Water-Soluble Ruthenium Alkylidene Complexes:

Synthesis and Application to Olefin Metathesis in Protic Solvents

Thesis by

David Michael Lynn

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To My Family

Acknowledgment

I would like to start by thanking my advisor, Professor Bob Grubbs. It's difficult for me to come up with a new twist on all of the other things that have been said. He is an incredibly insightful man, and has managed to combine great science with a "hands-off" management style to yield a truly unique scientific environment. He is also a genuinely nice person to have around, which is an desirable quality in a boss. He has encouraged my ideas, even the lame ones, and has supported me through times when nothing worked. How he knew it would eventually come together in the end I will never know. He has given me a number of great opportunities, and for that I am grateful. I know that I will look back upon my experiences with Bob as one of the highlights of my scientific career. I would also like to thank Professors John Bercaw, Harry Gray, and Dave Tirrell for taking the time to serve on my committee.

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Anyway, that brings me to other members of the Grubbs group. First, I'd like to thank a rather impressive list of postdocs who have passed through the lab, among them: Scott Miller, Geoff Coates, Osamu Fujimura, Mike Marsella, Mike Giardello, Peter

Schwab, and, more recently, Adam Matzger. Each of these people have left an indelible impression on me—some for their commitment to science, some for their senses of humor, and many of them for pleasant combinations of both. Each of them have, in their own ways, taken the group in important new directions. In a research group as large as ours, many people have come and gone. Postdocs play a special role in our group, and I apologize to all of the current and former postdocs that I do not have the time or space to mention. I do remember you.

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I feel very lucky to have joined Bob's group with a relatively large group of first years (Marcus Weck, Helen Blackwell, Tom Kirkland, Delwin Elder, and Tom Wilhelm) during a very exciting time in the group's history. Marcus made every day exciting, and when he wasn't yelling "redneck" at the top of his lungs in a crowded bar full of strangers bigger than us, I was proud to have many beers with him. The lab has been much quieter since he took off for Harvard. Tom Kirkland, along with Eric Dias and Todd Younkin, was part of the late-night crowd, all of whom are acknowledged for

things I ought not get into right now. Tom also donated considerably to the ring-closing metathesis work in Chapter 7. Delwin is "a generally happy guy," and was very seldom seen far apart from his big, toothy smile. I'd like to thank him for going out to seedy bars with the rest of us, even if he only had a few cokes. Not everyone would do that, and I think that helped make the bonds in our class even stronger. Tom Wilhelm deserves credit (along with Adam Matzger and Thomas Rolle) for keeping our computer networks running smoothly. It's a thankless job, so I am thanking them now.

That brings me to the rest of our current group: Mike Ulman, Heather Maynard, Erika Bellmann, Todd Younkin, Melanie Sanford, Matt Scholl, Chris Bielawski, J.P. Morgan, and Tina Trnka. I also think of our lone undergraduate, Alex Dunn, as having been a graduate student in our group, and he often worked more diligently on his projects than many of us. One of the greatest things about the Grubbs group is that even the bad times here have been pretty damned good.

I'd also like to thank Bob Grubbs for introducing me to the sport of rock climbing. After several years of talking about how I would "never want to do anything as pointless as that," Bob dragged me up a rock in Yosemite valley. Since that time I've been able to see many parts of California from radically different vantage points and build up memories that I will not soon forget. Steve Cox and Hoffman "Hoffman" Hoffman were excellent teachers, and their climbing class kept me encouraged at an early stage. I'd like to thank Todd Younkin, Chris Bielawski, and Adam Urbach for jumping in at the beginner level at the same time as me, and especially Todd for taking off to go climbing at the drop of a hat (kudos to Todd's mom Terry for coming up with the phrase

"momma's little climber"). Ken Brameld and Kirk Hansen were remarkably patient teachers, and I'd like to thank them for taking us out and pushing us past our limits.

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Finally, I would like to thank my girlfriend, Helen Blackwell. Dating someone in the same research group can be a uncertain venture, but it's certainly one of the better risks I've taken. She has been responsible for some of my most memorable times here at Caltech, and has put up with a lot. She also proofred (sic) this entire thesis, which is not an easy thing to do. Thank you for keeping me around.

Last, but not least, I'd like to thank my family—especially my mother, who has done nothing but encourage me and tell me to get a haircut for many years.

Abstract

This thesis describes the application of well-defined ruthenium alkylidene complexes to olefin metathesis in protic solvents. Chapter 2 describes the application of $(Cy_3P)_2Cl_2Ru{=}CHPh$ to the living ring-opening metathesis polymerization (ROMP) of functionalized monomers in aqueous emulsions. In these systems, monomers were dispersed in water using a cationic surfactant, and polymerization was initiated by injection of a catalyst solution. These polymerizations were shown to take place in the absence of chain transfer and chain termination reactions, passing all experimental criteria for living systems.

Chapter 4 describes the synthesis, characterization, and application of ruthenium alkylidenes of the type $(Cy_2RP)_2Cl_2Ru{=}CHPh$ bearing charged phosphine ligands. These complexes were completely soluble and stable in protic, high-dielectric solvents such as methanol and water. Interestingly, the alkylidene protons in these new complexes were found to exchange with deuterons when they were dissolved in perdeuterated protic solvents (as described in Chapter 5).

Chapter 6 describes the application of these new water-soluble alkylidenes to ROMP in aqueous solution. The propagating alkylidenes in these reactions were found to decompose on the time scale of the polymerizations. In the presence of a Brønsted acid, however, polymerization was rapid and quantitative. The effect of the acid in these systems was twofold—in addition to eliminating hydroxide ions, catalyst activities were enhanced by protonation of phosphine ligands. These activated alkylidenes were used to initiate *living* polymerizations in aqueous solution. Both chain termination and chain transfer reactions were demonstrated to be absent on the time scale of the

polymerizations, and this living polymerization protocol was used to synthesize water-soluble block copolymers.

Chapter 7 describes the application of water-soluble alkylidenes to the ring-closing metathesis (RCM) of diene substrates in water and methanol. These alkylidenes could not be used to cyclize α,ω-dienes due to the instability of the catalytically-active methylidene complexes in these reactions. Substrates containing an internal olefin, however, were readily cyclized. The activities of these alkylidene complexes were found to correlate with predicted activities based on analyses of the steric and electronic character of the phosphine ligands in these complexes (as described in Chapter 3).

Table of Contents

List of Figures, Tables, and Schemes

Chapter 1

Chapter 2

Chapter 3

Chapter 4

Chapter 5

Chapter 6

Chapter 7

"If I have seen farther than others, it is because
I was standing on the shoulders of giants."

—Sir Isaac Newton

"I am the Lizard King, I can do anything."

—James Douglas Morrison

Chapter 1

Introduction to Olefin Metathesis

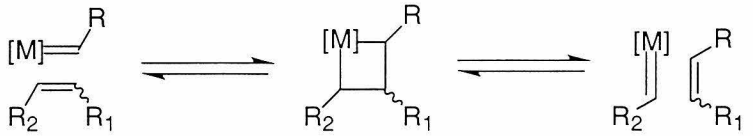
And Survey of Aqueous Metathesis Systems[†]

The Olefin Metathesis Reaction

The olefin metathesis reaction is a transition metal catalyzed, carbon-carbon bond-forming reaction in which olefin bonds are cleaved and the resulting fragments are redistributed to form new olefins.[1,2,3] For example, in the presence of a transition metal alkylidene, *cis*-2-pentene is converted to an equilibrium statistical mixture of both *cis* and *trans* butenes, pentenes, and hexenes (Eq 1).[1]

(Eq 1)

The general mechanism for this reaction, originally proposed by Chauvin,[4] has been shown to proceed *via* the formal [2+2] cycloaddition of an olefin and a metal alkylidene, yielding a metallocyclobutane intermediate (Eq 2). The productive retrocycloaddition of this intermediate generates a new metal alkylidene and a new olefin product, while unproductive cleavage regenerates the original starting materials. The elementary steps in this process are generally reversible, and the reaction is under thermodynamic control.



(Eq 2)

The versatility of the metathesis reaction has attracted the attention of chemists with interests ranging from polymer chemistry to the synthesis of complex natural products. In addition to the simple acyclic cross-metathesis reaction described above (Eq 1), transition metal alkylidenes also catalyze ring-opening metathesis polymerization (ROMP), ring-closing metathesis (RCM), and acyclic diene metathesis (ADMET). These three processes are fundamentally related, *via* the relationship shown in Figure 1. The particular products generated during an olefin metathesis reaction are typically a function of both olefin structure and thermodynamic considerations.[1]

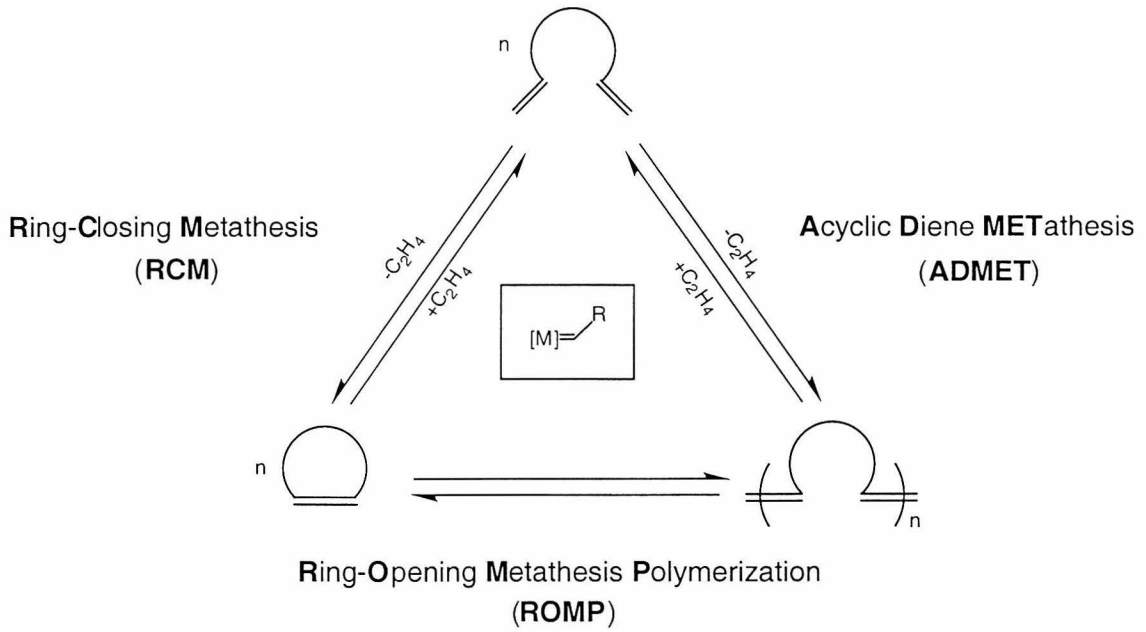
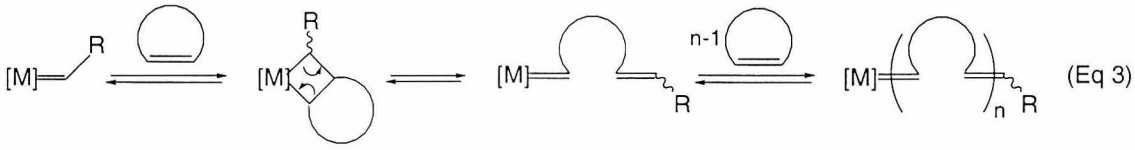


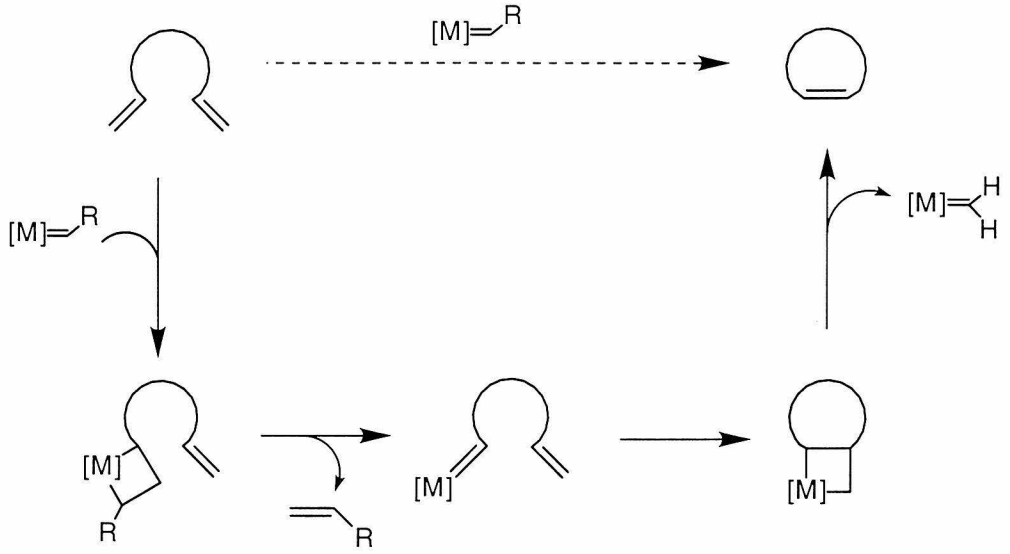
Figure 1: Competing olefin metathesis pathways.

In the presence of a suitable alkylidene catalyst, cyclic olefins can undergo ROMP to yield polymers having backbone unsaturation (Eq 3).[1,5,6] ROMP is particularly well-suited to the polymerization of highly-strained monomers such as norbornene and cyclobutene. Since polymerization is an entropically disfavored process, ROMP is driven forward enthalpically by relief of ring strain in these monomers.



Many metathesis catalysts will also initiate the ROMP of less-strained olefins such as cyclooctene and cyclopentene; however, cyclohexene will not polymerize under equilibrium conditions.[7] Several well-defined metal alkylidenes (discussed below) initiate the living polymerization of strained, cyclic olefins, and have enabled the synthesis of a wide variety of functionalized and unfunctionalized polymers having predictable molecular weights, narrow polydispersities, and well-defined endgroups.[1,5]

Olefin metathesis was originally discovered within the context of polymer chemistry. However, the application of olefin metathesis to the synthesis of small molecules and natural products *via* RCM has recently received much attention (Scheme 1).[8,9] Contrary to the thermodynamic profile of ROMP, the formation of cyclic olefins *via* the RCM of an α,ω-diene is enthalpically disfavored. Thus, RCM is driven forward entropically, *via* the loss of a volatile small molecule such as ethylene, and is limited by the relative ring strain of the cyclic olefin product. RCM has been widely applied toward the synthesis of 5- to 8-membered cyclic olefins, as well as the synthesis of larger macrocyclic systems, and has been the topic of several recent reviews. [8]



Scheme 1: Ring-closing metathesis (RCM) of an acyclic diene.

ADMET was recently introduced as new technique for the metathesis polymerization of α,ω-dienes.[10] This polymerization process resembles RCM thermodynamically, in that the reaction is driven forward entropically by the evaporative loss of a small molecule. The reaction must typically be carried out in neat monomer under vacuum, and often suffers from low conversion and the formation of cyclic byproducts. To date, ADMET has not been developed as extensively as ROMP for the synthesis of poly(olefins).

Olefin Metathesis Catalysts: A Historical Perspective

Over the last 20 years, metathesis catalysts have evolved from the poorly-defined, heterogeneous mixtures that characterized early systems (such as $TiCl_4/AlR_3$-based systems) to well-defined, single-component metallocycles and alkylidenes based on a variety of transition metals (Figure 2).[11,12] These well-defined complexes react in controlled, consistent ways, and their activities can often be attenuated through simple ligand substitution. In contrast to heterogeneous systems, for example, several of these well-defined alkylidenes initiate the living ROMP of monomers such as norbornene[5] (i.e., these polymerizations take place in the absence of chain termination and chain transfer reactions.).

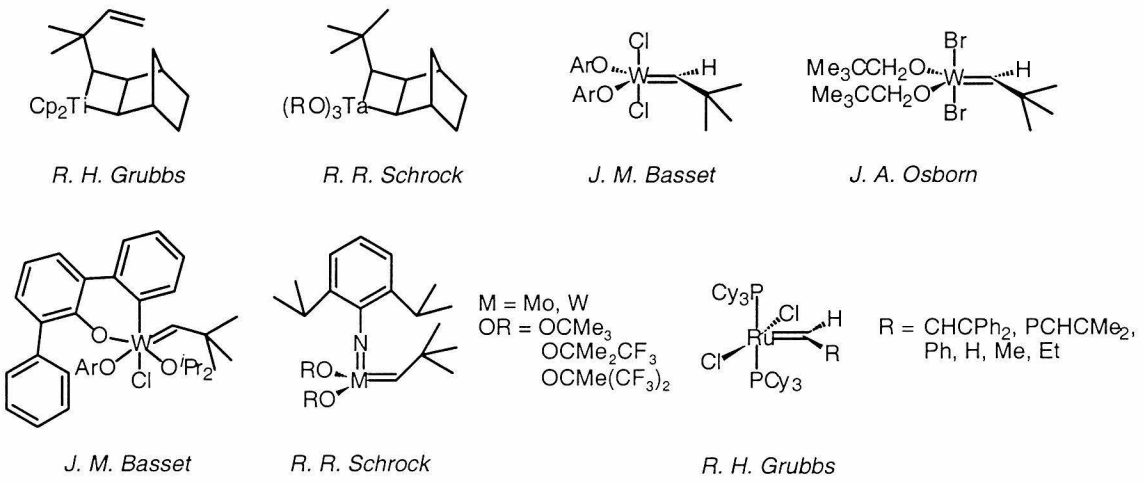


Figure 2: Selected single-component transition metal alkylidene complexes.

Historically, olefin metathesis has been limited to transformations on un-functionalized cyclic hydrocarbons in rigorously-purified organic solvents, due to the extreme sensitivities of original early transition metal catalyst systems to oxygen, water, and polar functional groups.[13] The eventual development of well-defined catalysts based on a *variety* of transition metals enabled the observation of trends in catalyst functional group tolerance.[14,15] In particular, it was found that as the metal centers in these complexes were chosen from further right in the periodic table, the resulting alkylidenes reacted more selectively with olefins in the presence of other harder, Lewis-basic functional groups

(Figure 3).[3] For example, while titanium- and tungsten-based catalysts efficiently olefinate ketones, the molybdenum-based catalysts developed by Schrock react preferentially with olefins in the presence of ketones. Unfortunately, these more tolerant and highly-active molybdenum catalysts react with aldehydes and are deactivated by other polar and protic functional groups such as alcohols and water.

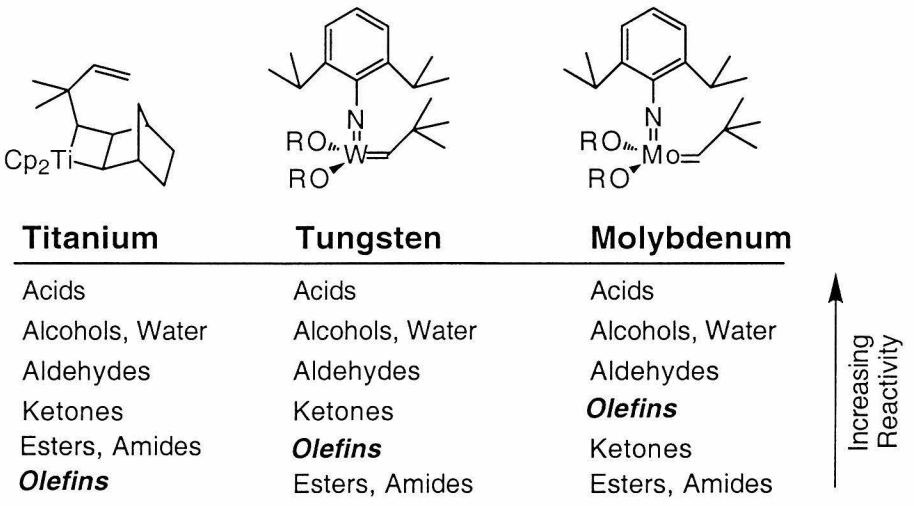


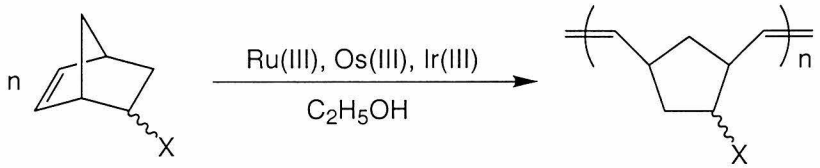
Figure 3: Functional group tolerance of selected alkylidene complexes.

It was quickly realized that the development of metathesis catalysts that were tolerant of *polar and protic* functional groups would offer several synthetic advantages, the most obvious being the use of substrates and solvents without the rigorous purification and drying required for the use of titanium, tungsten, and molybdenum alkylidenes. More tolerant catalysts would also broaden the scope of the reaction, enabling the metathesis of highly-functionalized substrates and obviating the need for tedious and costly functional group protection/deprotection strategies. Additionally, the possibility of water-tolerant and, ultimately, water-soluble catalysts could enable the metathesis of olefinic substrates in aqueous solution. These potential benefits prompted a search for active catalysts based on "softer," more polarizable late transition metals that would be stable toward functional groups and which might function homogeneously in water.

The following sections survey the events leading to the discovery of new functional group tolerant late metal Group VIII catalysts, and briefly discuss important characteristics of individual catalyst systems. These initial discoveries contributed to the development of the well-defined ruthenium alkylidenes shown in Figure 2. The chapter concludes with a brief overview of several recent advances made in applying these new catalysts to olefin metathesis in aqueous environments, the work which forms the body of this thesis.

Olefin Metathesis in Water: "Classical" Group VIII Catalysts

Early after the original discovery of the olefin metathesis reaction, reports indicated that complexes of ruthenium, osmium, and iridium could initiate ROMP. Michelotti *et al.* initially reported the polymerization of norbornene and norbornene derivatives catalyzed by the hydrates of $RuCl_3$, $OsCl_3$, and $IrCl_3$ in refluxing ethanol (Eq 4).[16,17]

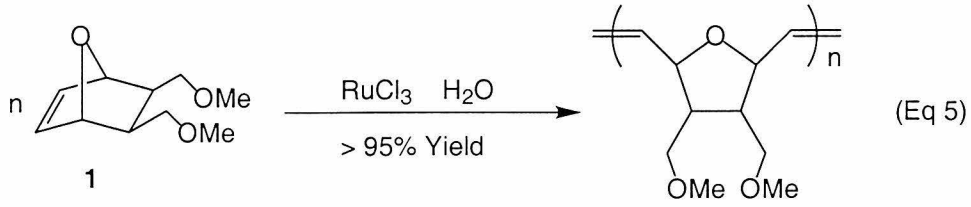


X = H, CH_2Cl, CH_2OH, CO_2H (Eq 4)

These complexes also functioned well in benzene, although small amounts of ethanol were necessary to initiate polymerization. The order of activity for these catalysts was Ir(III) > Os(III) > Ru(III), and they were found to polymerize norbornene monomers with *exo* substituents more readily than *endo* isomers. Rinehart *et al.* later demonstrated that these complexes initiated the aqueous polymerization of a substituted norbornene derivative in the presence of anionic emulsifiers and suitable reducing agents.[18] While this reaction gave only low yields of polymer (typically less than 9%), the overall tolerance of these complexes to polar and protic functionalities made them ideal candidates for further study.

For the ROMP of functionalized 7-oxanorbornenes (possible only *via* these late transition metal catalysts) it was found that the best catalyst was $RuCl_3$ in a mixture of

ethanol and benzene.[15,19] However, the lack of a preformed alkylidene in this "precatalyst" limited its practical usefulness, as polymerizations were preceeded by lengthy initiation periods ranging from several hours to several days.[19,20] Rigorous exclusion of water and oxygen from these systems was found to lengthen initiation periods, while the addition of small amounts of water substantially increased initiation rates. The conclusion that water functioned as a co-catalyst in these systems eventually led to the discovery that $RuCl_3$ functioned as an excellent ROMP initiator in entirely aqueous environments.[21,22] For example, the emulsion polymerization of *exo*-5,6-bismethoxymethyl-7-oxanorbornene **1** (Eq 5) proceeded quantitatively with initiation periods as short as 30 minutes.[21]

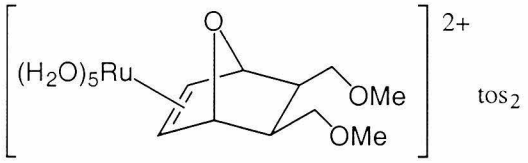


(Eq 5)

The molecular weights of poly(**1**) synthesized in aqueous media were typically high ($M_n \approx 10^6$), and polydispersities were often lower (PDI < 2.0) than the polydispersities of polymers produced by classical systems in organic solvents.[21,23,24] These low polydispersities have been attributed to the low occurrence of termination reactions during the polymerization and the relative inactivity of the propagating species toward the acyclic olefins in the polymer, which suppresses chain transfer reactions.[19] Although initiation occurred more quickly in aqueous systems, the extent of initiation was still low. In fact, it has been estimated that less than 1% of the metal centers in these reactions are converted to active alkylidenes. As a result, polymer properties were inconsistent from run to run and depended heavily on the purity of the $RuCl_3$ complexes.[19,23,24] Molecular weights were generally independent of monomer/catalyst ratios, indicating that these aqueous polymerizations were not living.

The problems outlined above prompted an investigation of the mechanism through which initiation occurred in these ill-defined systems. During the examination of recovered aqueous ruthenium solutions, it became evident that these solutions could be used to initiate additional polymerizations, and that the catalytic species in these solutions became more active upon successive use.[19,21] Initiation periods for these recycled solutions were as low as 10 seconds after two or three polymerizations, and catalyst solutions could be reused up to 14 times without a decrease in activity. This effect was observed for aqueous polymerizations initiated by other Ru(III) complexes, including K_2RuCl_5 and $[Ru(NH_3)_5Cl]Cl_2$, which displayed the same limiting initiation time of 10 seconds upon reuse.[19]

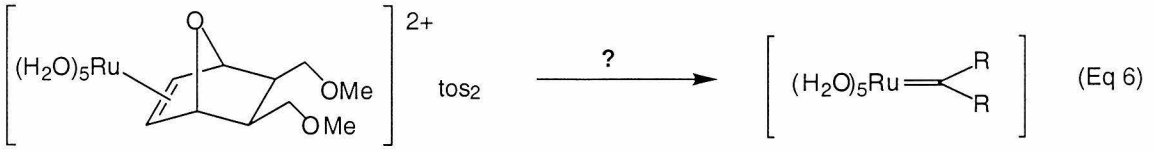
Studies employing Ru(II) complexes, such as $[(C_6H_6)Ru(H_2O)_3]tos_2$ and $Ru(H_2O)_6tos_2$ (tos = *p*-toluenesulfonate), revealed similar effects upon recycling, although these complexes were initially more active than their Ru(III) counterparts. For example, in aqueous polymerizations of monomer **1** catalyzed by $Ru(H_2O)_6tos_2$, induction periods were initially as short as 50 seconds. An important step in the identification of the active species in this polymerization was made when a ruthenium-olefin complex (**2**) was observed after polymerization of **1** initiated by $Ru(H_2O)_6tos_2$.[19,21]



2

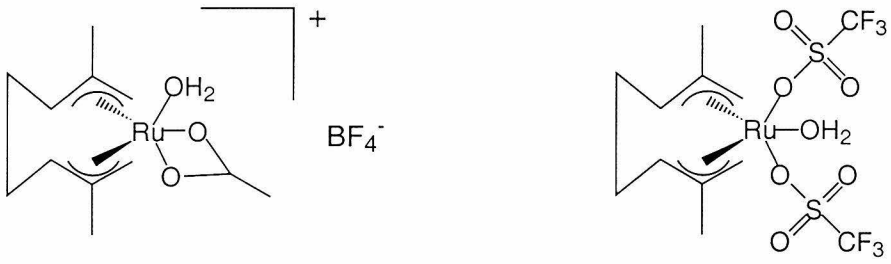
Recycled solutions of **2** initiated ROMP as quickly as the recycled Ru(III) solutions, and closer examination of the recycled Ru(III) solutions revealed NMR resonances identical to those of the olefin protons in **2**.[19] It was therefore suggested that a key step in the initiation process using Ru(III) was the *in situ* formation of a Ru(II)-olefin complex.[21] Current evidence supports the disproportionation of the Ru(III) species to form Ru(II) and

Ru(IV) species, followed by formation of a Ru(II)-olefin complex.[19] The equilibrium constant for disproportionation is small, accounting for the poor initiation efficiency of the Ru(III) systems.[24] An alternative, the disproportionation of an equilibrium amount of Ru(III)-olefin complex to a Ru(II)-olefin complex and a Ru(IV) species, is unlikely since Ru(III)-olefin complexes are generally unstable. Formation of a ruthenium alkylidene, the requisite active species in these polymerizations, has been proposed *via* rearrangement of **2** (Eq 6), although the mechanism for this reaction is not known.[15]



2

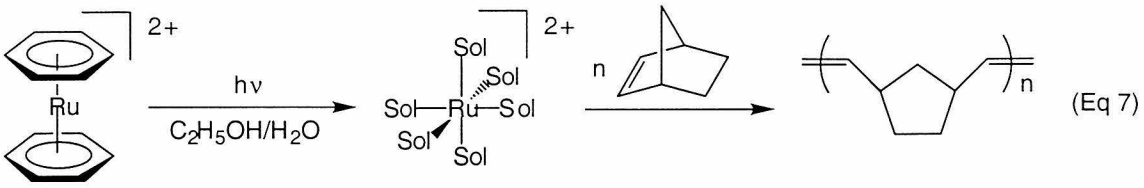
Water soluble bisallyl Ru(IV) complexes **3** and **4** also initiate the emulsion polymerization of norbornene.[25] The lack of preformed alkylidenes in these complexes limits initiation efficiency, although the onset of initiation is not subject to lengthy induction periods. Speculation on the active species in polymerizations initiated by these bisallyl complexes has not been reported.



3 **4**

Karlen *et al.* have described a photoinitiated ROMP (PROMP) system in water/ethanol mixtures using a variety of cationic ruthenium complexes with photo-labile ligands.[26,27] For example, the irradiation of $[Ru(CH_3CN)_6](tos)_2$ or $[(C_6H_6)_2Ru](tos)_2$

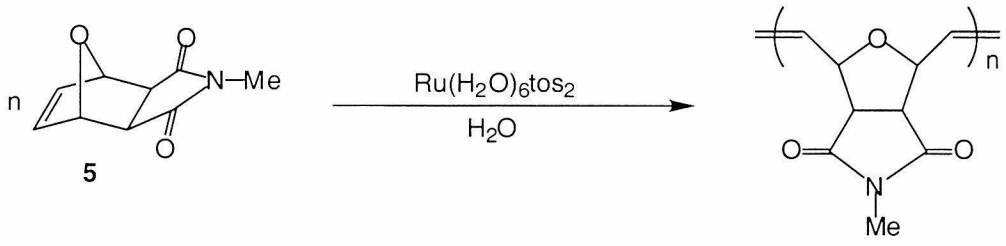
leads to partially- and fully-solvated Ru(II) species which initiate the ROMP of highly-strained olefins, presumably in the manner outlined above (Eq 7).



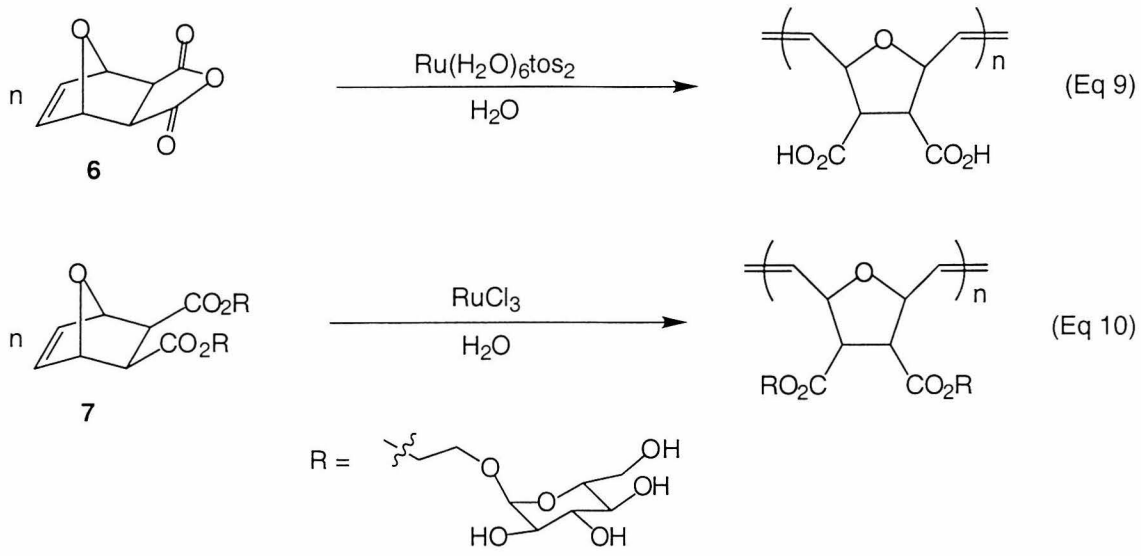
(Eq 7)

Polymers Prepared *via* Aqueous ROMP

The application of the Group VIII complexes discussed above is generally limited to the ROMP of functionalized norbornenes and 7-oxanorbornenes. (These "classical" complexes do not react with acyclic olefins, and therefore are not useful in initiating either cross-metathesis reactions or RCM in aqueous solution.) These complexes have been used to initiate the polymerization and copolymerization of monomers containing alkyl,[16,17,28] aryl,[24] ether,[21,23,29] alcohol,[19] ester,[24,28] anhydride,[19,28,30,31] carboximide,[32,33] and fluoromethyl[24] functionalities in aqueous environments. Aqueous polymerization of dicarboximide functionalized monomer **5** initiated by $Ru(H_2O)_6tos_2$ gave quantitative yields of a polymer having excellent thermal properties (Eq 8).[32] Additionally, polyacid materials were synthesized *via* the ROMP of anhydride-functionalized monomer **6**, which spontaneously opened to the diacid upon polymerization in aqueous environments (Eq 9).[19,30,31] Kiessling *et al.* have recently used $RuCl_3$ to initiate the polymerization of **7** and other carbohydrate-containing monomers to produce a variety of new glycopolymers having biological activities (Eq 10).[34,35,36] Many polymers based on the ROMP of functionalized 7-oxanorbornenes have been investigated as potential ionophoric materials.[20,37]



(Eq 8)



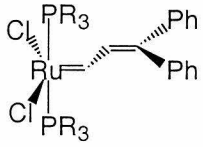
As previously mentioned, the molecular weights of the polymers obtained from these aqueous reactions are generally higher than desired due to the small number of active species. Although the propagating species in these polymerizations do not typically react with acyclic olefins, modest control over molecular weight is possible when certain acyclic chain transfer agents are employed.[29,38] For example, Feast *et al.* have used very high concentrations of *cis*-2-butene-1,4-diol or its dimethyl ether as chain transfer agents.[29] The chain transfer constants in these reactions were small, and inclusion of these olefins in the reaction mixture was shown to effect initiation periods and catalyst activities in complex ways.

The microstructures of polymers synthesized in aqueous media have been well-studied by ^{1}H and ^{13}C NMR. While most polymers prepared using these catalysts contain a high degree of *trans* olefin bonds, the ratio of *trans* to *cis* olefins has been found to vary considerably from catalyst to catalyst.[29] For example, poly-**1** prepared in water using $RuCl_3$ generally contains 60% *trans* olefins, while polymer samples prepared from $OsCl_3$ and $IrCl_3$ contain 75% and 90% *trans* olefins, respectively. In all cases, poly-**1** prepared by these catalysts was atactic. For the polymerization of *exo*-5,6-bis(methoxycarbonyl)-7-oxanorbornene, $RuCl_3$ gave a polymer having 88% *trans* olefin bonds, while [Ru(η^6-

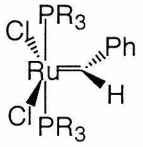
$C_6H_6)(H_2O)_3]tos_2$ and $Ru(H_2O)_6tos_2$ gave polymers containing equal amounts of *cis* and *trans* olefins.[24] In the $RuCl_3$ initiated polymerizations, the ratio of *trans* to *cis* olefins remained constant over prolonged reaction times, again demonstating the relative absence of chain transfer reactions that would eventually result in thermodynamic equilibration. A notable reversal in the *trans-cis* selectivities in these reactions is observed in the emulsion polymerization of norbornene initiated by bisallyl ruthenium complexes **3** and **4**, which yield polynorbornene having 85-90% *cis* olefin bonds.[25]

Well-Defined Ruthenium Alkylidenes

The insight derived from the investigation of ill-defined ruthenium ROMP initiators was eventually successfully applied to the development of Ru(II) alkylidenes **8** and **9**.[12]



8a, R = Ph
8b, R = Cy



9a, R = Ph
9b, R = Cy

In contrast to the "classical" Group VIII complexes, these well-defined alkylidenes initiated ROMP quickly and quantitatively, reacted readily with acyclic olefins, and could be used to initiate *living* polymerizations in organic solvents. Furthermore, as expected based on earlier work with their "classical" counterparts, these well-defined ruthenium alkylidenes displayed extraordinary functional group tolerance (Figure 4).

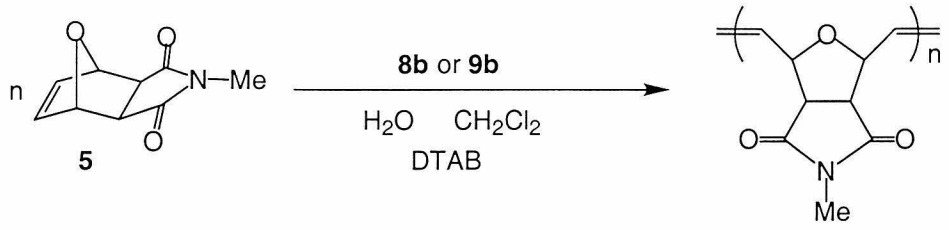
Titanium	Tungsten	Molybdenum	Ruthenium
Acids	Acids	Acids	***Olefins***
Alcohols, Water	Alcohols, Water	Alcohols, Water	Acids
Aldehydes	Aldehydes	Aldehydes	Alcohols, Water
Ketones	Ketones	***Olefins***	Aldehydes
Esters, Amides	***Olefins***	Ketones	Ketones
Olefins	Esters, Amides	Esters, Amides	Esters, Amides

Increasing Reactivity

Figure 4: Functional group tolerance of selected alkylidene complexes.

Thesis Research

Although these well-defined complexes were highly tolerant of protic and polar functional groups, the ligand spheres designed to protect and stabilize the alkylidene species rendered these catalysts completely insoluble in water. Chapter 2 of this thesis describes the initial efforts to address this insolubility issue through the application of complexes **8b** and **9b** to ROMP in aqueous environments (Eq 11).[39,40]



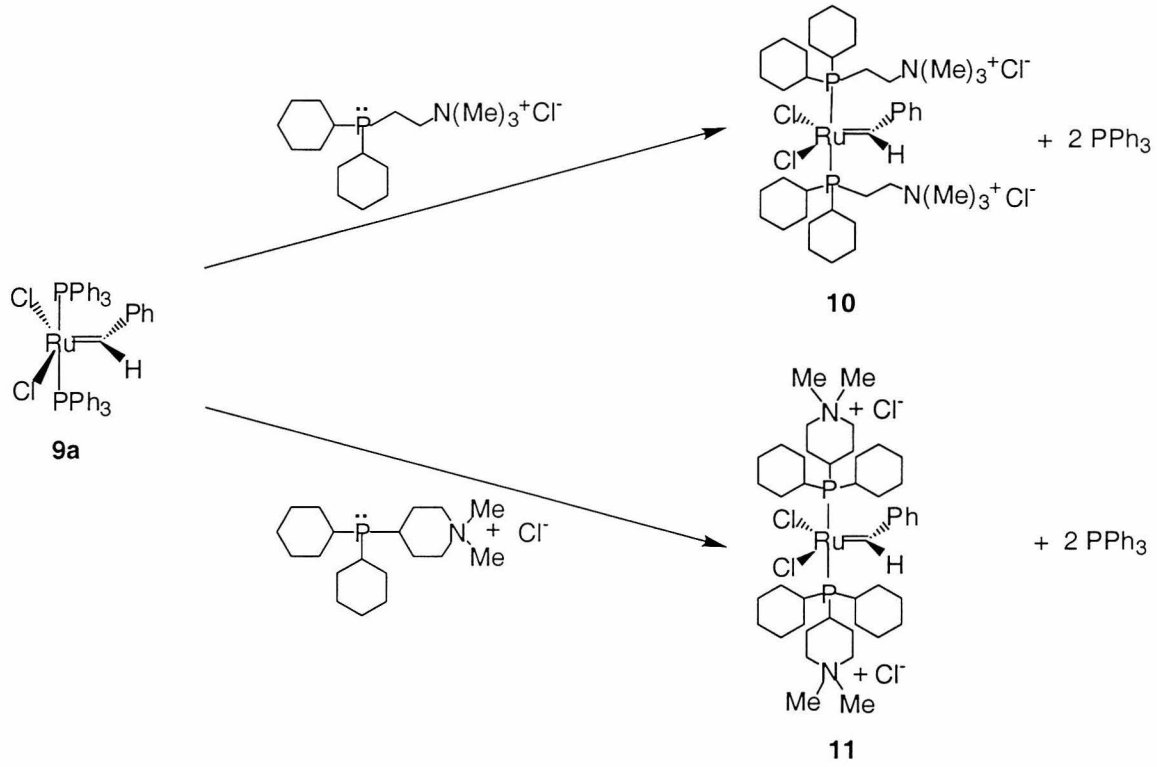
(Eq 11)

Initiation was fast and complete in these aqueous systems, and polymer molecular weights were found to vary linearly with the ratios of monomer to initiator, indicating that these aqueous ROMP systems were living.[39] Polymers having narrow polydispersities (PDI ≤1.10) were prepared from hydrophilic and hydrophobic monomers, and well-defined block copolymers were synthesized *via* sequential monomer addition. Kiessling *et al.* have recently applied this methodology to the synthesis of water-soluble, biologically-active glycopolymers.[41]

Water-Soluble Alkylidenes

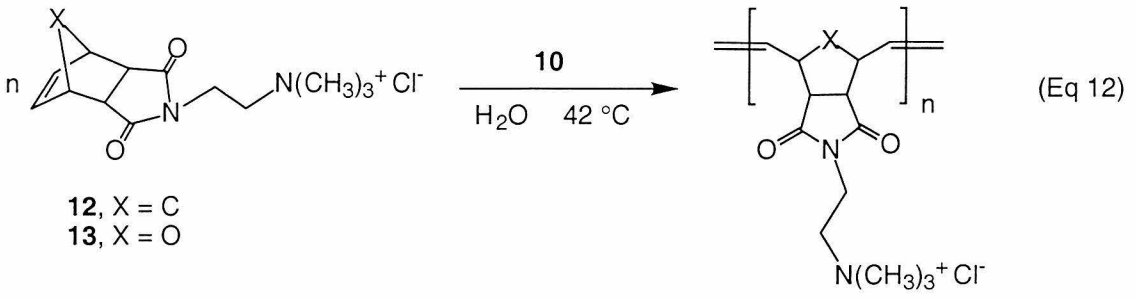
Chapter 4 of this thesis describes the synthesis of water-soluble derivatives of alkylidenes **8** and **9**, designed to overcome the insolubility of these catalysts in aqueous solvents. Previous work had demonstrated that the exchange of the phosphines in **8a** for $PhP(p\text{-}C_6H_4SO_3Na)_2$ afforded a water-soluble vinyl alkylidene.[15] This alkylidene was soluble in water, however the triarylphosphine ligands were too small, and not electron-donating enough, to produce an active catalyst.[42] Analogous substitution of the phosphines

in **9a** for more sterically-demanding, electron-rich, water-soluble phosphines (described in Chapter 3) yielded ruthenium alkylidenes **10** and **11**, which were soluble in both water and methanol (Scheme 2).[43]



Scheme 2: Synthesis of new water-soluble ruthenium alkylidene complexes.

In contrast to earlier "classical" catalysts, alkylidenes **10** and **11** initiated ROMP quickly and quantitatively in water and methanol.[43,44] A propagating alkylidene species was directly observed *via* ^{1}H NMR during the polymerization of most monomers, although the catalyst often decomposed before polymerization was complete. In the ROMP of water-soluble monomers **12** and **13** initiated by **10**, for example, conversions ranging from 45-80% were generally observed (Eq 12).[44]



12, X = C
13, X = O

(Eq 12)

It was found, however, that monomers could be quantitatively polymerized by **10** and **11** in aqueous solution in the presence of stoichiometric amounts of a strong Brønsted acid.[44] As described in Chapter 6, the effect of the acid in these systems was determined to be twofold, eliminating small concentrations of detrimental hydroxide ions, and accelerating the rate of metathesis with respect to termination reactions. Remarkably, the added acids did not react to decompose the ruthenium alkylidene, and a propagating alkylidene species was clearly observed following complete consumption of monomer. Addition of more monomer to the reaction mixture resulted in further quantitative polymerization, enabling the synthesis of block copolymers. These experiments established the extraordinary stability of the alkylidenes in these reactions, and suggested that **10** and **11** could initiate living polymerizations in aqueous solution.

In contrast to earlier "classical" ruthenium catalyst systems, these new water-soluble alkylidenes also reacted readily with less-strained cyclic olefins and acyclic olefins, allowing cross-metathesis and RCM reactions to be performed in homogeneous aqueous solution for the first time. Chapter 7 describes the application of alkylidenes **10** and **11** to the formation of cyclic olefins in water and methanol.

Summary

The recent development of alkylidenes incorporating late transition metals has resulted in olefin metathesis catalysts having unprecedented functional group tolerance. In particular, the discovery that complexes of Group VIII transition metals were efficient

ROMP catalysts introduced several advantages. In contrast to their early transition metal counterparts, these catalysts functioned well in the presence of a variety of polar and protic functional groups (Figure 4), and functioned *homogeneously* in water.

The lessons learned from early experiments with these complexes were eventually applied to the synthesis of well-defined ruthenium alkylidenes **8** and **9**. Although these new complexes were completely insoluble in water, they could be used to initiate the living ROMP of functionalized norbornenes and 7-oxanorbornenes in aqueous emulsions. Substitution of the phosphine ligands in **9** for bulky, electron-rich, water-soluble phosphines produced water-soluble alkylidenes **10** and **11**, which served as excellent initiators for the living ROMP of water-soluble monomers in aqueous solution. These ruthenium alkylidene complexes are potentially powerful tools for the synthesis of highly-functionalized polymers and organic molecules in both organic and aqueous environments.

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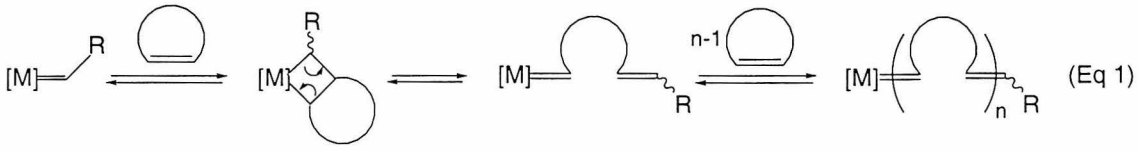
Chapter 2

Living Ring-Opening Metathesis Polymerization in Aqueous Media Using Well-Defined Ruthenium Alkylidene Complexes[†]

ABSTRACT: In aqueous media, two well-defined ruthenium carbene complexes [$(Cy_3P)_2Cl_2Ru{=}CHCH{=}CPh_2$ (**1**) and $(Cy_3P)_2Cl_2Ru{=}CHPh$ (**2**), Cy = cyclohexyl] catalyzed the living ring-opening metathesis polymerization (ROMP) of functionalized norbornenes and 7-oxanorbornenes. Monomers were dispersed in water using a cationic surfactant, and polymerization was initiated by injection of a catalyst solution to yield a polymer latex. The polymerization of a hydrophilic 7-oxanorbornene monomer and a hydrophobic norbornene monomer displayed similar behavior in aqueous media, with polymerization rates being slower relative to corresponding reactions carried out in anhydrous organic solvents. The polydispersity indices (PDIs) of polymers prepared using catalyst **1** in the presence of water were narrower (PDI = 1.20) than those obtained in dichloromethane solution (PDI = 2.11). PDIs for polymers prepared using catalyst **2** remained low in both the presence of water and in anhydrous solution (PDI $\approx$ 1.13), reflecting the relative differences in the initiation rates of these two complexes. The linear relationship between molecular weight and monomer/catalyst ratios demonstrated the absence of chain transfer and termination processes, and indicated that these polymerization systems were living. Finally, this new ROMP technique was shown to be an efficient method for the preparation of well-defined block copolymers.

Introduction

Polymerization reactions which proceed in the absence of termination steps and chain transfer reactions are considered living.[1,2,3] The development of new living polymerization systems has been the subject of intense academic and industrial interest, as living polymerizations generally afford polymers with specified molecular weights, narrow polydispersities, and allow the efficient synthesis of block copolymers.[4] Living polymerizations have been achieved *via* anionic, cationic, group transfer, radical, olefin insertion, and ring-opening polymerization mechanisms.[3] In recent decades, ring-opening metathesis polymerization (ROMP), catalyzed by well-defined transition metal complexes, has emerged as a versatile tool for the living polymerization of strained, cyclic olefins (Eq 1).[5]



(Eq 1)

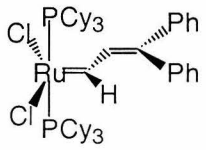
As described in Chapter 1, molybdenum-based alkylidenes are capable of polymerizing strained, cyclic olefins functionalized with a limited set of polar functional groups.[6] However, the sensitivity of these early metal catalysts to air and protic sources severely limits their application as living ROMP catalysts. Polymers currently prepared industrially by ROMP contain only olefinic functionality.[7] Tolerance toward functionalized substrates is essential to the practical utilization of olefin metathesis catalysts.

Recently-developed late transition metal metathesis catalysts exhibit remarkable functional group tolerance compared to early transition metal analogs.[8,9] For example, the ROMP of functionalized norbornenes and 7-oxanorbornenes in aqueous media has been achieved by simple ruthenium, iridium, and osmium salts (as outlined in Chapter 1).[10] Such "classical" catalysts do not contain preformed alkylidenes, however, and the catalytically active species in these systems have not yet been identified. In general,

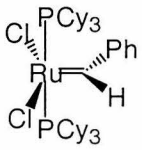
initiation is extraordinarily slow and inefficient, and "classical" catalyst systems do not initiate living polymerizations.

The benefits of performing polymerizations in aqueous media in an industrial setting are numerous,[3,11] and a variety of commodity polymers and polymer latexes are prepared by techniques such as suspension and emulsion polymerization.[3,12] Current efforts have focused on the development of aqueous living polymerization systems for the production of functionalized specialty polymers with unique qualities.[13] Novak has reported a nickel allyl initiator ($[(\eta^3\text{-}C_3H_5)Ni(OC(O)CF_3)]_2$) which catalyzes the polymerization of isocyanides in a living fashion. [14] Interestingly, this system remains living upon the exposure of the propagating species to air and water. More recently, advances made in the "living"/controlled polymerization of vinyl monomers by atom transfer radical polymerization (ATRP) and "persistent-radical" mediated polymerization have yielded systems which are also well-behaved in aqueous environments.[15]

Recently reported ruthenium-based alkylidene complexes **1** and **2** (Cy = cyclohexyl) have been shown to initiate the living polymerization of functionalized norbornenes, 7-oxanorbornenes, and cyclobutenes in a variety of organic solvents.[16]



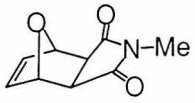
1



2

As with the "classical" late transition metal metathesis catalysts mentioned above, these alkylidenes are exceptionally tolerant of polar functionalities and are stable in unpurified, "wet" organic solvents. The development of such well-defined, water-tolerant catalysts prompted an examination of the activities of these complexes as catalysts for the ROMP of strained, cyclic olefins in aqueous media.[17] This chapter describes the application of alkylidenes **1** and **2** to the ROMP of a 7-oxanorbornene derivative (**3**) and two

norbornene derivatives (**4** and **5**) in aqueous emulsions. As differences in polymerization behavior could be observed for hydrophobic and hydrophilic monomers in such systems, the monomers used in these initial studies were chosen from both classes. Finally, block copolymerizations and the relationship between polymer molecular weight and monomer/catalyst ratios were investigated in order to determine the living nature of these systems.



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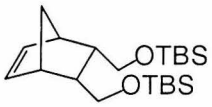

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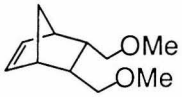


5

Results and Discussion

Initial Studies

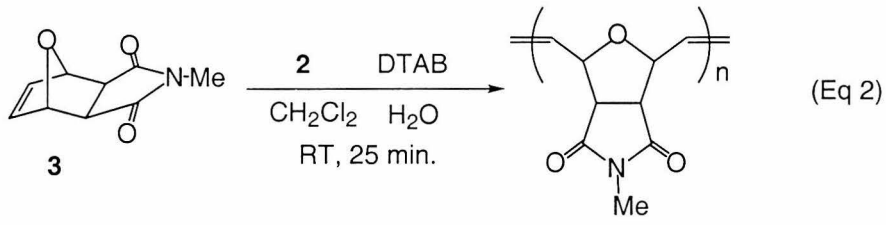
Although **1** and **2** are both highly-active, well-behaved olefin metathesis catalysts in organic solvents, they are completely insoluble in water. The aqueous ROMP of norbornene, therefore, was first examined using the triphenylphosphine derivative of catalyst **1** in the presence and absence of surfactants. This catalyst polymerized norbornene in both systems, although polymer yields were low and PDIs were broad relative to polymers prepared in organic solvents. Additionally, much of the water-insoluble catalyst remained suspended in the aqueous phase throughout the polymerization. The higher molecular weights and broader PDIs for these heterogeneous reactions, relative to polymerization in organic solution, were a result of low initiation efficiencies. Increased catalyst solubility would be required to achieve controlled initiation and prepare well-defined polymers.

In subsequent reactions, catalysts **1** and **2** were introduced to aqueous dispersions of monomer as solutions employing a small amount of organic solvent (5:1 water/organic solvent in a typical polymerization). In these systems, initiation and propagation is believed to have occurred in the organic phase in a controlled manner, and polymerization behavior and polymer characteristics could be altered by the presence of water, choice of monomer,

and emulsifier concentration. For example, aqueous polymerizations in the presence of DTAB resulted in polymer latexes (although the organic and aqueous components of these emulsions separated in the absence of vigorous stirring over a period of hours). Dichloromethane and 1,2-dichloroethane (DCE) were found to be the most favorable cosolvents for aqueous systems initiated by **1**, generally yielding more monodisperse polymers than those prepared in benzene or in the absence of cosolvent. Additionally, higher yields of polynorbornene were produced when a cationic emulsifying agent (dodecyltrimethylammonium bromide, DTAB) was employed, relative to systems employing an anionic surfactant (sodium dodecyl sulfate, SDS).

ROMP of Hydrophilic Monomer **3**

Alkylidenes **1** and **2** efficiently initiated the polymerization of hydrophilic monomer **3** in both suspension and emulsion-type systems (Eq 2).



(Eq 2)

Polymerizations in the presence of DTAB (emulsion systems) resulted in a polymer latex, while polymerizations in the absence of emulsifier (suspension systems) phase-separated in the absence of vigorous stirring. ^{1}H NMR spectroscopic data for polymers obtained in aqueous media are consistent with the data previously reported for polymers of **3** prepared *via* ROMP in organic solvents (Figure 1).[18] The reaction rates for polymerizations carried out in the presence of water were slower than the rates of polymerizations run under anhydrous conditions, yet polymer PDIs remained low in every case (Table 1).

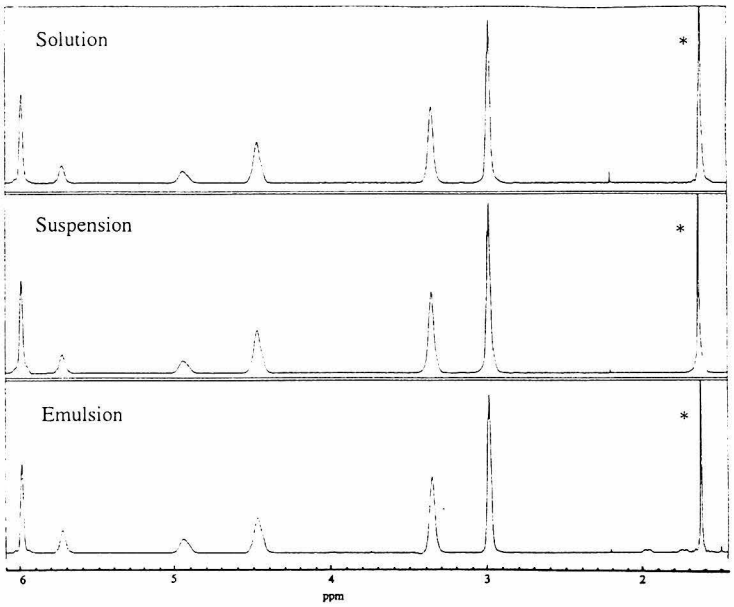


Figure 1. Representative ^1H NMR spectra ($CDCl_3$, 400 MHz) of the polymer obtained from monomer **3** initiated by alkylidene **2** in solution, suspension, and as an aqueous emulsion (* = H_2O).

Table 1. Polymerization of Monomer 3 by Alkylidenes 1 and 2.

Alkylidene	Polym Type[a]	[M]/[C]	Yield, %	M_n x10^{-4} [b]	PDI [b]
1	Solution	155	95	8.47	2.11
1	Suspension	147	82	6.81	1.37
1	Emulsion	144	85	4.95	1.20
2	Solution	100	99	4.41	1.13
2	Suspension	100	84	2.93	1.12
2	Emulsion	100	78	2.46	1.07

[a] Polymerizations with **1** were run at 50 °C; polymerizations with **2** were run at room temperature.
[b] Determined from GPC data in methylene chloride, relative to polystyrene standards.

When **1** was used to initiate polymerization in the presence of water, PDIs were lower than those obtained by polymerization in anhydrous organic solvent. A linear relationship between M_n and [**3**]/[**2**] was observed for the polymerization reactions in the presence of water, as well as for the reaction in anhydrous solution (Figure 2), indicating that these polymerizations were indeed living.

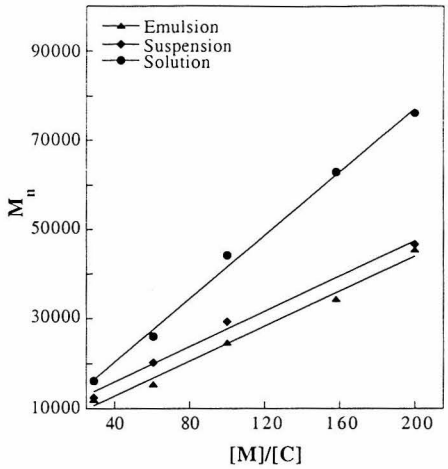


Figure 2. Plot of M_n versus [M]/[C] for poly-**3** initiated by alkylidene **2** in solution, suspension, and as an emulsion.

The data presented in Table 1 suggest that the presence of water in the suspension and emulsion polymerizations of monomer **3** exerts an influence on polymerization rates. For example, the yields and molecular weights of polymers obtained from these systems were lower than those obtained under anhydrous conditions (on the same reaction timescale). In experiments where aqueous polymerizations were quenched concomitantly with side-by-side, completed solution-phase reactions, careful analysis of the aqueous phase revealed the presence of unreacted monomer. Increasing the reaction time for these polymerizations resulted in complete monomer consumption, and polymer yields and molecular weights were comparable to those of polymers prepared in solution.

While the PDIs remained low in these aqueous systems (Table 1), molecular weight distributions of poly-**3** occasionally became bimodal in the later stages of the polymerization, indicative of cross-metathesis between polymer chains. Particularly at higher [M]/[C] ratios, the rate of monomer diffusion into the "monomer-starved" organic phase in the late stages of the reaction may be sufficiently slow to allow the rate of cross-metathesis to compete with the rate of propagation. Notably, this cross-metathesis is not a chain termination step, since the number of propagating species does not change and, although the molecular weight distribution changes, the number average molecular weight remains unaffected.

Because monomer **3** is soluble in both water and organic solvent, the partitioning of monomer between the aqueous and organic phases during polymerization results in *decreased* monomer concentrations in the organic phase (relative to an anhydrous solution polymerization employing the same amount of organic solvent). This suggests that this monomer phase equilibrium could be responsible for the diminished rates in the polymerization of this hydrophilic monomer, although these experiments do not unambiguously rule out other possibilities (as described below).

The lower PDIs of the polymers obtained with catalyst **1** in both suspension and emulsion systems suggest that the relative rates of initiation and propagation change in aqueous environments, resulting in lower PDIs relative to polymerization in organic solvent (Table 1). However, it is not clear that this kinetic effect is a direct result of the monomer phase equilibrium mentioned above, as k_i and k_p are both first order processes with respect to monomer concentration. The relative rates of initiation and propagation would be affected *equally* by a lower monomer concentration in the organic phase. However, preferential coordination of water to the propagating species could potentially serve to slow the rate of propagation relative to the rate of initiation, resulting in more monodisperse polymers.

For polymerization in organic solvents, the ratio of initiation to propagation has been shown to be much greater for derivatives of alkylidene **2** (k_i/k_p = 9) than for derivatives of **1** ($k_i/k_p = 6 \times 10^{-3}$).[16c] Therefore, for polymerizations employing **2**, any phenomena which would serve to alter rates of initiation and propagation in the presence of water should be masked by this 1,500-fold increase in the relative rates of initiation and propagation. Accordingly, narrower polydispersities in the presence of water are not observed for polymerizations initiated with **2** (Table 1).

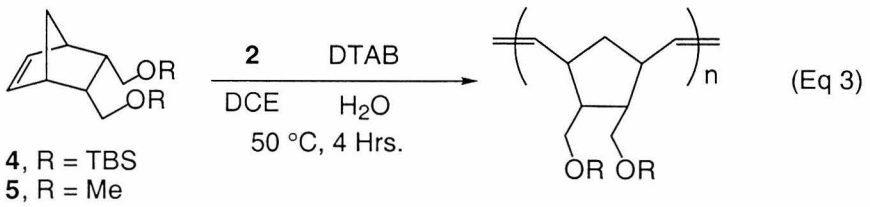
When k_i/k_p is large, and catalyst initiation occurs quantitatively, living systems can be used to produce polymers with either narrow or low polydispersities. When ROMP is conducted in solution, catalyst initiation is typically probed directly by ^{1}H NMR, since

alkylidene proton signals for the initiating and propagating species can be clearly distinguished. In aqueous emulsion systems, however, direct experimental observation of carbene species by ^{1}H NMR is experimentally complicated due to the heterogeneity of the reaction mixture. The exceptionally narrow PDIs observed for polymerizations in aqueous media are evidence of fast and complete initiation relative to propagation in aqueous systems employing **2**.

Finally, the molecular weight of a living polymer is controlled by the stoichiometry of the reaction,[1] and a linear relationship exists between the number average molecular weight (M_n) of the polymers and the corresponding monomer/catalyst ([M]/[C]) feed ratios. A linear relationship was observed in solution, suspension, and emulsion systems for the polymerization of **3** initiated by **2**, providing experimental support for the living nature of the aqueous systems (Figure 2). As the propagating species for polymers initiated by alkylidene **1** is identical to the propagating species for polymers initiated by **2**, it is expected that polymerizations initiated by **1** in the presence of water should be living as well. However, PDIs are broader due to the inherent differences in k_i and k_p for catalyst **1** as discussed above.

ROMP of Hydrophobic Monomers **4** and **5**

Aqueous polymerizations of monomers **4** and **5** were also examined, as any rate differences resulting from a monomer concentration equilibrium between aqueous and organic phases should be negligible with these hydrophobic monomers (Eq 3).



4, R = TBS
5, R = Me

(Eq 3)

For the polymerization of monomer **5** initiated by alkylidene **2**, the relationship between M_n and [**5**]/[**2**] was found to be linear for solution, suspension, and aqueous emulsion systems (Figure 3), and PDIs were similar in all cases (Table 2). However, the rates of reactions in the presence of DTAB were found to be lower than those prepared in either solution or suspension systems. Studies conducted with monomer **4** employing alkylidene **2** revealed the polymerization to be living in both solution and suspension systems. Interestingly, however, the polymerization was not living in the presence of DTAB under emulsion conditions (Figure 4).

Table 2. Polymerization of Monomer 5 by Alkylidene 2.

Polym Type[a]	[M]/[C]	Yield, %	M_n x10^{-4} [b]	PDI [b]
Solution	159	99	2.23	1.18
Suspension	159	99	2.34	1.19
Emulsion	159	68	1.32	1.10

[a] Polymerizations were run at 50 °C. [b] Determined from GPC data in methylene chloride, relative to polystyrene standards.

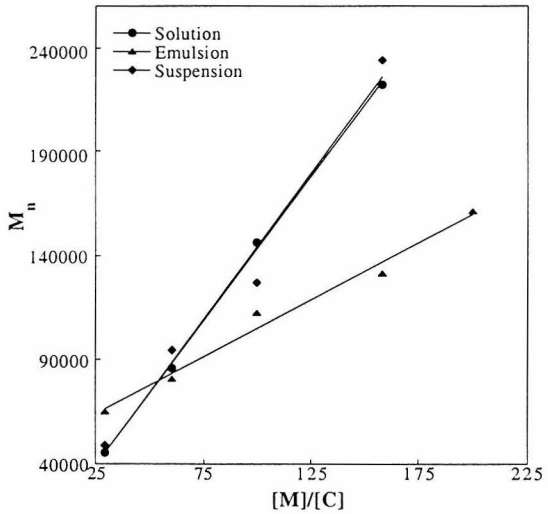


Figure 3. Plot of M_n versus [M]/[C] for poly-**5** initiated by **2** in solution, suspension, and as an aqueous emulsion.

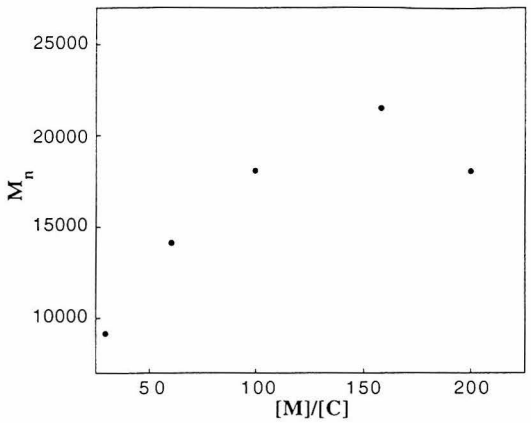
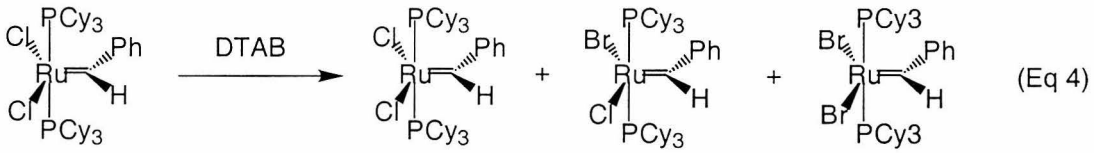


Figure 4. Plot of M_n versus [M]/[C] for poly-**4** initiated by **2** in an aqueous emulsion.

The data for polymerizations in suspension and solution systems employing monomer **5** are nearly identical (Figure 3), indicating that the lower molecular weights in the emulsion-type polymerizations result from the presence of emulsifier, and not from monomer solubility in the water phase or coordination of water to the propagating species during polymerization. Subsequent investigations into the effect of the emulsifier on this reaction revealed that the bromide anion of DTAB undergoes a facile exchange with the chloride ligands of alkylidene **2**. For example, in the presence of 10 equivalents of DTAB, alkylidene **2** is converted to a mixture of the dichloro, dibromo, and mixed-halide species in organic solvents (Eq 4).



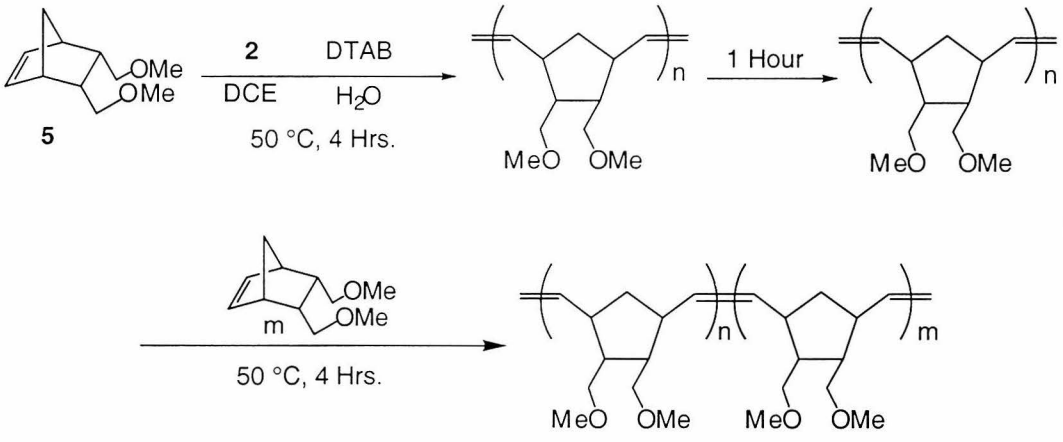
2 **2** (Eq 4)

Ruthenium alkylidene complexes of this type, having larger, less electronegative anionic ligands have been shown to be less active than the parent dichloro-substituted alkylidene **2**.[19] In view of the gross excess of DTAB used in the above reactions (up to 500 equivalents relative to catalyst), it is likely that this ligand substitution reaction occurs to yield a slower, dibromo-substituted catalytic species. Future applications of these aqueous

emulsion-type polymerizations should be conducted with this potential ligand exchange in mind. The use of dodecyltrimethylammonium chloride (DTAC), for example, would eliminate this exchange and preserve the robust activities of alkylidenes **1** and **2**. It is notable that while this exchange process may yield a less active catalyst, the polymerization of monomer **5** still remains living. The reasons for the nonlinear relationship between M_n and [M]/[C] for the polymerization of monomer **4** in the presence of emulsifier, however, remain unclear.

Block Polymerizations Using Alkylidene **2**

In living systems, polymerization proceeds until monomer is consumed, and further addition of monomer results in continued polymerization.[1] To clearly illustrate this important criterion, a two-step block polymerization of monomer **5** was performed using catalyst **2** (Eq 5). First, monomer **5** was polymerized in an aqueous emulsion system until all monomer was consumed. The reaction was allowed to sit for an additional hour, after which time a second aliquot of monomer **5** was added to the emulsion, resulting in continued polymerization.



(Eq 5)

Polymer M_n increased from 34,000 for the first block in this experiment to 126,700 for the final polymer, as determined by GPC (Figure 5). The M_n for the final polymer shifted dramatically (to within baseline separation by GPC) relative to the initial block with

an increase in PDI from 1.08 to 1.25 (Figure 5). The PDI of the initial block remained at 1.08 after sitting for an additional hour, and no residual peaks were observed in the GPC trace after continued polymerization. These data reflect the relative absence of chain transfer and termination reactions under aqueous conditions on the timescale of the polymerization reaction.

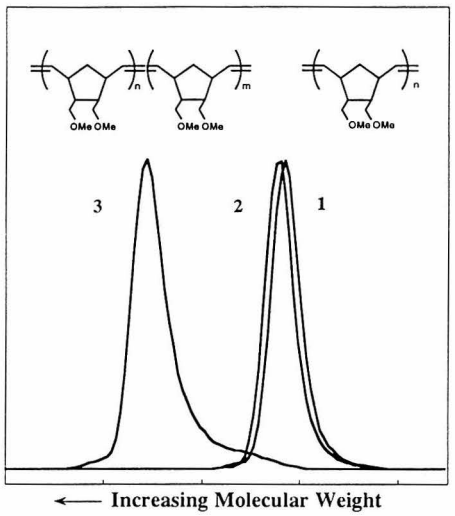
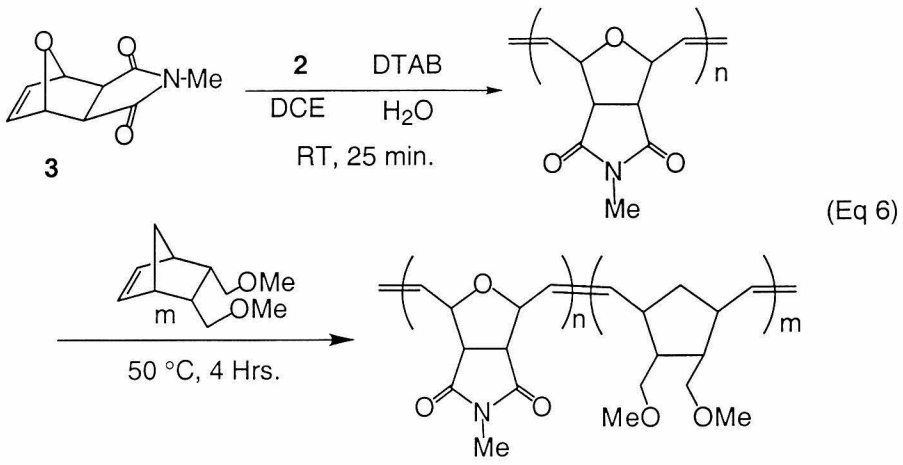


Figure 5. GPC traces for poly-**5** initiated by **2**. The peaks represent: 1) polymer after complete incorporation of monomer, 2) polymer after standing for 1 additional hour, and 3) the polymer after continued polymerization of additional monomer.

Block copolymers of monomers **3** and **5** were also prepared in aqueous media using alkylidene **2** in a procedure analogous to that described above (Eq 6). In this example, M_n for the block copolymer shifted dramatically, and the PDI increased from 1.06 to 1.32, while the polydispersity of the principal portion of the peak was calculated to be 1.08 (Figure 6). The formation of the low molecular weight material in these reactions may be due to a "back-biting" reaction of the propagating species in these polymers under the relatively high reaction temperatures.[20]



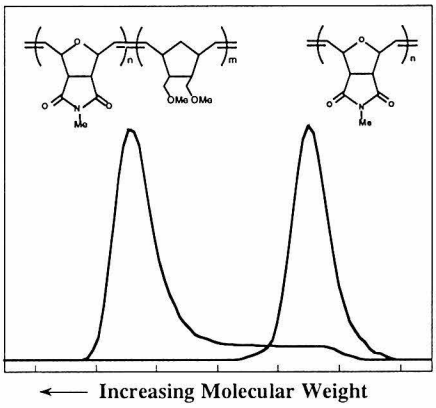


Figure 6. GPC traces for poly-**3** and the block copolymer obtained after addition of monomer **5**.

The observed tailing could also be attributed to the inefficient manner in which the propagating chain end of polymer **3** serves as an initiating species for the newly-introduced monomer **5**. While the polymerization of monomer **3** is carried out at room temperature, monomer **5** will only polymerize efficiently at 50 °C. An aliquot of monomer **5** was added to the polymerized **3** concurrent with the transfer of the reaction medium to a 50 °C sand bath. The time required for the system to reach thermal equilibrium should effect the initiation of the second monomer, and may also explain the tailing observed in the molecular weight distribution of the block copolymer. ^{1}H NMR spectra for poly-**3**, poly-**5**, and the block copolymer of **3** and **5** are shown in Figure 7.

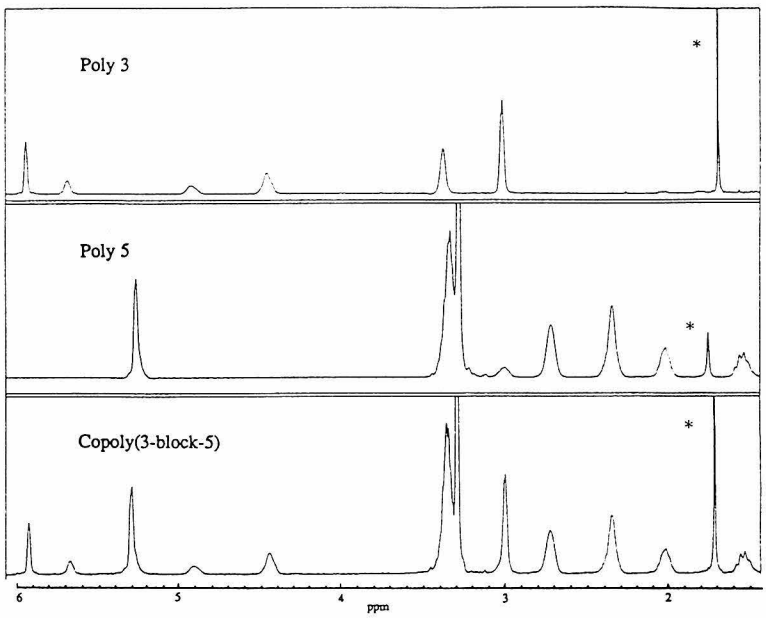


Figure 7. Representative ^1H NMR spectra ($CDCl^3$, 400 MHz) of the poly-**3** (top), poly-**5** (middle), and the block copolymer obtained from **3** and **5**. (* = H_2O).

Summary

Ruthenium alkylidenes **1** and **2** efficiently catalyze the living ring-opening metathesis polymerization of functionalized norbornenes and 7-oxanorbornenes in the presence of water. This report represents the first example of a living polymerization occurring entirely in the presence of water. Due to the insolubility of alkylidenes **1** and **2** in water, the introduction of a small amount of organic solvent is necessary to achieve controlled initiation. Block copolymerization and the relationship between polymer molecular weight and monomer/catalyst feed ratios were examined to demonstrate the living nature of the polymerizations in the presence of water. With proper experimental design, these living polymerization systems can be used to prepare latexes of nearly monodisperse homopolymers and block copolymers of both water soluble and water insoluble monomers.

Acknowledgement. This work was supported by the Caltech Consortium (DuPont, Kodak, and 3M), the Rohm and Haas Company, and the National Science Foundation. The author would like to thank Shoky Kanaoka for his and assistance, Peter Schwab for

providing the alkylidene complexes, and Bobby Maughon and Marcus Weck for helpful discussions.

Experimental Section

General Considerations. Argon was purified by passage through columns of BASF R3-11 catalyst (Chemalog) and 4 Å molecular sieves (Linde). ^{1}H NMR spectra were recorded on a JEOL GX-400 spectrometer (400 MHz) at 25 °C. All chemical shift values are given in ppm and are referenced with respect to residual protons in the solvent. Gel permeation chromatographs (GPC) were obtained using an Altex Model 110A pump, a Rheodyne Model 7125 injector with a 100-μL injection loop, through an American Polymer Standards 10-μm mixed-bed column, and a Knauer differential refractometer; dichloromethane was used as the eluent at a flow rate of 1.0 mL/min. The molecular weights and polydispersities of the polymers are reported relative to monodisperse polystyrene standards.

Materials. Distilled deionized water was used for the polymerizations, and was degassed by purging with argon and then stirring under high vacuum prior to use. 1,2-Dichloroethane was vacuum transferred from calcium hydride prior to use. Dichloromethane was purified by passage through solvent purification columns containing activated alumina.[21] Ruthenium carbene complexes **1**[16a] and **2**[16c] and monomers **3**[18] and **4**[16d] were prepared as previously reported. Dodecyltrimethylammonium bromide (DTAB) (Aldrich, purity 99%), sodium dodecylsulfate, ethyl vinyl ether, methanol, and other reagents were used without further purification unless otherwise noted.

General Polymerization Procedure. Typical polymerization reactions were conducted in the following manner. Deviations from this general procedure are indicated below for specific cases. In a nitrogen-filled dry box, monomer (0.558 mmol) was added

to a 4 dram vial equipped with a teflon-coated stirbar. For emulsion-type polymerizations, DTAB (0.516 g, 1.67 mmol) was added. The vial was capped with a rubber septum and secured with copper wire. Catalyst was added to a 1 dram vial and capped with a rubber septum, and organic solvent (0.8 mL) was added to the catalyst *via* syringe. Outside the dry box, water (4 mL) was added to the vial containing the monomer (for emulsion and suspension polymerizations only), and the contents were stirred vigorously (1300 rpm) at room temperature for 0.5 hours. The catalyst solution was sonicated briefly to ensure complete dissolution of the catalyst, and the polymerization reaction was initiated by adding the catalyst solution to the vial containing the monomer *via* a gas-tight syringe. Polymerization was terminated by adding an excess of ethyl vinyl ether (2 mL) to inactivate the catalyst, and a small amount of methylene chloride to prevent precipitation. Stirring was continued for 0.5 hours after termination. Polymers were typically purified by precipitation from methanol and were dried under dynamic vacuum overnight at room temperature prior to analysis. Reactions used to study the living nature of the polymerizations were not purified; water and organic solvent were removed *in vacuo* after catalyst termination, and the crude polymer samples were analyzed directly by GPC.

Synthesis of Endo-5,6-dimethoxymethylbicyclo[2.2.1]hept-2-ene (5). An oven-dried 500 mL, 3-necked flask was equipped with a teflon-coated stirbar, a pressure-equalizing addition funnel, and a Vigreux condenser. Under argon purge, the reaction vessel was charged with NaH (3.50 g, 0.146 mol) in dry THF (100 mL). Endo-5,6-dicarbinolbicyclo[2.2.1]hept-2-ene (9.00 g, 58.36 mmol) was dissolved in dry THF (30 mL) and added dropwise through the addition funnel. After complete addition, the reaction was stirred for an additional 0.5 hrs. CH_3I (39.80 g, 0.280 mol) was added slowly through the addition funnel. An exotherm was observed during the addition of the CH_3I, and the reaction was placed in an ice bath and allowed to stir for 2 hours after complete addition. Water was added dropwise to quench remaining NaH. The reaction

mixture was poured into diethyl ether (500 mL) and filtered. The filtrate was washed four times with water (200 mL), dried over Na_2SO_4, filtered, and volatiles were removed *in vacuo* to yield the crude product as a yellow oil (8.87 g, 83.36%). The product was purified by Kugelrohr distillation (55 °C, 4 mTorr) to yield the product as a clear oil in 76% yield. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.37 (dd, 2H, J=8.3 Hz), 2.43 (m, 2H), 2.88 (br s, 2H), 2.97 (t, 2H, J=9.0 Hz), 3.15 (dd, 2H, J=7.5 Hz), 3.27 (s, 6H), 6.10 (m, 2H) ppm. ^{13}C NMR (Proton decoupled, $CDCl_3$, 400 MHz) 135.30, 72.82, 58.68, 49.11, 45.59, 41.47 ppm. IR (Neat) 3057 (m), 2978 (s), 2919 (s), 2870 (s), 2870 (s), 2828 (s), 2807 (s), 2755 (w), 1480 (m), 1459 (m), 1389 (m), 1347 (m), 1245 (w), 1199 (m), 1168 (m), 1133 (s), 1102 (s), 970 (m), 958 (m), 911 (m), 892 (w), 826 (w) cm^{-1}. Anal calcd $C_{11}H_{18}O_2$: C, 72.49%; H, 9.95%. Found: C, 72.02%; H, 9.97%.

Polymerization of 3 and 4. The general polymerization procedure outlined above was followed. Dichloromethane was used to dissolve the catalyst. Reactions were run at room temperature and terminated 25 minutes after initiation.

Polymerization of 5. The general polymerization procedure outlined above was followed. DCE, a higher boiling solvent, was used to dissolve the catalyst since polymerization conditions required heating at 50 °C for 4 hours before termination. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.42 (br s), 1.95 (br s), 2.27 (br s), 2.67 (br s), 2.97 (br s), 3.28 (s), 3.35 (br s), 5.39 (br s) ppm. ^{13}C NMR (Proton decoupled, $CDCl_3$, 400 MHz) 132.15, 71.42, 58.68, 45.88, 44.12, 38.23 ppm.

Two-Step Polymerization of 5. Monomer **5** was polymerized according to the procedure outlined above. After 4 hours, an aliquot (0.2 mL) was removed and

precipitated into methanol for analysis by GPC. The reaction was allowed to proceed for an additional hour at 50 °C, and another aliquot (0.2 mL) was removed. Additional monomer **5** (0.408 g) was added neat via a gas-tight syringe and the reaction was stirred for an additional 4 hours. The polymerization was terminated and purified as outlined above.

Synthesis of copoly(3-block-5). Monomer **3** was polymerized according to the procedure outlined above. After 25 minutes, an aliquot (0.2 mL) was removed from the reaction with a gas-tight syringe and precipitated into methanol for analysis by GPC. Simultaneously, the reaction was transferred to a 50 °C sand bath, monomer **5** (0.408 g) was added neat via a gas-tight syringe, and vigorous stirring was continued. Four hours after monomer **5** was added, a small amount of polymer precipitate was observed, and the polymerization was terminated and purified as outlined above.

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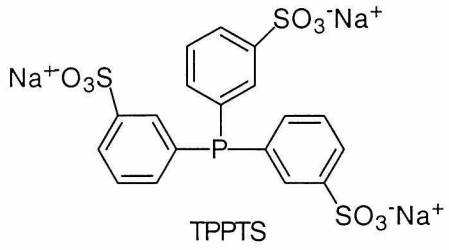
Chapter 3

Characterization of Bulky, Aliphatic, Water-Soluble Phosphines[†]

ABSTRACT: This chapter describes the characterization of water-soluble, aliphatic phosphines **4**-**7**. These phosphines were designed to be both sterically and electronically similar to tricyclohexylphosphine, a ligand of significant importance to the activities and reactivities of ruthenium alkylidene complexes of the type $(PR_3)_2Cl_2Ru(=CHPh)$. Spectroscopic investigations of corresponding $Pd(PR_3)_2Cl_2$ complexes were used to estimate the steric parameters of these new phosphines. Phosphines **4**, **5**, and **6** were determined to have cone angles approximating those of tricyclohexyl phosphine. Infrared spectroscopic investigations of corresponding $Ni(CO)_3PR_3$ complexes were used to determine the electronic character of these phosphines. These studies indicated that phosphines **4** and **5**, bearing positively-charged functionalities, are less electron-donating than tricyclohexylphosphine, while the presence of the sulfonate group in **6** increases the electron-donating character of this phosphine.

Introduction

The chemistry of water-soluble phosphines and their application as ligands for homogeneous and aqueous biphase catalysis have received considerable attention.[1,2] Much work in this area has been devoted to the development of water-soluble aryl phosphines, such as trisulfonated triphenylphosphine (TPPTS).

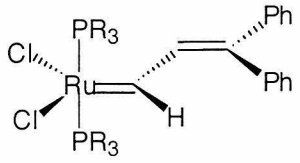


TPPTS

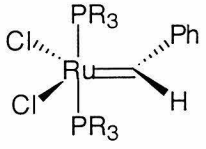
In contrast, relatively little effort has been directed toward the development of water-soluble aliphatic phosphines.[3] Compounds of this type are of considerable interest, as the selectivities, activities, and reactivities of many catalytic processes are often subject to the steric and electronic influences of phosphine ligands.[4,5] For example, electron-donating trialkylphosphines enhance selectivities for linear products when coordinated to certain cobalt carbonyl hydroformylation catalysts, while less electron-withdrawing phosphines do not provide good selectivities.[5]

The effects of phosphine steric and electronic parameters on the activities of well-defined, ruthenium-based metathesis catalysts were recently demonstrated.[6] For alkylidenes of the type $(PR_3)_2Cl_2Ru{=}CHR$, catalyst activities are generally maximized by the coordination of sterically-demanding, electron-donating phosphines to the ruthenium center.[6f] Tricyclohexylphosphine has been shown to be an optimal ligand for these complexes, having the requisite combination of bulk and electron density to impart a desirable mix of catalyst stability and reactivity. In contrast, alkylidenes of this type bearing triphenylphosphine ligands are less stable and react only with a limited set of highly-strained olefins. For example, while alkylidenes **1b** and **2b** react primarily with

norbornene, alkylidenes **1a** and **2a** will polymerize both high- and low-strained olefins and react readily with acyclic olefins.[6c-e]

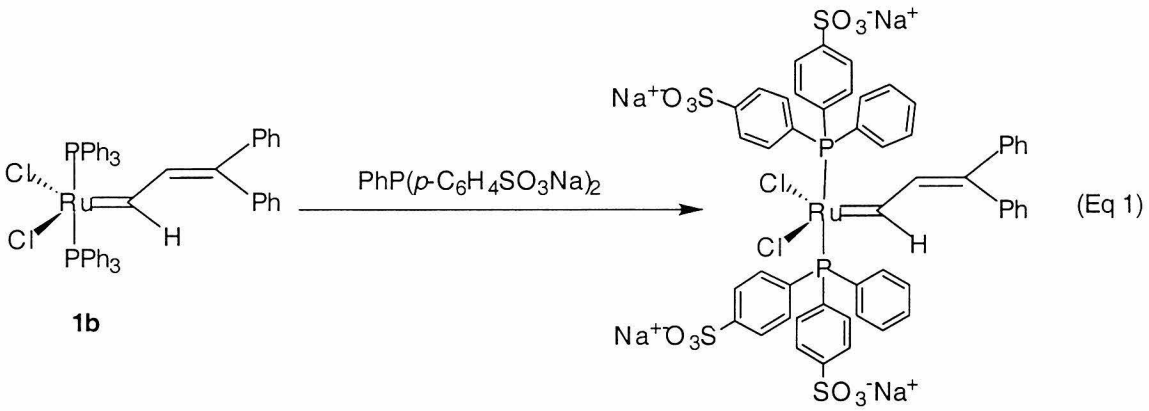


1a, R = Cy_3
1b, R = PPh_3



2a, R = Cy_3
2b, R = PPh_3

The synthesis of a ruthenium alkylidene (**3**) bearing charged phosphine ligands was recently accomplished *via* the exchange of the triphenylphosphine ligands in alkylidene **1b** with $PhP(p\text{-}C_6H_4SO_3Na)_2$ (Eq 1).[7] Alkylidene **3** was soluble in water, however the triarylphosphine ligands were neither large enough or electron-donating enough to produce an active metathesis catalyst. From this example, it became evident that the development of robust, water-soluble ruthenium alkylidenes would require the synthesis of bulkier, more electron-rich water-soluble phosphines.



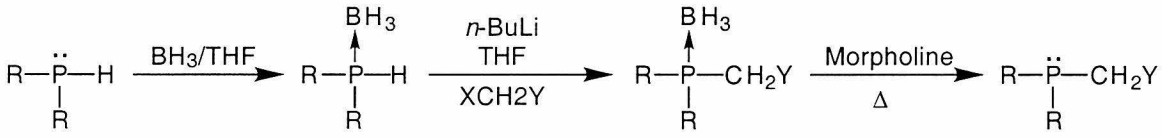
1b **3** (Eq 1)

Synthesis of Water-Soluble, Aliphatic Phosphines

Traditionally, the preparation of aliphatic phosphines has been complicated by both their nucleophilicities and the sensitivities of these compounds toward oxidation. Bartik *et al.*, however, recently prepared a series of electron-donating, water-soluble phosphines *via*

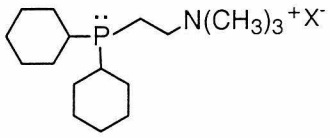
the direct *para*-sulfonation of tris(ω-phenylalkyl)phosphines. These sulfonated alkyl phosphines, having the general formula $P[(CH_2)_x(C_6H_5)]_3$, were found to be sterically and electronically similar to linear alkyl phosphines such as $P(n\text{-}Bu)_3$.[3a] Another synthetic approach is based on alkylation of PH_3 with ω-chloroalkylamines, followed by selective N-quaternization with alkyl iodides.[3b-d]

Grubbs *et al.* recently reported the synthesis of bulky, water-soluble, aliphatic phosphines (**4**-**7**) mediated by borane-protected phosphorus intermediates.† Phosphine-borane complexes[8,9] have become increasingly useful intermediates in the synthesis of phosphine derivatives.[10] For example, borane-protected phosphines are stable to metallation with lithium reagents, and can subsequently be treated with electrophiles to yield functionalized phosphine boranes (Scheme 1). Additionally, the integrity of the phosphorus-boron bond allows the modification of otherwise oxidatively-unstable alkyl phosphine complexes using standard benchtop techniques in air. The borane moiety can be conveniently removed in the final stages of synthesis under mild conditions by treatment with a large excess of a nucleophilic amine, such as morpholine.[8a]

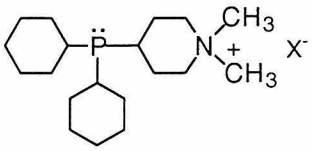


Scheme 1: Synthesis of functionalized phosphines *via* borane-protected intermediates.

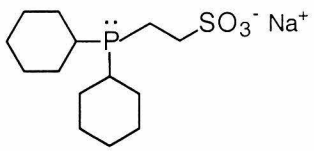
This phosphine-borane mediated approach was used to synthesize aliphatic, water-soluble phosphines **4**-**7**.† Interestingly, the counterions of the cationic phosphines **4** and **5** were discovered to play a crucial role in the water-solubility of these phosphines. For example, iodide salts **4a** and **5a** were soluble only in methanol, while corresponding chloride salts **4b** and **5b** were completely-soluble in both methanol and water. The solubility of difunctionalized phosphine **7** was not subject to this counterion influence, and sulfonated phosphine **6** was completely soluble in both solvents.



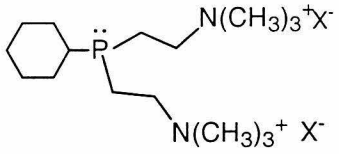
4a, $X^- = I^-$
4b, $X^- = Cl^-$



5a, $X^- = I^-$
5b, $X^- = Cl^-$



6



7a, $X^- = I^-$
7b, $X^- = Cl^-$

As phosphines **4-7** were designed to be both sterically and electronically similar to tricyclohexylphosphine, a determination of their steric and electronic parameters was of considerable interest. The following sections describe the determination of the steric and electronic parameters of these new phosphines *via* spectroscopic investigation of corresponding $Pd(PR_3)_2Cl_2$ and $Ni(CO)PR_3$ complexes. In Chapter 4, these phosphines will be applied to the synthesis of well-defined, water- and methanol-soluble ruthenium alkylidene complexes.

Results and Discussion

Determination of Phosphine Steric Parameters

The steric bulk of a phosphine is generally expressed as a cone angle, usually the Tolman cone angle (θ_{Tol}) originally derived from space-filling models,[4] or the Musco cone angle (θ_{Mus}), derived from phosphine X-ray diffraction data.[11] Space-filling molecular models were not employed in this study to mechanically estimate the cone angles of new phosphines **4-7**, as uncertainty existed regarding the steric demands of the charged moieties and the spatial requirements of the counterions. Accordingly, attempts to estimate the cone angles of these new phosphines were made through the preparation of the corresponding *trans*-$Pd(PR_3)_2Cl_2$ complexes, as an empirical linear relationship has been

demonstrated between the ^{31}P NMR chemical shift and both θ_{Tol} and θ_{Mus}.[12] *trans*-$Pd(PR_3)_2Cl_2$ complexes of phosphines **4b**, **5b**, **6**, and **7b** were prepared by the reaction of *cis/trans*-$Pd(PhCN)_2Cl_2$ with two equivalents of phosphine (Eq 2).[12,13]

$$\textit{cis/trans}\text{-}Pd(PhCN)_2Cl_2 + 2\,PR_3 \xrightarrow{CH_2Cl_2} \textit{trans}\text{-}Pd(PR_3)_2Cl_2 + 2\,PhCN \qquad \text{(Eq 2)}$$

The ^{31}P NMR spectrum for each complex was recorded directly *in situ*. Each spectrum consisted of a sharp singlet, and neither uncoordinated phosphine nor the sterically-discouraged *cis*-$Pd(PR_3)_2Cl_2$ complexes[12,13] were observed. Table 1 provides the spectral data obtained for the palladium complexes of the new phosphines. The reference value for *trans*-$Pd(PCy_3)_2Cl_2$ has been recorded for comparison.

Table 1. ^{31}P NMR Chemical Shifts for *Trans*-$Pd(PR_3)_2Cl_2$ Complexes.[a]

Phosphine	Chemical Shift (ppm)
PCy_3	25.12
4b	25.16
5b	26.67
6	26.90
7b	18.08

[a]Spectra recorded in CH_2Cl_2, referenced to H_3PO_4.

While investigating these water-soluble palladium complexes, we noted a substantial difference between our experimental data and the value previously reported for the tricyclohexylphosphine complex. We determined the ^{31}P NMR chemical shift for *trans*-$(PCy_3)_2PdCl_2$ to be 25.12 ppm, and a similar value of 25.4 ppm was recently reported independently.[14] These values differ significantly from the previously reported value of 58.4 ppm and cannot be extrapolated to the correct cone angle of 170° *via* the relationship described above.[12] Since this correlation could not be used reliably to determine the cone angle for PCy_3, it was not employed to numerically derive cone angles for phosphines **4b**, **5b**, **6**, and **7b**. However, the ^{31}P NMR chemical shift values were

used for a qualitative estimation of the cone angles of these phosphines relative to PCy_3.

The ^{31}P NMR chemical shift values for the *trans*-$Pd(PR_3)_2Cl_2$ complexes of the dicyclohexyl-derived phosphines **4b**, **5b**, and **6** are within ±1.5 ppm of the value for *trans*-$Pd(PCy_3)_2Cl_2$. This suggests that these new phosphines are sterically similar to PCy_3. By analogy, the difunctionalized phosphine **7b** has a chemical shift which is 7 ppm upfield from that of PCy_3, and may therefore be sterically less-demanding. It should be noted that the ^{31}P NMR chemical shifts these $Pd(PR_3)_2Cl_2$ complexes could be affected by the charged nature of the substituents and the presence of Cl^- ions in solution. Therefore, an assessment of the cone angles for these phosphines based on these data should be made with discretion.

Determination of Phosphine Electronic Parameters

Phosphine ligands may also be organized in an electronic series based on the carbonyl stretching frequencies of monosubstituted nickelcarbonyl complexes of the type $Ni(CO)_3PR_3$.[3a,4,15] Tolman has defined the phosphine electronic parameter, χ, as

$$\chi_{PR_3} = \nu(CO)A_{1\ PR_3Ni(CO)_3} - \nu(CO)A_{1\ P(tBu)_3Ni(CO)_3}$$

where the A_1 carbonyl stretching mode, $\nu(CO)$, is measured in CH_2Cl_2.[4] By this relationship, the value of χ decreases as the electron donating character of a phosphine approaches the electron donating character of $P(t\text{-}Bu)_3$. Alkylphosphines readily form monosubstituted complexes with $Ni(CO)_4$ under mild reaction conditions.[3a,15] Accordingly, the $Ni(CO)_3PR_3$ complexes of phosphines **4b**, **5b**, **6**, and **7b** were prepared by the reaction of $Ni(CO)_4$ with one equivalent of phosphine in CH_2Cl_2 at room temperature (Eq 3).

$$Ni(CO)_4 + PR_3 \xrightarrow{CH_2Cl_2} Ni(CO)_3PR_3 + CO \qquad \text{(Eq 3)}$$

The corresponding nickel complexes were not isolated, but were identified by their characteristic carbonyl stretching modes in the infrared spectrum. ^{31}P NMR spectra for each complex consisted of a sharp singlet with no evidence of uncoordinated phosphine or polysubstituted species. The spectral data and χ values for all new phosphines are presented in Table 2, as well as parameters for several other representative phosphines.[4]

Table 2. FTIR Stretching Frequencies, ν_{A_1}, and Electronic Parameters, χ, for $Ni(CO)_3PR_3$ Complexes.[a]

Phosphine	ν_{A_1} (cm^{-1})	χ (cm^{-1})
6	2054.0	-2.1
P(*t*-Bu)$_3$	2056.1	0.0
PCy_3	2056.4	0.3
P(*i*-Pr)$_3$	2059.2	3.1
5b	2061.1	5.0
PEt_3	2061.7	5.6
4b	2065.3	9.2
PPh_3	2068.9	12.8
7b	2071.9	15.8

[a]Spectra recorded in CH_2Cl_2 on CsF_2 plates.

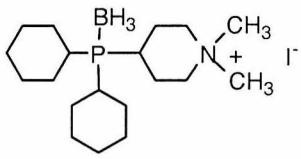
From the data in Table 2, it is evident that phosphine electron-donating capability is strongly influenced by the nature of the pendant functional group. Anionic phosphine **6**, for example, is more electron-donating than both PCy_3 and P(*t*-Bu)$_3$, whereas the cationic phosphines **4b**, **5b**, and **7b** are significantly less electron-donating. In fact, difunctionalized phosphine **7b** has a χ value which *exceeds* that of PPh_3. Presumably, the negatively-charged, sulfonate group on **6** inductively increases the electron density on the phosphorus atom, whereas the positively-charged, quaternary ammonium functionalities on **4**, **5**, and **7** withdraw electron density by the same mechanism.

This hypothesis is supported by the observation that the electronic parameter for **7b**, which contains two quaternary groups, is nearly twice the value of the electronic

parameter for **4b**, which contains only one. Additionally, the quaternary functionality on **5b** is further removed from the phosphorus center than the functionalities in **4b** or **7b**. Consequently, **5b** is more electron-donating than **4b** or **7b**. Although this analysis is consistent with the trends observed in Table 2, it should be taken into account that this method has been used only once previously to determine the electronic contributions of phosphines bearing charged substituents.[3a] Nevertheless, the results of the above investigations suggested that phosphines **4**, **5**, and **6** might be useful in the development of metathesis-active, water-soluble ruthenium alkylidene complexes.

X-ray Diffraction Analysis of the Borane Adduct of Phosphine **5a**.

In order to obtain additional data regarding the steric character of phosphines **4-6**, the borane adduct **8** of iodide salt **5a** was investigated by single-crystal X-ray diffraction.



8

Crystallization of **8** from a methanol/dichloromethane/hexane mixture yielded clear prisms suitable for analysis. An ORTEP plot of the data from this diffraction analysis is shown in Figure 1 (included dichloromethane solvent and iodide counterion omitted for clarity). The coordination sphere around the phosphorus atom is distorted tetrahedral. Each of the cyclohexyl groups in **8** were disordered in two chair conformations; the view provided in Figure 1 displays the cyclohexyl rings in their most populated sites. This disorder did not result in two discrete positions for **8**, and the molecule was found to pivot slightly about the P-B bond. This pivoting was reflected in the final bond distances and angles determined for this complex. Selected bond lengths and angles are provided in Table 3. The details of the X-ray diffraction experiment can be found in Appendix 1.

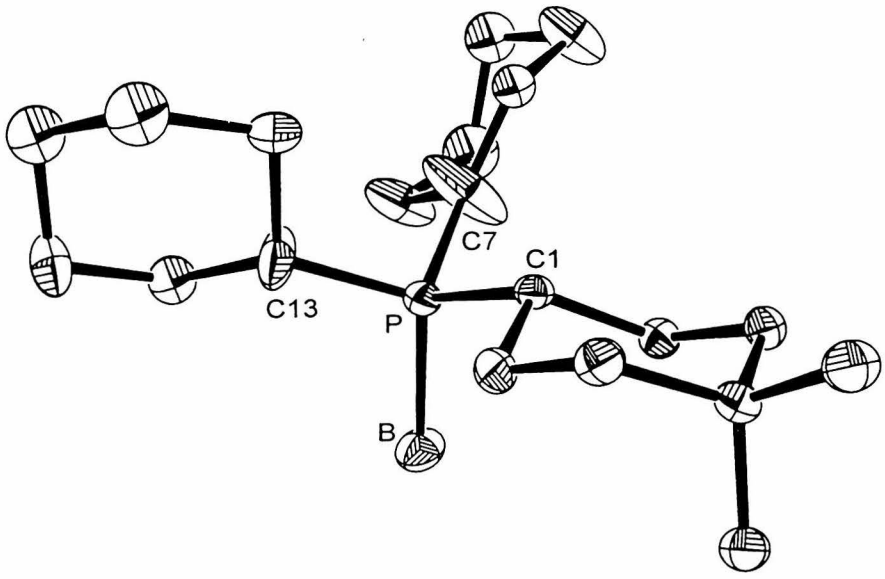


Figure 1: ORTEP drawing of phosphine-borane **8**. Cyclohexyl groups are depicted in their most populated conformations (See Appendix 1 for details). Thermal ellipsoids are drawn at 50% probability.

Table 3: Selected Bond Lengths (Å) and Angles (°) for Phosphine-Borane **8**.

	Bond Lengths (Å)		
P-C1	1.839(3)	P-C13b	1.831(5)
P-C7b	1.828(5)	P-B	1.912(4)
	Bond Angles (°)		
C1-P-B	110.68(18)	C7b-P-B	111.5(3)
C1-P-C13b	104.0(2)	C7b-P-C13b	110.4(3)
C1-P-C7b	107.13(19)	C13b-P-B	112.7(2)

Summary

The cone angles of phosphines **4**-**7** were estimated through the preparation of corresponding $Pd(PR_3)_2Cl_2$ complexes. Phosphines **4**, **5**, and **6** were determined to have cone angles approximating those of tricyclohexyl phosphine. Infrared spectroscopic investigations of corresponding $Ni(CO)_3PR_3$ complexes were then used to determine the electronic character of these phosphines. These studies indicated that phosphines **4** and **5**, bearing positively-charged functionalities, are less electron-donating than tricyclohexylphosphine, while the presence of the sulfonate group in **6** increases the

electron-donating character of this phosphine. Chapter 4 describes the application of these bulky, aliphatic phosphines to the synthesis of water-soluble ruthenium carbene complexes which initiate olefin metathesis in protic solvents.

Acknowledgments. The author wishes to thank Dr. Bernhard Mohr for his intellectual and experimental contributions central to the development of the work presented in this chapter. The X-ray diffraction analysis of phosphine-borane complex **8** was performed by Lawrence M. Henling. This work was supported by the Caltech Consortium (DuPont, Kodak, and 3M), the Rohm and Haas Company, and the National Science Foundation.

Experimental Section

General Considerations. All manipulations involving free phosphines were performed in a nitrogen-filled drybox or by using standard Schlenk techniques under an atmosphere of argon. Argon was purified by passage through columns of BASF R3-11 catalyst (Chemalog) and 4 Å molecular sieves (Linde). ^{1}H NMR (300.1 MHz) and ^{13}C NMR (75.49 MHz) spectra were recorded on a GE QE-300 spectrometer, ^{31}P NMR (161.9 MHz) spectra were recorded on a JEOL GX-400 spectrometer. All chemical shift values are given in ppm and are referenced with respect to residual protons in the solvent for proton spectra, or to phosphoric acid for phosphorus spectra. FTIR spectra were recorded on a Perkin Elmer 1600 Series FTIR spectrometer using cesium fluoride salt plates.

Materials. Dichloromethane was purified by passage through solvent purification columns containing activated alumina. Methanol was degassed by stirring under vacuum for 15 minutes prior to use. Bis(benzonitrile)palladium dichloride, and nickeltetracarbonyl were purchased from Strem Chemicals, Inc. Phosphines **4-7** were prepared as previously reported.[†] All other reagents were reagent grade and used without further purification.

General Procedure for the Preparation of $(PR_3)_2PdCl_2$ Complexes (PR_3 = 4a, 5a, 6, 7a). In a nitrogen-filled drybox, *cis, trans*-bis(benzonitrile) palladium dichloride (14.60 mg, 0.038 mmol) was dissolved in CH_2Cl_2 (0.25 mL) to yield an orange solution. Phosphine (2.0 eq) was dissolved in CH_2Cl_2 (0.25 mL) to yield a colorless solution. The two solutions were mixed together to yield a clear, bright yellow solution. After 5-6 minutes, small amounts of precipitate were noted, and a minimum amount of methanol (approx. 2 drops) was added to redissolve the complexes. ^{31}P NMR spectra were recorded directly on this solution.

$[Cy_2PCH_2CH_2N(CH_3)_3^+Cl^-]_2PdCl_2$, *trans*-isomer.

^{31}P NMR δ (CH_2Cl_2): 25.16 (s) ppm, (D_2O): 25.20 (s) ppm.

$[Cy_2P$(*N,N*-dimethylpiperidinium chloride)$]_2PdCl_2$, *trans*-isomer.

^{31}P NMR δ (CH_2Cl_2): 26.67 (s) ppm, (D_2O): 27.08 (s) ppm.

$[Cy_2PCH_2CH_2SO_3^-Na^+]_2PdCl_2$, *trans*-isomer.

^{31}P NMR δ (CH_2Cl_2): 26.90 (s) ppm.

$[CyP(CH_2CH_2N(CH_3)_3^+Cl^-)_2]_2PdCl_2$, *trans*-isomer.

^{31}P NMR δ (CH_2Cl_2): 18.08 (s) ppm.

General Procedure for the Preparation of $Ni(CO)_3(PR_3)$ Complexes (PR_3 = 14a, 15a, 16, 17a). In a nitrogen-filled drybox, phosphine was weighed into a 1 dram vial and dissolved in CH_2Cl_2 (3.0 mL). A minimum amount of methanol (approx. 2 drops) was added to aid solubility. $Ni(CO)_4$ (0.178 mmol, 1.0 equiv.) was added neat to this solution via syringe and immediate bubbling was observed. (NOTE: Extreme care should be exercised when handling $Ni(CO)_4$, as it is extremely toxic.) The reaction was sealed with a teflon-lined cap, and allowed to sit for 10 minutes. ^{31}P NMR spectra were recorded directly on this solution. A small portion of this solution was further dissolved in CH_2Cl_2 (1.0 mL) for FTIR analysis using a stop-flow injection cell.

[$Cy_2PCH_2CH_2N(CH_3)_3^+Cl^-$]$Ni(CO)_3$.

^{31}P NMR δ (CH_2Cl_2): 37.41 (s) ppm. IR (CH_2Cl_2) ν(CO): 2065.3 (w), 1991.5 cm^{-1}.

[Cy_2P(*N,N*-dimethylpiperidinium chloride)]$Ni(CO)_3$.

^{31}P NMR δ (CH_2Cl_2): 47.37 (s) ppm. IR (CH_2Cl_2) ν(CO): 2061.1 (w), 1987.5 cm^{-1}.

[$Cy_2PCH_2CH_2SO_3^-Na^+$]$Ni(CO)_3$.

^{31}P NMR δ (CH_2Cl_2): 35.59 (s) ppm. IR (CH_2Cl_2) ν(CO): 2054.0 (w), 1983.6 cm^{-1}.

[$CyP(CH_2CH_2N(CH_3)_3^+Cl^-)_2$]$Ni(CO)_3$.

^{31}P NMR δ (CH_2Cl_2): 24.99 (s) ppm. IR (CH_2Cl_2) ν(CO): 2071.9 (w), 2001.5 cm^{-1}.

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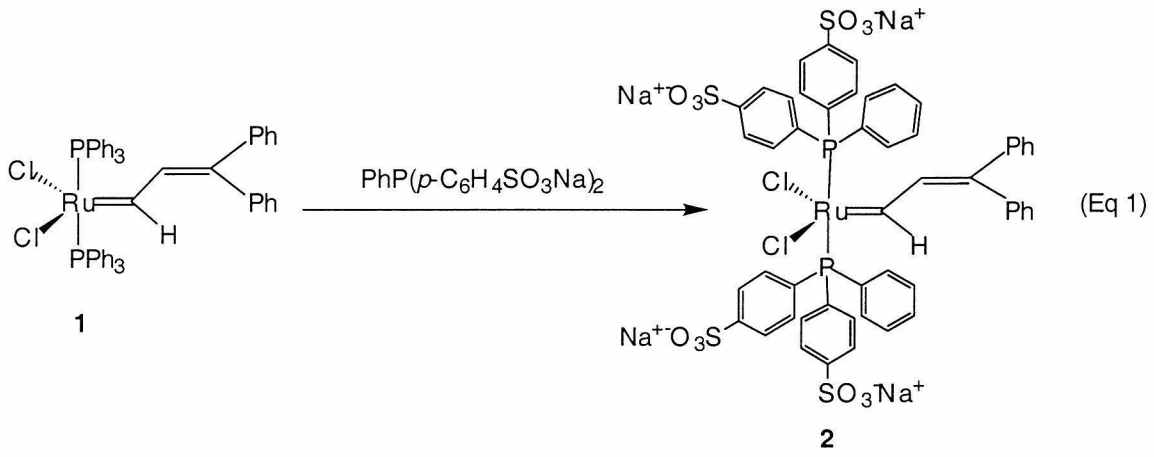
Chapter 4

Synthesis and Characterization of Well-Defined, Water-Soluble Ruthenium Alkylidenes[†]

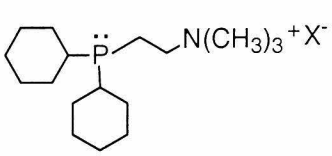
ABSTRACT: This chapter describes the application of bulky, electron-rich, water-soluble phosphines to the synthesis of well-defined, ruthenium benzylidene complexes. Alkylidenes **8** and **9** were synthesized *via* the exchange of the triphenylphosphine ligands in alkylidene $(PPh_3)_2Cl_2Ru{=}CHPh$ with phosphines **3b** and **4b**. Alkylidene **9** was also synthesized *via* a one-pot procedure starting from $(PPh_3)_2RuCl_2$, phenyldiazomethane, and phosphine **4b**. These complexes were completely-soluble in protic solvents such as water and methanol, and were insoluble in other common organic solvents such as acetone, tetrahydrofuran, and benzene. NMR spectroscopy data and X-ray diffraction analysis of alkylidene **8** suggested that these new alkylidenes are structurally similar to other ruthenium alkylidene complexes of the type $(PR_3)_2Cl_2Ru{=}CHR$ having bulky, electron-rich phosphine ligands. Initial experiments indicated that these new complexes could initiate olefin metathesis reactions in methanol, water, and in aqueous emulsions. Subsequent sections focus on the application of alkylidenes **8** and **9** to ring-opening metathesis polymerization (ROMP), cross-metathesis, and ring-closing metathesis (RCM) in these solvents.

Introduction

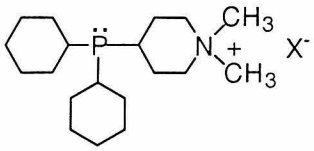
As described Chapter 3, the synthesis of a ruthenium alkylidene (**2**) bearing charged phosphine ligands was achieved *via* the exchange of the triphenylphosphine ligands in alkylidene **1** with PhP(*p*-$C_6H_4SO_3Na)_2$ (Eq 1).[1] While alkylidene **2** was soluble in water, it was not an active olefin metathesis catalyst in aqueous solution. This lack of activity was attributed to the relatively small size and electron-donating character of the coordinated triarylphosphine ligands. In general, the metathesis activities of alkylidenes of the type $(PR_3)_2Cl_2Ru{=}CHR$ are maximized by the coordination of sterically bulky, electron-rich trialkyl phosphines such as tricyclohexyl phosphine (PCy_3).[2]



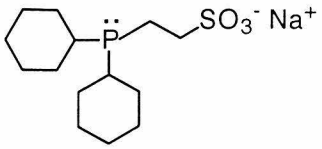
Chapter 3 also described the determination of the steric and electronic parameters of phosphines **3**, **4**, and **5**.[3] These water-soluble ligands were designed to be sterically and electronically similar to PCy_3, in order to overcome the lack of activity observed with alkylidene **2**. Phosphines **3**, **4**, and **5** were estimated to be sterically similar to PCy_3, and the determination of the electronic parameters for these phosphines suggested that these phosphines were attractive candidates as ligands for the development of new water-soluble alkylidenes.



3a, $X^- = I^-$
3b, $X^- = Cl^-$



4a, $X^- = I^-$
4b, $X^- = Cl^-$



5

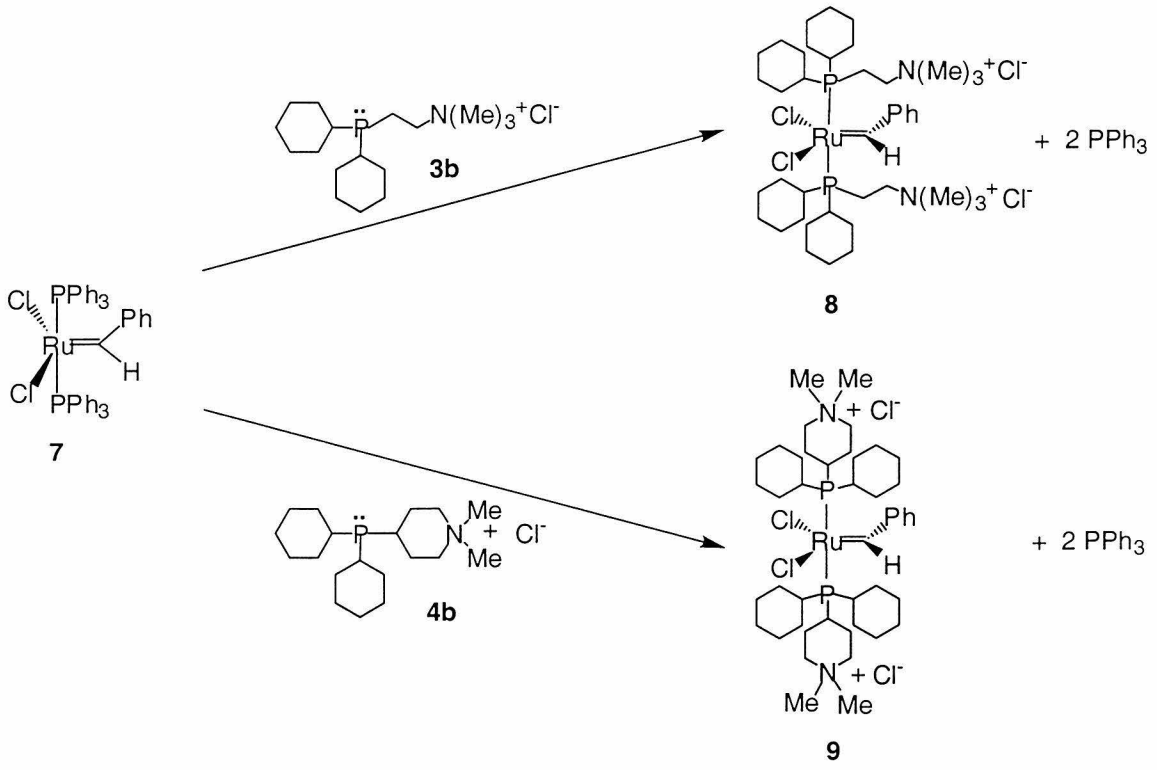
This chapter describes the application of phosphines **3**-**5** to the synthesis of well-defined, water-soluble ruthenium alkylidene complexes. The synthesis and characterization of these new complexes is addressed, and the initial experiments designed to probe the activities of these new catalysts as olefin metathesis catalysts in protic media are presented.

Results and Discussion

Synthesis of Water-Soluble Ruthenium Alkylidene Complexes

Initial investigations into the development of new, water-soluble ruthenium alkylidenes were focused on the development of new ruthenium *benzylidene* complexes. Phenyl-substituted ruthenium alkylidenes[4] (benzylidenes) have been shown to be highly stable, and initiate olefin metathesis reactions much more rapidly than otherwise equivalent vinyl-substituted alkylidenes[5] (such as **1**). Additionally, triphenylphosphine-containing ruthenium benzylidene precursor $(PPh_3)_2Cl_2Ru{=}CHPh$ (**7**) is more synthetically-accessible than vinyl-alkylidene complex **1**.[4]

Initial attempts to synthesize water-soluble ruthenium alkylidenes employing the phosphines described above centered on the application of quaternary amine-containing phosphines **3** and **4**. Ruthenium benzylidenes **8** and **9** were prepared in a single step by direct exchange of the triphenylphosphine ligands in alkylidene **7** with phosphines **3b** and **4b** (Scheme 1), in analogy to the synthesis of the PCy_3-containing alkylidene $(PCy_3)_2Cl_2Ru{=}CHPh$ (**10**).[4]

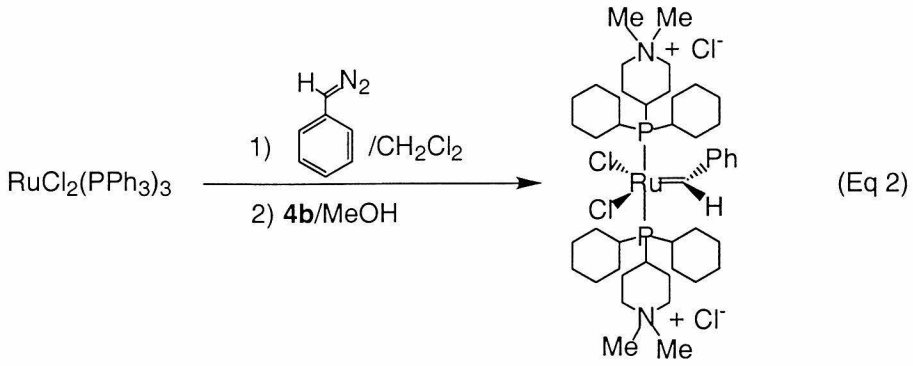


Scheme 1: Synthesis of water-soluble alkylidenes **8** and **9** *via* direct phosphine exchange.

The addition of a methanol solution of phosphine **3b** to a solution of **7** in dichloromethane yielded alkylidene **8**, recognized as an apparent singlet at 19.95 ppm in the ^{1}H NMR spectrum of the crude reaction mixture. The addition of phosphine was concomitant with an immediate change in the color of the reaction mixture from dark green to dark red. A slight excess of phosphine was used in these substitution reactions (from 2.05 - 2.2 equivalents relative to ruthenium complex). Alkylidene **8** was obtained in 86% yield as an analytically pure, purple microcrystalline solid following repeated precipitation from dichloromethane/pentane. This complex could be recrystallized at room temperature from a methanol/dichloromethane/diethyl ether mixture to yield dark purple needles.

Alternatively, complexes **8** and **9** could be prepared in a one-pot procedure from $RuCl_2(PPh_3)_3$ and phenyldiazomethane, following a protocol modified slightly from the procedure for the synthesis of **10** (Eq 2).[4] For example, alkylidene **9** was generated *in situ*

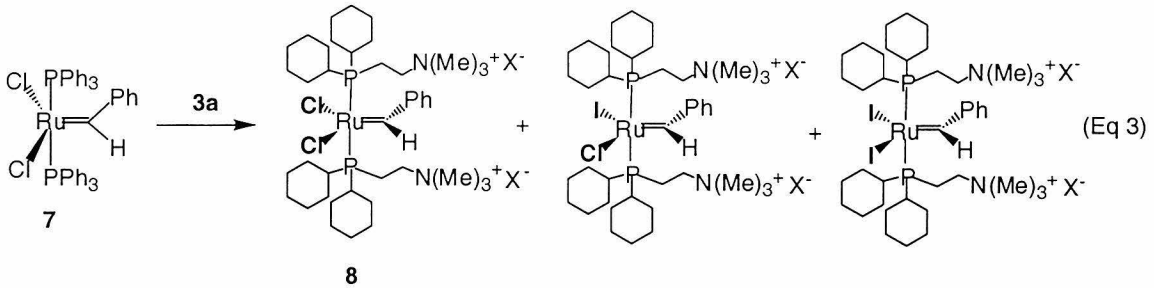
via the addition of phenyldiazomethane to a solution of $RuCl_2(PPh_3)_3$. Alkylidene **9** was isolated in 54% yield as a purple microcrystalline solid after repeated precipitation from dichloromethane/pentane and tetrahydrofuran/pentane.



(Eq 2)

9

It is noteworthy that cationic phosphines **3a** and **4a**, having iodide rather than chloride counterions, also exchange with the triphenylphosphine ligands in alkylidene **7** to yield new substituted alkylidenes. However, this particular phosphine exchange is concomitant with an anion metathesis reaction between the ammonium-iodide substituents on the phosphine and the ruthenium-chloride bonds in the alkylidene complexes. This exchange process is remarkably facile, and proceeds to yield a mixture of dichloro, diiodo, and chloro/iodo mixed-halide alkylidene species (Eq 3), as determined by ^1H NMR spectroscopy.



(Eq 3)

7

8

Chen *et al.* recently confirmed this observation by direct mass spectrometric observation of mixed-halide species following electrospray ionization of alkylidenes synthesized with phosphine **3a**.[6] As ruthenium alkylidenes of the type $(PR_3)_2X_2Ru{=}CHR$

having iodides as anionic ligands are generally less active than their dichloro-substituted counterparts in organic solvents,[2] iodide salts **3a** and **4a** were not investigated further as ligands for the synthesis of water-soluble, ruthenium alkylidene complexes.

Properties of Alkylidene Complexes **8** and **9**

Alkylidenes **8** and **9** were completely soluble in protic, high dielectric solvents such as water, methanol, ethanol, and water/THF mixtures. The complexes were insoluble in other common organic solvents including acetone, THF, and benzene. Complex **9** was additionally soluble in dichloromethane, however it decomposed rapidly (over a period of hours) in this solvent. Surprisingly, both complexes were also completely insoluble in Lewis acidic, Lewis basic, and Lewis neutral chloroaluminate-imidazolium ionic liquid melts.[7]

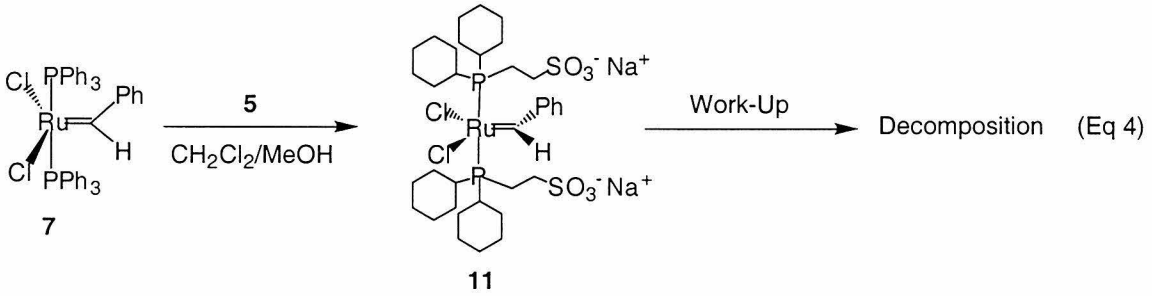
Alkylidenes **8** and **9** were stable in methanol solution for over three weeks, however significant decomposition was observed after only two days in aqueous solution. The nature of this unexpectedly rapid decomposition in water is not known. Although bimolecular decomposition may be involved, stilbene (the organic fragment expected from a bimolecular coupling process) is not observed by ^{1}H NMR in solutions of decomposed **8** or **9**. The detection of stilbene in solutions of these decomposed alkylidenes may be complicated, however, by the observation that **8** and **9** undergo a novel deuterium exchange process in deuterated solvents. This exchange reaction, in which the alkylidene protons of complexes **8** and **9** exchange rapidly with deuterons in perdeuterated protic solvents, is discussed in detail in Chapter 5. A more general analysis of the decomposition of these complexes will be presented in Chapter 8.

Alkylidenes **8** and **9** are highly air-sensitive in solution, and even the slightest trace of adventitious oxygen results in rapid decomposition (within minutes) to a brilliant green solution. Solutions of these alkylidenes which have been exposed to air contain phosphine oxide as the single phosphorus-containing species (as determined by ^{31}P NMR); the nature of the inorganic decomposition products is unknown. This conversion to a green solution

has been observed for structurally-related ruthenium alkylidenes upon exposure to air in organic solution.[8] However, oxidative decomposition occurs much more slowly in these systems. Therefore, in contrast to the use of more oxidatively-stable alkylidene **10**, the solvents used to dissolve alkylidenes **8** and **9** must be rigorously degassed and all manipulations should be carried out using standard Schlenk techniques. Both alkylidenes **8** and **9** also decompose slowly under an atmosphere of air in the solid state, and should be stored and manipulated under an inert atmosphere.

Synthesis of Other Water-Soluble Alkylidenes

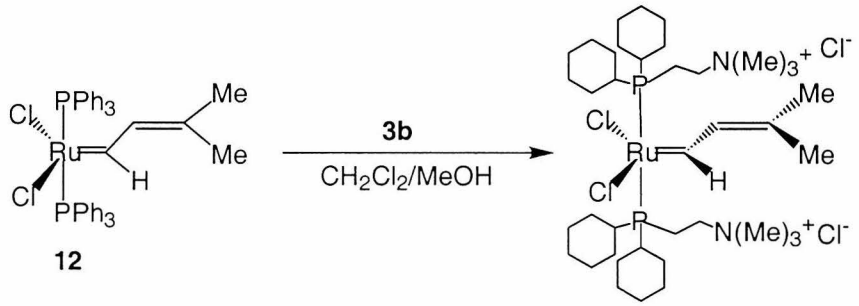
Treatment of alkylidene **7** with 2.2 equivalents of sulfonated phosphine **5** in a mixture of methanol and methylene chloride was not sufficient to achieve complete phosphine exchange. Instead, the reaction proceeded to generate a mixed-phosphine species, as determined by the presence of an A-B quartet in the ^{31}P NMR spectrum of the crude reaction mixture. Treatment of **7** with 4.0 equivalents of **5** yielded a single new alkylidene species **11** (Eq 4).



This exchange reaction proceeded to high conversion, as determined by NMR spectroscopy [^1H NMR: singlet, 20.66 ppm (alkylidene-H); ^{31}P NMR: singlet, 35.58 ppm]. The observed downfield chemical shift of the alkylidene proton relative to complexes **8** and **9** is consistent with the coordination of more electron-rich phosphine **5**.[2] Alkylidene **11** was stable for over 12 hours in the crude reaction mixture, however repeated attempts to isolate this new species resulted in rapid decomposition. Considering

the relatively nonpolar solvents employed in the work-up of this complex, this observed decomposition may have been due to the intramolecular displacement of a chloride ligand by a sulfonate group, resulting in the formation a 6-membered chelate and the precipitation of NaCl. The instability of alkylidene **11** was unfortunate, as the analysis of the electronic character of anionic phosphine **5** in Chapter 3 ($\chi = -2.1$ cm^{-1}) suggested that alkylidene **11** would be an extraordinarily robust water-soluble metathesis catalyst.

As mentioned above, synthetic approaches to the synthesis of water-soluble alkylidenes concentrated on the development of ruthenium benzylidene complexes, primarily due to: 1) the stability of these species, 2) their superior activities as initiators for ring-opening metathesis polymerization (ROMP), and 3) the general availability of triphenylphosphine-containing starting materials such as **7**. The recent development of a facile synthetic route to dimethylvinyl ruthenium alkylidene **12**,[9] however, prompted an investigation into the synthesis of water-soluble derivatives of this alkylidene (Eq 5). Treatment of **12** with 2.2 equivalents of phosphine **3b** yielded new alkylidene **13**. This dimethylvinyl-substituted alkylidene was soluble in water, methanol, and methylene chloride.



12 **13** (Eq 5)

Determination of Alkylidene Structure and Geometry

The spectroscopic features of alkylidenes **8** and **9** are suggestive of the structures and geometries presented in Scheme 1, in which the disposition of the chloride ligands is *cis*, the two coordinated phosphine ligands are *trans*, and the alkylidene substituents lie in

the Cl-Ru-Cl plane. These assignments have been made in analogy to the structures of parent alkylidene **10** and other complexes of the type $(PR_3)_2Cl_2Ru{=}CHR$ bearing bulky trialkyl phosphines.[2,4,5b]

The ^1H NMR resonances for the alkylidene protons in these complexes were observed as singlets (19.95 ppm for complex **8**; 20.14 ppm for complex **9**). The lack of observable P-H coupling in these complexes is consistent with a proposed Karplus-type relationship for P-H coupling constants in complexes of this type, in which a dihedral angle of 90° between the Ru-P and alkylidene C-H bonds is assumed to result in a near-zero P-H coupling constant.[2,4,5b,8] This empirical relationship between the spatial orientation of the alkylidene substituents and P-H coupling constants has been suggested for several related ruthenium alkylidene complexes, including **10**.[4b] The ^{31}P NMR resonances of these complexes appear as singlets (29.38 ppm for complex **8**; 35.30 ppm for complex **9**), reflecting the equivalent, *trans*-disposition of the two coordinated phosphines. No evidence for the formation of analogous complexes having *cis*-phosphines was observed in any case. Collectively, the above data provide additional experimental support for the steric parameters of these phosphines determined in Chapter 3.

A definitive determination of the structure of alkylidene **8** was made by X-ray diffraction analysis of a single crystal of this complex. As mentioned above, alkylidene **8** was recrystallized from a methanol/methylene chloride/diethyl ether mixture to provide dark purple needles. An ORTEP plot of the data from this analysis is shown in Figure 1 (solvent molecules and hydrogen atoms omitted for clarity). The coordination sphere around the ruthenium atom is distorted square pyramidal, with the phosphines and chloride ligands forming the base of the pyramid. Selected bond lengths and angles (Table 1) are consistent with those obtained for related complexes, such as **10**.[4b,5b] The alkylidene substituents are twisted 4.7° out of the Cl1-Ru-Cl2 plane (roughly orthogonal to the P1-Ru-P2 plane), suggesting that the proposed solution structure of this complex is retained in the solid state. The details of the X-ray diffraction experiment can be found in Appendix 2.

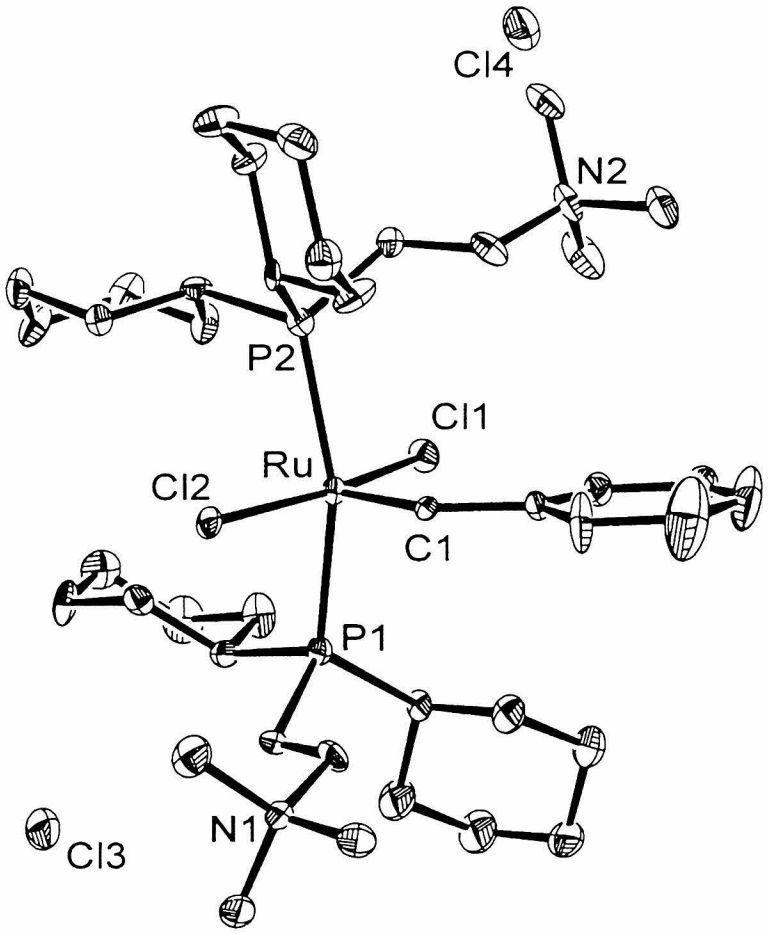


Figure 1: ORTEP drawing of alkylidene **8**. Thermal ellipsoids are drawn at 50% probability.

Table 1: Selected Bond Lengths (Å) and Angles (°) for Alkylidene **8**.

	Bond Lengths (Å)		
Ru-P1	2.384(2)	Ru-Cl1	2.393(2)
Ru-P2	2.393(2)	Ru-Cl2	2.399(2)
Ru-C1	1.816(7)		
	Bond Angles (°)		
C1-Ru-P1	99.5(2)	P1-Ru-P2	160.39(8)
C1-Ru-P2	99.8(2)	P1-Ru-Cl2	89.81(7)
C1-Ru-Cl1	103.6(2)	P2-Ru-Cl2	87.07(8)
C1-Ru-Cl2	88.1(2)	Cl1-Ru-P2	90.03(8)
P1-Ru-Cl1	89.11(8)	Cl1-Ru-Cl2	168.26(8)

Olefin Metathesis Activities of Alkylidenes 8 and 9 in Protic Solvents

Ring-Opening Metathesis Polymerization (ROMP)

Preliminary experiments demonstrated that alkylidenes **8** and **9** served as efficient initiators for the ROMP of several functionalized norbornene and 7-oxanorbornene derivatives in water, methanol, and in aqueous emulsions. Figure 2 shows some representative examples of monomers which will polymerize using these alkylidenes.

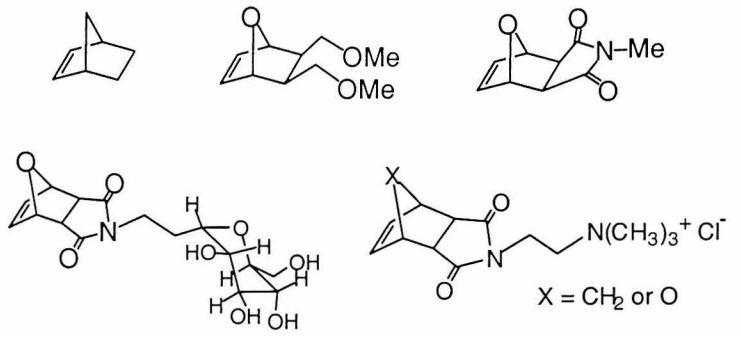


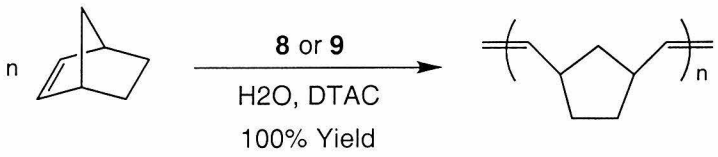
Figure 2: Selected norbornene and 7-oxanorbornene derivatives which will polymerize employing alkylidenes **8** and **9** in water, methanol, and aqueous emulsions.

These alkylidenes were active enough to polymerize less-strained cyclic olefins, such as 1,5-cyclooctadiene (COD). For example, the addition of **8** to a concentrated solution of COD in methanol at 45 °C resulted in the precipitation of poly(COD), a polymer structurally identical to 1,4-polybutadiene, within 15 minutes. These alkylidenes also initiated the aqueous polymerization of highly-functionalized monomers such as the unprotected α-C-glucoside-functionalized monomer shown in Figure 2.[10]

Initiation of monomer generally occurred rapidly in these systems and polymer polydispersities (PDIs) were low (PDIs = 1.10 - 1.30). Polymer yields and molecular weights were lower than expected, however, and subsequent analysis of polymerization reaction mixtures by ^{1}H NMR spectroscopy revealed that the propagating species in these reactions were decomposing over the time scale of the reaction. Accordingly, these aqueous polymerizations were not living. The factors affecting the longevity of alkylidenes **8** and **9** in aqueous solution are discussed in more detail in Chapter 6, which outlines the

activation of these complexes and their application to the *living* ROMP of functionalized norbornenes and 7-oxanorbornenes.

A notable exception to the problems discussed above was the polymerization of norbornene as an aqueous emulsion initiated by alkylidenes **8** and **9** (Eq 6, DTAC = dodecyltrimethylammonium chloride).



(Eq 6)

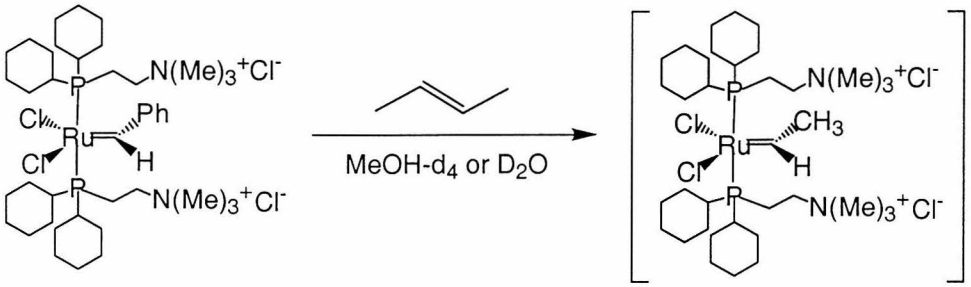
In these cases, polymerization was rapid and quantitative. Apparently, the relative reactivity of this unsubstituted monomer, relative to the substituted monomers shown in Figure 2, resulted in a rate of propagation that was sufficiently competitive with catalyst decomposition. The PDIs for polynorbornene produced in this system were as low as 1.18, however the molecular weight distributions were sometimes bimodal, having small fractions of high molecular weight material observed as a small shoulder in the gel permeation chromatograph (GPC) traces of these samples. The reasons for this peak shouldering were unclear. Dodecyltrimethylammonium chloride was employed as the emulsifier in these reactions, rather than the corresponding bromide salt used in Chapter 2, in order to avoid potential anionic ligand exchange reactions which could affect the structures and activities of alkylidenes **8** and **9**.

Reactivity With Acyclic Olefins

The applications of the "classical" ruthenium complexes discussed in Chapter 1 are generally limited to the ROMP of functionalized norbornenes and 7-oxanorbornenes. These "classical" complexes lack preformed alkylidene moieties, and the presence of highly-strained, cyclic olefins is required to generate the active species in the polymerization of those monomers. Thus, these complexes are not useful in initiating

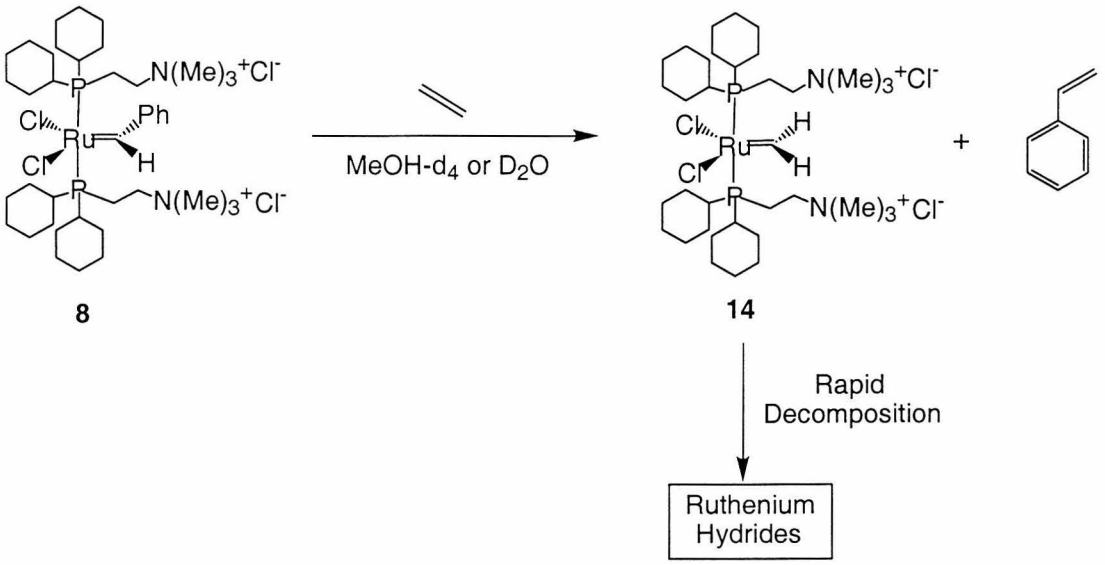
reactions with acyclic olefins and cannot be used to perform cross-metathesis reactions or ring-closing metathesis (RCM) reactions in aqueous solution or methanol.

In contrast to "classical" ruthenium complexes, well-defined alkylidenes **8** and **9** react readily with terminal and internal acyclic olefins. For example, simply bubbling a stream of *trans*-2-butene through a solution of alkylidene **8** in either methanol or water resulted in quantitative conversion to a new ruthenium *ethylidene* complex as an orange solution (Eq 7, determined by ^{1}H and ^{31}P NMR spectroscopy). This new species decomposed gradually over a period of hours in solution, and could not be isolated.



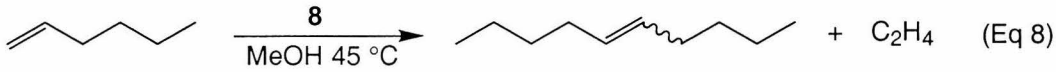
8 (Eq 7)

The reaction of alkylidene **8** with ethylene in methanol or water also proceeded to yield an orange solution. However, analysis of this solution by ^{1}H NMR spectroscopy yielded no alkylidene resonances. Several new resonances were observed in the far upfield region of the ^{1}H NMR spectrum (-15.9 ppm) and were assigned as ruthenium hydride species. Due to the rapid rate of this apparent decomposition reaction, a definitive determination of the decomposition pathway could not be made. However, the presence of styrene in the reaction mixture suggested that ethylene reacted first *via* metathesis with alkylidene **8** to produce a new *methylidene* species (**14**, Scheme 2) which then rapidly decomposed to ruthenium hydrides. The results of this experiment carry implications for the application of these alkylidenes to the RCM of α,ω-dienes (as discussed below), because methylidene **14** would be the catalytically active species in these reactions.



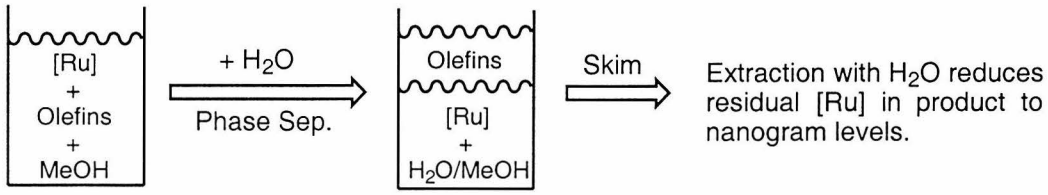
Scheme 2: The reaction of **8** with ethylene proceeds rapidly to yield styrene and ruthenium hydrides.

The demonstrated reactivities of these complexes with acyclic olefins introduced the opportunity to apply these catalysts to the cross-metathesis of terminal olefins in protic solvents. The dimerization of 1-hexene to 5-decene in methanol at 45 °C was chosen as a model reaction (Eq 8). The reaction proceeded to yield 5-decene in 20% yield, as determined by gas chromatographic (GC) analysis (the ratio of E/Z-isomers was not determined).



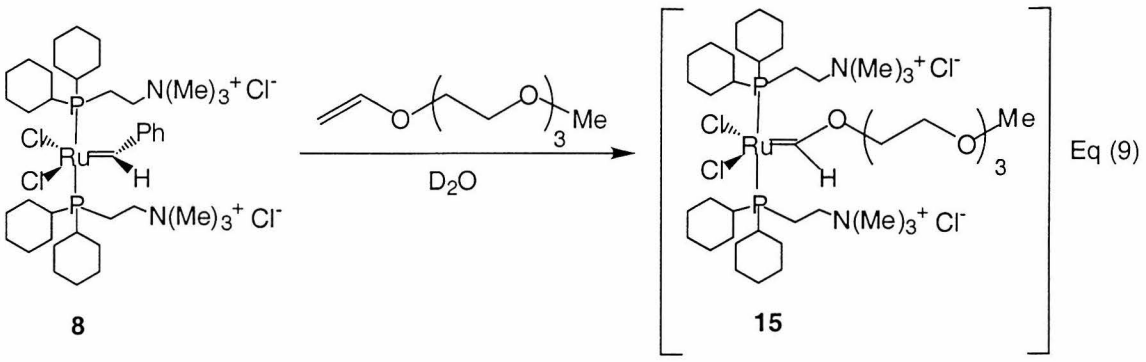
The yield for this reaction was not high. However, this reaction represented the first example of a cross metathesis reaction in a protic solvent. The reaction was carried out in a sealed reaction vessel without removal of ethylene, which may have contributed to the low yield in this reaction. It is likely, however, that the predominant factor influencing yield was the instability of the catalytically-active methylidene species (as described above). No attempts were made to optimize the yields in this reaction.

Despite the low yield in Eq 8, a benefit of performing the reaction in methanol employing alkylidene **8**, relative to applying alkylidene **10** in an organic solvent, was the ease with which **8** could be removed from the desired product. In this reaction, the separation of catalyst from olefin products was facilitated simply by the addition of non-degassed water to the reaction mixture.[11] As shown in Scheme 3, the addition of water to the reaction mixture yielded a biphasic system consisting of a colorless organic layer and a green aqueous phase. A 50 mg sample of the organic phase collected from this biphasic mixture contained less than 30 ng of detectable ruthenium, as determined by inductively-coupled plasma mass spectrometry (ICP-MS) analysis. This experiment suggested that these water-soluble alkylidenes may be useful for the metathesis of organic substrates in applications where removal of residual ruthenium is critical or otherwise problematic.[12]



Scheme 3: Aqueous extraction procedure demonstrating the removal of ruthenium from olefin metathesis reactions in methanol initiated by water-soluble alkylidenes **8** and **9**.

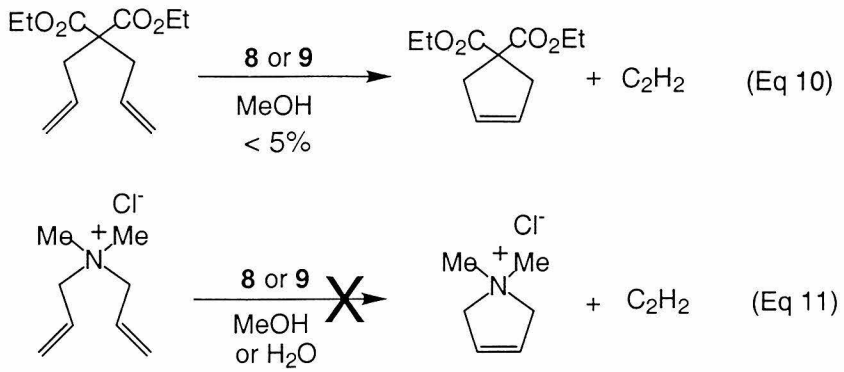
Ruthenium alkylidenes of the type $(PR_3)_2Cl_2Ru{=}CHR$ have also been shown to react with vinyl ethers to yield metathesis-inactive Fischer-carbene complexes.[13] For example, ethyl vinyl ether reacts with ruthenium benzylidene **10** to yield styrene and a new Fischer-carbene complex. Alkylidenes **8** and **9** react in an analogous manner with vinyl ethers in protic solvents—the treatment of alkylidene **8** with an excess of tri(ethylene glycol) methyl vinyl ether in aqueous solution yielded water-soluble Fischer-carbene complex **15** (Eq 9).



Carbene complex **15** could not be isolated, but was identified by the characteristic upfield resonance of the carbene proton (singlet, 14.34 ppm), which has been observed for structurally-similar ruthenium Fischer-carbene complexes in organic solvents.[13] Vinyl ethers have been used effectively as terminating reagents for ROMP initiated by well-defined ruthenium alkylidene complexes.[14] The use of water-soluble tri(ethylene glycol) methyl vinyl ether as a terminating reagent for *aqueous* ROMP reactions initiated by alkylidenes **8** and **9** is described in Chapter 6.

Ring-Closing Metathesis (RCM)

Initial attempts to probe the activities of **8** and **9** toward RCM centered upon the cyclization of α,ω-dienes such as diethyl diallylmalonate (Eq 10) and dimethyldiallylammonium chloride (Eq 11). The cyclization of diethyldiallylmalonate initiated by alkylidenes **8** or **9** in methanol generally proceeded in <5% yield (as determined by ^{1}H NMR spectroscopy). The RCM of dimethyldiallylammonium chloride in water did not yield observable product.



It is believed that the failure of these alkylidenes to cyclize these substrates is rooted in the instabilities of the catalytically-active methylidene species **14** generated upon the first turnover step. A more thorough treatment of these issues and the successful application of these complexes to the RCM of diene substrates can be found in Chapter 7 of this thesis.

Summary

This chapter described the application of water-soluble phosphines **3-5** to the synthesis of well-defined, water-soluble ruthenium alkylidenes. Benzylidene complexes **8** and **9** were synthesized directly *via* the exchange of the triphenylphosphine ligands in $(PPh_3)_2Cl_2Ru$=CHPh (**7**) with phosphines **3b** and **4b**. Dimethylvinyl alkylidene **13** was synthesized by an analogous procedure. Alkylidene **9** could also be synthesized *via* a one-pot procedure starting from $(PPh_3)_2RuCl_2$, phenyldiazomethane, and phosphine **4b**. While sulfonate-functionalized phosphine **5** was observed to undergo substitution reactions with the triphenylphosphine ligands in **7** to yield a new alkylidene, this complex was unstable to work-up conditions and could not be isolated.

Alkylidene complexes **8** and **9** were completely soluble in protic solvents such as water and methanol, and were insoluble in other common organic solvents such as acetone, tetrahydrofuran, and benzene. NMR spectroscopy data and X-ray diffraction analysis of alkylidene **8** suggested that these new alkylidenes were structurally similar to previously-reported ruthenium alkylidene complexes of the type $(PR_3)_2Cl_2Ru$=CHR bearing bulky, electron-rich phosphine ligands.

Alkylidenes **8** and **9** were shown to initiate olefin metathesis reactions in methanol, water, and in aqueous emulsions. Both complexes initiated the ROMP of a variety of functionalized norbornenes and 7-oxanorbornenes in these solvents. In contrast to "classical" ruthenium complexes, these new alkylidenes also reacted readily with less-strained monomers and with acyclic olefins. Initial investigations revealed that the application of these complexes to cross-metathesis and RCM in protic solvents may be limited by the stability of the catalytically-active methylidene species (**14**) generated in these reactions. The applications of these complexes to the *living* ROMP of functionalized monomers and the successful RCM of diene substrates in both water and methanol is discussed in more detail in Chapters 6 and 7 of this thesis.

Acknowledgments. The author wishes to thank Dr. Bernhard Mohr for his intellectual and experimental contributions to the work presented in this chapter, Professor Laura Kiessling, Kathy Mortell, and Ross Weatherman for providing several carbohydrate-functionalized water-soluble monomers, and Dr. Peter Green for help with the ICP-MS analysis. The X-ray diffraction analysis of alkylidene **8** was performed by Lawrence M. Henling and Dr. Michael W. Day. This work was supported by the Caltech Consortium (DuPont, Kodak, and 3M), the Rohm and Haas Company, and the National Science Foundation.

Experimental Section

General Considerations. All manipulations involving free phosphines and ruthenium complexes were performed in a nitrogen-filled drybox or by using standard Schlenk techniques under an atmosphere of argon. Argon was purified by passage through columns of BASF R3-11 catalyst (Chemalog) and 4 Å molecular sieves (Linde). ^{1}H NMR (300.1 MHz) and ^{13}C NMR (75.49 MHz) spectra were recorded on a GE QE-300 spectrometer, ^{31}P NMR (161.9 MHz) spectra were recorded on a JEOL GX-400

spectrometer. All chemical shift values are given in ppm and are referenced with respect to residual protons in the solvent for proton spectra, or to phosphoric acid for phosphorus spectra. Gel permeation chromatographs were obtained using an Altex Model 110A pump, a Rheodyne Model 7125 injector with a 100-μL injection loop, through an American Polymer Standards 10-μm mixed-bed column, and a Knauer differential refractometer; dichloromethane was used as the eluent at a flow rate of 1.0 mL/min. The molecular weights and polydispersities of the polymers are reported relative to monodisperse polystyrene standards.

Materials. Dichloromethane, tetrahydrofuran, and pentane were purified by passage through solvent purification columns containing activated alumina. Deionized water and methanol used for the polymerizations were degassed by purging with argon and then stirring under vacuum prior to use. Phosphines **3**-**5**,[3] Tris(triphenyl-phosphine)rutheniumdichloride,[15] phenyldiazomethane,[16] and $RuCl_2(=CHPh)(PPh_3)_2$[4] were prepared as previously reported. Carbohydrate-functionalized norbornene and 7-oxanorbornene monomers were kindly provided by Professor Laura Kiessling's research group at the University of Wisconsin. All other reagents were reagent grade and used without further purification.

$RuCl_2(=CHPh)[Cy_2PCH_2CH_2N(CH_3)_3^+Cl^-]_2$ (8). $RuCl_2(=CHPh)(PPh_3)_2$ (1.20 g, 1.53 mmol) was placed in a Schlenk flask equipped with a stirbar, capped with a rubber septum, and purged with argon. CH_2Cl_2 (15.0 mL) was added and the dark green solution was cooled to -78°C. Phosphine **3b** (1.0 g, 3.13 mmol, 2.05 equiv.) was dissolved in methanol (10 mL) under argon, cooled to -78 °C, and slowly added to the Schlenk flask *via* syringe. The reaction mixture was stirred at -78 °C for 30 min while a color change to dark red was observed. Stirring was continued for 30 min as the reaction warmed to room temperature. Removal of the solvent *in vacuo* yielded a dark purple

solid. The solid material was dissolved in CH_2Cl_2 (10 mL), stirred, and pentane (100 mL) was added to precipitate a purple solid. The brownish red supernatant was removed and discarded *via* cannula filtration, and this procedure was repeated until the supernatant became colorless. At this point, the solid product was insoluble in CH_2Cl_2 and was further treated with neat CH_2Cl_2, until the washings became colorless. The product was dissolved in methanol (15 mL), cannula filtered from an insoluble dark purple material, and solvent was removed *in vacuo* to yield the desired product as a purple solid (0.680 g, 49%). ^{1}H NMR (D_2O): δ 19.76 (s, alkylidene-H), 8.45 (d, J = 7.5 Hz, *o*-H of C_6H_5), 7.82 (t, J = 7.5 Hz, *p*-H of C_6H_5), 7.57 (t, J = 7.5 Hz, *m*-H of C_6H_5), 3.13 (br m, N-CH_2), 2.96 (s, N-CH_3), 2.36 (br m), 2.00 (br m), 1.85-1.66 (m), 1.53-1.15 (m). ^{13}C NMR (D_2O): δ 151.70, 132.14, 130.48, 130.11, 62.17, 52.28, 33.20, 33.07, 32.94, 28.86, 28.56, 28.34, 26.76, 26.59, 26.55, 26.39, 25.55, 25.46, 25.31, 12.26, 12.17. ^{31}P NMR δ (D_2O): 29.38 (s). ^{1}H NMR (CD_3OD): δ 19.95 (s, carbene-H), 8.55 (d, J = 7.8 Hz, *o*-H of C_6H_5), 7.81 (t, J = 7.8 Hz, *p*-H of C_6H_5), 7.57 (t, J = 7.8 Hz, *m*-H of C_6H_5), 3.20 (br m, N-CH_2), 3.06 (s, N-CH_3), 2.42 (br m), 2.08 (br m), 1.90-1.75 (m), 1.57-1.25 (m). ^{13}C NMR (CD_3OD): δ 301.93, 152.20, 131.13, 130.25, 129.65, 61.96, 51.54, 33.29, 33.15, 33.01, 28.80, 28.43, 26.80, 26.72, 26.60, 26.53, 25.35, 12.14, 12.04, 11.92. ^{31}P NMR (CD_3OD): δ 31.21 (s). Elemental analysis: Calcd for $C_{41}H_{76}N_2Cl_4P_2Ru$ (M_r = 901.87): C, 54.60; H, 8.49; N, 3.11. Found: C, 53.60; H, 8.27; N, 2.74. High-resolution FAB MS: Calcd for [M-Cl^-]: 867.359. Found: 867.359. The observed isotopic abundance for the corresponding [M-Cl^-] peaks identically matched the predicted isotope pattern for the [M-Cl^-] fragment of the title compound.

$RuCl_2$(=CHPh)[Cy_2P(*N,N*-dimethylpiperidinium chloride)]$_2$ (9).

$RuCl_2(PPh_3)_3$ (1.38 g, 1.44 mmol) was placed in a Schlenk flask and purged with argon. CH_2Cl_2 (15.0 mL) was added and the dark red solution was cooled to -78°C. Phenyldiazomethane (0.340 g, 2.88 mmol, 2.0 equiv.) was quickly weighed under air,

dissolved in pentane (1.0 mL), cooled to -78 °C, and added to the Schlenk flask *via* pipette under an argon purge. Upon addition of the diazo compound, an instantaneous color change from dark red to dark green was observed. The reaction was stirred for 5 min, and a solution of **4b** (1.10 g, 3.18 mmol, 2.2 equiv.) in methanol (10 mL) was added *via* syringe. The solution became dark-red, and stirring was continued for 30 min as the reaction warmed to room temperature. Solvent was removed *in vacuo* and dried overnight to yield a burgundy solid. The solid material was dissolved in CH_2Cl_2 (15 mL), stirred, and pentane (100 mL) was added to precipitate a burgundy solid. Pentane should be added quickly, as **9** slowly decomposes in CH_2Cl_2. The dark red supernatant was removed and discarded *via* cannula filtration, and the product was reprecipitated until the supernatant was colorless. The solid was dissolved in CH_2Cl_2 (10 mL), precipitated by addition of THF (150 mL), and cannula filtered. This process was continued until the supernatant was colorless. The product was dissolved in methanol (10 mL), cannula filtered from insoluble material, and solvent was removed *in vacuo* to yield the desired product as a burgundy solid (0.740 g, 54%). ^{1}H NMR (D_2O): δ 20.14 (s, alkylidene-H), 8.44 (d, J = 7.5 Hz, *o*-H of C_6H_5), 7.77 (t, J = 7.5 Hz, *p*-H of C_6H_5), 7.47 (t, J = 7.5 Hz, *m*-H of C_6H_5), 3.58-3.52 (m, P-CH), 3.35-3.13 (m, N-CH_2), 3.08 (s, N-CH_3), 2.97 (s, N-CH_3), 2.75-2.70 (m), 2.58-2.50 (m), 2.10-1.99 (m), 1.80-1.55 (m), 1.30-1.10 (m). ^{13}C NMR (D_2O): δ 292.60, 152.41, 130.61, 129.09, 62.44, 52.26, 32.67, 32.55, 32.42, 29.48, 29.29, 27.82, 27.70, 27.58, 26.98, 26.79, 26.85, 26.90, 25.60, 22.80. ^{31}P NMR (D_2O): δ 35.3 (s). Elemental analysis: Calcd for $C_{45}H_{80}N_2Cl_4P_2Ru$ (M_r = 953.99): C, 56.66; H, 8.45; N, 2.93. Found: C, 56.51; H, 8.08; N, 2.91. High-resolution FAB MS: The observed isotopic abundance for the corresponding [M-Cl^-] peaks identically matched the predicted isotope pattern for the [M-Cl^-] fragment of the title compound.

$RuCl_2(=CH\text{-}CH=Me_2)[Cy_2PCH_2CH_2N(CH_3)_3{}^+Cl^-]_2$ (13). $RuCl_2(=CH\text{-}Ch=Me_2)(PPh_3)_2$ (500 mg, 0.654 mmol) was placed in a Schlenk flask equipped with a stirbar, capped with a rubber septum, and purged with argon. CH_2Cl_2 (10.0 mL) was added to yield a dark red solution. Phosphine **3b** (502 mg, 1.57 mmol, 2.4 equivalents) was dissolved in methanol (10 mL) and slowly added to the Schlenk flask *via* syringe. The resulting dark red reaction mixture was stirred at room temperature for 30 minutes. Removal of the solvent *in vacuo* yielded a dark purple solid. The solid material was dissolved in CH_2Cl_2 (10 mL), stirred, and pentane (100 mL) was added to precipitate a red/purple solid. The supernatant was removed *via* cannula filtration, and this procedure was repeated until the supernatant became colorless. The resulting solid was dissolved in CH_2Cl_2 (5 mL), precipitated by addition of THF (150 mL), and cannula filtered. This process was continued until the supernatant was colorless. The product was dissolved in methanol (10 mL), cannula filtered from insoluble material, and solvent was removed *in vacuo* to yield a red/purple solid. ^1H NMR (CD_3OD, 400 MHz): δ 19.15 (d, J = 11.8, alkylidene-H), 7.90 (d, J = 11.8 Hz, β-H of alkylidene). ^{31}P NMR (CD_3OD): δ 35.11 (s).

General Polymerization Procedure. In a nitrogen-filled dry box, monomer was added to a septum-capped vial equipped with a teflon-coated stirbar. For emulsion-type polymerizations, dodecyltrimethylammonium bromide was added. Catalyst was added to second a vial and capped with a rubber septum. Outside the dry box, water or methanol was added to each vial *via* a gas-tight syringe, and the polymerization was initiated by adding the catalyst solution to the vial containing the monomer. Polymerizations were terminated either by adding an excess of ethyl vinyl ether, or by removing solvent under vacuum prior to analysis.

Emulsion Polymerization of Norbornene. In a nitrogen-filled dry box, norbornene (65.0 mg, 0.690 mmol) and dodecyltrimethylammonium chloride (550 mg) were added to

a 10 mL screw-necked pressure flask equipped with a magnetic stirbar, and the flask was sealed with a Teflon needle valve. Alkylidene **8** (5.0 mg, 0.0055 mmol) was weighed into a 1 dram vial, and the vial was capped with a rubber septum. Outside the dry box, water (3 mL) was added to the flask containing monomer and emulsifier *via* syringe under an argon purge, and the mixture was stirred at room temperature until it became an optically-clear microemulsion. Occasionally, mild heat was applied to expedite this process. Alkylidene **8** was dissolved in water (1mL) and the resulting red/orange solution was added to the monomer emulsion *via* syringe under an argon purge. An immediate color change from orange/red to pale yellow was observed upon addition of the catalyst solution to the monomer emulsion. The flask was resealed with a Teflon needle valve, and the reaction was allowed to stir at room temperature. After 10 minutes, the flask was opened to air, and the contents were precipitated into methanol (750 mL) to yield polynorbornene (65 mg) as a fluffy white solid.

Dimerization of 1-Hexene. In a nitrogen-filled dry box, alkylidene **8** (10.0 mg, 0.011 mmol) was dissolved in methanol (1 mL). This catalyst solution was added to a solution of 1-hexene (187 mg, 200 equivalents relative to **8**) in MeOH (1 mL) in a 1 dram vial equipped with a magnetic stirbar. The vial was capped with a Teflon-lined cap, and the homogeneous reaction mixture was heated to 45 °C. The red/orange reaction mixture turned bright orange within 10 minutes of heating. After 14 hours, the reaction was vented by temporarily loosening the cap under an atmosphere of nitrogen. At 30 hours, the reaction was allowed to cool, and water (2 mL) was added to the reaction mixture to yield a biphasic mixture. The clear top layer was collected *via* pipette and analyzed directly. The yield of 5-decene was found to be 20% as determined by gas chromatographic analysis. A 50 mg sample of the organic product layer was found to contain 27.6 ng of residual ruthenium as determined by inductively-coupled plasma mass spectrometry (ICP-MS).

Reaction of Alkylidene 8 With Tri(ethylene glycol) Methyl Vinyl Ether. Alkylidene **8** (10 mg, 0.011 mmol) was dissolved in D_2O (0.250 mL). Tri(ethylene glycol) methyl vinyl ether (25 mg, 0.131 mmol, 12 equivalents relative to **8**) was dissolved in D_2O (0.250 mL), and the two solutions were mixed. Upon mixing, the color of the reaction mixture changed from red/orange to light orange. This solution was placed in an NMR tube, and the tube was capped with a rubber septum. The reaction mixture was kept at room temperature, and the progress of the reaction was monitored *via* ^1H NMR spectroscopy. The resulting Fischer-carbene complex was observed as a singlet at 14.34 ppm. This complex decomposed after 1 hour and could not be isolated.

General RCM Procedure. In a typical reaction, diethyldiallyl malonate was placed in a vial and dissolved in CD_3OD. Alkylidene **8** or **9** was placed in a separate vial and dissolved in CD_3OD. The catalyst and substrate solutions were combined, placed in an NMR tube, and the tube was sealed with a rubber septum. The reaction was heated to 45 °C, and monitored by ^1H NMR spectroscopy. Conversion to product was determined *via* integration of the allylic protons in the cyclized product (2.95 ppm, s) relative to the allylic protons of the uncyclized substrate (2.68 ppm, d).

General Procedure for Reaction of Alkylidene 8 with Acyclic Olefins. A solution of alkylidene **8** (10 mg, 0.11 mmol) in CD_3OD (0.5 mL) was placed in a NMR tube capped with a rubber septum. This solution was heated to 45 °C and purged with propene, resulting in a rapid color change from purple to orange. The reaction was monitored by ^1H NMR spectroscopy after 15 minutes. The reaction proceeded to yield a new alkylidene resonance at 19.29 ppm, as well as the resonance for **8**, observed at 19.94 ppm. Styrene was also observed in the reaction mixture. Analysis of the reaction mixture *via* ^{31}P NMR spectroscopy revealed a new alkylidene species, observed as a singlet at 33.3

ppm. Evaporation of solvent from the reaction mixture yielded an orange powder. Rapid decomposition precluded the isolation of this new complex.

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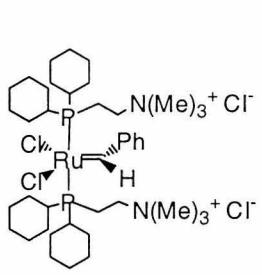
Chapter 5

Novel Reactivity of Ruthenium Alkylidenes in Protic Solvents

ABSTRACT: Alkylidene complexes **1-3** were designed for use as initiators for olefin metathesis reactions in protic solvents. During the isolation and characterization of these complexes, however, an additional and completely unexpected mode of reactivity was discovered. Specifically, the alkylidene protons in complexes **1-3** were found to exchange rapidly and quantitatively with deuterons when they were dissolved in perdeuterated protic solvents such as D_2O and CD_3OD. This exchange reaction was found to be general for a variety of other ruthenium alkylidenes in protic, high dielectric solvents. This chapter describes the nature of this new reaction, and details a kinetic investigation designed to provide insight into potential mechanisms for this transformation.

Introduction

Chapter 4 described the synthesis and characterization of complexes **1** and **2**, ruthenium alkylidenes bearing charged phosphine ligands.[1] These compounds represent the first transition metal alkylidenes that are soluble and stable in protic, high dielectric solvents such as methanol and water. Although alkylidenes **1** and **2** were designed to initiate olefin metathesis in these solvents, an additional and completely unexpected mode of reactivity was discovered during the synthesis and isolation of these new complexes. Specifically, the alkylidene protons in complexes **1** and **2** were found to exchange rapidly and quantitatively with deuterons when they were dissolved in perdeuterated protic solvents such as D_2O and CD_3OD. This chapter describes the nature of this new reaction.



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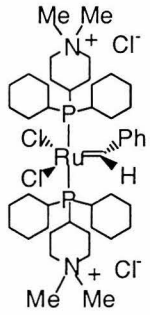

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Results and Discussion

During the synthesis and isolation of alkylidenes **1** and **2**, these complexes were dissolved in perdeuterated protic solvents for spectroscopic analysis. Initially, the expected resonances for the alkylidene protons in these complexes were not observed when D_2O solutions of **1** or **2** were analyzed by ^1H NMR spectroscopy. More careful analysis of these solutions revealed that the resonances of the alkylidene protons *could* be observed, provided that the solutions were analyzed immediately after the complexes were dissolved. In these cases, the resonances for the alkylidene protons disappeared completely over a period of 15 minutes. Similar behavior was observed when these complexes were dissolved in CD_3OD, although the rates of the disappearance of the alkylidene resonances

were much slower than the corresponding rates in D_2O (as described below).

The disappearance of the alkylidene proton resonances in the above examples suggested that alkylidenes **1** and **2** decomposed when dissolved in water or methanol. However, all other aspects of the ^1H NMR spectra of these complexes remained unchanged, even after the alkylidene protons had disappeared. For example, the diagnostic chemical shifts and coupling constants of the aromatic protons in the benzylidene moiety of this complex did not change [8.45 (d, J = 7.5 Hz, *o*-H), 7.82 (t, J = 7.5 Hz, *p*-H), 7.57 (t, J = 7.5 Hz, *m*-H)]. No new proton resonances were observed in this experiment, and the ^{31}P NMR spectrum remained unchanged throughout the course of the reaction. Representative portions of the ^1H NMR spectra for complexes **1** and **1-D** are shown in Figure 1.

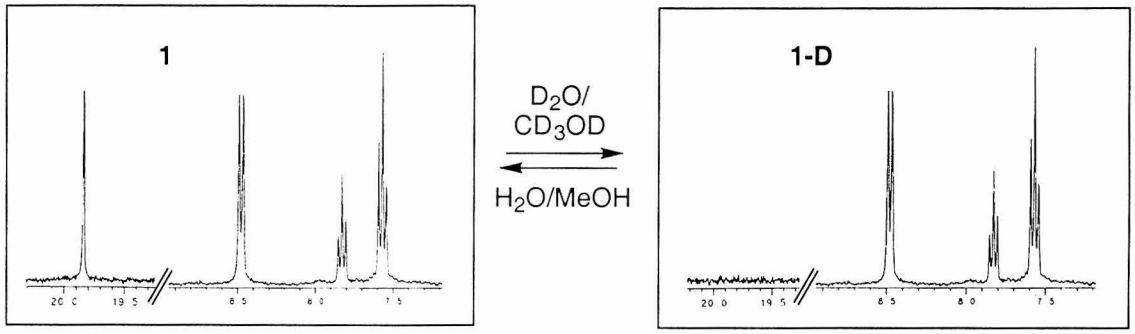
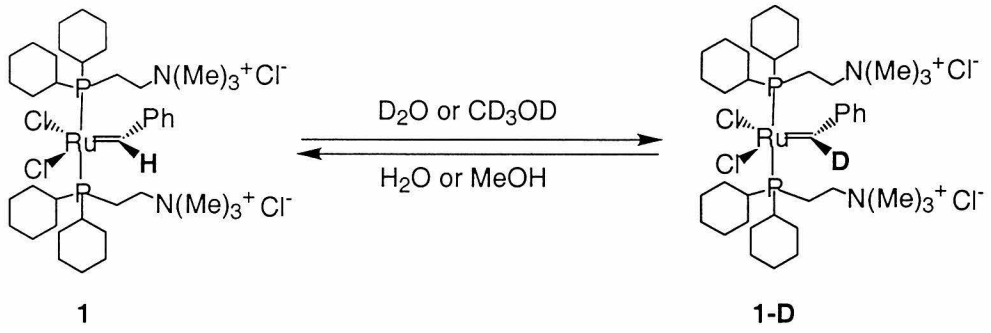


Figure 1: Representative ^1H NMR spectra (400 MHz, D_2O/CD_3OD) showing the diagnostic regions of alkylidene **1** before (left) and after (right) exchange of the alkylidene proton with solvent deuterons. This reaction was reversible in the presence of H_2O or MeOH.

The data above suggested that alkylidene **1** did *not* decompose to a structurally-unrelated species in aqueous solution, but rather underwent a well-defined transition to deuterated alkylidene complex **1-D** (Eq 1).



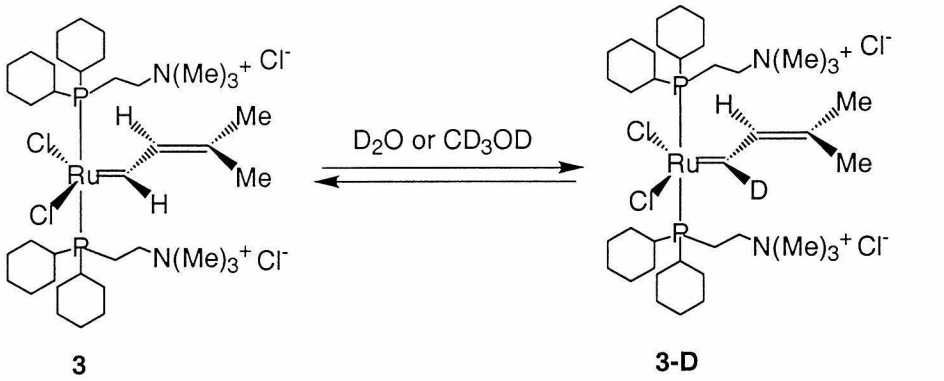
1 **1-D** (Eq 1)

This proton-deuteron exchange reaction was completely reversible when alkylidene **1-D** was dissolved in nondeuterated protic solvents. For example, alkylidene **1-D** was isolated *via* evaporation of deuterated solvent in the above experiment, and dissolution of this new complex in either D_2O or MeOH regenerated protio-alkylidene **1** (as determined by ^1H NMR spectroscopy after redissolving the complex in D_2O or CD_3OD). This proton-deuteron exchange was repeated up to three times with no observable decomposition.[2]

Further analysis of complex **1-D** by high-resolution fast atom bombardment (FAB) mass spectrometry yielded an observed mass of m/z = 868.3646. This value is in excellent agreement with the predicted mass of the [M-Cl] fragment of deuterated alkylidene **1-D** (predicted m/z = 868.3648).[3] The incorporation of deuterium at the alkylidene carbon in **1-D** was further confirmed *via* direct observation of this species by ^2H NMR spectroscopy. The ^2H NMR spectrum of this complex consisted of a single deuterium resonance, which appeared as a very broad singlet at a diagnostic chemical shift of 20.00 ppm. The expected C-D coupling at the alkylidene carbon of **1-D** was observed by ^{13}C NMR spectroscopy (500 MHz, CD_3OD, 301.89 ppm, J = 19.4 Hz), although peaks were broad and the splitting pattern for this resonance was additionally complicated by unresolved coupling to phosphorus. This carbon resonance sharpened considerably upon analysis by deuterium-decoupled ^{13}C NMR spectroscopy.

Dimethylvinyl alkylidene **3** displayed similar behavior in deuterated protic solvents (Eq 2). When alkylidene **3** was dissolved in either D_2O or CD_3OD proton-deuteron

exchange occurred exclusively at the alkylidene H_α position, and coupling between this deuterium atom and the adjacent vinyl proton (H_β) was manifest as a broad singlet at 7.85 ppm (the H_β proton in **3** is observed as a doublet (7.85 ppm, J = 8.25 Hz)).



3 **3-D** (Eq 2)

Investigation of Reaction Kinetics

As mentioned above, the rates observed for the proton-deuteron exchange in alkylidenes **1**-**3** varied considerably with solvent. For example, while this exchange was complete in 15 minutes for alkylidene **1** in D_2O, the reaction required three weeks to reach completion in CD_3OD under otherwise equivalent conditions. Exchange rates were also found to vary markedly according to catalyst structure—the alkylidene proton in **2** exchanged much faster than the alkylidene proton in **1**, suggesting that the rates of exchange were influenced by the electronic character of the bound phosphine ligands. These observations, in addition to the novelty of this transformation, prompted an investigation into the mechanism of this reaction.

The disappearance of the alkylidene proton in the above reactions provided a convenient handle for the investigation of the reaction kinetics by ^1H NMR spectroscopy. However, investigation of these reactions by ^1H NMR introduced several problems. First of all, the rates of exchange in water were too rapid to be followed accurately by ^1H NMR at room temperature, and these reactions could not be cooled below 5 °C due to the

relatively high freezing point of D_2O. Conversely, the deuterium exchange reaction proceeded too slowly in CD_3OD to be experimentally feasible. Although the rates of reaction in CD_3OD were accelerated at elevated temperatures, significant decomposition of alkylidenes **1-3** was observed over the course of the exchange process under such conditions.

It was observed that the exchange reaction proceeded at intermediate rates in mixtures of D_2O and CD_3OD, and that the rates in such solvent mixtures varied considerably according to the volume fraction of D_2O. As a result of this relationship, the rates of exchange in alkylidenes **1-3** could be "tuned" to values slow enough to allow investigation by ^1H NMR, but fast enough to be experimentally practical. An investigation of the reaction kinetics in D_2O/CD_3OD solvent mixtures would be simplified the basic assumption that the rates of exchange due to CD_3OD were negligible relative to the rates of exchange due to D_2O. This relationship was initially assumed to be valid in view of the dramatic differences in the relative reaction rates in these solvents (as discussed above).

In order to gain insight into the mechanism of the proton-deuteron exchange reaction, the reaction kinetics were studied by monitoring the disappearance of the alkylidene proton in **1** over time. As shown in Figure 2, the exchange reaction in a 30% D_2O/70% CD_3OD (v/v) solvent mixture at 30 °C exhibited pseudo-first-order kinetics. A good linear correlation was observed, and the pseudo-first-order rate constant, k_{obs}, for this reaction was calculated to be 17.2 ($\pm$0.2) x 10^{-3} min^{-1}.

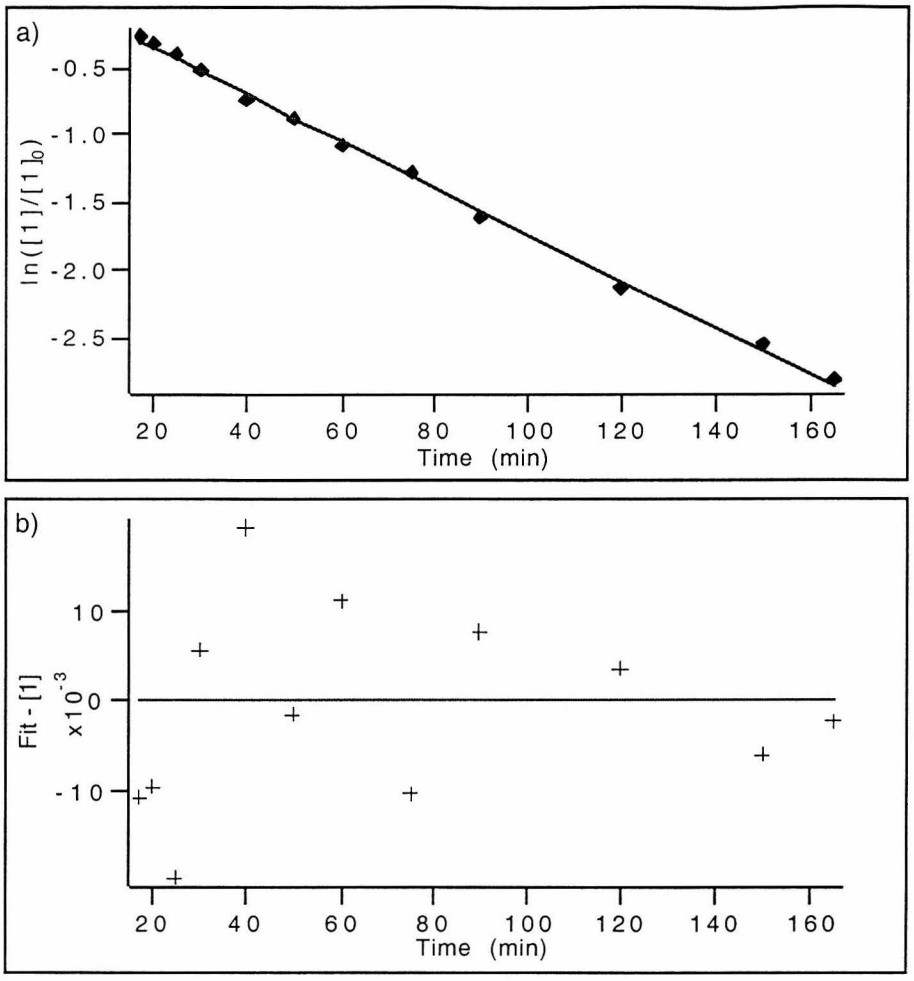


Figure 2: (a) Representative plot of $\ln([\mathbf{1}]/[\mathbf{1}]_0)$ vs. time for alkylidene **1**. The reaction was carried out with $[\mathbf{1}]_0 = 0.022$ M, in a 30% D_2O/70% CD_3OD solvent mixture at 30 °C. The filled diamonds are the data points and the solid line is the best linear fit to the data. b) Plot of the residuals from the fit in a) found by taking the difference between the data and the curve fit at each point.

Next, the rates of this reaction for alkylidene **1** were investigated as a function of D_2O concentration. As shown in Figure 3, the observed rate constants (k_{obs}) for these reactions varied exponentially with increasing concentrations of D_2O. Unfortunately, a plot of $\ln(k_{obs})$ vs. $\ln[D_2O]$ derived from this data did not permit the extraction of a reliable value for the order of D_2O in these reactions (although this relationship was linear, the order of D_2O derived from this relationship was calculated to be 2.50 ±0.23).

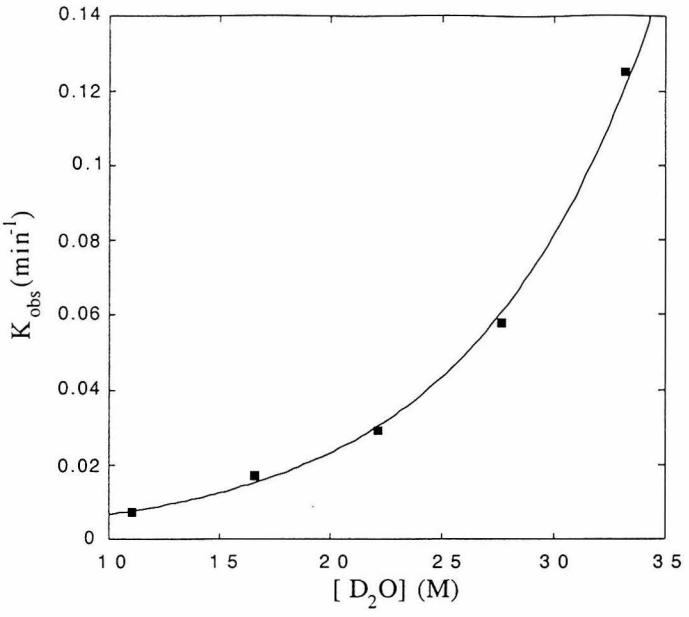


Figure 3: Plot of k_{obs} vs. [D_2O] for alkylidene **1**. Reactions were carried out in mixtures of D_2O and CD_3OD as solvent at 30 °C. The filled squares are the data points, and solid curve represents the best calculated exponential fit ($R^2 = 0.997$)

Influence of Solvent Dielectric on Reaction Rates

It is known that a linear relationship exists between the concentration of water and solvent dielectric constants in methanol/water mixtures.[4] In accordance with this relationship, the data above also revealed that the rate of the proton-deuteron exchange for alkylidene **1** varied exponentially with increasing solvent dielectric constant. As shown in Figure 4, a plot of $\ln(k_{obs})$ vs. 1/D yielded a linear relationship (D = dielectric constant of solvent mixture). These data may be useful in determining the nature of the reactants and/or transition states, and thus the mechanism, of this reaction.[5]

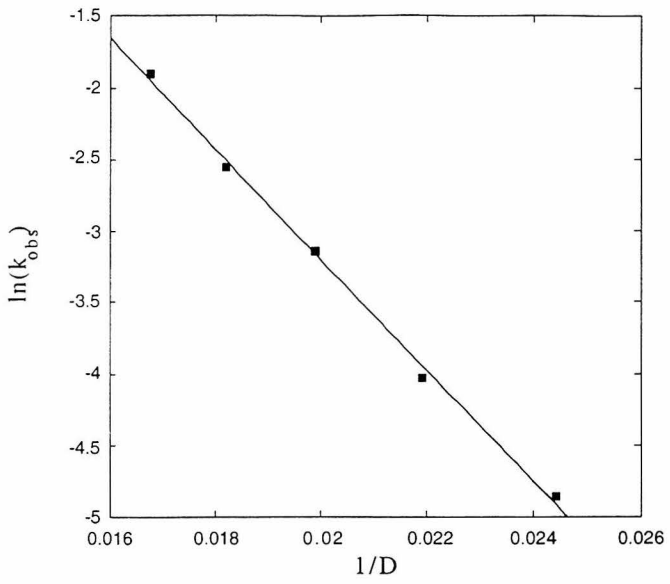


Figure 4: Plot of $\ln(k_{obs})$ vs. 1/D for alkylidene **1** (D = dielectric constant of solvent). Reactions were carried out in mixtures of D_2O and CD_3OD as solvent at 30 °C. The filled squares are the data points, and the solid line represents the best calculated linear fit. Intercept = 4.56 (±0.24); slope = -388.01 (±11.64); linear correlation coefficient (R^2) = 0.997.

When the rates of exchange for alkylidene **1** were studied in THF-d_8/D_2O mixtures rather than in D_2O/CD_3OD mixtures, the reaction rates were much slower at equivalent D_2O concentrations (Figure 5). The dielectric constant of THF is much lower than the dielectric constant of methanol. Accordingly, mixtures of THF and water have lower dielectric constants than methanol/water mixtures at equivalent water concentrations.[6] The results in Figure 5 suggested that the rates of proton-deuteron exchange reactions in alkylidene **1** were primarily dictated by solvent dielectric, and not the actual concentration of D_2O present in the solvent mixture (or that the initial assumption that the rate of exchange due to methanol in D_2O/CD_3OD mixtures may not be as negligible as originally assumed). An overlayed plot of k_{obs} versus D suggests that that both conclusions may be true (Figure 6). For example, the overlay of the two plots reveals that the differences between the rates of exchange in both solvent mixtures are negligible with respect to dielectric constant at lower D_2O concentrations ([D_2O] < 40% (v/v)). The deviation in the curves at higher D_2O concentrations ([D_2O] > 40% (v/v)), however, suggests that the contribution of methanol to exchange rates may become significant at higher dielectric constants.

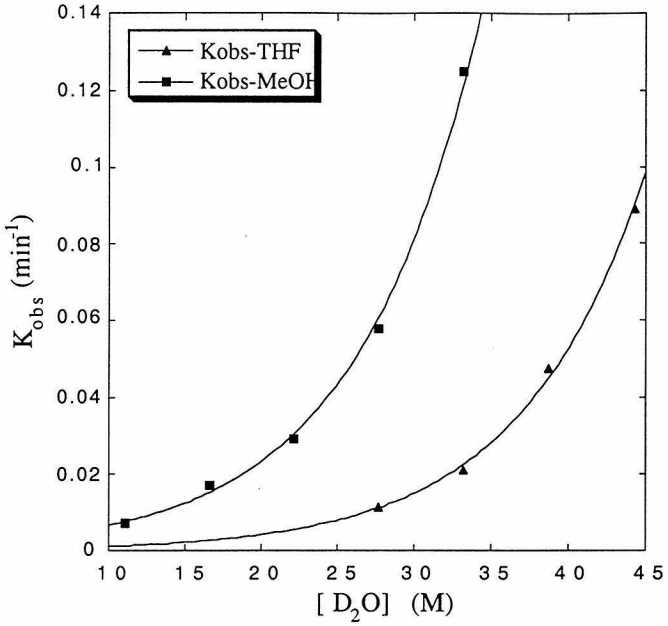


Figure 5: Plot of k_{obs} vs. [D_2O] for the deuterium exchange in alkylidene **1** in mixtures of D_2O/THF-d_8 and D_2O/CD_3OD. Reactions were carried out at 30 °C. The filled squares are the data points for the reactions in D_2O/CD_3OD, the filled triangles are the data points for the reactions in D_2O/THF-d_8. The solid curves represent the best calculated exponential fits to these data.

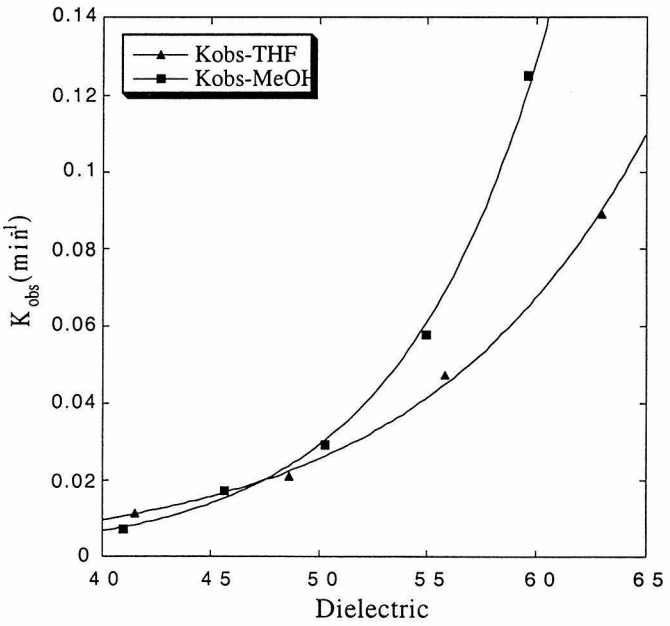


Figure 6: Plot of k_{obs} vs. D for the deuterium exchange in alkylidene **1** in mixtures of D_2O/THF-d_8 and D_2O/CD_3OD. Reactions were carried out at 30 °C. The filled squares are the data points for the reactions in D_2O/CD_3OD, the filled triangles are the data points for the reactions in D_2O/THF-d_8. The solid curves represent the best calculated exponential fits to these data.

Activation Parameters for Alkylidene Proton-Deuteron Exchange

An analysis of the reaction kinetics as a function of temperature permitted an estimation of the activation parameters for the exchange reaction. Figure 7 shows an Eyring plot [$\ln(k_{obs}/T)$ vs. 1/T] of data derived from the exchange of the alkylidene proton of **1**. From this plot, the enthalpy and entropy of activation ($\Delta H^{\ddagger}$ and $\Delta S^{\ddagger}$) were determined to be 16.94 (±0.8) kcal/mol and –8.24 (±2.82) e.u., respectively. An Arrhenius plot of the same data yielded a value of 17.52 (±0.84) kcal/mol as the energy of activation (E_A) for this exchange process (graph not shown). It is important to note that the rate data used in the above calculations could only be collected over a relatively narrow temperature range (from 10-37 °C) due to problems associated with solvent freezing points and reaction rates. The solvents in these reactions could not be cooled lower than 10 °C, and the reaction rate was already sufficiently rapid at 37 °C that the kinetics could only be studied over the final 45% of the exchange process.

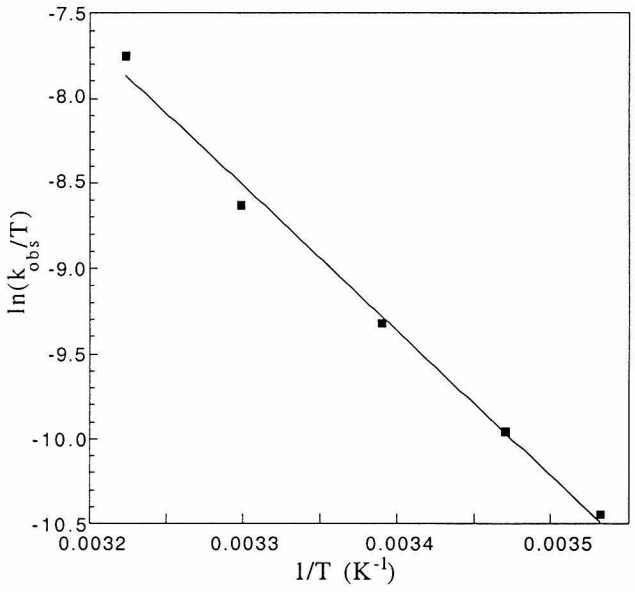


Figure 7: Eyring plot [$\ln(k_{obs}/T)$ vs. 1/T] for alkylidene **1**. Reactions were carried out in 50% D_2O/50% CD_3OD solvent mixtures (v/v) at temperatures ranging from 283.15-310.15 K. The filled squares are the data points, and the solid line represents the best calculated linear fit. Intercept = 19.61 (±1.42); slope = -8522.6 (±489.0); linear correlation coefficient (R) = 0.996.

Reaction Kinetics for Proton-Deuteron Exchange in Alkylidene **2**

An investigation of the kinetics for the exchange of the alkylidene proton in **2** revealed that this reaction was also pseudo-first-order with respect to alkylidene in D_2O/CD_3OD mixtures over a range of D_2O concentrations. The rates of exchange for this alkylidene were generally much faster than the rates of exchange of alkylidene **1**. For example, in a 30% D_2O/70% CD_3OD (v/v) solvent mixture at 30 °C, the observed rate constant, k_{obs}, for the exchange of the alkylidene proton in **2** [k_{obs} = 200.0 (±7.0) x 10^{-3} min^{-1}] was 11.6 times the value for the rate of exchange in alkylidene **1** [k_{obs} = 17.2 (±0.2) x 10^{-3} min^{-1}].

This result suggested that rates of exchange in alkylidenes **1** and **2** were strongly influenced by the electronic character of the coordinated phosphine ligands. For example, an exchange mechanism invoking a nucleophilic alkylidene carbon would be facilitated by the increased electron density on the metal center in alkylidene **2** (see Chapter 3). In contrast to the data shown in Figure 3 for alkylidene **1**, the observed rate constants for the exchange of the alkylidene proton in **2** did not appear to correlate exponentially with increasing D_2O concentration. Likewise, the relationship between these data could not be expressed as a linear correlation. As shown in Figure 8, the observed rate constants for the exchange in alkylidene **2** were best described as a quadratic function of D_2O concentration.

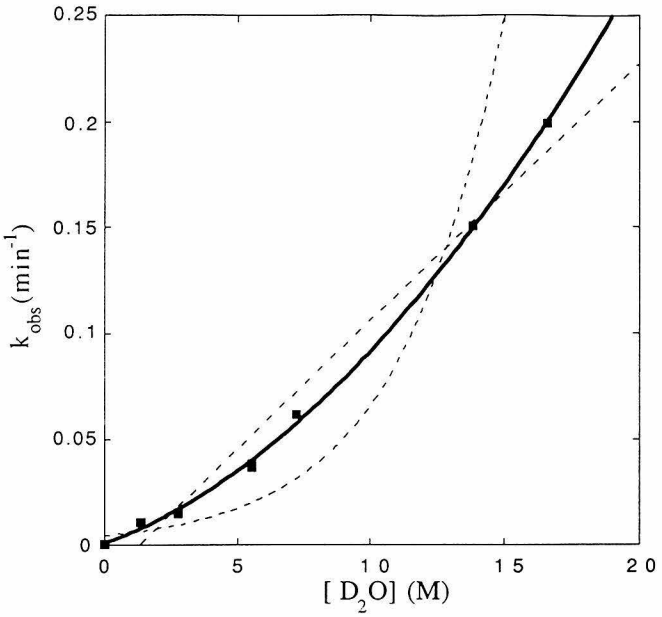


Figure 8: Plot of k_{obs} vs. [D_2O] for alkylidene **2**. Reactions were carried out in mixtures of D_2O and CD_3OD as solvent at 30 °C. The filled squares are the data points. The dashed line represents the best linear fit (R^2 = 0.971) and the dashed curve represents the best exponential fit to the data (R^2 = 0.915). The solid curve is the best fit of the data to a quadratic equation of the form ($y = ax^2 + bx + c$); R^2 = 0.999.

Effect of Ligand Concentration on Exchange Rates

In developing potential mechanisms for the proton-deuteron exchange behavior of alkylidenes **1** and **2**, we considered an active intermediate resulting from the dissociation of a chloride or phosphine ligand from the metal center. In order to investigate this possibility, the kinetics for the exchange reaction of alkylidene **1** were investigated in a 50% D_2O/50% CD_3OD solvent mixture at 30 °C in the presence of added phosphine. The half-life for the exchange reaction in the presence of 1.0 equivalent of added phosphine was 13.41 (±1.48) minutes [k_{obs} = 52.0 (±6.0) x 10^{-3} min^{-1}].

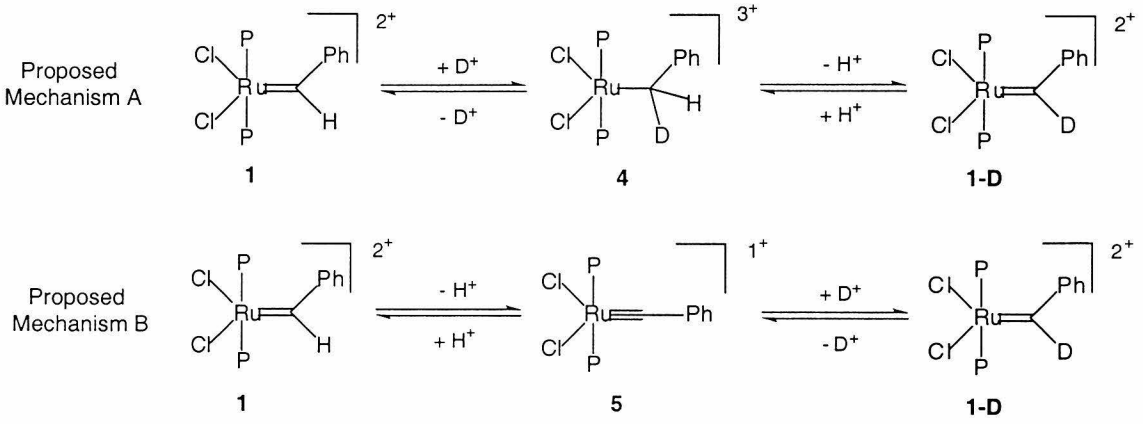
The half-life of that reaction did not differ significantly from the half-life for the same reaction in the *absence* of added phosphine [12.01 (±0.28) minutes, k_{obs} = 58.0 (±1.0) x 10^{-3} min^{-1}] within the estimated errors for these measurements. The estimated error for the reaction in the presence of added phosphine is larger in this case, as the magnitude of the proton resonances arising from the methyl groups on the phosphine introduced significant uncertainties into the integration of the alkylidene proton. These data

suggested that phosphine dissociation did not occur in the rate-determining step of this reaction.

A similar experiment was performed employing 5.0 equivalents of added phosphine. The alkylidene proton of **1** could not be reliably integrated under these conditions. However a qualitative assessment of reaction rate provided further evidence that the rate of this reaction was not dependent on phosphine concentration. As the addition of phosphine in the above reactions necessarily added an equivalent of chloride (present as the counterion of the trimethylammonium moiety), the above experiments also suggested that the rate of these reactions was independent of chloride concentration. In view of the facile anion-exchange reactions presented in Chapters 2 and 4, however, it is likely that a chloride dissociation step could be involved in the context of the overall reaction mechanism, perhaps as a fast preequilibrium preceeding the rate-determining step.

Analysis of Reaction Mechanism

It is possible to propose a variety of potential mechanisms for the alkylidene proton-deuteron exchange reaction in Eq 1. We initially considered two potential mechanisms [A and B, Scheme 1 (substituents on phosphorus omitted for clarity)].



Scheme 1: Possible mechanisms for alkylidene proton-deuteron exchange reactions.

In mechanistic pathway A, it was proposed that the ruthenium-carbon alkylidene bond in **1** could be "protonated" by a solvent-derived deuteron (D^+) to yield a ruthenium alkyl species (**4**); subsequent deprotonation of this intermediate would generate deuterated alkylidene **1-D**. Mechanistic pathway B proposed the initial deprotonation of the ruthenium alkylidene bond to yield a ruthenium benzylidyne species (**5**); "protonation" of this complex by D^+ would yield a deuterated alkylidene. In either mechanism, the rate-determining step of the reaction could also be thought to be preceeded by dissociation of chloride in a fast preequilibrium step.

We initially considered mechanistic pathway A, since this pathway invoked the generation of intermediate **4** having an overall charge of +3 (including the two cationic charges contributed by the cationic phosphine ligands). In contrast, intermediate **5** generated in pathway B bears an overall charge of +1. We reasoned that the generation of a more highly-charged intermediate was consistent with the observed dependence of the rates of exchange on solvent dielectric constants (as shown in Figures 3 and 4).

If the reaction were taking place through mechanistic pathway A, the rate of alkylidene proton-deuteron exchange would be accelerated by the addition of acid (D^+) to the reaction mixture. Unfortunately, this key experiment could not be performed with reliable certainty, because the addition of acid to solutions of alkylidenes **1** and **2** resulted in the protonation of phosphine ligand (as described in more detail in Chapter 6). This ligand protonation generated a mixture of bisphosphine and monophosphine alkylidenes, significantly changed the chemical nature of the species present in solution. This reaction was performed nonetheless, through the addition of 0.3 equivalents of DCl to a solution of alkylidene **1** in D_2O. A qualitative evaluation of the data suggested that the addition of acid did not have a significant impact on the rate of the exchange reaction.

If the exchange reaction were proceeding *via* the mechanism in pathway B, the overall rate of the reaction should be accelerated upon addition of base to the reaction mixture. This key experiment could not be performed, however, because the addition of

NaOH to aqueous solutions of **1** or **2** resulted in immediate conversion of these alkylidenes to an unidentified new species which rapidly decomposed (as described in Chapter 6). It should be noted that the rate of an exchange reaction occurring by this mechanism would also have been affected by the experiments above conducted in the presence of excess phosphine ligand, since these electron-rich ligands are significantly basic. As described above, however, the rates of exchange were independent of the amount of added phosphine ligand.

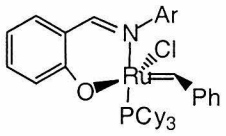
The significant variation in the relative rates of exchange for the alkylidene protons in **1** and **2** may also offer information regarding the mechanism of proton-deuteron exchange. For example, the dramatic rate enhancments observed for alkylidene **2**, which contains more electron-rich phosphines than alkylidene **1**, strongly implicate a mechanism involving a nucleophilic alkylidene carbon (such as pathway A above). A detailed analysis of the general nucleophilic or electrophilic character of ruthenium alkylidenes is currently being investigated by others.[7]

Summary and Perspective

Alkylidenes **1** and **2** represent the first examples of well-defined transition metal alkylidenes which are soluble and stable in protic solvents, and the observation of an alkylidene proton-deuteron exchange reaction was completely unexpected. Although the protonation of ruthenium dihalo-alkylidenes and rhenium alkylidene complexes has been investigated by others,[8] the alkylidenes in these examples generally undergo well-defined, *irreversible* transformations to metal-alkyl (non-alkylidene) intermediates or products.

This chapter described several experiments designed to gain insight into the mechanism and overall nature of this new exchange reaction. Although a considerable amount has been learned about this transformation, the data presented above do not currently support any particular proposed mechanism. However, with the recent development of new ruthenium alkylidenes which are also soluble and stable in methanol

and/or water, additional examples of this novel reactivity have been discovered. For example, methanol-soluble ruthenium alkylidenes such as **6**[9] also undergo an alkylidene-deuteron exchange in CD_3OD.



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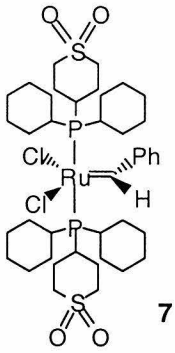

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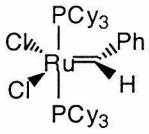

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In the case of alkylidene **6**, the rate of proton-deuteron exchange is approximately *54 times faster* in methanol than the rate of exchange for alkylidene **2** under equivalent conditions. Additionally, ruthenium complex **7** has been observed to undergo this exchange reaction in both methanol and methanol/water mixtures.[10] Finally, this proton-deuteron exchange reaction has been observed for alkylidene **8**[11] in a mixture of dichloromethane and methanol.

These final examples suggest that the novel reactivity occurring at the alkylidene carbon may be general for an entire class of ruthenium alkylidenes, provided that protic species are available in solution and that the dielectric constant of the reaction medium is sufficiently high. As alkylidenes **6-8** are also soluble in non-protic organic solvents such as dichloromethane and benzene, the investigation of these complexes may present opportunities to study the mechanisms of this novel behavior under reaction conditions conducive to more detailed kinetic analysis. For example, reactions employing alkylidenes **6-8** could be run under true first-order conditions through addition of stoichiometric amounts of protic species to the complexes in organic solvents, potentially enabling the derivation of a more complete rate law for this reaction. Additionally, the use of organic

solvents would facilitate the investigation of these processes at both higher and lower temperatures than possible using alkylidenes **1** or **2** in water or methanol.

In addition to addressing the novel aspects of this reaction, the mechanism for the proton-deuterium exchange shown in Eq 1 should be investigated for several other reasons. As described in Chapter 4, alkylidenes **1** and **2** decompose more rapidly in aqueous and methanolic solution than alkylidenes such as **8** in organic solvents. While the exchange reaction is not itself a decomposition reaction, we suggest the possibility that intermediates along the reaction coordinate from **1** to **1-D** may be responsible for the accelerated rates of decomposition observed for these complexes. Finally, it is anticipated that the investigation of this (currently) novel reaction will eventually lead to the development of new and potentially useful non-metathesis applications of ruthenium alkylidene complexes in organic and organometallic chemistry.

Acknowledgments. The author wishes to thank Dr. Eric Dias for his assistance with the kinetic experiments presented above, and for many late-night discussions regarding this work. We also thank Drs. Bernhard Mohr, Adam Matzger, Thomas Rolle, and Melanie Sanford for helpful discussions and insight. Dr. Robert Lee is thanked for his assistance with NMR spectroscopy experiments. This work was supported by the National Science Foundation.

Experimental Section

General Considerations. All manipulations involving ruthenium alkylidene complexes were performed using standard Schlenk techniques under argon or in a nitrogen-filled dry box. Argon was purified by passage through columns of BASF R3-11 catalyst (Chemalog) and 4 Å molecular sieves (Linde). ^{1}H NMR (300.1 MHz) were recorded on a GE QE-300 spectrometer. ^{31}P NMR (161.9 MHz) spectra were recorded on a JEOL GX-400 spectrometer. ^{13}C NMR (125.78 MHz) spectra were recorded on a Varian Inova 600

spectrometer. All chemical shift values are given in ppm and are referenced with respect to residual protons in the solvent for proton spectra, or to phosphoric acid for phosphorus spectra.

Materials. Dichloromethane and tetrahydrofuran were purified by passage through solvent purification columns containing activated alumina. CD_3OD, D_2O, and THF-d_8 were degassed by purging with argon and stirring under vacuum prior to use. Rigorously dried CD_3OD used in kinetics experiments was purchased directly from Acros Organics (Lot # A010250901). Alkylidenes **1** and **2**,[1] **3**,[12] **6**[9] and **8**[11] were prepared as previously reported. All other reagents were reagent grade and used without further purification.

$RuCl_2(=CDPh)[Cy_2PCH_2CH_2N(CH_3)_3^+Cl^-]_2$ (1-D). Alkylidene **1** (20 mg) was placed in a Schlenk flask equipped with a stirbar, and capped with a rubber septum. D_2O (1 mL) was added *via* syringe, and the solution was stirred for 30 minutes at room temperature. Solvent was removed under vacuum to yield the deuterated alkylidene in quantitative yield as a red/brown solid. A singlet (corresponding to the alkylidene deuteron) was observed at δ 20.00 ppm in the ^2H NMR spectrum (d_4-MeOH). ^1H, ^{13}C, and ^{31}P NMR spectra for this compound were identical to alkylidene **1**, with the following exceptions: In the ^1H NMR spectrum, no alkylidene resonance was observed. In the ^{13}C NMR spectrum, the expected C-D coupling at the alkylidene carbon of **1-D** was observed (500 MHz, CD_3OD, 301.89 ppm, J = 19.4 Hz), although peaks were broad and the splitting pattern for this resonance was additionally complicated by unresolved coupling to phosphorus. This carbon resonance sharpened considerably upon analysis by deuterium-decoupled ^{13}C NMR spectroscopy. High-resolution FAB MS: calculated for [M-Cl^-], 868.3648; found, 868.3646. The observed isotopic abundance for the corresponding [M-Cl^-] peaks identically matched the predicted isotope pattern for the [M-Cl^-] fragment of the title compound.

Kinetic Investigation of Alkylidene Proton-Deuteron Exchange. Reactions for kinetic studies were performed in NMR tubes capped with rubber septa. All reactions were conducted at a constant temperature of 30.0 °C (with the exception of the reactions used to obtain activation parameters), and all reactions were performed at constant volume (500 μL) and catalyst concentration (0.022 M). Reactions were conducted in the following general manner. In a dry box, alkylidene (0.011 mmol) was weighed into an NMR tube, dissolved in a desired amount of CD_3OD (from 0-500 μL), and the NMR tube was capped with a rubber septum. The NMR tube was removed from the dry box, wrapped with parafilm, and lowered into the NMR probe (preheated at 30 °C) for 2 minutes to allow the solution of alkylidene to reach thermal equilibrium. The sample was ejected from the NMR probe, and a volume of D_2O (the amount necessary to bring the total volume of the reaction to 500 μL) was injected *via* gas tight syringe. The NMR tube was shaken vigorously and immediately lowered back into the NMR probe for data collection. The disappearance of the alkylidene proton resonances in these experiments was monitored by integrating the alkylidene proton versus methylene chloride as an internal standard or the ortho protons on the alkylidene substituent.

References and Notes

1) Mohr, B.; Lynn, D.M.; Grubbs, R.H. *Organometallics* **1996**, *15*, 4317.

2) As determined by ^{1}H, ^{13}C, and ^{31}P NMR spectroscopy.

3) Although it is possible that this result represents the observation of an [M-Cl+H] fragment resulting from protio-alkylidene **1**, the analysis of authentic **1** by FAB mass spectrometry from the same ionization matrix yielded the mass of the [M-Cl] ion, suggesting that the observed ionized species in the present FAB mass spectrometry experiment is also the [M-Cl] species and not the protonated [M-Cl+H] fragment. Unfortunately, this complex could not be examined by electron impact (EI) mass spectrometry.

4) Akerlof, G. *J. Am. Chem. Soc.* **1932**, *54*, 4125.

5) The rates of ion-ion and ion-dipole reactions are often significantly influenced by the dielectric constant of the reaction medium. As a result, many equations have been derived to correlate solvent dielectric constants with reaction rates. The rate constants for ion-ion reactions have been shown to vary with solvent dielectric according to the following equation proposed by Eyring and Laidler:

$$\frac{\partial \ln(k)}{\partial (1/D)} = \frac{-\varepsilon^2 Z_a Z_b}{krT}$$

where Z_a and Z_b are the effective nuclear charges on reactants A and B. By this relationship, it is expected that a plot of ln(k) vs 1/D for the rate constants of an ion-ion reaction should yield a linear relationship. The sign of the slope of the line resulting from this relationship often conveys information about the charges of the reacting species. For example, the reaction between a negatively-charged molecule (Z_a is negative) and a positively charged molecule (Z_b is positive) would yield a line with a positive slope. The negative correlation observed in Figure 4 reveals that the rate-determining step in the alkylidene proton-deuteron exchange reaction likely

occurs between either two positively-charged or two negatively-charged species. A similar equation has been derived to describe ion-dipole reactions. These reactions, however, generally yield positive correlations and were discounted in view of the data in Figure 4. A more detailed explanation of these concepts is beyond the scope of this thesis. Interested readers can find a more detailed analysis in: a) Laidler, K.J. *Chemical Kinetics*, Harper and Row: New York, **1987**.

6) a) Renard, E.; Justice, J-C. *Journal of Solution Chemistry* **1974**, *3*, 633. b) Justice, M-C.; Justice, J-C.; Kay, R.L. *Journal of Solution Chemistry* **1990**, *19*, 1211.

7) M.S. Sanford, R.H. Grubbs. 1999, Unpublished results.

8) a) For examples of amphiphilic carbenes and the reaction of ruthenium alkylidenes with strong acids, see: a) Casey, C.P.; Vosejpka, P.C.; Askham, F.R. *J. Am. Chem. Soc.* **1990**, *112*, 3713. b) Clark, G.R.; Hoskins, S.V.; Jones, T.C.; Roper, W.R. *J. Chem. Soc., Chem. Commun.* **1983**, 719. c) Brothers, P.J.; Roper, W.R. *Chem. Rev.* **1988**, *88*, 1293.

9) Chang, S.; Jones, L.; Wang, C.M.; Henling, L.M.; Grubbs, R.H. *Organometallics* **1998**, *17*, 3460.

10) T. Rolle and R.H. Grubbs. 1999, Unpublished results.

11) (a) Schwab, P.E.; France, M.B.; Grubbs, R.H.; Ziller, J.W. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 2039. (b) Schwab, P.E.; Grubbs, R.H.; Ziller, J.W. *J. Am. Chem. Soc.* **1996**, *118*, 100.

12) See Chapter 4 of this thesis.

Chapter 6

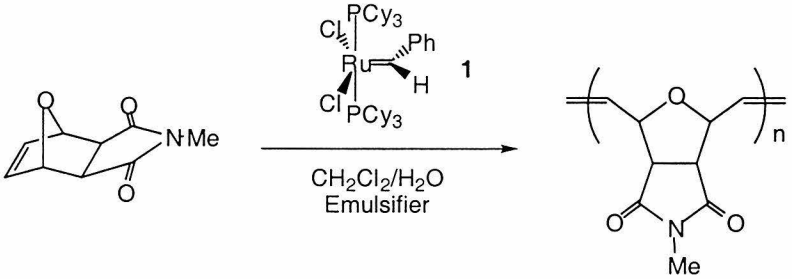
Living Ring-Opening Metathesis Polymerization in Water[†]

ABSTRACT: This chapter describes the application of alkylidenes **2** and **3** to the ring-opening metathesis polymerization (ROMP) of strained, cyclic olefins in water. Both alkylidenes **2** and **3** initiated the ROMP of water-soluble monomers **4** and **5** in aqueous solution. However, the propagating species in these reactions were observed to decompose prior to complete consumption of monomer. In the presence of a Brønsted acid, polymerization was observed to be rapid and quantitative, and alkylidenes **2** and **3** were found to initiate the *living* polymerization of these monomers. Furthermore, both chain termination and chain transfer reactions were demonstrated to be absent on the time scale of the polymerizations. The stabilities of the propagating species in these reactions were quantified spectroscopically, and this living polymerization protocol could be used to synthesize water-soluble block copolymers. The effect of the acid in these systems was proposed to be twofold—in addition to eliminating hydroxide ions, which would cause catalyst decomposition, catalyst activity was enhanced by protonation of phosphine ligands.

Introduction

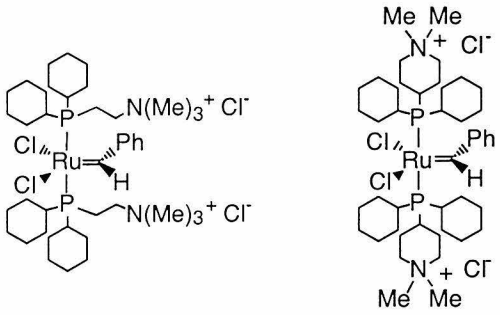
The development of polymerization systems that are living[1] in water and capable of polymerizing water-soluble monomers, represents a formidable challenge in synthetic polymer chemistry. For example, the addition of water to traditional living anionic or cationic systems results in rapid termination.[1a] The benefits of performing polymerization reactions in water are numerous,[2] and the development of living aqueous polymerization techniques would allow the controlled synthesis of water-soluble polymers from either water-soluble or water-insoluble monomers. Additionally, such systems would afford precise control over the composition of highly-functionalized, water-soluble block copolymers for use in biomedical and other applications.[3]

The advent of late transition metal catalysts which are tolerant of polar and protic functionalities has resulted in recent advances toward this goal. For example, Chapter 2 of this thesis described the application of a water-tolerant ruthenium alkylidene complex (**1**) to the ring-opening metathesis polymerization (ROMP) of strained, cyclic alkenes in aqueous environments (Eq 1).[4a] This methodology has recently been applied to the polymerization of water-soluble, carbohydrate-functionalized norbornene derivatives to produce a variety of new glycopolymers having biological activities.[4b,c] Additionally, Novak has described a nickel allyl initiator which polymerizes isocyanides in a living manner in the presence of water.[4e,f] Finally, advances made in the transition metal mediated "living"/controlled polymerization of vinyl monomers have yielded systems which are well-behaved in aqueous environments.[4d]



(Eq 1)

Although these examples represent significant advances toward entirely aqueous polymerization systems, the transition metal catalysts themselves are insoluble in water and the polymerization reactions basically occur in "wet" organic phases (as described Chapter 2). Chapter 4 described the synthesis of new ruthenium alkylidenes **2** and **3** which bear two water-soluble phosphine ligands. These new alkylidenes are completely soluble in both methanol and water, and initiate olefin metathesis reactions in these solvents.



2 **3**

This chapter details the application of complexes **2** and **3** to the ROMP of strained, cyclic monomers in aqueous solution. The chapter begins with a brief analysis of factors controlling the stabilities of **2** and **3**, and describes a method for the activation of these complexes toward polymerization employing Brønsted acids. The chapter concludes with the first examples of living polymerizations taking place in entirely aqueous solution, and details the synthesis of water-soluble polymers and block copolymers.

Results and Discussion

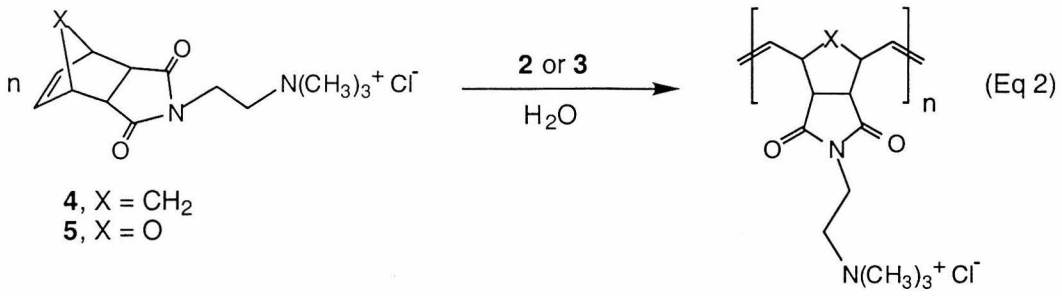
The aqueous ROMP of strained, cyclic olefins initiated by Group VIII salts and coordination complexes is well-documented.[5] As described in Chapter 1, these complexes do not contain preformed alkylidene fragments, and generally initiate polymerization poorly and inefficiently. For example, in reactions employing $RuCl_3$ it has been estimated that fewer than 1% of the metal centers are converted to catalytically-active species over the course of the reaction. As a result, the properties of polymers produced in these systems generally vary considerably from reaction to reaction, and these aqueous polymerizations

are not living. In contrast to "classical" catalysts, however, water-soluble alkylidenes **2** and **3** *do* contain preformed alkylidene fragments and initiate olefin metathesis rapidly and quantitatively.[6] This dramatic increase in initiation efficiency prompted an investigation into the potential of alkylidenes **2** and **3** to initiate *living* ROMP in entirely aqueous solution.

Initial Studies

Preliminary experiments demonstrated that alkylidenes **2** and **3** served as efficient initiators for the ROMP of a variety of functionalized norbornenes and 7-oxanorbornene derivatives in water, methanol, and in aqueous emulsions (as described in Chapter 4). Initiation occurred rapidly and quantitatively in these reactions, as determined by the quantitative conversion of the initiating benzylidenes to broad upfield alkylidene resonances (≈ 19.2 ppm) in the ^{1}H NMR spectrum of these reactions. The observation of propagating alkylidenes in these aqueous polymerizations was immediately significant, because propagating species had never been observed for polymerizations initiated by "classical" ruthenium complexes. Importantly, the direct observation of propagating species in these reactions allowed the extent of chain termination to be addressed spectroscopically throughout the course of the reaction.

It quickly became evident that the propagating species in the above reactions decomposed before polymerization was complete. For example, in the ROMP of water-soluble monomers **4** and **5** (Eq 2), conversions ranging from 45-80% were observed in aqueous and methanol solutions under a variety of experimental conditions. The color of these polymerization reactions progressed from a light orange color, indicative of the propagating species, to a dark orange color, and a propagating alkylidene was no longer observed by ^{1}H NMR spectroscopy. The polydispersity indices (PDIs) for the polymers produced were broad (Figure 1, PDI ≈ 2.3). Molecular weights were lower than anticipated, and these polymerizations could not be considered living.



4, X = CH_2
5, X = O

(Eq 2)

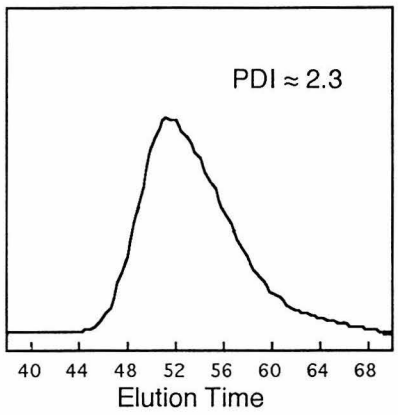


Figure 1: Aqueous GPC trace of poly-**4** initiated by alkylidene **2** in H_2O at 45 °C.

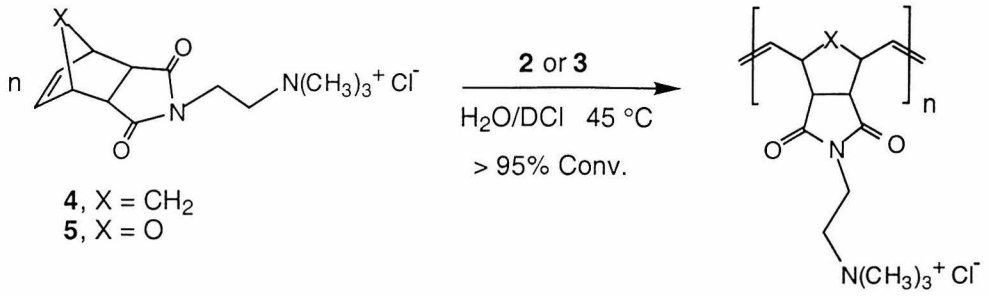
Activation of Alkylidenes **2** and **3**

During previous work with "classical" ruthenium catalysts in water, it was discovered that initiation periods for these complexes were shorter at lower pH, and that catalyst deactivation occurred rapidly in alkaline solution.[7] Consistent with these earlier observations, it was found that the presence of hydroxide ions in aqueous solutions of **2** and **3** also promoted the rapid decomposition of these well-defined alkylidene species. For example, the addition of one equivalent of NaOD to alkylidene **2** in D_2O resulted in an instantaneous change in the color of the reaction solution from red/orange to dark orange. Further examination of this reaction *via* ^1H NMR spectroscopy suggested that NaOD reacted stoichiometrically with **2** to yield a new, non-alkylidene species which then underwent rapid decomposition to a mixture of products. The nature of this reaction and the identity of this new non-alkylidene species was not determined.

The observed color change upon addition of NaOD in the above reaction was interesting, however, as a similar progression from light orange to dark orange was also observed in the later stages of the polymerization of monomers **4** and **5** (as described above). This observation suggested that the low yields and observed catalyst deactivation during these reactions could potentially be due to the presence of adventitious hydroxide ions. In these systems, hydroxide ions could be generated from the autoprotolysis of water or from the basic nature of the phosphines employed. In an attempt to eliminate small concentrations of hydroxide ions, we began to investigate the polymerization of monomers **4** and **5** in the presence of Brønsted acids.

For several reasons, deuterium chloride (DCl) in D_2O was chosen as the Brønsted acid used in subsequent experiments. First, alkylidenes **2** and **3** undergo facile anionic ligand exchange reactions in aqueous solutions (as described in Chapter 4). Because the activities of these catalysts could be directly influenced by these ligand exchange reactions, DCl, having only a Cl^- anion, was chosen in order to minimize the impact of potential counterion exchange processes. Additionally, stock solutions of DCl/D_2O are commercially available and are well-suited for use in ^1H NMR studies. Finally, DCl is a strong acid (pK_a = -8) and is completely dissociated in aqueous solution. Thus, precise concentrations of protons (deuterons) could be delivered to polymerization systems without regard to the equilibria governing the dissociation of weaker acids.

It was found that monomers **4** and **5** could be *quantitatively* polymerized when small amounts of DCl (from 0.3 to 1.0 equivalent relative to alkylidene complexes **2** or **3**) were added to the reaction mixture (Eq 3).



4, X = CH_2
5, X = O

(Eq 3)

Additionally, the presence of acid was found to have a profound effect on polymerization rates: polymerizations were up to ten times faster than those to which no acid had been added. More significantly, two propagating alkylidene species were observed by ^{1}H NMR spectroscopy (at room temperature) both *during* polymerization and *after* complete consumption of monomer (the nature of the two propagating species observed in these reactions will be discussed below). The PDIs of polymers produced in the presence of acid were considerably lower (Figure 2, PDI = 1.24) than the PDIs of polymers synthesized in the absence of acid (Figure 1, PDI ≈ 2.3). The injection of additional monomer into these completed polymerization reactions resulted in further quantitative polymerization, suggesting that these polymerizations could be living.

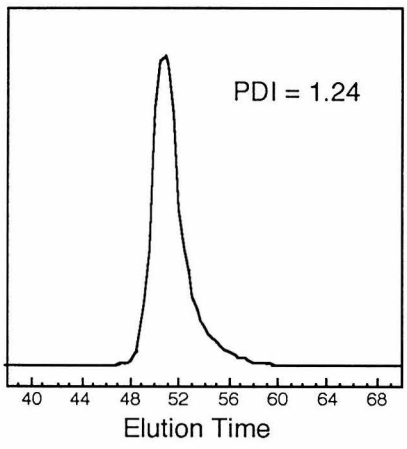
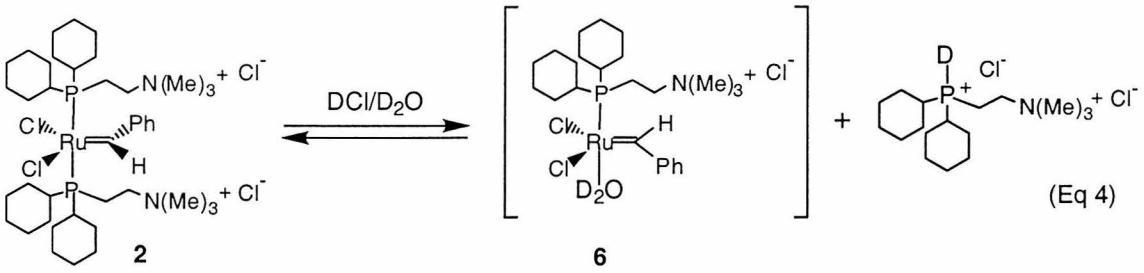


Figure 2: Aqueous GPC trace of poly-**4** initiated by alkylidene **2** in D_2O in the presence of 1.0 equivalent of DCl at 45 °C (Mn = 11,500, PDI = 1.24).

Spectroscopic Analysis of Activated Alkylidenes

In order to better understand the role of the acid in the above reactions, the reaction of DCl with alkylidene **2** was studied in the absence of monomer. The addition of 0.3 equivalents of DCl to a solution of complex **2** in D_2O generated 0.3 equivalents of a new alkylidene species (**6**), in addition to the parent alkylidene (Eq 4). New alkylidene **6** was not isolated, but was identified *via* ^1H and ^{31}P NMR spectroscopy as a monophosphine derivative of **2**.



A resonance for the alkylidene proton of new alkylidene **6** was observed in the ^1H NMR spectrum at 20.12 ppm (d, J_{PH} = 12.0 Hz), slightly downfield of that of alkylidene **2** (s, 19.76 ppm). Additionally, the resonances for the protons on the phenyl group were shifted approximately 0.1 ppm downfield. These data indicated that the added acid did not react irreversibly with the ruthenium-carbon bond, but rather reacted with **2** to yield a new alkylidene species. Examination of this reaction by ^{31}P NMR spectroscopy indicated that the acid protonated an equivalent of phosphine to yield a new alkylidene species and an equivalent of a phosphonium salt (Eq 4). The phosphonium salt generated *in situ* was identified through comparison to spectroscopic data characteristic of the independently synthesized material. A resonance observed at 46.18 ppm in the ^{31}P NMR spectrum was assigned as alkylidene **6**. The structure of alkylidene **6** is assumed to be that shown in Eq 4, in which the alkylidene substituents are perpendicular to the Cl-Ru-Cl plane, based on the observation of phosphorus coupling to the alkylidene proton in the ^1H NMR spectrum of this complex (d, J_{PH} = 12.0 Hz).

A well-known reaction pathway for the decomposition of transition metal alkylidenes is bimolecular coupling to generate an internal olefin and a dimeric metal-containing species.[8] For ruthenium alkylidenes of the type $(PR_3)_2Cl_2Ru{=}CHR$, this type of bimolecular coupling is sterically discouraged by the two coordinated phosphine ligands which surround the alkylidene moiety.[9] Considering this, it might be anticipated that a monophosphine complex, having a more sterically-accessible metal center, would be predisposed to rapid bimolecular decomposition. Indeed, this has been observed for alkylidenes such as **1** in organic solution in the presence of phosphine scavengers such as $CuCl_2$.[10]

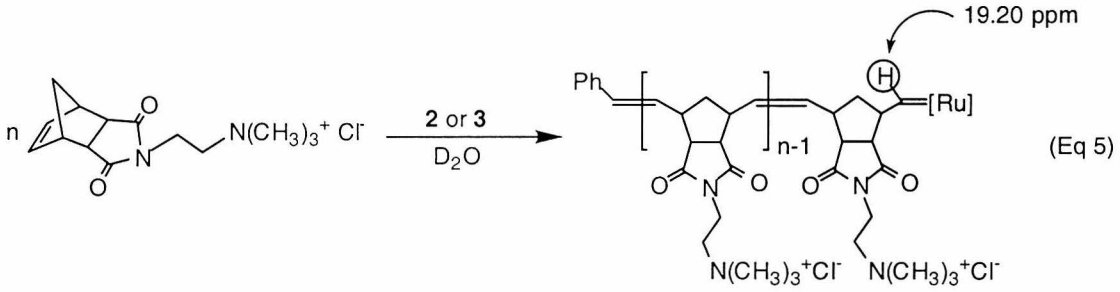
Surprisingly, accelerated decomposition was not observed upon the protonation of phosphine in aqueous solution. The monophosphine species formed upon addition of 0.3 equivalents of DCl in the above reaction was remarkably stable—addition of excess phosphine to the reaction mixture up to 1.5 hours after the addition of acid reversed the equilibrium in Eq 4, regenerating alkylidene **2** with less than 5% detectable decomposition. In these aqueous systems, it is believed that the coordination of water molecules to the monophosphine species stabilizes the alkylidene and prevents bimolecular decomposition. The coordination of water would yield a potentially more stable, sterically-protected 16- or 18-electron species, although no direct evidence for this type of water coordination has been observed.

The addition of 1.0 equivalent of DCl to alkylidene **2** yielded an equilibrium mixture of monophosphine and bisphosphine alkylidene species in a ratio of 1:2. The reasons for this nonstoichiometric protonation behavior were not fully understood, and both alkylidenes decomposed more rapidly under these conditions in the absence of monomer. In the presence of monomer, however, the propagating bisphosphine and monophosphine propagating species were *significantly* more stable than the respective initiating species **2** or **3**. For example, alkylidene **2** decomposes in aqueous solution over a period of days at room temperature. However, both the bisphosphine (**2**) and

monophosphine (**6**) propagating species in polymerization reactions to which acid had been added could be observed for *over three months*. In addition to the relatively reduced concentration of the monophosphine species dictated by the equilibrium in Eq 4, stability toward bimolecular decomposition was presumably imparted *via* the relative steric bulk of the propagating alkylidene.

Experimental Determination of Living Polymerizations

The results above suggested that the aqueous polymerizations carried out in the presence of acid could indeed be living. In order to determine experimentally that a polymerization is living, propagation must be shown to take place in the absence of termination and chain transfer reactions.[1,11] To assess the living character of these polymerizations, an NMR-scale polymerization of monomer **4** was conducted in D_2O employing DCl (1.0 equivalent relative to alkylidene), and the relative amount of propagating species was quantified *via* integration of the alkylidene protons against the aromatic protons of the polymer endgroups (Eq 5).



(Eq 5)

As previously described, two propagating species, corresponding to bisphosphine alkylidene **2** and monophosphine alkylidene **6**, were observed for acid-activated polymerization reactions initiated by alkylidene **2** at room temperature. The ^{1}H NMR resonances for these two alkylidenes coalesced at higher temperatures, however, indicating rapid equilibration *via* phosphine scrambling. Accordingly, the above NMR-scale experiment was carried out at 45 °C, as the resonances for the two propagating alkylidene

species were observed as a single broad resonance at 19.2 ppm at this temperature. After 15 minutes, the reaction was >95% complete and the relative integration of the alkylidene protons of the propagating species did not decrease either during the reaction or after all monomer had been consumed (Figure 3).[12] In fact, the propagating species remained intact for an additional 15 minutes (at this temerature) in the absence of monomer before beginning to slowly decompose. The stability of the propagating species for alkylidene **3** upon addition of acid was demonstrated in a similar manner.

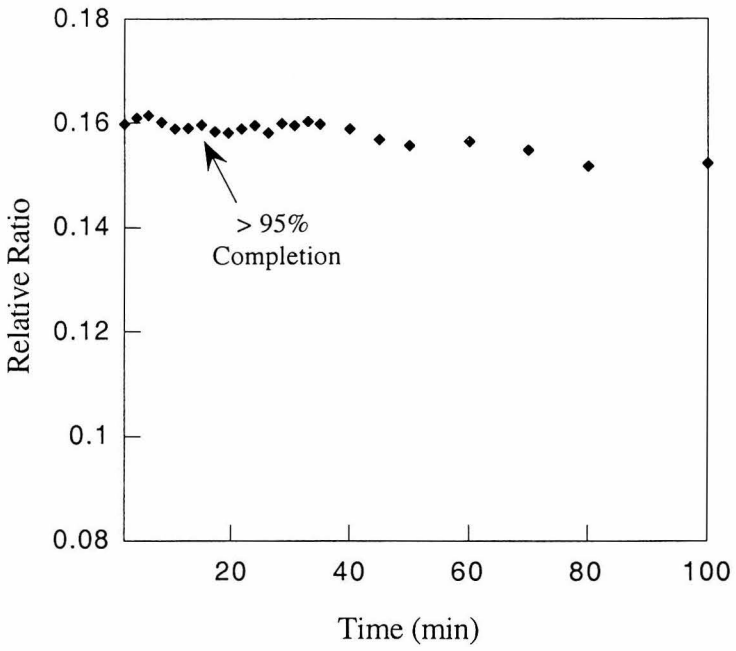
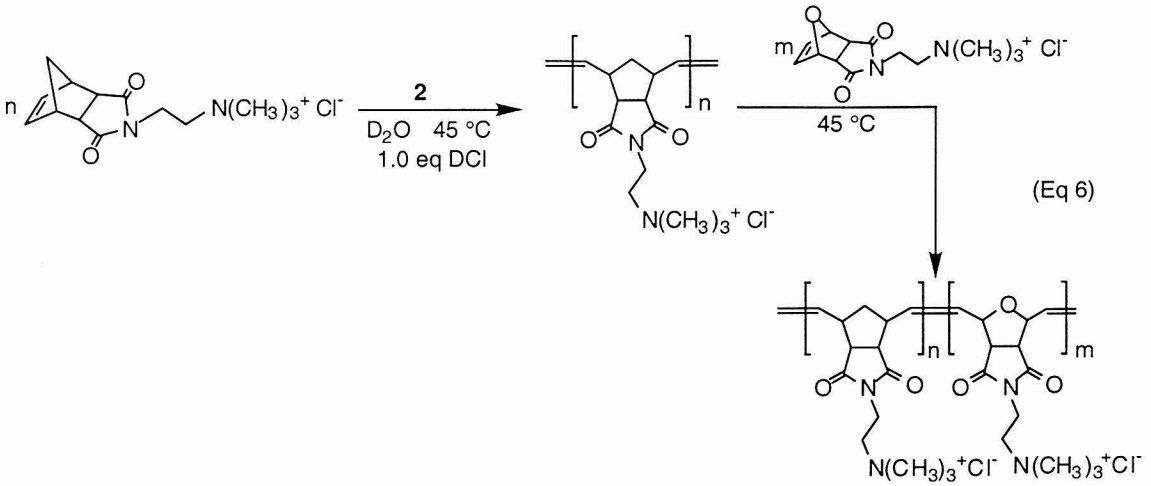


Figure 3: Ratio of the propagating alkylidene (relative to polymer endgroups) over time for the polymerization of monomer **4** initiated by **2** at 45 °C in D_2O in the presence of 1.0 equivalent of DCl. The arrow indicates the time at which the polymerization was complete by ^1H NMR.

A block copolymerization of monomers **4** and **5** was carried out *via* sequential monomer addition to further demonstrate the robust nature of the propagating species in these reactions. After complete polymerization of monomer **4**, 20 equivalents of monomer **5** were injected. Monomer **5** was rapidly and completely consumed (Eq 6). The concentration of the propagating species remained constant both during and after the

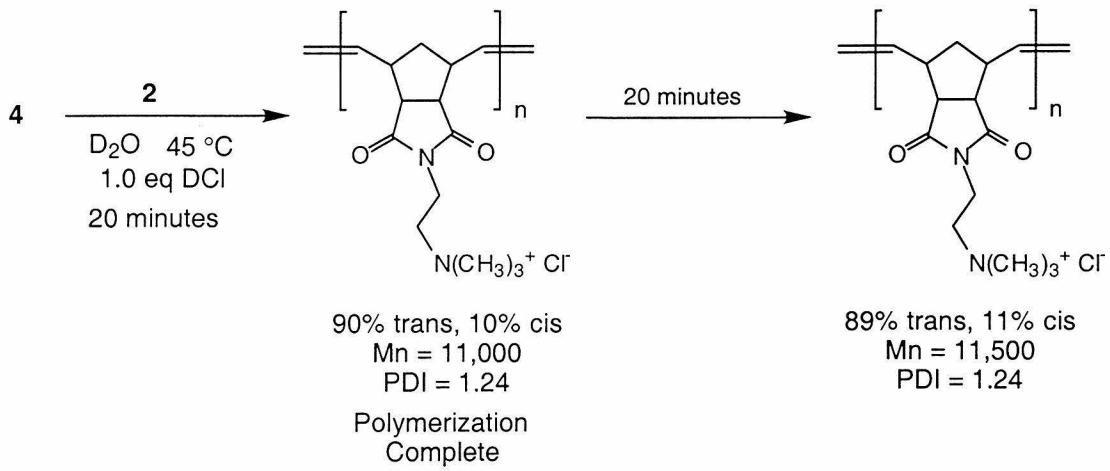
polymerization of the second block (as determined by ^{1}H NMR spectroscopy), again highlighting the robust nature of the propagating species under these conditions.



Within the limits of NMR sensitivity, the direct observation and quantification of the propagating alkylidenes in the above experiments demonstrated the absence of chain termination in these reactions. The fact that the alkylidene resonances did not disappear over a time period twice as long as the time scale of the reaction indicated that these systems were indeed living. The above experiments did not, however, provide information regarding the absence of *chain transfer* reactions on the time scale of the polymerization.

To demonstrate the absence of chain transfer in these reactions, the polymerization of monomer **4** was initiated by alkylidene **2** in the presence of 1.0 equivalent of DCl, and the PDI of the resulting polymer was determined by gel permeation chromatography (GPC) at various points in the reaction. As shown in Scheme 2, monomer **4** was polymerized quantitatively over a period of 20 minutes, and an aliquot of the reaction mixture was removed for analysis. The reaction was allowed to stand for an additional 20 minutes before polymerization was terminated. The PDI obtained for the initial aliquot was 1.24, and the PDI did not broaden upon standing. The lack of broadened PDIs in this experiment demonstrates the relative absence of chain transfer reactions on the time scale of the polymerization reaction. Additionally, the ratio of *trans* to *cis* olefins in the backbone of the

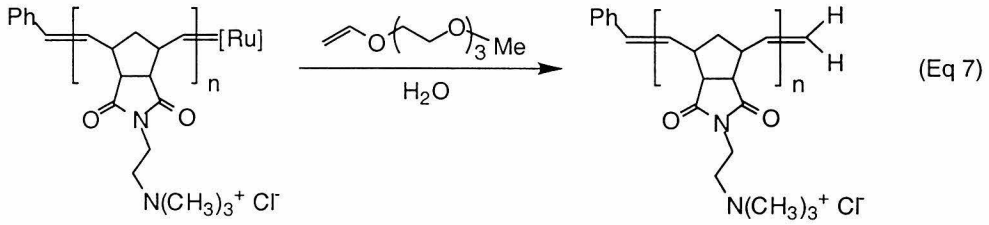
polymer (as determined by ^{1}H NMR integration) remained constant over the entire reaction period (Scheme 2), providing further evidence for the absence of chain transfer reactions that would eventually result in thermodynamic equilibration.



Scheme 1: Experiment demonstrating the absence of chain transfer reactions in the polymerization of monomer **4** initiated by alkylidene **2** in the presence of DCl.

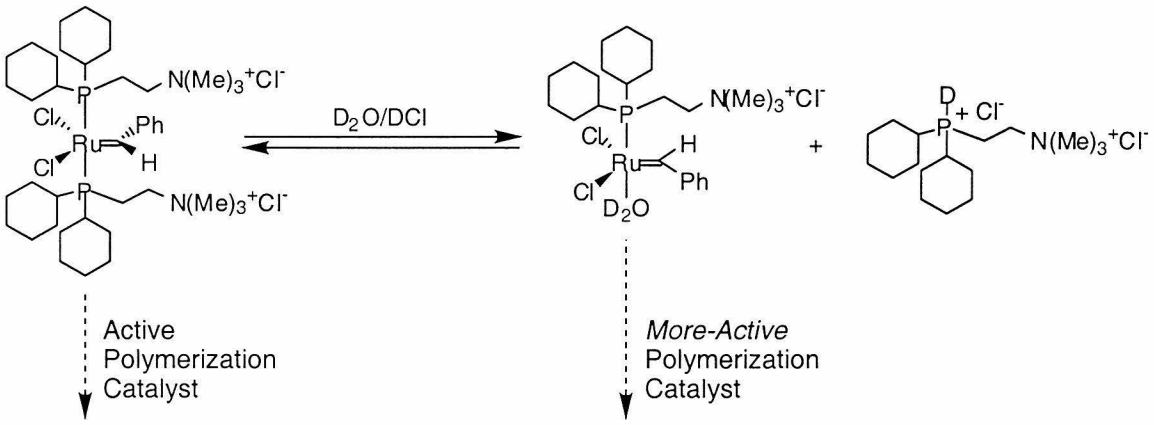
Termination of Aqueous Polymerizations

Ethyl vinyl ether has been used as an effective terminating reagent for living ROMP initiated by alkylidene **1** in organic solvents.[13] This reagent could not be applied to the termination of the aqueous living polymerizations described above, however, because ethyl vinyl ether is insoluble in water. As described in Chapter 4, alkylidenes **2** and **3** react with tri(ethylene glycol) methyl vinyl ether in aqueous solution to yield an analogous Fischer-carbene complex. Treatment of the living polymerization reactions shown in Eq 3 with an excess of this water-soluble vinyl ether quantitatively terminated polymerization and endcapped these water-soluble polymers with a methylene (=CH_2) moiety (Eq 7).



Brønsted Acids as Phosphine Scavengers

The equilibrium presented in Eq 4 provides a convenient explanation for the rate enhancements, and thus the living nature, of the polymerizations described above. For alkylidene complexes of the type $(PR_3)_2Cl_2Ru=CHR$, olefin metathesis has been shown to proceed through a mechanism in which a phosphine dissociates from the metal center.[10] Rates of olefin metathesis in organic systems have been increased by the addition of phosphine scavengers, although the catalysts rapidly decompose under these conditions. In analogy to organic systems, protons appear to act as phosphine scavengers in aqueous polymerizations employing alkylidenes **2** and **3** (Scheme 2). In these systems, the rate of olefin metathesis is increased *without* concomitant acceleration of catalyst decomposition. The differences in the rates of propagation and termination under acidic conditions allows for rapid, quantitative conversion of monomer in a living manner.



Scheme 2: Activation of alkylidene **2** by addition of DCl.

It should be noted that the activation of alkylidenes **2** and **3** with strong acids should not preclude application to the ROMP of acid-sensitive monomers. The stoichiometric amount of acid initially added to the alkylidene complex reacts to form a phosphonium salt, and acid-labile monomers could theoretically be added to this significantly less-acidic solution of activated catalyst to effect polymerization.

Summary

This chapter described the application of alkylidenes **2** and **3** to the ROMP of strained, cyclic olefins in water. Both alkylidenes **2** and **3** initiated the ROMP of water-soluble monomers **4** and **5** in aqueous solution. However, the propagating species in these reactions were observed to decompose prior to complete consumption of monomer. In the presence of a Brønsted acid, polymerization was rapid and quantitative, and alkylidenes **2** and **3** were found to initiate the *living* polymerization of these monomers. The effect of the acid in these systems was proposed to be twofold—in addition to eliminating hydroxide ions, which would cause catalyst decomposition, catalyst activity was enhanced by protonation of phosphine ligands. Remarkably, the acid did not react with the ruthenium alkylidene bond. Both chain termination and chain transfer reactions were demonstrated to be absent on the time scale of the polymerizations, indicating that these polymerizations satisfied the criteria for living systems. These systems represent the first examples of living polymerization reactions taking place in homogeneous aqueous solution.

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Experimental Section

General Considerations. All manipulations and reactions involving ruthenium alkylidenes were performed in a nitrogen-filled dry box or by using standard Schlenk techniques under an atmosphere of argon. Distilled deionized water and reagent grade methanol were used for the polymerizations, and were rigorously degassed by purging with argon and stirring under high vacuum prior to use. Solutions of DCl in D_2O were

purchased from Cambridge Isotopes and were transferred and diluted using Schlenk techniques. All other reagents were used without further purification unless otherwise noted. Ruthenium carbene complexes **2** and **3** were prepared as previously reported.[6] Argon was purified by passage through columns of BASF R3-11 catalyst (Chemalog) and 4 Å molecular sieves (Linde). ^{1}H NMR (300.1 MHz) and ^{13}C NMR (75.49 MHz) spectra were recorded on a GE QE-300 spectrometer, ^{31}P NMR (161.9 MHz) spectra were recorded on a JEOL GX-400 spectrometer. All chemical shift values are given in ppm and are referenced with respect to residual protons in the solvent for proton spectra, or to phosphoric acid for phosphorus spectra. GPC measurements were made by Dr. Rudolf Bruessau at BASF AG Ludwigshafen. Molecular weights are reported versus pullulan standards.

***exo*-N-(N',N'-dimethylammonio)ethyl-bicyclo[2.2.1]hept-5-ene-2,3-dicarboximide.** *Exo*-bicyclo[2.2.1]hept-5-ene-2,3-dicarboxylic anhydride (1.0 g, 6.09 mmol) and N,N-dimethylethylenediamine (0.537 g, 6.09 mmol) were dissolved in benzene (50 mL) in a round bottom flask equipped with a Dean-Stark apparatus and a condenser, and the solution was heated at 110 °C for 12 hours. Upon cooling to room temperature, the solvent was removed *in vacuo*. The solid product was dissolved in water, acidified, and extracted 5 times with ether (30 mL). The aqueous layer was then neutralized with sodium bicarbonate and extracted 5 times with ether (30 mL). Ether was removed *in vacuo* to yield 0.96 g of a white powder (67% yield). ^{1}H NMR ($CDCl_3$): δ 6.23 (s, 2H), 3.55 (t, J = 6.45 Hz, 2H), 3.21 (s, 2H), 2.64 (s, 2H), 2.45 (t, J = 6.45 Hz, 2H), 2.20 (s, 6H), 1.40 (dd, J = 1.2 Hz, J = 6.9, 2H). ^{13}C NMR ($CDCl_3$): δ 178.75, 138.39, 56.53, 48.36, 45.76, 45.86, 43.18, 36.96. Anal. Calc., C: 66.65, H: 7.74, N: 11.95. Found, C: 66.39, H: 7.62, N: 12.10.

***exo*-N-(N',N',N'-trimethylammonio)ethyl-bicyclo[2.2.1]hept-5-ene-2,3-dicarboximide chloride (4).** *exo*-N-(N',N'-dimethylammonio)ethyl-bicyclo[2.2.1] hept-5-ene-2,3-dicarboximide (1.2 g, 5.12 mmol) was dissolved in THF (20 mL) and treated with 5 equivalents of methyl iodide at room temperature. The resulting white precipitate was filtered, washed liberally with THF, and dried under vacuum to yield the title compound as an iodide salt. Iodide/chloride ion exchange as previously described[6] afforded **3** as a white flaky solid (98% yield). ^{1}H NMR (CD_3OD): δ 6.38 (s, 2H), 4.0 (t, J = 7.05 Hz, 2H), 3.54 (t, J = 7.2 Hz, 2H), 3.25 (s, 2H), 3.22 (s, 9H), 2.90 (s, 2H), 1.37 (dd, J = 9.9 Hz, J = 9.9 Hz, 2H). ^{13}C NMR (CD_3OD): δ 177.53, 137.26, 61.86, 52.29, 47.54, 44.73, 42.07, 31.60. HRMS (FAB), *m/z* for M^+ ion Calc., 249.1603. Found, 249.1605.

***exo*-N-(N',N'-dimethylammonio)ethyl-7-oxabicyclo[2.2.1]hept-5-ene-2,3-dicarboximide.** *Exo*-7-oxabicyclo[2.2.1]hept-5-ene-2,3-dicarboxylic anhydride (5.0 g, 30.01 mmol) and N,N-dimethylethylenediamine (2.65 g, 30.01 mmol) were dissolved in benzene (1000 mL) in a round bottom flask equipped with a Dean-Stark apparatus and a condenser, and the solution was heated at 110 °C for 18 hours. Upon cooling to room temperature, the solvent was removed *in vacuo*, and the resulting residue was recrystallized from hexanes to yield the title compound as a fluffy white crystalline solid (2.50 g, 35% yield). ^{1}H NMR ($CDCl_3$): δ 6.48 (s, 2H), 5.23 (s, 2H), 3.57 (t, J = 6.75 Hz, 2H), 2.84 (s, 2H), 2.45 (t, J = 6.0 Hz, 2H), 2.23 (s, 6H). ^{13}C NMR (CD_3OD): δ 175.89, 136.247, 80.59, 55.89, 47.20, 45.14, 36.57. Anal. Calc., C: 61.01, H: 6.83, N: 11.85. Found, C: 60.47, H: 6.85, N: 11.89.

***exo*-N-(N',N',N'-trimethylammonio)ethyl-7-oxabicyclo[2.2.1]hept-5-ene-2,3-dicarboximide chloride (5).** *exo*-N-(N',N'-dimethylammonio)ethyl-7-oxabicyclo[2.2.1]hept-5-ene-2,3-dicarboximide (1.2 g, 5.12 mmol) was dissolved in THF

(20 mL) and treated with 5 equivalents of methyl iodide at room temperature. The resulting white precipitate was filtered, washed liberally with THF, and dried under vacuum to yield the title compound as an iodide salt. Iodide/chloride ion exchange as previously described[6] afforded **4** as a white flaky solid (98% yield) ^{1}H NMR (CD_3OD): δ 6.56 (s, 2H), 5.19 (s, 2H), 3.94 (t, J = 6.0 Hz, 2H), 3.58 (t, J = 6.44 Hz, 2H), 3.18 (s, 9H), 3.00 (s, 2H). ^{13}C NMR (CD_3OD): δ 176.58, 136.34, 81.03, 62.28, 52.59, 52.50, 32.49. HRMS (FAB), *m/z* for M^+ ion Calc., 251.1396. Found, 251.1399.

General Polymerization Procedure. In a typical experiment, alkylidene **2** (5.0 mg, 0.055 mmol) and monomer **4** (30 mg, 0.011 mmol) were weighed into separate vials in a nitrogen-filled drybox. A stirbar was added to the vial containing **4**, and the vials were capped with rubber septa. Outside the drybox, **2** was dissolved in 250 μl of a rigorously degassed solution of HCl in H_2O (0.022M, an amount containing 1.0 eq of HCl relative to **2**), and monomer **4** was dissolved in degassed H_2O. The solution of **2** was quickly added to the vial containing **4** *via* syringe, and the reaction mixture was heated to 45 °C. Upon completion, the polymerization reactions were terminated by adding tri(ethylene glycol) methyl vinyl ether and precipitating the polymer from tetrahydrofuran, or were analyzed directly after evaporation of solvent.

References and Notes

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12) The slight deviation from the theoretical ratio of 0.2 observed in Figure 3 is also observed for complexes **2** and **3**, as well as other ruthenium carbene complexes.

13) For recent examples, see reference 4a and Weck, M.; Schwab, P.; Grubbs, R.H. *Macromolecules*, **1996**, *29*, 1789.

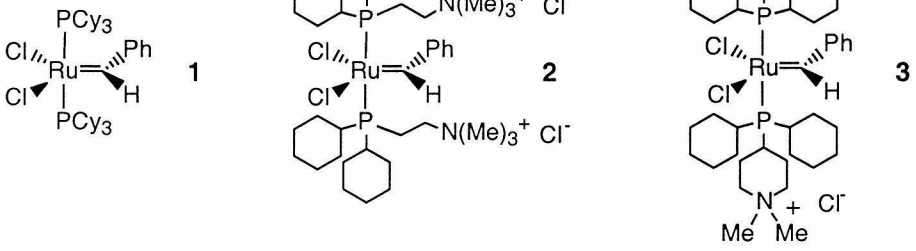
Chapter 7

Ring-Closing Metathesis in Methanol and Water[†]

ABSTRACT: This chapter describes the application of alkylidenes **2** and **3** to the ring-closing metathesis (RCM) of diene substrates in water and methanol. Alkylidenes **2** and **3** did not promote the RCM of α,ω-dienes due to the instability of the catalytically-active methylidene complexes in these reactions. However, substrates containing an internal olefin were readily cyclized. Alkylidene **3** was found to be a more active catalyst for RCM than alkylidene **2**. Several factors influenced the success of these cyclization reactions. In particular, the choice of olefin substituents was critical, as it directly impacted the stabilities and reactivities of the catalytic alkylidenes. These systems represent a metal-catalyzed carbon-carbon bond forming process which proceeds to high conversion in aqueous solution, and provides a framework for the application of RCM to more structurally-complex water-soluble substrates.

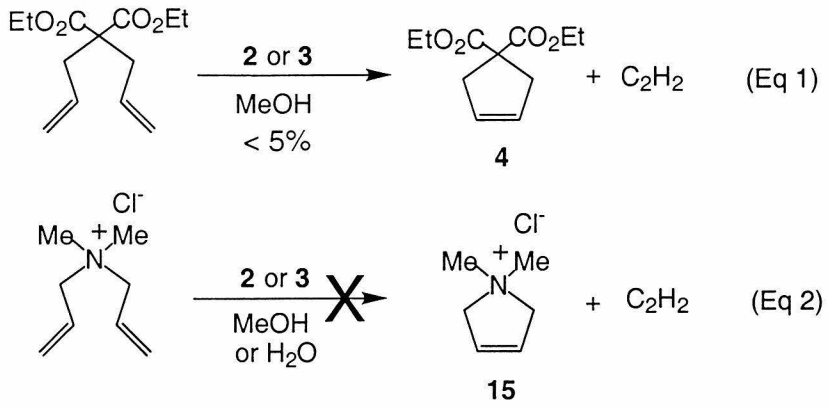
Introduction

Ring-closing metathesis (RCM) has emerged as a powerful method for the synthesis of highly-functionalized carbocycles and heterocycles.[1] Of the transition metal alkylidenes which initiate this reaction, ruthenium alkylidene **1** has become an important reagent for the cyclization of highly-functionalized substrates in organic solvents,[2] primarily because it remains active in the presence of numerous polar and protic functional groups. This complex is soluble in a variety of organic solvents, but is insoluble in protic solvents such as methanol and water (as described in Chapter 2).[3] This insolubility has prevented the application of RCM to the cyclization of water-soluble dienes and biologically-interesting substrates such as peptides and proteins.[2d] The transformation of unprotected substrates and the selective formation of carbon-carbon bonds in water has remained an important goal.[4]

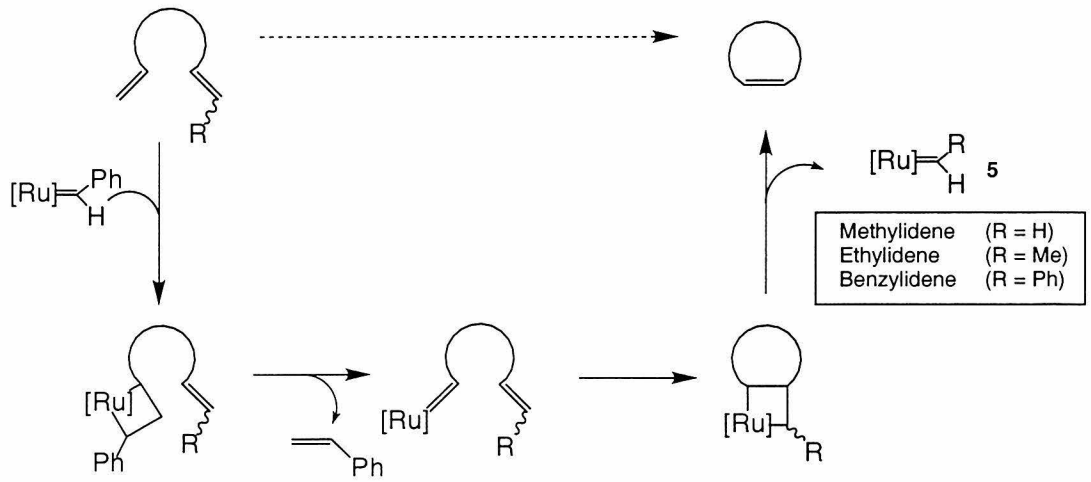


Chapter 4 outlined the synthesis[5] of water-soluble ruthenium alkylidenes **2** and **3** and the application[6] of these complexes to olefin metathesis in methanol and water. As previously described, initial attempts to probe the activities of **2** and **3** toward RCM centered upon the cyclization of α,ω-dienes such as diethyl diallylmalonate (Eq 1) and dimethyldiallylammonium chloride (Eq 2). Although alkylidene **1** catalyzes the cyclization of diethyl diallylmalonate to cyclopentene diester **4** rapidly and quantitatively in organic solvents, the cyclization of this substrate initiated by alkylidenes **2** or **3** in methanol generally proceeded in <5% yield (as determined by ^{1}H NMR spectroscopy).

Furthermore, the RCM of dimethyldiallylammonium chloride in either methanol or water did not yield observable product. Both alkylidenes, however, reacted rapidly and quantitatively with substrate in the above reactions, as determined by ^{1}H NMR.



As depicted in Scheme 1, the first catalytic turnover in the RCM of an α,ω-diene using an alkylidene of the type $(PR_3)_2Cl_2Ru$=CHPh generates one equivalent of styrene, one equivalent of cyclized product, and a new ruthenium methylidene (**5**, R = H). In subsequent turnovers, methylidene **5** re-enters the catalytic cycle through reaction with another equivalent of substrate; therefore, **5** is the true catalytic species in the RCM of α,ω-dienes.



Scheme 1: The first turnover step of RCM.

The methylidene complex derived from alkylidene **1** is stable under a variety of conditions in organic solvents. However, transition metal methylidenes are generally less-stable than otherwise analogous substituted alkylidenes, and the limited stability of transition metal methylidenes over the course of cyclization reactions is often a limiting factor in RCM.[7]

The instability of the methylidenes derived from alkylidenes **2** and **3** in protic solvents was addressed in detail in Chapter 4. As previously described, experiments investigating the activities of alkylidenes **2** and **3** with acyclic olefins in methanol and water suggested that *alkyl*-substituted alkylidenes of this type were significantly more stable than the corresponding methylidene species. In the RCM of a diene containing one internal olefin (Scheme 1, R ≠ H), metathesis occurs initially at the less hindered terminal olefin[8] and the olefin substituent is transferred to the alkylidene upon cyclization. This then generates a significantly more stable substituted catalytic species (**5**, R ≠ H) at the end of each catalytic cycle.

Because the limiting factor in cyclizations using **2** and **3** appeared to be methylidene instability, we hypothesized that the incorporation of internal olefins into diene substrates would facilitate RCM. This chapter describes the application of alkylidenes **2** and **3** to substrates of this type. The chapter begins with an analysis of olefin substituents and their affects on both alkylidene stabilities and reactivities toward RCM in methanol. The chapter concludes with the application of these strategies to the first examples of ring-closing metathesis in aqueous solution.

Results and Discussion

The modifications in substrate design described above had a profound effect on RCM initiated by alkylidenes **2** and **3**. For example, treatment of methyl-substituted diene **6** with 5 mol% **2** or **3** in methanol resulted in up to 60% conversion to cyclic diester **4** (Eq

3, Table 1). A catalytic ethylidene species was clearly observed by ^1H NMR spectroscopy throughout the course of these reactions.

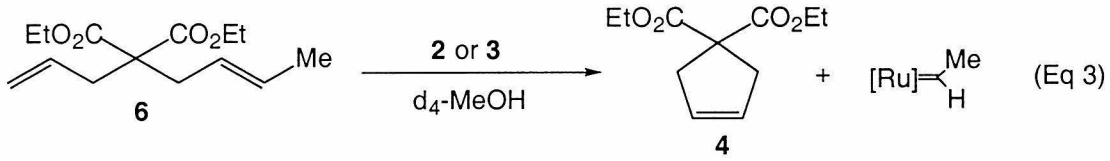
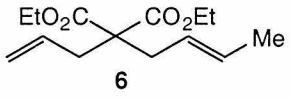
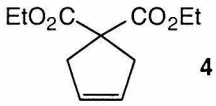
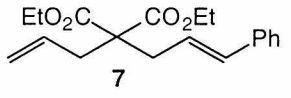
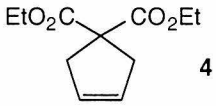
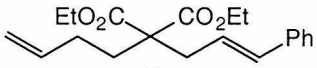
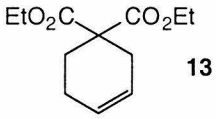
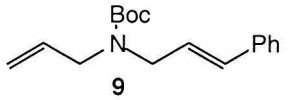
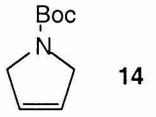
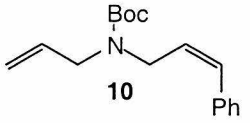
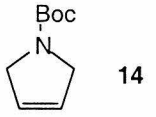
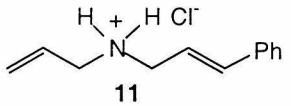
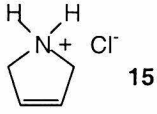
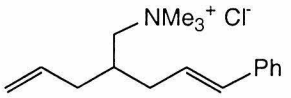
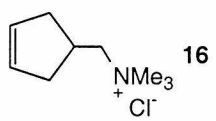


Table 1: RCM of functionalized dienes initiated by alkylidenes 2 and 3[a]

Substrate	Product	Solvent	Conversion[b,c]
 6	 4	MeOH	30% (**2**)[d] 60% (**3**)[d]
 7	 4	MeOH	80% (**2**) 95% (**3**)
 8	 13	MeOH	45% (**2**)[e] 55% (**3**)[e]
 9	 14	MeOH	40% (**2**) 90% (**3**)
 10	 14	MeOH	30% (**2**) >95% (**3**)
 11	 15	MeOH H_2O H_2O	75% (**2**) 10% (**2**) 5% (**3**)
 12	 16	MeOH H_2O H_2O	90% (**3**) 60% (**3**) 90% (**3**)[f]

[a]The following conditions were used unless otherwise noted: 5 mol% catalyst (**2** or **3**), 0.37M substrate, 45 °C. [b]Conversions were determined by ^1H NMR. [c]Number in parenthesis indicates catalyst used. [d]Substrate conc. = 0.24M. [e]Substrate conc. = 0.1M. [f]10 mol% **3** used.

The treatment of phenyl-substituted substrate **7** with alkylidene **2** resulted in 80% conversion to diester **4**, while cyclization proceeded nearly *quantitatively* in the presence of alkylidene **3** (Table 1). In this example, initiating benzylidenes **2** and **3** are actually regenerated in subsequent catalytic turnovers. The additional stability and reactivity of the catalytically-active benzylidene in these reactions, relative to the ethylidene in the Eq 3, resulted in greater activities, longer catalyst lifetimes, and higher conversions. The synthesis of a functionalized cyclohexene was also achieved *via* cyclization of diene **8**, although conversions were slightly lower.

These cyclizations proceeded cleanly to product, and conversions were limited only by catalyst decomposition—the reaction mixtures consisted primarily of product and unreacted starting material. It should be noted that while the incorporation of internal olefins alters the structure of the catalytically-active alkylidenes in these examples, the structure of the desired cyclized products remains unaffected.

As described in Chapter 3, the metathesis activities of alkylidenes of the type $(PR_3)_2Cl_2Ru{=}CHR$ are generally maximized by the coordination of large, electron-rich phosphines. Although the phosphines coordinated to alkylidenes **2** and **3** are sterically similar, the phosphines coordinated to **3** are considerably more electron-rich (as described in Chapter 3). Accordingly, alkylidene **3** has been predicted to be a more active catalyst than alkylidene **2.** While differences in the activities of these alkylidenes have not been particularly notable for ROMP, the cyclization reactions discussed above allow a qualitative assessment of their relative activities. For example, the treatment of substrate **7** with alkylidene **2** resulted in 30% conversion after 1.5 h, while the use of alkylidene **3** resulted in 85% conversion over the same time period. These results are in excellent accord with predictions made based on the differences in the steric and electronic character of these phosphines. Unfortunately, a quantitative assessment of catalyst activities could not be made because the catalysts steadily decompose during the course of these reactions.

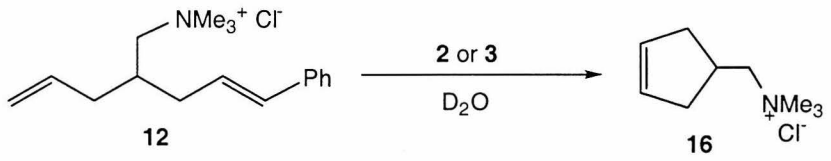
The geometry of the internal olefins in these substrates also had an impact on cyclization rates. For example, while the cyclization of *trans*-substituted substrate **9** with alkylidene **3** required 30 h to reach 90% conversion, the cyclization of *cis*-substituted derivative **10** proceeded *quantitatively* in 2 h (Table 1). This effect was not unexpected, as *cis*-substituted olefins generally coordinate to metal centers better than *trans*-olefins.[9] However, the dramatic rate increase observed using *cis*-olefins in this example may improve conversions in cases where cyclization is slow (such as in the cyclization of substrate **6** or in other larger ring systems).

RCM in Water

The cyclization of substituted diallylamine hydrochloride derivative **11** in methanol proceeded to pyrroline hydrochloride **15** in 75% conversion using catalyst **3** (Table 1). While conversions of this substrate in water were disappointingly low (5-10%), these reactions represented the first observation of a RCM reaction in aqueous solution. The cyclization of a *cis*-substituted analog yielded similar results, giving 15% conversion in the presence of catalyst **3**.

The reasons for the poor yields in these aqueous reactions remain unclear. It is possible that the acidic nature of these substrates could be responsible for low yields in these reactions. However, protons do not react to decompose these alkylidenes, and complexes **2** and **3** have been used to initiate ring-opening metathesis polymerization (ROMP) in the presence of acid (as described in Chapter 6). The failure of a dimethyl analog of **11** to cyclize under the same conditions suggests that electronic factors may be responsible for these low conversions. Presumably, the electron-withdrawing nature of the quaternary ammonium functionality deactivated these substrates. As shown in the last entry in Table 1, placing the ammonium functionality one methylene unit further from the olefins in substrate **12** resulted in a dramatic increase in conversion to desired cyclopentene

16 in both water and methanol (Eq 4). In the presence of 10 mol% **3**, the cyclization of this substrate proceeds to 90% conversion in aqueous solution.



12 **16** (Eq 4)

Summary

This chapter described the application of alkylidenes **2** and **3** to the ring-closing metathesis (RCM) of dienes in methanol and water. Alkylidenes **2** and **3** did not promote the RCM of α,ω-dienes due to the instability of the catalytically-active methylidene complexes in these reactions. However, diene substrates containing a terminal olefin and one internal olefin were readily cyclized. In the RCM of these substrates, metathesis was believed to occur initially at the terminal olefin. The olefin substituent was transferred to the alkylidene upon cyclization, resulting in a significantly more stable, substituted alkylidene after each catalytic cycle. Alkylidene **3** was found to be a more active catalyst for RCM than alkylidene **2**, as predicted based on previous spectroscopic predictions.

Several factors influenced the success of these cyclization reactions. In particular, the choice of olefin substituents was critical, as it directly impacted the stabilities and reactivities of the catalytic alkylidenes. These systems represent an efficient metal-catalyzed carbon-carbon bond forming process which proceeds to high conversion in aqueous solution. The methodology described herin provides a solid framework for the application of RCM to the cyclization of more structurally-complex, water-soluble substrates.

Acknowledgments. The author wishes to thank Tom Kirkland for the synthesis of substrates **6**, **7**, and **9-12**, as well as for his intellectual contributions and collaborative efforts central to the development of this work. This work was supported by the National Institutes of Health and the National Science Foundation.

Experimental Section

General Considerations. All manipulations and reactions involving ruthenium alkylidenes were performed in a nitrogen-filled dry box or by using standard Schlenk techniques under an atmosphere of argon. Argon was purified by passage through columns of BASF R3-11 catalyst (Chemalog) and 4 Å molecular sieves (Linde). ^{1}H NMR (300.1 MHz) and ^{13}C NMR (75.49 MHz) spectra were recorded on a GE QE-300 spectrometer. Distilled deionized water and reagent grade methanol were used for the polymerizations, and were rigorously degassed by purging with argon and stirring under high vacuum prior to use. Alkylidenes **1-3**, substrates **6**, **7**, **11**, and products **4**, **13-15**, and **16** have been previously prepared and reported.[†] All other reagents were used without further purification unless otherwise noted.

General RCM Procedure. In a typical reaction, substrate **6** was placed in a vial and dissolved in CD_3OD. Alkylidene **2** or **3** was placed in a separate vial and dissolved in CD_3OD. The catalyst and substrate solutions were combined, placed in an NMR tube, and the tube was sealed with a rubber septum. The reaction was heated to 45 °C, and monitored by ^{1}H NMR spectroscopy. Conversion to product was determined *via* integration of the allylic protons in the cyclized product (2.95 ppm, s) relative to the allylic protons of the uncyclized substrate (2.68 ppm, d).

4,4-Dicarboethoxy-1-phenyl-1,7-octadiene (8). Diester **8** was synthesized from 1,1-dicarboethoxy-4-pentene and cinnamyl bromide according to a previously published procedure.[10] 1,1-Dicarboethoxy-4-pentene was synthesized according to the same method. Diester **8** was isolated as a clear, colorless oil (33%): ^{1}H NMR ($CDCl_3$): δ 7.32-7.17 (m, 5H), 6.44 (d, J = 7.8 Hz, 1H), 6.11-6.00 (m, 1H), 5.84-5.73 (m, 1H), 5.04 (d, J = 8.6 Hz, 1H), 4.96 (d, J = 5.1 Hz, 1H), 4.19 (q, J = 5.3 Hz, 4H), 2.06-2.03 (m, 4H), 1.24 (t,

J = 4.8 Hz, 6H); ^{13}C NMR ($CDCl_3$): δ 170.8, 137.3, 136.8, 133.5, 128.2, 127.1, 125.9, 123.8, 114.8, 61.0, 57.3, 36.2, 31.6, 28.2, 13.9; HRMS (EI) calcd for $C_{20}H_{26}O_4$ [M^+] 330.1831, found 330.1825.

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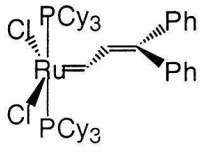
Chapter 8

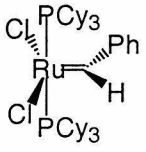
Olefin Metathesis in Protic Solvents: Summary and Perspectives

Introduction

The development of well-defined ruthenium alkylidene complexes **1** and **2** significantly broadened the scope of the olefin metathesis reaction. Specifically, these functional group tolerant alkylidenes enabled the ROMP, RCM, and cross-metathesis of olefins containing polar and protic functional groups (such as unprotected alcohols and aldehydes) that deactivated alkylidenes based on earlier transition metals. The stabilities of these alkylidenes to *water* also introduced significant practical advantages, the most obvious being the use of substrates and solvents without the rigorous purification and drying required for the use of titanium, tungsten, and molybdenum alkylidenes.



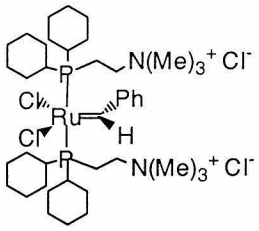
1



2

As described in Chapter 1, the development of alkylidenes **1** and **2** resulted from earlier work conducted on ROMP in water initiated by "classical" ill-defined (non-alkylidene) ruthenium complexes. These early systems were not without limitations, but they functioned well in aqueous solution and served as important platforms for the development of complexes **1** and **2**. These well-defined alkylidenes were highly-active toward olefin metathesis and tolerant of various functional groups. However, the ligand spheres designed to protect and stabilize the alkylidene moieties had rendered these new catalysts completely insoluble in water. Chapter 2 described the initial efforts to address this insolubility issue through the application of complex **2** to ROMP in biphasic environments. Since this initial work, this emulsion methodology has been successfully extended to the ROMP of water-soluble, carbohydrate-functionalized monomers to yield new polymers having potent biological activities.[1]

Chapter 4 described the synthesis of water-soluble derivatives of alkylidenes **1** and **2**, designed to overcome the insolubility of these catalysts in aqueous solvents.



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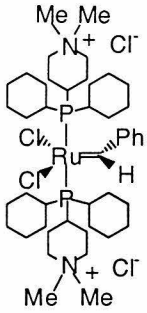


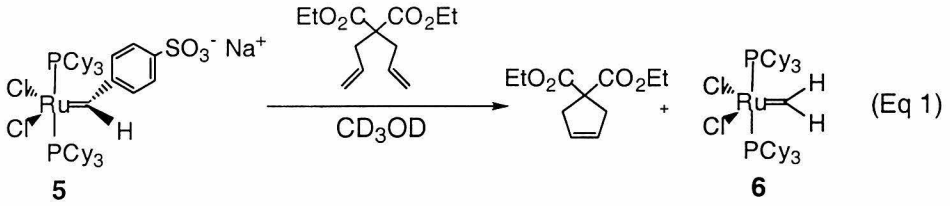
4

Alkylidenes **3** and **4** were completely soluble in protic solvents such as methanol and water, and served as well-defined initiators for the ROMP, RCM, and cross-metathesis of functionalized olefins in these solvents (as described in Chapters 4, 6, and 7). These complexes represented the first transition metal alkylidenes that were soluble and stable in protic solvents, and resulted in the observation of unique trends in reactivity and stability. For example, Chapter 5 described a novel process by which the alkylidene protons in these complexes exchanged with deuterons in perdeuterated protic solvents. This process had not been observed for other alkylidenes in organic solvents, and is believed to be related to the dielectric constants and protic nature of the solvents in which these complexes are soluble. This novel behavior has since been observed for several other alkylidene complexes, including **2**.[2]

More generally, it was observed that while alkylidenes **1** and **2** were exceedingly stable in the presence of large amounts of water, complexes **3** and **4** were *significantly* less stable in aqueous solution. Another unexpected observation was the instability of alkylidenes derived from **3** and **4** on the time scale of typical olefin metathesis reactions. The decomposition of these propagating species during ROMP, and the instabilities of the methylidenes derived from **2** and **3** were discussed in Chapter 4. These limitations were eventually overcome, and resulted in the application of these alkylidenes to living ROMP (Chapter 6) and RCM (Chapter 7) in methanol and water.

Instability of Ruthenium Alkylidenes in Protic Solvents

Subsequent experiments have suggested that the instabilities of alkylidenes **3** and **4** in methanol and water may not be restricted to these cationically-functionalized complexes, but that the observations above may be indicative of general limitations to the application of ruthenium alkylidenes to olefin metathesis in these solvents. For example, a new *p*-sulfonated benzylidene (**5**) was synthesized and used to initiate the cyclization of diethyl diallylmalonate in methanol (Eq 1). This cyclization proceeded to 80% conversion as determined by ^{1}H NMR spectroscopy.



5 **6** (Eq 1)

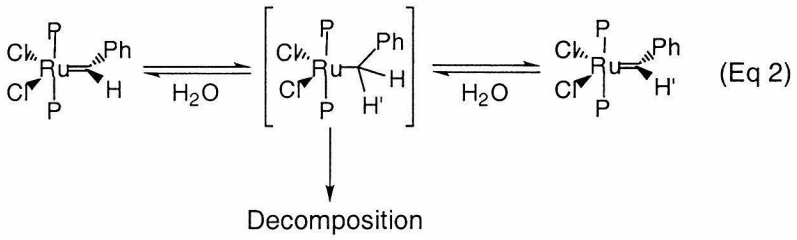
This reaction was interesting for several reasons. First, the catalytically-active species in Eq 2 was methylidene **6** (generated from substituted benzylidene **5** after the initial turnover step in this reaction; see Chapter 7, Scheme 1). Methylidene **6** is structurally identical to the methylidene derived from alkylidenes **1** and **2**; as previously described, this species is generally stable and active for extended periods in organic solvents. This experiment indicated that methylidene **6** was thermodynamically soluble and active in methanol. The reduced yield observed in Eq 1, however, suggested that this normally robust methylidene was decomposing on the time scale of the cyclization in methanol (methylidene **6** generally cyclizes this substrate quantitatively in organic solvents).

Subsequent cyclization experiments employing authentic methylidene **6**, as well as benzylidene **2**, revealed that these species could also initiate RCM in methanol. (These complexes were only marginally soluble in this solvent, and the majority of alkylidenes **6** and **2** remained insoluble throughout the reactions.) These reactions proceeded

quantitatively, however the dark yellow colors of the reaction mixtures suggested that methylidene **6** was also decomposing during these reactions.

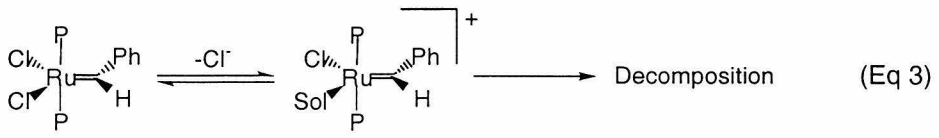
Potential Decomposition Pathways

The experiments above suggest that while ruthenium-based alkylidenes are generally stable to polar and protic functional groups in organic solvents, they are significantly less stable when *dissolved* in polar, protic solvents. The reasons for this accelerated decomposition are not entirely clear. However, we suggest the possibility that the proton-deuteron exchange process described in Chapter 5 may play a key role in this process. Although this reaction is not itself a decomposition reaction, it is possible that intermediates along the reaction coordinate of this degenerate transformation may be responsible for the accelerated rates of decomposition observed for these complexes (Eq 2).



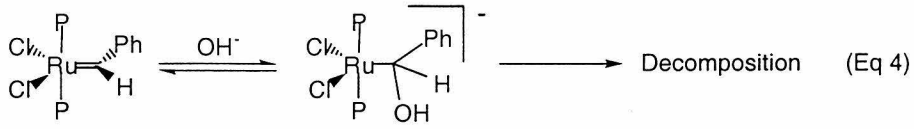
(Eq 2)

Alternatively, dissociation of a chloride ligand from these complexes would lead to the generation of a cationic metal alkylidene complex which could be less stable than the parent alkylidenes (Eq 3). Although no direct evidence for such a species has been observed, there is considerable evidence that the dissociation of chloride from alkylidenes **3** and **4** is facile in protic, high-dielectric solvents such as methanol and water (as discussed in Chapters 2 and 4).



(Eq 3)

A final explanation for the increased rates of decomposition for ruthenium alkylidenes in methanol and water may involve irreversible nucleophilic attack of a solvent-derived species at the alkylidene carbon of these complexes (Eq 4). Although methanol, water, and hydroxide are generally poor nucleophiles, there is current evidence suggesting that the alkylidene carbon in alkylidene **2** possesses electrophilic character.[3] The dissociation of a chloride ligand from these alkylidenes (as proposed in Eq 3) could facilitate such a pathway, as the resulting cationic metal center would render the alkylidene carbons of these complexes more electrophilic. A detailed analysis of the electronic character of the alkylidene carbons these complexes is the subject of an ongoing investigation in our group.[4]



Summary

This thesis described the design, synthesis, and application of ruthenium alkylidenes **3** and **4**. These complexes were soluble in methanol and water, and represented significant advances over "classical" aqueous ROMP initiators. Alkylidenes **3** and **4** reacted with olefins in a controlled, consistent manner and enabled living ROMP, RCM, and cross-metathesis in protic solvents. It is hoped that this research has provided a firm basis for the application of alkylidenes **3** and **4** to more complex aqueous systems.

As described above, the stabilities of alkylidenes **3** and **4** in water and methanol were somewhat limited relative to alkylidenes **1** and **2** in organic solvents. Although these limitations were eventually overcome, the data above suggest that the protic, high-dielectric character of water and methanol may impose *general* restrictions to the application of ruthenium alkylidenes in these solvents. Decomposition manifolds such as those proposed in equations 2, 3, and 4, acting alone or in tandem, may become sufficiently facile under

protic, high-dielectric conditions to ultimately limit the stability of this entire class of alkylidene complexes. These concepts should be borne in mind with respect to the design of new generations of alkylidene complexes intended for use in water or methanol.

Experimental Section

General Considerations. RCM reactions were carried out according to the general protocol in Chapter 7. Other general experimental and analytical considerations may be found in preceeding chapters.

Synthesis of Sulfonated Alkylidene 5. In a nitrogen-filled dry box, **2** (200 mg, 0.024 mmol) and the sodium salt of 4-styrenesulfonic acid (100 mg, 0.048 mmol) were placed in a Schenk flask equipped with a stirbar. Dichloromethane (20 mL) was added, and the dark purple heterogeneous reaction mixture was allowed to stir at room temperature. After 1 hour, methanol (10 mL) was added and the reaction was allowed to stir overnight. The dark red supernatant was cannula filtered from excess sodium salt, and the solvent was removed *in vacou* to yield a reddish-brown solid. ^{1}H NMR (400 MHz) δ 20.10 (s, alkylidene-H). 31P NMR (161.9 MHz) δ 37.0 (s). This alkylidene was employed as an initiator for RCM reactions without further purification.

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2) For a general discussion, see Chapter 5.

3) Hansen, S.M.; Rominger, F.; Metz, M.; Hofmann, P. *Chemistry—A European Journal* **1999**, *5*, 557.

4) M.S. Sanford and R.H. Grubbs. 1999, Unpublished results.

Appendix 1

X-Ray Diffraction Analysis of

$Cy_2P(BH_3)$(*N*,*N*-dimethylpiperidinium) Iodide

Table 1. Crystal data and structure refinement for DML2.

Empirical formula	$C_{19.70}H_{41.40}BCl_{1.40}INP$ $[C_{19}H_{40}BINP \cdot 0.70CH_2Cl_2]$
Formula weight	510.68 [451.22 · 59.45]
Crystallization Solvent	CH_2Cl_2 / MeOH / Hexanes
Crystal Habit	prism
Crystal size	0.45 x 0.30 x 0.19 mm^3
Crystal color	colourless

Data Collection

Type of diffractometer	CAD4	
Wavelength	0.71073 Å MoKα	
Data Collection Temperature	84 K	
Theta range for reflections used in lattice determination	14 to 16°	
Unit cell dimensions	a = 13.133(4) Å b = 20.566(8) Å c = 9.943(3) Å	α= 90° β= 112.82(2)° γ = 90°
Volume	2475.3(14) $Å^3$	
Z	4	
Crystal system	Monoclinic	
Space group	*Cc*	
Density (calculated)	1.370 Mg/m^3	
F(000)	1054	
Theta range for data collection	1.5 to 25.0°	
Completeness to theta = 25.0°	100 %	
Index ranges	-15<=h<=15, -24<=k<=24, -11<=l<=11	
Data collection scan type	Ω–scan	
Reflections collected	11504	
Independent reflections	4353 [R_{int}= 0.015; GOF_{merge}= 0.97]	
Absorption coefficient	1.514 mm^{-1}	
Absorption correction	Ψ–scan (North, Phillips & Matthews, 1968)	
Max. and min. transmission	1.05 and 0.93	
Number of standards	3 reflections measured every 75min.	
Variation of standards	0.97%.	

Table 1 (cont.)

Structure solution and Refinement

Structure solution program	SHELXS-97 (Sheldrick, 1990)
Primary solution method	Direct methods
Secondary solution method	Structure factor / difference map
Hydrogen placement	Calculated positions
Structure refinement program	SHELXL-97 (Sheldrick, 1997)
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	4353 / 2 / 234
Treatment of hydrogen atoms	no refinement
Goodness-of-fit on F^2	1.775
Final R indices [$I>2\sigma(I)$]	R1 = 0.0257, wR2 = 0.0569
R indices (all data)	R1 = 0.0278, wR2 = 0.0575
Type of weighting scheme used	calculated
Weighting scheme used	$w=1/\sigma^2(F_o)^2$
Max shift/error	0.036
Average shift/error	0.002
Absolute structure parameter	-0.014(16)
Largest diff. peak and hole	0.639 and -0.312 e.Å^{-3}

Special Refinement Details

Refinement of F^2 against all reflections. The weighted R-factor wR and goodness of fit S are based on F^2, conventional R-factors R are based on F, with F set to zero for negative F^2. The threshold expression of $F^2 > 2\sigma(F^2)$ is used only for calculating R-factors(gt) etc. and is not relevant to the choice of reflections for refinement. R-factors based on F^2 are statistically about twice as large as those based on F, and R- factors based on ALL data will be even larger.

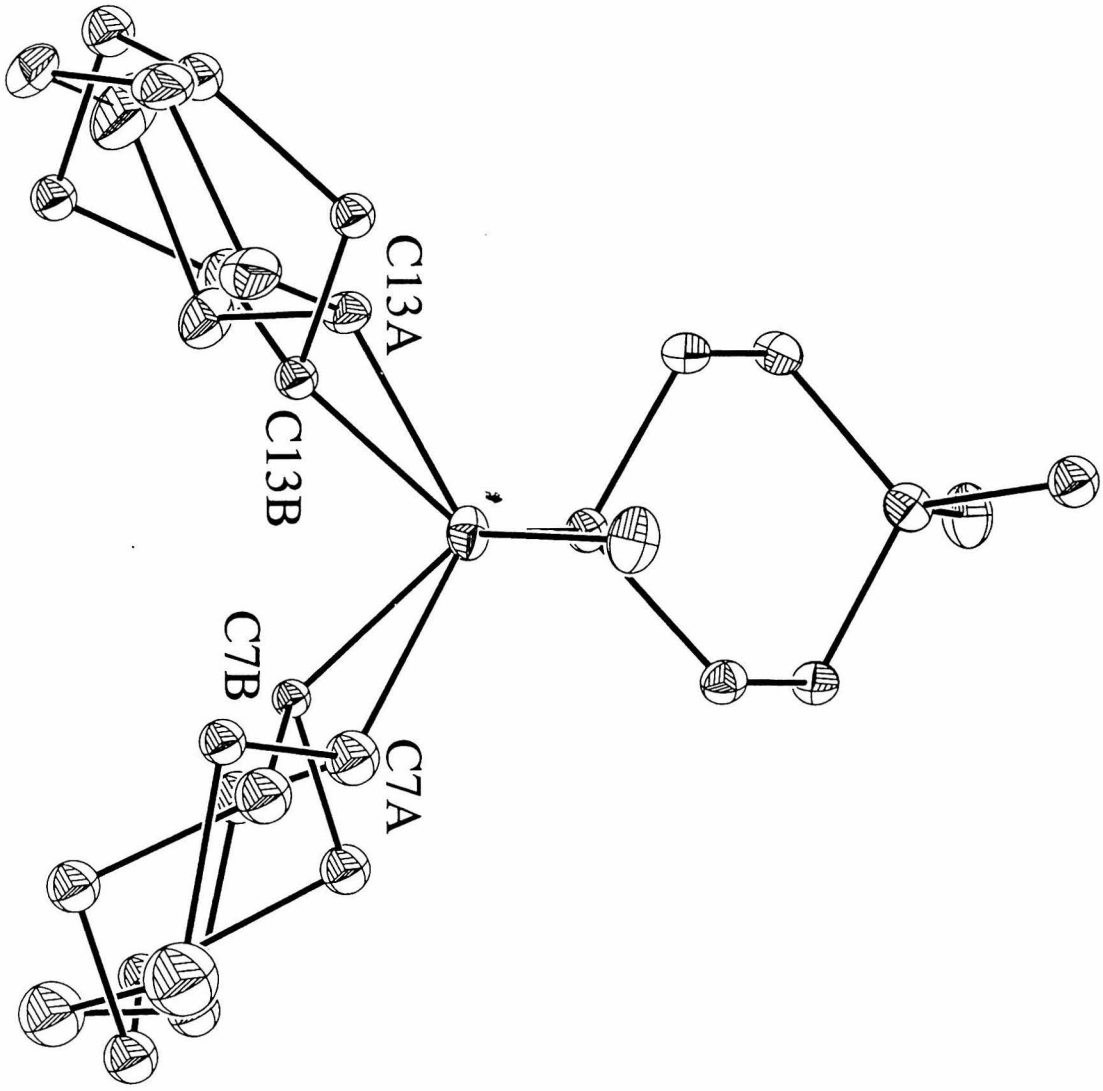
Data were collected with 1.60 degree ω-scans. The individual backgrounds were replaced by a background function of 2θ derived from those reflections with $I < 8\sigma(I)$. The GOF_merge was 0.968 (4236 multiples) in point group *m*; R_int was 0.015 for 3706 duplicates with $F_o > 0$. One outlier reflection (0 2 0) was deleted.

Weights w are calculated as $1/\sigma(F_o^2)$; variances ($\sigma^2(F_o^2)$) were derived from counting statistics plus an additional term, $(0.014I)^2$; variances of the merged data were obtained by propagation of error plus another additional term, $(0.014\langle I\rangle)^2$.

A dichloromethane molecule is present 70% of the time in the structure. The two cyclohexyl groups of the cation are each disordered in two chair conformations; the relative population values refined to 55.6:44.4 and 68.9:31.1. Unfortunately, this disorder does not result in two discrete positions. Instead the rest of the cation pivots slightly around the P-B bond. As a result, some of the final bond distances and angles are chemically unreasonable. In the final model, each of the two disordered cyclohexyl groups was modelled by two separate sets of six carbon atoms. The most populated site was refined with anisotropic displacement parameters; the other three were refined isotropically. All hydrogen atoms were placed at calculated positions with displacement parameters 20% larger than those of the attached atom. [In an alternate model, three atoms of each disordered cyclohexyl were refined anisotropically and the other three treated as two isotropic atoms. This model was a little worse, but as all carbons

bonded to the phosphorus were modelled as single atoms, the geometry around the phosphorus atom is a more reasonable average of the disordered model, with P-C bonds of 1.828(5), 1.831(5) and 1.839(4)Å and C-P-C bond angles of 104.0(2), 107.1(2) and 110.4(3)°. However the internal cyclohexyl distances and angles are again affected by the disorder.] Despite the similarity between the solvent population parameter and that of one of the disordered cyclohexyl groups, there seems to be no significant steric interaction.

The closest contacts to the iodide anion are a number of carbon atoms (including the two methyl carbons) at ~3.9 - 4.0Å. Viewed down the c-axis, the cations form sheets of slightly interleaved stacks . The iodide anions are packed between the four methyl groups of two adjacent cations. The solvent molecules form zigzag chains between the sheets (closest contacts of 3.385Å, near the ends of the cations.



View of the title compound showing all four cyclohexyl positions. Displacement ellipdoids are drawn at 30% and hydrogen atoms have been omitted. The view is perpendicular to the best plane through atoms P, C&A, C&B, C13A, and C13B.

Appendix 2

X-Ray Diffraction Analysis of

$RuCl_2(=CHPh)[Cy_2PCH_2CH_2N(CH_3)_3^+Cl^-]_2$

Table 1. Crystal data and structure refinement for DML1A.

Empirical formula	$C_{44.78}H_{77.93}Cl_{11.57}N_2P_2Ru$ $\{[C_{41}H_{58}N_2P_2Cl_2Ru][Cl_2]\cdot 3.8CH_2Cl_2]\}$
Formula weight	1217.61 (883.78•333.82)
Crystallization Solvent	Dichloromethane/methanol/petroleum ether
Crystal Habit	Fragment
Crystal size	0.41 x 0.33 x 0.07 mm^3
Crystal color	Dichroic; purple and orange

Data Collection

Preliminary Photos	None
Type of diffractometer	CAD-4
Wavelength	0.71073 Å MoKα
Data Collection Temperature	85 K
θ range for reflections used in lattice determination	12.6 to 13.8°
Unit cell dimensions	a = 13.958(6) Å b = 25.919(11) Å β= 101.45(3)° c = 16.819(5) Å
Volume	5964(2) $Å^3$
Z	4
Crystal system	Monoclinic
Space group	$P2_1/n$
Density (calculated)	1.356 Mg/m^3
F(000)	2525
θ range for data collection	1.57 to 24.97°
Completeness to θ = 24.97°	100.0 %
Index ranges	$-16 \le h \le 16$, $-30 \le k \le 27$, $-19 \le l \le 19$
Data collection scan type	ω scans
Reflections collected	21914
Independent reflections	10474 [R_{int}= 0.051; GOF_{merge}= 1.00]
Absorption coefficient	0.866 mm^{-1}
Absorption correction	None
Number of standards	3 reflections measured every 75min.
Variation of standards	-1.5%.

Table 1 (cont.)

Structure solution and Refinement

Structure solution program	SHELXS-97 (Sheldrick, 1990)
Primary solution method	Patterson method
Secondary solution method	Difference Fourier map
Hydrogen placement	Geometric calculated sites
Structure refinement program	SHELXL-97 (Sheldrick, 1997)
Refinement method	Full matrix least-squares on F^2
Data / restraints / parameters	10474 / 19 / 565
Treatment of hydrogen atoms	Riding
Goodness-of-fit on F^2	2.306
Final R indices [$I>2\sigma(I)$]	R1 = 0.0897, *w*R2 = 0.1518
R indices (all data)	R1 = 0.1464, *w*R2 = 0.1600
Type of weighting scheme used	Sigma
Weighting scheme used	$w=1/\sigma^2(Fo^2)$
Max shift/error	0.006
Average shift/error	0.000
Largest diff. peak and hole	2.642 and -1.460 e.Å^{-3}

Special Refinement Details

This crystal contains disordered solvent molecules. These are modeled as six molecules of dichlormethane with partial occupancies which altogether add to 3.8 full occupancy molecules.

The variances [$\sigma^2(Fo^2)$] were derived from counting statistics plus an additional term, $(0.014I)^2$, and the variances of the merged data were obtained by propagation of error plus the addition of another term, $(0.014\langle I\rangle)^2$.

Refinement of F^2 against ALL reflections. The weighted R-factor (*w*R) and goodness of fit (S) are based on F^2, conventional R-factors (R) are based on F, with F set to zero for negative F^2. The threshold expression of $F^2 > 2\sigma(F^2)$ is used only for calculating R-factors(gt) etc. and is not relevant to the choice of reflections for refinement. R-factors based on F^2 are statistically about twice as large as those based on F, and R-factors based on ALL data will be even larger.

All esds (except the esd in the dihedral angle between two l.s. planes) are estimated using the full covariance matrix. The cell esds are taken into account individually in the estimation of esds in distances, angles and torsion angles; correlations between esds in cell parameters are only used when they are defined by crystal symmetry. An approximate (isotropic) treatment of cell esds is used for estimating esds involving l.s. planes.