are the same as defined for eqs 4.4–4.7.

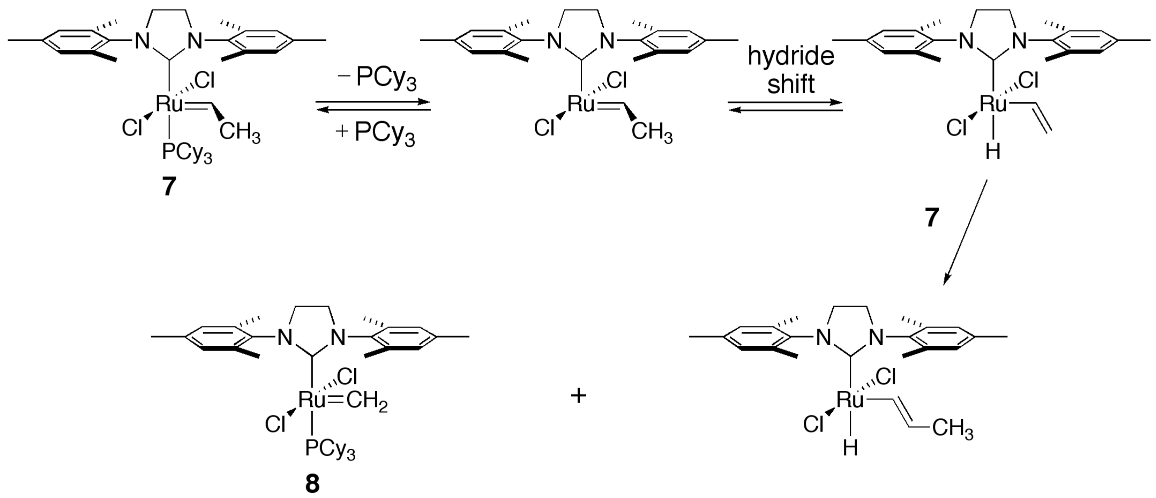
The observed reduction of complex **7**'s decomposition rate when its initial concentration is 0.046 M can then be best explained by an examination of eq 4.10. Given that, in the presence of water, decomposition does not involve a preequilibrium, k_D is greater than k_{-1}. Assuming that k_D is sufficiently greater than k_{-1}, **7**'s decomposition rate will be independent of $[PCy_3]$ at low values of $[PCy_3]$. However, as the value of $[PCy_3]$ grows sufficiently large, the rate of **7**'s decomposition will decrease as the value of $k_{-1}[PCy_3]$ approaches the value of k_D. From Figure 4.6, the decomposition of a sample where **7**'s initial concentration is 0.023 M does not generate enough PCy_3 to retard the decomposition rate even after extensive decomposition. Consistent with this observation is the fact that the reduction of **7**'s decomposition rate for a sample with an initial concentration of 0.046 M does not occur until 50% of the sample has decomposed.

A second interesting result is the observation of a new alkylidene hydrogen resonance in the ^1H NMR spectra as ethylidene complex **7** decomposes, both in the presence and absence of water. This observation was also made by Wagener and co-workers upon examining the decomposition of complex **7** in benzene. They speculate that the identity of this new peak is ruthenium methylidene complex **8**.[38] Indeed, the new resonance appears at 17.8 ppm, which is identical with the chemical shift of **8**'s alkylidene hydrogen peak in THF. Moreover, an examination of the ^{31}P NMR spectra of **7** after decomposition at 35 °C reveals a major phosphorus resonance at 37.2 ppm, consistent with the phosphorus resonance of complex **8**. Additionally, the ^{31}P NMR spectrum reveals a large peak at 34.8 ppm matching the phosphorus resonance of Cy_3PMeCl whose presence would be expected from decomposition of the *in situ* generated **8**.

The decomposition of a sample containing known initial amounts of complexes **7** and **8** provides further confirmation of this identification. An examination of the ^{1}H NMR spectrum of this sample after brief decomposition reveals only two sharp alkylidene peaks at 18.5 and 17.8 ppm, corresponding to the alkylidene hydrogen resonances of **7** and **8** respectively. Had the newly observed compound not been **8**, three alkylidene hydrogen resonances should be present in this spectrum, or complex **8**'s alkylidene hydrogen resonance should have broadened or shown a shoulder. Therefore, the newly formed alkylidene hydrogen peak observed during **7**'s decomposition is confidently ascribed to the *in situ* generation of complex **8**.

The formation of ruthenium methylidene complex **8** during the decomposition of ethylidene compound **7** is likely indicative of a process like the one outlined in Scheme 4.5. A hydride shift to the ruthenium center from a carbon beta to the metal center is believed to play a role in the decomposition of ruthenium benzylidene complexes in the presence of various alcohols.[21,39] Similarly, a β-hydride shift from complex **7**'s alkylidene ligand's terminal methyl group to the ruthenium center is proposed to form a ruthenium hydride with a sigma-bound ethylene molecule (Scheme 4.5). This first step is proposed to occur on the phosphine-dissociated fourteen-electron species, which contains an open coordination site appropriately positioned to accept a hydride ligand. Methylidene complex **8** is then produced by a metathesis reaction between the sigma-bound ethylene molecule and residual complex **7**.

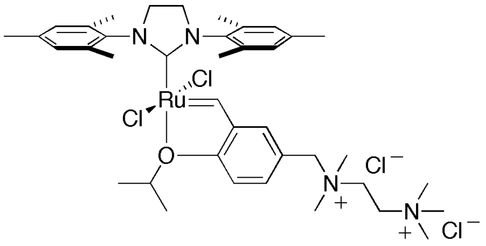
Scheme 4.5.



Ethylidene complex **7** is not overly stable at elevated temperatures in a polar environment. At 35 °C in THF, 50% of **7** decomposed in ~3.6 hours. In contrast, Wagener and co-workers extrapolate that 50% decomposition of **7** requires 100 hours at 55 °C in benzene.[38] In the presence of water, **7** is even less stable. In 4 M water/THF, 50% decomposition of **7** occurs after ~1.3 hours at 35 °C and ~7.5 hours at 25 °C. Unfortunately, these data indicate that the use of substrates containing internal olefins with terminal methyl groups is unlikely to be a successful strategy for aqueous metathesis at elevated temperatures. While not promising, the potential success of this strategy for aqueous metathesis at room temperature remains unclear.

Summary

To summarize, this research demonstrates that ruthenium benzylidene complex **2** is reasonably stable in the presence of water while ruthenium ethylidene complex **7** and ruthenium methylidene complex **8** show much lower stability. The decomposition of methylidene complex **8** is not significantly affected by added chloride ion and is only moderately affected by added PCy_3. An examination of the products arising from the decomposition of **8** reveals multiple decomposition pathways though most involve the generation of Cy_3PMeCl. The decomposition behavior of complex **8** in aqueous THF is first order in **8** itself and may indicate a direct interaction between **8** and water. While not approaching the stability of **2**, ethylidene complex **7** is more stable towards water than **8**. In 4 M water/THF, complex **7** shows a brief period of slow decomposition prior to a large increase in the decomposition rate. However, in the absence of added water, the decomposition rate of **7** follows a typical exponential decay. Finally, ethylidene complex **7** generates methylidene complex **8** during its decomposition.



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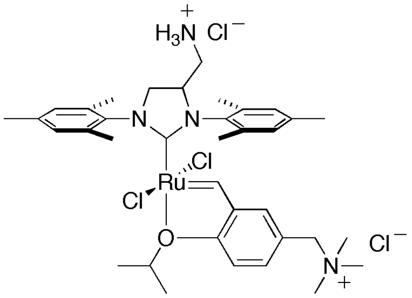

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In conclusion, the successful generation of a ruthenium-based, water-soluble metathesis catalyst containing an NHC ligand must overcome the obstacles of the relative instabilities of methylidene and alkylidene ruthenium complexes toward water. The formation of Cy_3PMeCl indicates that PCy_3 plays an active role in ruthenium methylidene complex **8**'s decomposition. Therefore, water-soluble compounds lacking a phosphine ligand may be better targets for an aqueous metathesis catalyst. Catalysts containing 2-isopropoxybenzylidene ligands, such as catalysts **15** and **16**, are thus attractive water-soluble catalyst targets. The successful development of these water-soluble metathesis catalysts is described in Chapter 5.

Acknowledgements

First and foremost, the author acknowledges the contributions of Dr. Soon Hyeok Hong to the research described in this chapter. He synthesized ruthenium complexes **7** and **8** and assisted with the described decomposition experiments. Drs. Scott Ross and Christine Thomas are gratefully acknowledged for their aid with solvent suppression and HMQC NMR spectroscopy respectively. Drs. Jonathan Owen, Sebastian Smidt, Joseph Samec, and Greg Beutner also contributed to this research with helpful discussions. The National Institute of Health funded this research (5R01GM068647).

Experimental

Materials and methods. All decomposition trials were measured on a Varian Inova 500 spectrometer (499.85 MHz for ^1H; 202.34 MHz for ^{31}P; 125.69 MHz for ^{13}C) under temperature control. Temperature calibration at elevated temperatures was accomplished with an ethylene glycol standard. All other NMR spectra were obtained on a Varian Mercury 300 spectrometer (299.817 MHz for ^1H, 75.4 MHz for ^{13}C, and 121 MHz for ^{31}P). ^1H NMR chemical shifts are reported in ppm relative to $SiMe_4$ ($\delta = 0$) and are internally referenced to residual solvent proton peaks. ^{31}P NMR spectra are externally referenced to 98% phosphoric acid (δ = 0). With the exception of the initiation of complex **8**, all the reported decomposition or initiation measurements were performed at least twice, and the provided data is the average of all of the trials. Slow decomposition and time constraints prevented data collection over a period of more than two half-lives for the decomposition of methylidene **8** in THF. Otherwise, all decomposition and initiation collections were acquired over a period of at least three half-lives.

All samples, sans water, were prepared in a N_2-filled Vacuum Atmospheres glove box (O_2 < 3 ppm). Ruthenium benzylidene complex **2** was obtained from Materia and was used as received. Ruthenium ethylidene complex **7** and ruthenium methylidene complex **8** were made according to literature procedures.[37,7] Puriss water was purchased from Fluka (Aldrich). PCy_3 and zone-refined anthracene were obtained from Aldrich and used without further purification. Puriss $^{n}Bu_4NCl$ was acquired from Fluka (Aldrich) and dried under high vacuum at 90 °C for 2 days prior to storage and use in a glove box. Deuterated THF was purchased from Cambridge Isotopes Laboratories and dried over flame-activated 4 Å molecular sieves. Ethyl vinyl ether was acquired from Aldrich and distilled from CaH_2. All liquids were degassed by either 3 freeze, pump, and thaw cycles or a generous argon sparge.

Procedure for a typical decomposition measurement. In a N_2-filled glove box, ruthenium methylidene complex **8** (12.4 mg, 0.016 mmol) and anthracene (1 mg, 0.0056 mmol) were weighed into a 1-dram vial. Deuterated THF (650 µL) was used to transfer the sample to a screw-cap NMR tube. A septa-cap was used to seal the NMR tube before removing the tube from the glove box and reinforcing the seal with parafilm. The sample was placed into the spectrometer and allowed to equilibrate at the probe temperature (25 °C) for 10 minutes prior to the injection of water (50 μL, 4 M) from an air-tight syringe. Mixing was accomplished by three tube inversions. The sample was reinserted into the spectrometer and rapidly locked and shimmed prior to collecting data through the use of a time-delayed array of ^{1}H NMR spectra (referred to as a preacquisition delay, PAD, by Varian software). A custom macro was used to export the time and integration data from the spectral array as a text file. These data were imported into GraphPad Prism 4.0b for Macintosh (trial version) and fitted to an exponential decay. The reported uncertainty represents the 95% confidence intervals of the fit.

Examination of the effect of additives. For PCy_3, the procedure is identical to that described above for measuring the decomposition of complex **8** except that the PCy_3 is also weighed into the sample vial. However, $^nBu_4NCl$ was weighed directly into the NMR tube through the use of a weighing boat. Full dissolution of 10 equivalents of $^nBu_4NCl$ occurred only upon the addition of water.

Procedure for a typical ethyl vinyl ether initiation experiment. In a N_2-filled glove box, ruthenium benzylidene complex **2** (10.1 mg, 0.012 mmol) and anthracene (1 mg, 0.0056 mmol) were weighed into a 1-dram vial. Deuterated THF (620 μL) was used to transfer the sample to a screw-cap NMR tube. The tube was sealed with a septa-cap and brought out of the box, and the seal was reinforced with parafilm. Water (50 μL, 4M) was injected using an air-tight syringe. The sample was inserted into the spectrometer and allowed to equilibrate at the probe temperature (25 °C) for 10 min. Sample locking and shimming were performed just prior to the injection of ethyl vinyl ether (33.5 μL, 0.35 mmol, 29 equiv) with an air-tight syringe. Mixing was accomplished by three rapid tube inversions, and the sample was immediately reinserted into the spectrometer. Data collection and analysis waere accomplished as described for the decomposition of complex **8**. For the initiation of ruthenium methylidene complex **8** in the presence of water, a blank sample containing the appropriate amounts of deuterated THF, water, and ethyl vinyl ether was used to lock and shim the spectrometer. After temperature equilibration, both water and ethyl vinyl ether were injected into the methylidene sample followed by immediate data collection.

References and Notes

Portions of this chapter have been published as: Jordan, J. P.; Hong, S. H.; Grubbs, R. H. *Organometallics* submitted, 2007.

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(16) The alkylidene hydrogen is the hydrogen attached to the carbon, which is double bonded to the ruthenium center as shown in Scheme 4.1.

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(21) $^1H/^{31}P$ HMQC NMR spectroscopy reveals two proton/phosphorus cross-peaks for the phosphorus resonance at 34.8 ppm. These cross-peaks indicate coupling interactions between this phosphorus and protons with chemical shifts of 2.49 ppm and 1.95 ppm as observed in the ^1H NMR spectrum. Comparison with an authentic sample of Cy_3PMeCl reveals that these protons correspond to the cyclohexyl methine and the methyl group of Cy_3PMeCl respectively.

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