Metathesis Catalysts in Tandem Catalysis: Methods and Mechanisms for Transformation

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Abstract

The ever-worsening environmental crisis has stimulated development of less wasteful “green” technologies. To this end, tandem catalysis enables multiple catalytic cycles to be performed within a single reaction vessel, thereby eliminating intermediate processing steps and reducing solvent waste. Assisted tandem catalysis employs suitable chemical triggers to transform the initial catalyst into new species, thereby providing a mechanism for “switching on” secondary catalytic activity.

This thesis demonstrates the importance of highly productive secondary catalysts through a comparative hydrogenation study involving prominent hydrogenation catalysts of tandem ring-opening metathesis polymerization (ROMP)-hydrogenation, of which hydridocarbonyl species were proved superior. This thesis illuminates optimal routes to hydridocarboxylics under conditions relevant to our ROMP-hydrogenation protocol, using Grubbs benzylidenes as isolable proxies for ROMP-propagating alkylidene species. Analogous studies of ruthenium methylidenes and ethoxylidenes illuminate optimal routes to hydridocarboxylics following ring-closing metathesis (RCM) and metathesis quenching, respectively. The formation of unexpected side products using aggressive chemical triggers is also discussed, and emphasizes the need for cautious design of the post-metathesis trigger phase.
Acknowledgements

First and foremost, thank you Deryn for teaching me to see the forest for the trees, and to be mindful of where the forest stands. Your constant guidance and contagious enthusiasm have transformed the way I view chemistry, and science in general. Greg, the skills I acquired during my Honours and Masters gave me the confidence to pursue this degree, and for that I thank you.

Ken, thanks for schooling me in the art of “bombcraft”; our day-long hydrogenolysis experiments were the most fun I’ve had in the lab. Jo, our many discussions never failed to provide new and exciting approaches to complicated problems. Cheers to Lummiss for always asking “what’s the point?”, and for maintaining a light atmosphere regardless of the chemistry. Jennifer and Carolyn, I greatly enjoyed the work we did together, however brief. To Seb, Heather, Titel, Adrien, Josh, Debbie, and Matt(s): thank you for the insightful discussions and the fun times.

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To Mom, Dad, Mikey and Miss, and to Paul and all my aunts, uncles, and cousins, thanks for all your support and encouragement through yet another degree, and for making it easy to come home.

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### Abbreviations

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ac</td>
<td>Acetyl, -C(O)CH$_3$</td>
</tr>
<tr>
<td>ADMET</td>
<td>Acyclic diene metathesis</td>
</tr>
<tr>
<td>atm</td>
<td>Atmosphere (1 atm = 14.7 psi)</td>
</tr>
<tr>
<td>Ar</td>
<td>Aryl</td>
</tr>
<tr>
<td>ATRP</td>
<td>Atom transfer radical polymerization</td>
</tr>
<tr>
<td>Bn</td>
<td>Benzyl, -CH$_2$Ph</td>
</tr>
<tr>
<td>BOC</td>
<td>-C(O)O'Bu</td>
</tr>
<tr>
<td>Cat.</td>
<td>Catalyst</td>
</tr>
<tr>
<td>CM</td>
<td>Cross metathesis</td>
</tr>
<tr>
<td>COD</td>
<td>1,5-cyclooctadiene, C$<em>8$H$</em>{12}$</td>
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<tr>
<td>Conv.</td>
<td>Conversion</td>
</tr>
<tr>
<td>Cy</td>
<td>Cyclohexyl, -C$<em>6$H$</em>{11}$</td>
</tr>
<tr>
<td>DEPT</td>
<td>Distortionless enhancement by polarization transfer</td>
</tr>
<tr>
<td>DFT</td>
<td>Density functional theory</td>
</tr>
<tr>
<td>DMB</td>
<td>2,4-dimethoxybenzyl</td>
</tr>
<tr>
<td>EPR</td>
<td>Electron paramagnetic resonance</td>
</tr>
<tr>
<td>equiv</td>
<td>Equivalents</td>
</tr>
<tr>
<td>Et</td>
<td>Ethyl, -C$_2$H$_5$</td>
</tr>
<tr>
<td>EVE</td>
<td>Ethyl vinyl ether, CH$_2$=CHOEt</td>
</tr>
<tr>
<td>GC-FID</td>
<td>Gas chromatography flame ionization detection</td>
</tr>
<tr>
<td>GC-MS</td>
<td>Gas chromatography mass spectrometry</td>
</tr>
<tr>
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<td>N,N'-bis-(2,4,6-trimethylphenyl)imidazolin-2-ylidene</td>
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<td>H$_2$IPr</td>
<td>N,N'-bis-(2,6-diisopropylphenyl)imidazolin-2-ylidene</td>
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<tr>
<td>H$_2$ITol</td>
<td>N,N'-bis-(2-methylphenyl)imidazolin-2-ylidene</td>
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<tr>
<td>HMBC</td>
<td>Heteronuclear multiple-bond correlation</td>
</tr>
<tr>
<td>HMQC</td>
<td>Heteronuclear multiple-quantum coherence</td>
</tr>
<tr>
<td>Hz</td>
<td>Hertz (s$^{-1}$)</td>
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<tr>
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<td>N,N'-bis-(2,4,6-trimethylphenyl)imidazol-2-ylidene</td>
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<tr>
<td>'Pr</td>
<td>Isopropyl, -CH(CH$_3$)$_2$</td>
</tr>
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<td>Abbreviation</td>
<td>Full Form</td>
</tr>
<tr>
<td>--------------</td>
<td>-----------</td>
</tr>
<tr>
<td>IR</td>
<td>Infrared</td>
</tr>
<tr>
<td>KA</td>
<td>Kharasch addition</td>
</tr>
<tr>
<td>Me</td>
<td>Methyl, -CH₃</td>
</tr>
<tr>
<td>Mes</td>
<td>Mesityl, 2,4,6-trimethylphenyl</td>
</tr>
<tr>
<td>MMA</td>
<td>Methylmethacrylate, CH₂=CH(Me)(C=O)(OMe)</td>
</tr>
<tr>
<td>NBR</td>
<td>Nitrile-butadiene rubber</td>
</tr>
<tr>
<td>n.d.</td>
<td>Not determined</td>
</tr>
<tr>
<td>NHC</td>
<td>N-heterocyclic carbene</td>
</tr>
<tr>
<td>NMR</td>
<td>Nuclear magnetic resonance</td>
</tr>
<tr>
<td>NOESY</td>
<td>Nuclear Overhauser effect spectroscopy</td>
</tr>
<tr>
<td>Ns</td>
<td>Nosyl, -SO₂(p-NO₂-C₆H₄)</td>
</tr>
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<td>OTf</td>
<td>Trflate, -OSO₂CF₃</td>
</tr>
<tr>
<td>OTMS</td>
<td>Trimethylsiloxy, -OSiMe₃</td>
</tr>
<tr>
<td>Oxone®</td>
<td>KHSO₅</td>
</tr>
<tr>
<td>PDI</td>
<td>Polydispersity index</td>
</tr>
<tr>
<td>Ph</td>
<td>Phenyl, -C₆H₅</td>
</tr>
<tr>
<td>ppm</td>
<td>Parts per million</td>
</tr>
<tr>
<td>py</td>
<td>Pyridine, C₅H₅N</td>
</tr>
<tr>
<td>RCEYM</td>
<td>Ring-closing enyne metathesis</td>
</tr>
<tr>
<td>ROMP</td>
<td>Ring-opening metathesis polymerization</td>
</tr>
<tr>
<td>RCM</td>
<td>Ring-closing metathesis</td>
</tr>
<tr>
<td>T₁(min)</td>
<td>Minimum temperature-dependent spin-lattice relaxation time</td>
</tr>
<tr>
<td>'Bu</td>
<td>Tert-butyl, -CMe₃</td>
</tr>
<tr>
<td>THF</td>
<td>Tetrahydrofuran, C₄H₈O</td>
</tr>
<tr>
<td>THN</td>
<td>1,2,3,4-tetrahydronaphthalene</td>
</tr>
<tr>
<td>TMB</td>
<td>1,3,5-trimethoxybenzene</td>
</tr>
<tr>
<td>TMS</td>
<td>Tetramethyilsilane, SiMe₄</td>
</tr>
<tr>
<td>-TMS</td>
<td>Trimethyilsilyl, -SiMe₃</td>
</tr>
<tr>
<td>TOF</td>
<td>Turnover frequency</td>
</tr>
<tr>
<td>TON</td>
<td>Turnover number</td>
</tr>
<tr>
<td>Ts</td>
<td>Tosyl, -SO₂(p-CH₃-C₆H₄)</td>
</tr>
<tr>
<td>Abbreviation</td>
<td>Definition</td>
</tr>
<tr>
<td>--------------</td>
<td>-----------------</td>
</tr>
<tr>
<td>TS</td>
<td>Transition state</td>
</tr>
<tr>
<td>UHP</td>
<td>Ultra High Purity</td>
</tr>
<tr>
<td>xs</td>
<td>Excess</td>
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List of Compounds

Ruthenium complexes

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<tr>
<td>a</td>
<td>Cl</td>
<td></td>
<td>Ru-1</td>
</tr>
<tr>
<td>b</td>
<td>Cl</td>
<td></td>
<td>Ru-1a</td>
</tr>
<tr>
<td>b'</td>
<td>IMes</td>
<td>Cl</td>
<td>Ru-1a&lt;sub&gt;re&lt;/sub&gt;</td>
</tr>
<tr>
<td>c</td>
<td>IMes</td>
<td>IMes</td>
<td>Ru-2</td>
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<tr>
<td>d</td>
<td>IMes</td>
<td>(py)&lt;sub&gt;2&lt;/sub&gt;</td>
<td>Ru-3</td>
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<tr>
<td>e'</td>
<td>H&lt;sub&gt;2&lt;/sub&gt;Itol</td>
<td>Cl</td>
<td>Ru-4</td>
</tr>
<tr>
<td>f'</td>
<td>H&lt;sub&gt;2&lt;/sub&gt;IPr</td>
<td>Cl</td>
<td>Ru-5</td>
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Ru-1: \[
\text{RuCl}_3(L)(L')_2\]

Ru-1a: \[
\text{RuCl}_3(PCy_3)(PCy_3)\]

Ru-1a<sub>re</sub>: \[
\text{RuCl}_3(PCy_3)\text{C}==\text{O}\text{Br}\text{PCy}_3\]

Ru-2: \[
\text{RuCl}_3(PCy_3)\text{Ph}\text{L'}\text{Cl}\]

Ru-3: \[
\text{RuCl}_3(PCy_3)\text{H}_2\text{IMes}\text{Cl}\]

Ru-4: \[
\text{RuCl}_3(PCy_3)\text{Mes}\text{L}\text{Cl}\]

Ru-5: \[
\text{RuCl}_3(PCy_3)\text{H}_2\text{IMes}\text{Cl}\]

Ru-6: \[
\text{RuCl}_3(PCy_3)\text{H}_2\text{L'}\text{Cl}\]

Ru-7: \[
\text{RuCl}_3(PCy_3)\text{H}\text{L'}\text{Cl}\]

Ru-8: \[
\text{RuCl}_3(PCy_3)\text{Ph}_3\text{L}\text{Cl}\]

Ru-9: \[
\text{RuCl}_3(PCy_3)\text{Ph}_3\text{L}\text{Cl}\]
Ru-30

Substrates

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<td>S5</td>
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<tr>
<td>N-heterocyclic carbenes</td>
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<tr>
<td>H₂ITol</td>
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List of Contributions


Chapter 1: Introduction

1.1 Tandem Catalysis

The improved quality of life enabled by industrialized societies has exacted an environmental price. Balancing the two constitutes a major challenge for our own and future generations. "Green Chemistry" seeks to address this challenge by fostering the development of energy- and resource-efficient technologies designed to reduce environmental impact. As a blueprint for the development of improved industrial practices, Anastas and Warner put forward "Twelve Principles of Green Chemistry", a core objective of which is the replacement of wasteful stoichiometric processes by catalytic methodologies.

Catalysis reduces the energy demands of chemical reactions by decreasing the barrier to activation ($E_a$; Figure 1.1a). In a simplified catalytic cycle, a reactant (e.g. A, Figure 1.1b) combines with the catalyst C to form intermediate CA, which reacts with another reactant B to yield product AB and regenerate C. This process constitutes a single "turnover" of the catalytic cycle. A kinetic benefit results from the decreased energy barrier, but the net thermodynamics of the system are unchanged.

![Figure 1.1](image.png)

**Figure 1.1.** (a) Potential energy diagram for reaction of A and B in the presence (green) or absence (red) of catalyst C. (b) A simple model in which reaction of A with B is catalyzed by C.
In most catalytic processes, the active species is generated via initiation of a precatalyst, while termination involves catalyst deactivation, whether incidental (e.g. decomposition) or deliberately induced (e.g. quenching). Catalyst activity is often expressed in terms of the turnover number (TON): that is, the number of catalytic cycles completed by each molecule of catalyst prior to termination. The TON is thus readily determined from the molar ratio of product vs. precatalyst. Also important is the turnover frequency (TOF), or the number of turnovers per unit time. To maximize catalyst efficiency, the lifetime of the active catalyst must be long relative to the timescale of catalyst decomposition. For less active or chemically sensitive catalysts, high loadings are often required to attain useful TOFs. This can drastically increase process costs where expensive precious metal catalysts are used.

The efficiency of chemical reactions is often described in terms of atom economy, or the molecular weight ratio of the desired product relative to all reactants. The term was coined by Trost in 1995 to aid synthetic organic chemists in recognizing more materials-efficient transformations. However, atom economy does not take into account materials expenditures arising from (e.g.) unused reactants, side-products, or solvents required for reaction or work-up. A broader metric for efficiency is the E factor (or Environmental factor) introduced by Sheldon, which reports on the kilograms of waste generated for each kilogram of isolated product. Process sustainability, as gauged by the E-factor, ranges from ca. 0.1 for the petroleum industry to >100 for pharmaceutical synthesis (Table 1.1). A major contributor to waste in the latter context is solvent use: a GlaxoSmithKline estimate puts solvent wastes at 85% of the total mass of chemical waste generated in pharma. Eliminating unnecessary reaction steps, as well as solvent-intensive workup and purification stages, can greatly improve process efficiencies.
Table 1.1. Typical E-factors for various sectors of the chemical industry.

<table>
<thead>
<tr>
<th>Sector</th>
<th>Production scale (t/y)</th>
<th>E-factor</th>
<th>Waste (t/y)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Petroleum industry</td>
<td>$10^6$-$10^8$</td>
<td>ca. 0.1</td>
<td>$10^5$-$10^7$</td>
</tr>
<tr>
<td>Commodity chemicals</td>
<td>$10^4$-$10^6$</td>
<td>$\leq$5</td>
<td>$10^4$-$5\times10^6$</td>
</tr>
<tr>
<td>Fine chemicals</td>
<td>$10^2$-$10^4$</td>
<td>5-50</td>
<td>$5\times10^2$-$5\times10^5$</td>
</tr>
<tr>
<td>Pharmaceuticals</td>
<td>10-$10^3$</td>
<td>25-100</td>
<td>2.5$\times10^2$-$10^5$</td>
</tr>
</tbody>
</table>

Tandem catalysis offers a potentially important means of reducing the waste associated with operating sequential catalytic reactions as separate steps. Much recent attention has focused on use of this approach to couple such transformations, thus enabling two or more originally independent reactions to be carried out within a single reaction vessel.\(^5,6\) Fogg and dos Santos put forward a taxonomy (Figure 1.2) to aid in analyzing the opportunities and limitations offered by different types of tandem catalytic processes. Of particular interest is assisted tandem catalysis (described in more detail below), which offers the opportunity to independently optimize each of the catalytic processes involved.

![Flowchart](image)

**Figure 1.2.** Flowchart for classification of one-pot processes in which an organic substrate is elaborated via multiple, sequential catalytic transformations.\(^5\)
Assisted tandem catalysis relies on use of a trigger reagent or condition, applied once the first cycle is complete, to switch between distinct modes of catalysis. As shown in Figure 1.3, the trigger converts **Catalyst A** into a new species (**Catalyst B**), and the latter drives transformation of organic **Product A** into **Product B**. Fast transformation of the catalyst is important to minimize the timescale of operations; efficient, high-yield transformation is essential to maximize capture of the initial catalyst charge. To date, however, few processes have attempted to optimize this step. The following sections describe progress in tandem metathesis-functionalization and metathesis-hydrogenation. Interest in such methodologies is high, due in part to the versatility of olefin metathesis (**Cycle A**) as a method for assembling new C=C bonds.\(^7,8\)

**Figure 1.3.** Schematic representation of assisted tandem catalysis.\(^5c\)

### 1.2 Assisted tandem catalysis utilizing Grubbs metathesis catalysts

The Grubbs metathesis catalysts (Chart 1.1) have been harnessed in a range of tandem catalysis processes. Developments prior to 2006 have been reviewed,\(^5\) and the majority of these will not be repeated here. The following section describes reports of tandem metathesis-functionalization that have emerged over the past five years, focusing in particular on *assisted* tandem catalysis\(^5c\) via the Grubbs catalysts. This is followed by a more detailed review of tandem metathesis-hydrogenation, a transformation central to the work presented in this thesis.
Chart 1.1. Grubbs and Hoveyda-Grubbs catalysts employed in assisted tandem catalysis.

1.2.1 Tandem metathesis-cyclopropanation

Snapper and coworkers used precatalyst Ru-1a to couple ring-closing enyne metathesis (RCEYM) with cyclopropanation. The cyclopropanation step was initiated by purging the metathesis reaction with N\textsubscript{2} to remove the ethylene atmosphere, following which the diazo reagent was added dropwise (Scheme 1.1). In situ NMR studies did not aid in identifying the cyclopropanation catalyst. However, no metathesis activity was retained following cyclopropanation, tending to argue against involvement of an ester-alkylidene species, as such complexes are known to be metathesis active.

Scheme 1.1. Ru-1a-catalyzed tandem RCEYM-cyclopropanation.

This methodology was later applied by Perez-Castells and coworkers in the RCM assembly and cyclopropanation of five- to seven-membered enamide rings (Scheme 1.2).
Poor control over regioselectivity of cyclopropanation was found for the six- and seven-membered rings, implying isomerization prior to cyclopropanation. Adopting a suggestion by Fustero and coworkers, the authors proposed that the isomerization catalyst could be dinuclear hydride Ru-4 (earlier observed on thermolysis of the resting-state methyldiene species Ru-2b)\textsuperscript{13}

![Scheme 1.2. Ru-1b'-catalyzed tandem RCM-isomerization-cyclopropanation.\textsuperscript{11}]

1.2.2 Tandem metathesis-Kharasch addition (KA)

*Tandem metathesis-Kharasch addition* (KA) involves the post-metathesis addition of a trihaloacetyl C-X bond across a newly-formed C=C bond. This addition may be intra- or intermolecular. For trichloroacetyl substrates, the metathesis and Kharasch cycles can be isolated by the elevated temperatures required for KA\textsuperscript{14,15} (provided that metathesis is efficient at ambient temperature). This is important to ensure that KA modification does not
occur prematurely on the diene substrate. The first-generation Grubbs catalyst Ru-1a, which exhibits high initiation efficiency at room temperature, promoted efficient RCM-KA of trichloroacetamide-functionalized 1,6-, 1,7- and 1,8-dienes,\textsuperscript{16} as well as trichloroacetate-functionalized 1,7-dienes (Scheme 1.3).\textsuperscript{17}

\begin{align*}
\text{Scheme 1.3. Ru-1a/b'-catalyzed RCM-Kharasch addition.} & ^{16,17}
\end{align*}

Thermal segregation of the metathesis and Kharasch steps also requires a relatively high C-X bond dissociation energy, a condition met by the C-Cl bond, but not by C-Br species.\textsuperscript{18} Thus, attempted RCM-KA of tribromoacetamides at ambient temperature suffers from poor product selectivity, owing to competing KA of the starting diene.

This chemistry was incorporated into the extended sequence depicted in Scheme 1.4. Thus, a Pd-catalyzed Overman rearrangement of trichloroacetimidates was followed by tandem RCM-KA.\textsuperscript{19} The bicyclic products were formed with excellent enantioselectivity ($\leq90\%$ e.e.) during the process of Scheme 1.4b, in particular, although the Overman rearrangement was slow.
Scheme 1.4. Overman rearrangement in sequence with Ru-1a-catalyzed RCM-KA.\textsuperscript{19}

The superior metathesis activity of the second-generation Ru-1b' enabled efficient RCM-KA of trichloroacetate-functionalized 1,6-dienes (Scheme 1.3).\textsuperscript{17} Cross-metathesis (CM) of N-phenyl-trichloroacetamide with various styrenes, followed by KA, was also employed by Quayle and coworkers (Scheme 1.5). However, yields of the KA products were low.\textsuperscript{20}

Scheme 1.5. Ru-1b'-catalyzed tandem CM-KA.\textsuperscript{20}

While the Kharasch catalyst was not identified during any of the above studies, Schmidt suggested the potential involvement of paramagnetic ruthenium species, formation of which was inferred from the severe broadening of NMR signals for crude RCM-KA reaction
mixtures. Chlorination of the metathesis catalyst to form Ru(III) products could account for the conversion of trichloroacetamides to their dichlorinated analogues during RCM-KA promoted by Ru-1a.16

1.2.3 Tandem metathesis-oxidation

Blechert and coworkers were the first to exploit the residual ruthenium present after olefin metathesis to carry out C=C oxidation (specifically dihydroxylation).21 Their protocol began by stripping off the CH2Cl2 solvent used for metathesis, and suspending the residue in 3:3:1 MeCN/EtOAc/H2O. The dihydroxylation stage was then initiated by cooling to 0 °C and adding the Lewis acid catalyst YbCl3•6 H2O, accompanied by excess NaIO4 oxidant. A screening study revealed superior dihydroxylation activity for the first-generation Grubbs catalyst Ru-1a relative to second-generation Ru-1b' (though see later). Use of Ru-1a for RCM-dihydroxylation of various 1,7- and 1,8-dienes (Scheme 1.6) enabled rapid dihydroxylation (≤40 min) to afford exclusively cis-1,2-diols.

\[
\begin{align*}
\text{Scheme 1.6. Ru-1a-catalyzed RCM-dihydroxylation.}\quad & \\
\text{Dihydroxylation of internal, electron-deficient olefins formed by CM was also examined. These experiments utilized the second-generation Hoveyda-Grubbs catalyst Ru-3b'. Dihydroxylation efficiency is lower than that found with Ru-1a. The nature of the olefin
}\\
\end{align*}
\]
substituent had a pronounced effect on diol geometry: acrylates led to cis-diols, and cyanide to trans-diols (Scheme 1.7).

\[
\begin{align*}
R_1 = & \quad \text{AcO}, \quad \text{Ns} \quad \text{H} \quad \text{R}_2 \\
R_2 = & \quad \text{CO}_2\text{Et}, \quad \text{CN} \quad \text{R}_2
\end{align*}
\]

\text{Scheme 1.7. Ru-3b'}-catalyzed CM-dihydroxylation.\textsuperscript{21}

A minor drawback to this protocol is the need to remove the metathesis solvent CH\(_2\)Cl\(_2\) prior to dihydroxylation.\textsuperscript{22,23} Snapper performed the metathesis reaction in EtOAc, and used CeCl\(_3\)•7 H\(_2\)O as the Lewis acid catalyst.\textsuperscript{24} The latter is thought to generate RuO\(_4\) (the putative olefin oxidation catalyst) more effectively than YbCl\(_3\)•6 H\(_2\)O.\textsuperscript{25} Olefin oxidation was complete within 20 minutes at 0 °C. \textit{Ru-1b'} was also employed as the metathesis catalyst, enabling efficient RCM-dihydroxylation of 1,6-dienes. Diol yields were comparable or higher than those found in the Blechert study of Scheme 1.6 above.\textsuperscript{21}

Snapper also applied an oxidation protocol developed by Plietker, in which Oxone® (i.e. KHSO\(_5\)) and NaHCO\(_3\)\textsuperscript{26,27} are added after metathesis to achieve tandem metathesis-ketohydroxylation. In contrast with the trends in dihydroxylation, in which \textit{Ru-1a} showed higher activity, the second-generation \textit{Ru-1b'} proved more effective for ketohydroxylation. Thus, RCM of disubstituted 1,6-, 1,7-, and 1,8-dienes and trisubstituted 1,6-dienes by \textit{Ru-1b'} was followed by rapid ketohydroxylation to yield the desired \(\alpha\)-hydroxyketones (Scheme 1.8).
Scheme 1.8. Ru-1b'-catalyzed RCM-ketohydroxylation.\textsuperscript{24}

This technique was also effective for tandem CM-ketohydroxylation of various olefins with methyl acrylate or methyl methacrylate (Scheme 1.9). However, CH\textsubscript{2}Cl\textsubscript{2} was required as solvent for efficient CM.

Scheme 1.9. Ru-1b'-catalyzed CM-ketohydroxylation.\textsuperscript{24}

Plietker later modified Snapper's CM-dihydroxylation protocol to include chloride abstraction from Ru-3b' by Bu\textsubscript{4}NIO\textsubscript{4}, prior to addition of NaIO\textsubscript{4}.\textsuperscript{28} Stereoselective dihydroxylation following CM of vinylcyclohexane was achieved with chirally pure camphorsulfamidate and camphorsultame substrates. Two sea anemone alarm pheromones (anthopleurine and \textit{ent}-anthopleurine)\textsuperscript{29} were obtained with >99\% e.e.

In the above examples of tandem metathesis-oxidation, the oxidation catalyst is believed to be RuO\textsubscript{4}, a well-known olefin oxidant.\textsuperscript{30} Plietker has postulated that the reaction of CeCl\textsubscript{3} \cdot 6 H\textsubscript{2}O with NaIO\textsubscript{4} results in formation of Ce(IV)-periodato complexes,\textsuperscript{25} which then
oxidize the metathesis catalysts to RuO₄. Differences in oxidation activity noted above may reflect variations in the efficiency with which RuO₄ is produced in situ. The efficiency of the oxidation step could potentially be improved further by a deeper mechanistic understanding of the processes involved.

1.2.4 Tandem metathesis-isomerization

In an early study of tandem RCM-isomerization promoted by Ru-1b', Snapper and coworkers screened various agents (HCO₂H, NaBH₄CN, methanolic NaOMe and H₂) for their ability to promote isomerization. Optimal isomerization activity was observed using H₂ diluted with N₂ (i.e. "regeneration gas"; 5% H₂) to suppress competing hydrogenation. α-Enol ethers were obtained from 1,7- and 1,8-dienes (Scheme 1.10), although small amounts (<10%) of saturated byproducts were also formed.

Schmidt later employed the inorganic hydrides NaH and NaBH₄ to promote similar reaction chemistry (Scheme 1.11). The precatalyst used was Ru-1a. Isomerization yielded only minor amounts of trisubstituted olefin, despite Snapper's proposed 4 kcal/mol preference for this product.
Scheme 1.11. Ru-1a-catalyzed RCM-isomerization.\textsuperscript{33}

This study was followed by an assessment of the capacity of various bases to turn on isomerization (Table 1.2).\textsuperscript{33} Isopropoxide (i.e. NaOH/PrOH) enabled much faster reaction. Unlike the hydride reagents, it also enabled isomerization even where an alcohol substituent was present (R = OH; Scheme 1.11). However, transfer hydrogenation was also observed.\textsuperscript{34}
In subsequent investigations, the isopropoxide system was used as the system of first resort, but NaH or NaBH\textsubscript{4} were used when transfer hydrogenation was found to compete.

Table 1.2. Dependence of isomerization yields on the trigger used to convert the metathesis catalyst into an isomerization catalyst in the reactions of Scheme 1.11.\textsuperscript{33}

<table>
<thead>
<tr>
<th>Trigger</th>
<th>Loading (mol%)\textsuperscript{a}</th>
<th>Time (h)\textsuperscript{b}</th>
<th>Ring size</th>
<th>Yield range (%)</th>
<th>A : B</th>
</tr>
</thead>
<tbody>
<tr>
<td>CH\textsubscript{2}=CHOEt</td>
<td>500</td>
<td>5-7</td>
<td>five</td>
<td>61-77</td>
<td>&lt;8:1</td>
</tr>
<tr>
<td>NaH (or NaBH\textsubscript{4})</td>
<td>30-50</td>
<td>5-7</td>
<td>five</td>
<td>53-79</td>
<td>&lt;8:1</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>six</td>
<td>73-94</td>
<td>&gt;19:1</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>seven</td>
<td>44-82</td>
<td>&gt;19:1</td>
</tr>
<tr>
<td>NaOH + 'PrOH'\textsuperscript{c}</td>
<td>50</td>
<td>1-2</td>
<td>six</td>
<td>63-91</td>
<td>&gt;19:1</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>seven</td>
<td>51-74</td>
<td>&gt;19:1</td>
</tr>
<tr>
<td>HSiEt\textsubscript{3}</td>
<td>110</td>
<td>10-16</td>
<td>six</td>
<td>71-84</td>
<td>&gt;19:1</td>
</tr>
</tbody>
</table>

\textsuperscript{a} Catalyst loading refers to the amount of Ru-1a initially used for RCM. \textsuperscript{b} Time is that required for complete consumption of the RCM product during isomerization. \textsuperscript{c} Isopropanol was used as cosolvent (25% v/v).

The Schmidt group used these methodologies to establish high-yield routes to enantiopure spirocycles,\textsuperscript{35} diastereopure dihydrofurans and dihydropyrans,\textsuperscript{36} unsaturated six- and seven-membered glycals, and eight-membered oxacycles.\textsuperscript{37} Various natural products were also prepared. These include L-rhodinal and L-amicetal,\textsuperscript{38} oligosaccharide side-chains present in
naturally-occurring antibiotic and anticancer agents, as well as the potent antibiotic centrolobine.\textsuperscript{40}

Blechert and coworkers have reported the enantioselective preparation of (−)-centrolobine using their methodology for diastereoselective ring-rearrangement metathesis (dRRM) via \textbf{Ru-1b}',\textsuperscript{41} followed by Schmidt's isomerization protocol involving post-RCM addition of NaBH\textsubscript{4} (40 mol%).\textsuperscript{42}

In all the above studies, the isomerization catalyst is reasonably presumed to be a ruthenium hydride. Such complexes can be highly active for olefin isomerization.\textsuperscript{53} Schmidt and coworkers observed several hydride signals by in situ \textsuperscript{1}H NMR analysis of crude RCM-isomerization reaction mixtures, although the chemical shifts (−7 > δ\textsubscript{H} > −15 ppm) suggested coordinative saturation. \textsuperscript{31}P NMR analysis of CH\textsubscript{2}=CHOEt-assisted reaction mixtures also revealed the presence of hydridocarbonyl complex \textbf{Ru-7a}, formed by thermolysis of ethoxylidene \textbf{Ru-22a}, as discussed in Section 1.4.\textsuperscript{44}

1.2.5 Tandem enyne metathesis-hydrovinylation

Snapper and coworkers reported tandem RCEYM-hydrovinylation of 1,6- and 1,7-enynes using the first-generation catalyst \textbf{Ru-1a} (Scheme 1.12).\textsuperscript{45} The hydrovinylation catalyst, hydride \textbf{Ru-7a}, was generated using the Mol strategy (see Section 1.4).\textsuperscript{46} Thus, after synthesis of the conjugated 1,3-dienes by ethylene-assisted enyne metathesis, methanolic NaOMe was added to convert the metathesis catalyst into \textbf{Ru-7a}.\textsuperscript{47,50} Reaction with ethylene yielded the 1,4-hydrovinylation products depicted. No 1,2-hydrovinylation was observed (cf. the behaviour of the \textbf{Ru-7a}-HBF\textsubscript{4} system; Figure 1.4). The preference for 1,4-addition was attributed to isomerization of the conjugated diene prior to hydrovinylation. The authors
suggested that this may be due to the ability of methanol to compete with ethylene for binding to Ru. Control experiments showed that hydrovinylation was faster for a 1:1 mixture of Ru-1a and Ru-7a than for Ru-7a alone. An unspecified cooperative interaction of the two catalysts was inferred. This implies that the reasonable yields seen in the tandem metathesis reactions rely upon incomplete conversion of Ru-1a into Ru-7a. In situ NMR analysis confirmed that this transformation is only ca. 50% over the 10 min period allowed.

Scheme 1.12. Ru-1a-catalyzed RCEYM-isomerization.\textsuperscript{45}

1.2.6 Tandem metathesis-hydrogenation

Saturation of metathesis polymers is key to preventing unwanted chemistry at the olefinic backbone, as discussed in more detail below. The simplest protocol entails exposure to H\textsubscript{2} after metathesis is complete. Grubbs extended this methodology to tandem RCM-hydrogenation, using Ru-1a/b' as the RCM catalyst. H\textsubscript{2}-hydrogenation yielded saturated cyclic alkanes, ethers, ketones, lactones, and lactams (Scheme 1.13).\textsuperscript{51} Yields of saturated products were lower for trisubstituted olefins than disubstituted olefins, owing to the steric encumbrance of the double bonds. This protocol was also applied to CM-hydrogenation of various olefins (Scheme 1.14).
This report also demonstrated transfer dehydrogenation of an alcohol to a ketone following CM of 3-butene-2-ol with 5-acetoxy-1-hexene, using NaOH and 3-pentanone to trigger formation of the hydrogenation catalyst (Scheme 1.15). Tandem RCM-transfer dehydrogenation-hydrogenation was then used in a one-pot preparation of (R)-(−)-muscone (Scheme 1.16).
Scheme 1.16. Ru-1b'-catalyzed RCM-transfer dehydrogenation-hydrogenation.\textsuperscript{51}

More recently, Yu and coworkers reported use of Ru-1b to promote tandem RCEYM-hydrogenation of chiral $\alpha,\beta$-acetylenic esters (Scheme 1.17).\textsuperscript{52}

Scheme 1.17. Ru-1b-catalyzed RCEYM-hydrogenation.\textsuperscript{52}

Ramharter and coworkers later employed the first-generation diphenylvinylidene Grubbs catalyst Ru-1a\textsuperscript{Ph2} to prepare the polycyclic scaffold of (+)-lycoflexine, a potent acetylcholinesterase inhibitor (Scheme 1.18).\textsuperscript{53}
Scheme 1.18. Ru-1a\textsuperscript{Ph2}-catalyzed RCEYM-hydrogenation.\textsuperscript{53}

Dixneuf and coworkers described tandem CM-hydrogenation using the Hoveyda-Grubbs isopropoxybenzylidene catalysts such as Ru-3b\textsuperscript{t}. In an initial report, saturated nitrile-esters were prepared via CM-hydrogenation of acrylonitrile with unsaturated fatty esters (Scheme 1.19).\textsuperscript{54}

Scheme 1.19. Ru-3b\textsuperscript{t}-catalyzed CM-hydrogenation.\textsuperscript{54}

The Dixneuf group later employed Ru-3e\textsuperscript{t} (in which the NHC ligand is H\textsubscript{2}ITol; Scheme 1.20) for tandem self-CM-hydrogenation of \( \omega \)-undecylenal.\textsuperscript{55} This process is of interest in the context of renewable feedstocks, as the olefinic precursor is obtained by cracking castor oil. Tandem CM-hydrogenation of \( \omega \)-undecylenal with acrolein was also investigated: yields of saturated \( \alpha,\omega \)-alcohols were on the order of 75\%.
Tandem metathesis-hydrogenation has attracted most attention in the context of metathesis polymerization, as a means of reducing the polymers obtained via acyclic diene metathesis (ADMET) and ring-opening metathesis polymerization (ROMP). Reduction of ROMP materials is of particular importance in enhancing the stability of these designer materials toward thermal and oxidative degradation. The following section describes in detail the developments in this area since the 1997 report by McLain, Brookhart and coworkers.

In this first, groundbreaking study, ROMP of a cyclooctene derivative was followed by hydrogenation at high temperatures and pressures to yield ester-functionalized polyethylene (Scheme 1.21). The process was presumed to involve transformation of the metathesis catalyst Ru-1a\(^{\text{Ph2}}\) into a hydride species formulated as "RuHCl(PCy\(_3\))\(_2". Saturation reached >99\%, but forcing conditions were required (135 °C), which could promote competitive crosslinking.

Scheme 1.20. Ru-3e\(^{\prime}\)-catalyzed CM-hydrogenation.\(^{55}\)

Scheme 1.21. Ru-1a\(^{\text{Ph2}}\)-catalyzed ROMP-hydrogenation of a cyclooctene substrate.\(^{57}\)
Grubbs extended this approach to concurrent ROMP of cyclooctadiene (COD) and atom transfer radical polymerization (ATRP) of methylmethacrylate (MMA). This study used the first-generation initiator Ru-1a<sup>Br</sup> (Scheme 1.22).<sup>58</sup> Hydride complex RuHCl(H<sub>2</sub>)(PCy<sub>3</sub>)<sub>2</sub> Ru-6a was presumed to be the hydrogenation catalyst.

Scheme 1.22. Ru-1a<sup>Br</sup>-catalyzed ROMP-hydrogenation of cyclooctadiene.<sup>58</sup>

Fogg and coworkers were able to reduce the hydrogen pressure required to 1 atm.<sup>59</sup> This advance rested on use of NEt<sub>3</sub> and MeOH as triggers to convert the ROMP catalyst Ru-1a into RuHCl(CO)(PCy<sub>3</sub>)<sub>2</sub> Ru-7a, a key hydrogenation catalyst (Section 1.4). The latter was indeed observed via in situ NMR analysis of crude reaction mixtures (Scheme 1.23).

Scheme 1.23. Ru-1a-catalyzed ROMP-hydrogenation of cyclooctene.<sup>59</sup>

Subsequent studies by the Fogg group integrated the high ROMP activity and chain-length control of the third-generation Grubbs catalyst Ru-1d with the high hydrogenation efficiency of Ru-1b. This approach was used to prepare saturated neoglycopolymers, as well as other saturated polymers. The key to overcoming the poor hydrogenation activity of Ru-1d lay in adding PCy<sub>3</sub> post-ROMP, thus converting the Ru-alkylidene endgroup into that formed in ROMP via Ru-1b.<sup>60</sup> Subsequent addition of NEt<sub>3</sub> and MeOH enabled generation
of a more robust, PCy₃-stabilized hydrogenation catalyst. This methodology was used to prepare saturated neoglycopolymers which proved effective as collagen crosslinking agents for construction of artificial corneas (Scheme 1.24). Nishihara and coworkers later used this protocol to prepare cyano- and ester-functionalized polynorbornanes.


The above studies demonstrate how understanding of the organometallic chemistry involved in "switching" the nature of the catalyst can aid in design of effective protocols for assisted tandem catalysis. It is noteworthy that the hydridocarbonyl complex RuHCl(CO)(PCy₃)₂ Ru-7a was implicated as "Catalyst B" during tandem metathesis-isomerization, RCEYM-hydrovinylation, and ROMP-hydrogenation. The diverse olefin functionalization activity of hydridocarbonyl complexes is illustrated further in the following section.
1.3 Olefin functionalization activity of RuHCl(CO)(L)(PCy$_3$)$_2$ Ru-7

The hydridocarbonyl complexes RuHCl(CO)(L)(PCy$_3$)$_2$ Ru-7, particularly bis-phosphine Ru-7a, promote many olefin transformations, ranging from simple hydrogenation and isomerization to coupling reactions (Figure 1.4).

![Olefin functionalization processes catalyzed by Ru-7](image)

**Figure 1.4.** Olefin functionalization processes catalyzed by Ru-7. Bold arrows denote compatibility with internal olefins (i.e. potential relevance to tandem (R)CM-functionalization).

Rempel carried out pioneering work on Ru-7a as a hydrogenation catalyst, with a particular focus on reduction of the C=C bonds in nitrile-butadiene rubber (NBR).$^{63-64}$ Forcing conditions were required (40 atm H$_2$, 160 °C) for these challenging polymer substrates. More recent work by de Souza and coworkers showed that this transformation can be carried out in ionic liquids.$^{65}$ Yi and coworkers have reported that Ru-7a effects efficient hydrogenation of cis and trans olefins, as well as terminal olefins, in molecular
substrates. This not surprising, given the much greater accessibility of the olefinic group in small molecules, relative to polymers. In subsequent work, Yi et al. included HBF$_4$ as a co-catalyst to sequester dissociated PCy$_3$ as [HPCy$_3$]BF$_4$ (and hence presumably to trap the catalyst as the four-coordinate active species RuHCl(CO)(PCy$_3$) Ru-7a'). Low pressures of H$_2$ (1-2 atm) could then be used, although the effect on catalyst lifetime (total TON) was not explored. Soon after, Yi and Nolan reported the related catalyst RuHCl(CO)(IMes)(PCy$_3$) Ru-7b. This exhibits lower hydrogenation activity than Ru-7a at ambient temperatures (presumably due to the low lability of the PCy$_3$ ligand trans to an NHC), but superior activity at 100 °C. In a comparative study of the hydrogenation activity of Ru-7a/b and the PPh$_3$-substituted analogues RuHCl(CO)(NHC)(PPh$_3$) Ru-14b/b', Fogg and coworkers correlated hydrogenation activity with phosphine lability.

The olefin isomerization activity of Ru-7a was noted by Yi in studies originally directed at hydrogenation, and similar behaviour was noted for Ru-7b and Ru-14 by Fogg. Since then, Arisawa explored isomerization of allyl amines to vinyl amines, using as a catalyst system Ru-1b' and vinylxytrimethylsilane. This system generates Ru-7b' in situ, as discussed in more detail below. The latter complex was observed by in situ NMR analysis. Likewise, Ru-7a was observed by NMR analysis on use of a Ru-1a-CH$_2$=CHOEt system used for tandem RCM-isomerization (Section 1.2.4).

To the multitude of reports concerning catalysis by Ru-7a, Marciniec and coworkers have contributed a very large body of work on silylative, borylative and germylative coupling of many terminal olefins with vinyl silanes, boronates and germanes, respectively.
Yi and coworkers reported that **Ru-7a** catalyzes the coupling of terminal olefins with secondary amines. The **Ru-7a/HBF$_4$** catalyst system was used for hydroamination of terminal olefins, including conjugated olefins, by primary arylamines and benzocyclic amines. Hydrovinylation of vinylarenes and conjugated internal olefins, as well as terminal and internal dienoates (typically at elevated temperatures), was also reported. RajanBabu and Connell were able to use mild conditions by adding AgOTf or AgSbF$_5$ as cocatalysts (1:1 vs. Ru). The activity was attributed to generation of four-coordinate $[\text{RuH(CO)(PCy}_3)_2]X$ ($X = \text{OTf, SbF}_5$) by chloride abstraction from **Ru-7a**.

The loadings of **Ru-7** employed in many of these studies (<2 mol%) are low compared to those typical of olefin metathesis (1-20 mol%). This is an asset in terms of the efficiency with which post-metathesis catalysis can be carried out, as it can compensate for the inefficient formation of **Ru-7**. As the catalyst loadings used in olefin metathesis are forced to improve, however, this luxury will disappear. Even in the current state of the art, the long reaction times and forcing conditions often required for the "alkylidene-to-hydride" or other transformations described above underscore the need for greater efficiency. The following section summarizes the efficiency with which **Ru-7** could be generated from the Grubbs catalysts at the outset of this thesis work.

### 1.4 Transformation of Grubbs catalysts into hydridocarbonyls

In the first mechanistic investigation of the reaction of **Ru-1a** with H$_2$ ("hydrogenolysis"), Fogg and coworkers reported that the benzylidene ligand of **Ru-1a** is evolved as toluene, with co-formation of Ru(H$_2$)Cl$_2$(PCy$_3)_2$ **Ru-5** and its dihydride tautomer Ru(H)$_2$Cl$_2$(PCy$_3)_2$ **Ru-5'**. Use of a base to abstract HCl yielded RuHCl(H$_2$)(PCy$_3)_2$ **Ru-6a** as the sole product.
Proton Sponge® (1,8-bis(dimethylamino)naphthalene) was used for convenience in NMR monitoring, but NEt₃ was also effective. A requirement for several equivalents of base was observed: this was attributed to rechlorination of the ruthenium species by the CH₂Cl₂ solvent. Subsequent catalytic studies showed that use of methanol as co-solvent greatly enhanced hydrogenation activity during ROMP-hydrogenation (Scheme 1.25).

In situ NMR analysis revealed the known, highly active hydrogenation catalyst RuHCl(CO)(PCy₃)₂ Ru-7a, which was presumed to form via decarbonylation of methanol by Ru-6a (a long-established process; see later). Higher hydrogenation activity was inferred for Ru-7a, vs. Ru-6a, but was not directly examined. The question of the efficiency with which both complexes can be obtained from Ru-1a, or the important second- and third-generation Grubbs catalysts, was taken up in the present work.

![Scheme 1.25. Hydrogenolysis of Ru-1a](image)

Subsequent work by Mol and coworkers reported that H₂ is not required in order to form the hydridocarbonyl complexes from Ru-1 (Ru-1a: L = PCy₃; Ru-1b': L = H₂IMes; Ru-1f': L = H₂IPr). Reaction of these benzylidene complexes with methanol in the presence of a base ("methanolysis", Scheme 1.26) likewise affords Ru-7, albeit in variable yields. The Ru-1a study employed the inorganic bases NaOH, NaOMe, and K₂CO₃ to effect rapid formation of Ru-7a in moderate yield. Methanolysis of second-generation Ru-1b' and Ru-
If' in the presence of NEt₃ afforded the related complexes Ru-7b' and Ru-7f' and multiple unidentified side-products. Ligand disproportionation during methanolysis of Ru-1b' is indicated by the formation of bis(PCy₃) species Ru-7a.

Scheme 1.26. Methanol-induced transformation of benzylidene complexes Ru-1a/b'/f' into carbonyl hydride Ru-7.⁴⁶,⁸³,⁸⁴

A plausible mechanism for methanolysis of Ru-1a (Scheme 1.27) was proposed by Mol and coworkers.⁴⁶ Dehydrohalogenation of Ru-1a and methanol was suggested to form a methoxide complex, which undergoes proton transfer to the benzylidene Cₓ to form a benzyl intermediate and formaldehyde. Abstraction of a proton from formaldehyde would liberate the benzyl ligand as toluene, following which formyl deinsertion would yield Ru-7a.

Scheme 1.27. Proposed mechanism for base-assisted methanolysis of Ru-1a.⁴⁶

A Grubbs report described the formation of hydridocarbonyl RuH(OC(O)CF₃)(CO)(PPh₃)₂ Ru-25 by decomposition of a Fischer carbene (Scheme 1.28).⁸⁵ A mechanism involving PPh₃
dissociation and formyl deinsertion was proposed. The resulting formyl intermediate may undergo reductive elimination of PhCH$_2$OC(O)CF$_3$ to form hydride **Ru-25** (Scheme 1.28, Path (a)) or of toluene to generate carbonyl **Ru-26** (Scheme 1.28, Path (b)). Both PhCH$_2$OC(O)CF$_3$ and PhCH$_2$D were observed (GC-MS) following decomposition of Ru(OC(O)CF$_3$)$_2$(PPh$_3$)$_2$(=CDOCH$_2$Ph) $\alpha$-d$_1$-**Ru-24**. The 8.5:1 ratio indicated a strong preference for hydridocarbonyl formation.

![Scheme 1.28. Proposed pathways for decomposition of Ru-24.](image)

Grubbs suggested that such a mechanism could also account for generation of **Ru-7a** on thermolysis of the Fischer carbene RuCl$_2$(PCy$_3$)$_2$(=CHOEt) **Ru-22a** (Scheme 1.29, Path (a)).$^{44}$ Arisawa later described a much more efficient process involving CM of **Ru-1b'$^\dagger$' with CH$_2$=CHOTMS. This affords RuHCl(CO)(H$_2$IMes)(PCy$_3$) **Ru-7b'$^\dagger$' in quantitative yields within 1 hour at 50 °C (Scheme 1.29, Path (b)).$^{71}$ Reactivity studies with **Ru-22a/b** are confined to metathesis and thermolysis, and the potential for combining metathesis quenching with tandem catalysis has not been considered to date.
Scheme 1.29. Formation of \textbf{Ru-7} by thermolysis of Fischer carbenes.\textsuperscript{44,71}

The organometallic chemistry of Grubbs methyldienes \ce{RuCl_2(L)(PCy_3)(=CH_2)} \textbf{Ru-2a/b} is even less studied, perhaps surprisingly given the importance of these species as catalyst resting states in Ru-catalyzed RCM\textsuperscript{86} and CM.\textsuperscript{87} A rare exception is a report by Caulton and coworkers, who described the clean hydrogenolysis of \textbf{Ru-2a} to \textbf{Ru-6a} (Scheme 1.30).\textsuperscript{88}

Scheme 1.30. Hydrogenolysis of \textbf{Ru-2a}.\textsuperscript{88}

Assessment of the efficiency with which the Grubbs catalysts \textbf{Ru-1a/b} can be converted into their hydridocarbonyl analogues \textbf{Ru-7a/b}, using the methods summarized above, could improve existing methodologies in tandem ROMP-hydrogenation. Insight into methods suitable for the corresponding transformation of methyldienes \textbf{Ru-2a/b} would open up new opportunities for (R)CM-functionalization, while such studies of Fischer carbenes \textbf{Ru-22a/b} would enable introduction of an intervening quenching step.
1.5 Scope of Thesis Work

This work was aimed at establishing the efficiency with which the Grubbs catalysts are transformed into Ru-hydrides using state-of-the-art protocols for ROMP-hydrogenation. The relative hydrogenation activity of the ruthenium products is also examined. Transformation of the first- and second-generation Grubbs benzylidenes into hydridocarbonyl complexes using various chemical agents is examined. The corresponding behaviour of ruthenium methylidenes and ethoxylidenes is also evaluated, to assess the compatibility of these transformations with tandem (R)CM-functionalization and metathesis quenching, respectively. Particular care is taken to examine disproportionation of Ru-NHC-catalysts, a potential vector for catalyst decomposition. In studying second-generation Grubbs catalysts, we chose to focus on the chemistry of the IMes derivatives, because preliminary studies of H₂IMes complex Ru-1b' in ROMP-hydrogenation indicated much lower hydrogenation activity (work carried out by Dr. Debbie Mitra of the Fogg group). This may point toward a lower thermal stability of the H₂IMes complexes (perhaps a function of the higher lability of the phosphine ligand in Ru-1b' relative to IMes complex Ru-1b), although this issue was not investigated.
1.6 References

22. Low yields of dihydroxylated product are obtained when trace amounts of CH₂Cl₂ are present.
23. It is notable that post-metathesis solvent removal violates the waste-reduction objectives of green chemistry (Section 1.1).
34. The authors speculate that unprotected alcohol groups and exocyclic olefinic bonds aid in transfer hydrogenation by coordinating to the metal center.
44. Louie, J.; Grubbs, R. H. Organometallics 2002, 21, 2153-2164.
63. Martin, P.; McManus, N. T.; Rempel, G. L. Ibid. 1992, 73, 161
Chapter 2. Carbonyl-Amplified Catalyst Performance: Assessing the Balance Between Stability and Activity for RuHCl(H₂)LL' and RuHCl(CO)LL' Catalysts.*

2.1 Introduction

The high volume of waste characteristic of fine chemicals and pharmaceutical manufacturing¹,² was discussed in Chapter 1. Such issues are coming under increasing scrutiny in a stringent economic climate in which the contribution of waste to process costs is no longer regarded as insignificant. Tandem catalysis has attracted much interest³-⁵ for the potential economic and environmental benefits that accrue from coupling multiple catalytic transformations in a single vessel. Particularly important is the potential to improve process efficiencies by eliminating unnecessary workup stages and solvent use, two major contributors to waste in pharmaceutical manufacturing.¹,⁶ Improved efficiencies in catalyst consumption confer added advantages in reducing direct catalyst costs, as well as indirect costs associated with purification of the organic products.

Within a program of study focusing on tandem catalysis, prior work in the Fogg group targeted development of efficient methodologies for tandem ROMP-hydrogenation (ROMP = ring-opening metathesis polymerization).⁷-¹⁰ These and improved methodologies, which enable important routes to "designer materials", are described in detail in Chapter 3. In general, they rest on the accessibility of five-coordinate Ru hydrides from Grubbs catalysts of type Ru-1 (Scheme 2.1). Earlier work by Samantha Drouin of this research group⁹ showed that the

hydrido-dihydrogen complex Ru-6a is formed cleanly by hydrogenolysis of Ru-1a in the presence of base: the corresponding hydridocarbonyl complexes Ru-7 are formed from both Ru-113 and Ru-67 by reaction with methanol or other primary alcohols, via established alcohol decarbonylation pathways.14-17 Small amounts of methanol cosolvent dramatically increased hydrogenation efficiency. Use of isopropanol led to smaller rate accelerations. An increase in the dielectric constant of the reaction medium almost certainly contributes to the beneficial effect. The higher activity in the presence of the primary alcohol, however, also correlates with formation of Ru-7a – by inference, a more reactive catalyst than Ru-6a.7

Scheme 2.1. Hydride complexes formed from first- and second-generation Grubbs metathesis catalysts.7,9,11-13

While ample precedents exist for hydrogenation via Ru-7a,11,18-23 catalysis via Ru-6a has gone less studied,24 and no direct comparison of the hydrogenation activity of the two complexes has been reported. The possibility that Ru-7a is more active is intriguing, given that much evidence correlates higher hydrogenation activity with a more electron-rich Ru center. Thus, Ru catalysts containing strongly σ-donating alkylphosphine ligands outperform those containing arylphosphines, and incorporation of a CO ligand is known to decrease hydrogenation activity in arylphosphine complexes of Ru, Rh, and Ir.22,25-27 The latter behaviour is consistent with the inhibiting effect of the π-acid ligand on both phosphine loss
(a required step in olefin hydrogenation via \textbf{Ru-7a} and related polyphosphine catalysts), and oxidative addition of dihydrogen. Further, in a computational study designed to probe the effect of a $\sigma$-donor, vs. a $\pi$-acid, ancillary ligand in RuHCl(L)(P$^{3}$Pr$_{3}$)$_{2}$ model systems (L = CO, PH$_{3}$), a systematically more stable reaction profile emerged for the PH$_{3}$ species. That is, this study revealed no electronic basis for increased hydrogenation activity on the part of the CO complex.

Given the apparent contradiction between these findings and the tandem catalysis data in the presence of methanol, a systematic experimental study was undertaken to compare the hydrogenation activity of the isolated, well-defined dihydrogen and carbonyl complexes. The complexes examined are those accessible from the first- and second-generation Grubbs catalysts, viz. RuHCl(H$_{2}$)(L)(PCy$_{3}$) (\textbf{Ru-6}) and RuHCl(CO)(L)(PCy$_{3}$) (\textbf{Ru-7}). This Chapter describes the synthesis of the previously unreported \textbf{Ru-6b}, and the higher hydrogenation efficiency of the carbonyl catalysts relative to their dihydrogen analogues. Finally, it demonstrates that this effect originates in the longer lifetimes of the CO complexes, rather than their higher reactivity.

\textbf{2.2 Results and Discussion}

\textit{2.2.1 Synthesis of RuHCl(H$_{2}$)LL' complexes Ru-6.}

We recently reported a clean, high-yield route to the hydridocarbonyl complexes \textbf{Ru-7}, in which RuHCl(CO)(PPh$_{3}$)$_{3}$ \textbf{Ru-8} is warmed with PCy$_{3}$ in benzene. The success of this approach led us to attempt synthesis of \textbf{Ru-6a} by the analogous reaction of RuHCl(PPh$_{3}$)$_{3}$ \textbf{Ru-9}. These efforts were thwarted, however, by the poor solubility of \textbf{Ru-9} in aromatic solvents, which resulted in only partial conversion to RuHCl(PCy$_{3}$)(PPh$_{3}$)$_{2}$ \textbf{Ru-10} (30% of
the soluble portion, and an undetermined amount of the suspended material; Scheme 2.2) over 24 h at room temperature. Complete conversion, moreover, was hindered by the onset of product decomposition on longer reaction, while use of methylene chloride, in which Ru-9 is soluble, is precluded by the susceptibility of the basic alkylphosphine to chlorination by this solvent. We therefore prepared Ru-6a by existing methods, involving hydrogenolysis of Ru-1a or ligand exchange30 of [RuCl₂(COD)]ₙ with PCy₃ (in the latter synthesis, we used isopropanol as a convenient alternative to the original sec-butanol solvent,30 and higher pressures of H₂).

Scheme 2.2. Attempted synthesis of Ru-6a. Dashed arrow indicates incomplete reaction: for details, see text.

Leitner and coworkers prepared dihydride complex Ru(H)₂(H₂)₂(IMes)(PCy₃) Ru-11b by ligand exchange of Ru(H)₂(H₂)₂(PCy₃)₂ Ru-11a with IMes at 55 °C under H₂.31 The room-temperature reaction did not yield product. We obtained RuHCl(H₂)(IMes)(PCy₃) Ru-6b by the corresponding reaction of Ru-6a under argon: in this case, reaction was complete within 2 h at 23 °C (Equation 2.1). No products other than Ru-6b and free PCy₃ were evident by NMR analysis, and the 1:1 ratio between the signals for free and bound PCy₃ confirmed clean formation of Ru-6b (i.e. free of paramagnetic byproducts; see below). Extraction of
the free phosphine with hexanes enabled isolation of clean **Ru-6b** in ca. 70% yield. Its identity is supported by spectroscopic and elemental analysis.

\[
\begin{array}{c}
\text{H} \\
\text{Cl} \\
\text{Cy}_3\text{P} \text{Ru} \text{PCy}_3 \\
\text{Ru-6a} \\
\end{array} \quad \xrightarrow{1.1 \text{ IMes} \ 23 \degree C, 2 \text{ h}} \quad \begin{array}{c}
\text{H} \\
\text{Cl} \\
\text{IMes} \text{Ru} \text{PCy}_3 \\
\text{Ru-6b} \\
\end{array}
\]

The NMR features for **Ru-6b** correspond well with those for **Ru-6a** (Table 2.1). Thus, a \(^{31}\text{P}\{^1\text{H}\}\) NMR singlet appears at 56.4 ppm, and the broad singlet due to the hydride/dihydrogen ligands at -16.44 ppm. The \(T_{1\text{(min)}}\) value for the latter signal, 36.6 ms in \(\text{C}_7\text{D}_8\) (253K, 300 MHz), corresponds to a H-H distance of 1.03 Å, assuming a fast-spinning H\(_2\) ligand.\(^{32}\) Both the breadth of this signal, and its comparatively long relaxation time, are characteristic of \(\eta^2\)-H\(_2\) perturbed by interaction with cis-hydride.\(^{32}\) In comparison, a value of ca. 30 ms was reported for **Ru-6a** at 243 K and 250 MHz.\(^{33}\) Exchange between classical and nonclassical hydrides occurs with a typical barrier of ca. 10-13 kcal/mol.\(^{34}\) The averaged NMR signal for these ligands in **Ru-6b** appears ca. 11 ppm downfield from the -27.6 ppm location of the doublet due to the unperturbed hydride in dinitrogen analogue **Ru-12a** (the latter complex is discussed in greater detail below). Well-resolved singlets appear for the IMes methyl, aromatic, and \(=\text{CCHN}\) groups for **Ru-6b**, integration of which against the H/H\(_2\) singlet is consistent with the proposed structure.
### Table 2.1. Key NMR data for Ru-hydride complexes relevant to this work (Ar, 298 K).

<table>
<thead>
<tr>
<th>Complex</th>
<th>Solvent</th>
<th>$\delta_p$ (ppm)</th>
<th>$\delta_h$ (ppm)</th>
<th>Ref.</th>
</tr>
</thead>
<tbody>
<tr>
<td>RuHCl(H$_2$)(PCy$_3$)$_2$ Ru-6$^a$</td>
<td>C$_6$D$_6$</td>
<td>54.2 (s)</td>
<td>$-16.3$ (br s)$^b$</td>
<td>$^9$,$^{33}$</td>
</tr>
<tr>
<td>RuHCl(N$_2$)(PCy$_3$)$_2$ Ru-12a</td>
<td>C$_6$D$_6$</td>
<td>43.7 (s)</td>
<td>$-27.26$ (t, $^2J_{HP} = 18$ Hz)</td>
<td>$^35$</td>
</tr>
<tr>
<td>RuHCl(H$_2$)(IMes)(PCy$_3$) Ru-6b</td>
<td>C$_6$D$_6$</td>
<td>56.4 (s)</td>
<td>$-16.44$ (br s)$^b$</td>
<td>this work</td>
</tr>
<tr>
<td>RuHCl(N$_2$)(IMes)(PCy$_3$) Ru-12b</td>
<td>C$_6$D$_6$</td>
<td>45.1 (s)</td>
<td>$-27.63$ (d, $^2J_{HP} = 21$ Hz)</td>
<td>this work</td>
</tr>
<tr>
<td>RuHCl(CO)(PCy$_3$) Ru-7a$^a$</td>
<td>C$_6$D$_6$</td>
<td>46.9 (s)</td>
<td>$-24.21$ (t, $^2J_{HP} = 18$ Hz)</td>
<td>$^29$</td>
</tr>
<tr>
<td>RuHCl(CO)(IMes)(PCy$_3$) Ru-7b</td>
<td>C$_6$D$_6$</td>
<td>47.8 (s)</td>
<td>$-24.82$ (d, $^2J_{HP} = 21$ Hz)</td>
<td>$^29$</td>
</tr>
<tr>
<td>Ru(H)$_2$Cl$_2$(PCy$_3$)$_2$ Ru-5</td>
<td>C$_6$D$_6$</td>
<td>91.3 (s)</td>
<td>$-12.0$ (t, $^2J_{HP} = 32$ Hz)</td>
<td>$^9$</td>
</tr>
</tbody>
</table>

$^a$ In C$_6$D$_6$, the $^{31}$P($^1$H) NMR singlet for Ru(H$_2$)Cl$_2$(PCy$_3$)$_2$ Ru-5'$^*$ is coincident with that for Ru-6a, but is accompanied by a singlet for the Ru(IV) tautomer Ru-5 (ratio 1:2). The corresponding hydride signals appear at $-16.2$ ppm (br s, Ru-5') and $-12.0$ ppm (t, $^2J_{HP} = 32$ Hz, Ru-5). In CD$_2$Cl$_2$, only Ru-5 is present. $^b$ The hydride and dihydrogen signals for Ru-6 appear as a single broad peak integrating to 3H. A chemical shift of $-16.8$ (br t, $^2J_{HP} = 11$ Hz) was originally reported for Ru-6a in CD$_2$Cl$_2$ (250 MHz). $^33$ The difference may reflect the presence of H$_2$ in the literature report.

#### 2.2.2 Catalytic Activity of Ru-6 vs. Ru-7.

Hydrogenation studies focused on the substrates shown in Chart 2.1. In a preliminary assessment of the relative hydrogenation activity of catalysts Ru-6 and Ru-7, we established their baseline activity toward styrene (S1) at 23 °C. The duration of these experiments was normalized to that required for quantitative formation of ethylbenzene by the most reactive catalyst, Ru-7a (Figure 2.1a). The lower activity of the IMes derivative Ru-7b at room temperature, vs. its "first-generation" analogue Ru-7a, has precedent. $^{37}$ the data for Ru-6 indicate that this trend is retained for the H$_2$ complexes. We attribute the drop in activity to the low lability of PR$_3$ trans to an NHC ligand, $^{38,39}$ originally described by the Grubbs group in a seminal paper on olefin metathesis. $^{38}$ Within both the bis(PCy$_3$) and the IMes-PCy$_3$ series, the activity of the CO complexes Ru-7 is consistently greater than that of their dihydrogen analogues Ru-6. The implications in terms of process efficiency are manifested most explicitly in the time profile for complete hydrogenation of styrene at a catalyst.
loading of 0.1 mol % (Figure 2.1b). Reduction by **Ru-7a** under the conditions specified is complete at 1.5 h, while quantitative reduction via **Ru-6a** requires 12 h.

We also evaluated the tendency of the more reactive catalysts **Ru-6a/Ru-7a** to promote competing isomerization, using allylbenzene **S2** as substrate. Hydridocarbonyl **Ru-7a** proves considerably more reactive than its H₂ analogue **Ru-6a** in both reduction and isomerization (Figure 2.1a). Of note, hydrogenation is ca. 30 times faster than isomerization for **Ru-6a**, but only 15 times faster for **Ru-7a**, suggesting that the higher activity of the latter may come at the price of reduced discrimination.

![Chemical structure of Ru catalysts](image)

**Figure 2.1.** (a) Relative catalyst performance in hydrogenation of styrene (**S1**, 1.5 h, filled bars) and allylbenzene (**S2**, 0.5 h, unfilled), showing turnover frequencies (TOF; mol product • mol catalyst⁻¹ h⁻¹), with isomerization TOF in parentheses. (b) Time for complete hydrogenation of styrene by **Ru-6a** vs. **Ru-7a**. All reactions carried out in benzene at 23 °C under 1000 psi H₂, using 0.1 mol% Ru and 1.0 M styrene or 0.7 M allylbenzene. Average of three trials (± 3%).
To assess the generality of the trends indicated in Figure 2.1, we turned to hydrogenation of several substrates of broader interest, which present successively greater challenges to reduction (Chart 2.1; Table 2.2).

**Chart 2.1.** Substrates employed in hydrogenation studies.

Reduction of lactone S3 affords the musk-odoured perfume Exaltolide, while the reduced ROMP polymers are of interest for their relevance to well-defined polymer platforms for further functionalization (S4), or for tissue engineering (S5). Other hydrogenated ROMP polynorbornenes find applications as engineering thermoplastics and fluoropolymers, as polymer supports in synthetic applications, as nanoporous materials, and as gradient polymers with potentially programmable thermal properties. We recently described tandem ROMP-hydrogenation of S5 via first, second, and third-generation Grubbs catalysts, using protocols that generate Ru-6 and, in the presence of methanol, Ru-7.

Reduction of these substrates in CH₂Cl₂ follows the trend established above, with the CO complexes Ru-7 outperforming their H₂ analogues Ru-6 in all cases. As well, the "first-generation" catalysts (series a) generally outperform the second-generation catalysts (series b) in reduction of all substrates, with the exception of neoglycopolymer S5. The challenging nature of S5 is illustrated by the low turnover numbers found even at 0.5 mol % Ru. While
the CO catalysts remain more effective than their H₂ analogues for reduction of this substrate, maximum conversions are found for the IMes derivative Ru-7b, rather than the bis-PCy₃ complex Ru-7a. We attribute this to the significant steric bulk present in S5, arising from its polymeric nature, the endo/exo disubstitution of the repeat unit, the bulk of the galactose groups, and the additional steric pressure exerted by the acetal protecting groups. The unexpectedly higher activity of the IMes catalyst Ru-6b may reflect the essentially two-dimensional steric bulk of the N-heterocyclic carbene, relative to PCy₃; we presume that one phosphine ligand is replaced by olefin during the hydrogenation cycle as for Ru-6a; vide supra.

Table 2.2. Relative efficiency of dihydrogen and carbonyl catalysts in hydrogenation of various olefinic substrates.ᵃ

<table>
<thead>
<tr>
<th>Substrate</th>
<th>mol % Ru</th>
<th>Time (h)</th>
<th>Cat.</th>
<th>TOF (h⁻¹)</th>
<th>Conv. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>S1</td>
<td>0.1</td>
<td>0.5</td>
<td>Ru-6a</td>
<td>1260</td>
<td>63</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Ru-7a</td>
<td>1840</td>
<td>92</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Ru-6b</td>
<td>540</td>
<td>27</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Ru-7b</td>
<td>1520</td>
<td>76</td>
</tr>
<tr>
<td>S3</td>
<td>0.1</td>
<td>1</td>
<td>Ru-6a</td>
<td>830</td>
<td>83</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Ru-7a</td>
<td>960</td>
<td>96</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Ru-6b</td>
<td>530</td>
<td>53</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Ru-7b</td>
<td>810</td>
<td>81</td>
</tr>
<tr>
<td>S4</td>
<td>0.1</td>
<td>1</td>
<td>Ru-6a</td>
<td>310</td>
<td>31</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Ru-7a</td>
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<td></td>
<td></td>
<td>Ru-6b</td>
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<td></td>
<td></td>
<td>Ru-7b</td>
<td>17</td>
<td>50</td>
</tr>
</tbody>
</table>

ᵃ Conditions: 1000 psi H₂, refluxing CH₂Cl₂ (except for S1: 23 °C); conversions measured by GC-FID or 'H NMR analysis; data represent average of two independent runs (±3%). ᵇ Conversions <10% at 0.1 mol % Ru.
A more detailed study focused on the effect of solvent and additives on hydrogenation of lactone S3 (Figure 2.2). Consistently higher conversions are found for reduction in methylene chloride, relative to benzene: the reactivity trends in both solvents follow the norm established above. Addition of base to the reactions in CH₂Cl₂ improves activity slightly, particularly for the IMes derivatives, suggesting some competing chlorination of the hydride catalyst by the chlorocarbon solvent (see later). Finally, the difference in activity between the H₂ and CO series of catalysts is minimized in the presence of MeOH, in which the dihydrogen catalysts undergo carbonylation, as discussed above.

![Figure 2.2. Effect of solvent and additives on hydrogenation of lactone S3 via catalysts Ru-6 and Ru-7: (a) CH₂Cl₂ solvent without additives (Table 2.2); (b) CH₂Cl₂, 3 equiv NEt₃; (c) 20 MeOH : 80 CH₂Cl₂, 3 equiv NEt₃; (d) C₆H₆ without additives. Conditions: 1000 psi H₂, 0.1 mol% Ru, bath temperature 55 °C, 1 h reaction time. Data represent average of two independent runs (±3%).](image)

2.2.3 Relative stability of Ru-6 and Ru-7.

The data above demonstrate that the carbonyl complexes Ru-7 are more effective hydrogenation catalysts than their dihydrogen analogues Ru-6. Given the similarly low bulk of the CO and H₂ ligands, we discount a steric origin for this higher activity. However, the
DFT study described in Section 2.1, which predicts a higher-energy reaction profile for hydrogenation via RuHCl(L)(PR₃)₂ species in which L is CO, vs. the σ-donor PH₃, implies that the π-acidity of the CO ligand should be detrimental to hydrogenation activity.²⁸ We speculated that the higher hydrogenation efficiency of Ru-7 might be due to an improved stability relative to Ru-6, and hence longer catalyst lifetime. This would translate into higher catalyst concentrations over the timescale of hydrogenation.

This hypothesis stemmed in part from the high reactivity characteristic of the related, classic H₂ complex Ru(H₂)(H₂)(PCy₃)₂ Ru-11a, a function of the electron-rich character of the metal and the lability of the dihydrogen ligand(s).⁴⁹ In Ru-11a and cyclohexylphosphine complexes, this reactivity is manifested in C-H bond activation even at ambient temperatures.⁴⁹⁻⁵² Of interest, Leitner and coworkers have reported that Ru(H₂)(H₂)(IMes)(PCy₃) is more reactive than Ru-11a in C-H activation chemistry.³¹ While this was of value in enabling intermolecular C-H bond activation at room temperature, it may also signify a greater susceptibility to deactivation via intramolecular bond activation.

The ease of H₂-N₂ exchange can afford a preliminary indicator of such lability.³² The relative robustness of the Ru-H₂ interaction in Ru-6a is suggested by the early comment that this complex resists exchange with 1 atm N₂ at room temperature.³³ We find that exchange does occur to afford Ru-12a, but slowly (5-15% after 24 h; Ru-12a identified on the basis of the reported chemical shifts³⁵ of –27.26 and 43.7 ppm for the hydride and ³¹P nuclei, respectively; Table 2.1). The higher lability of the dihydrogen ligand in Ru-6b is suggested by observation of ca. 70% conversion to RuHCl(N₂)(IMes)(PCy₃) Ru-12b after 24 h under N₂. Complex Ru-12b is identified from its well-resolved hydride doublet at –27.63 ppm (ca.
11 ppm upfield of the averaged hydride/dihydrogen signal for Ru-6b), which correlates in HMBC experiments with a new $^{31}$P{$^1$H} NMR singlet at 45.1 ppm. These chemical shifts agree well with the values for Ru-12a above.

In related cyclohexylphosphine complexes, loss of a stabilizing H$_2$ or N$_2$ ligand is often the entry-point to extensive intramolecular bond activation, as noted above. Under argon at 23 °C, neither Ru-6 or Ru-7 shows evidence of bond activation in C$_6$D$_6$ after 24 h, as judged by integration of their $^{31}$P{$^1$H} NMR signals against an internal standard. (Use of an internal standard in these experiments is important, as the potential paramagnetism of the product(s), and the consequent absence of an NMR "marker", means that losses can otherwise easily go unnoticed). In CH$_2$Cl$_2$, however, Ru-6a undergoes partial conversion to the known$^{37}$ Ru(IV) complex Ru(H)$_2$Cl$_2$(PCy$_3$)$_2$ Ru-5, with a ca. 1:1 ratio of Ru-6a: Ru-5 after 16 h. We earlier described the low catalytic activity of Ru-5.$^7$ Its identity was confirmed in the present experiment by HMBC correlation of the $^{31}$P{$^1$H} NMR singlet at 91.3 ppm with the expected hydride triplet for Ru-5 at −12.39 (t, $^2$J$_{HP}$ = 32 Hz; CD$_2$Cl$_2$). Chlorination of Ru-6a is consistent with earlier findings from the Toulouse group, which described the successive conversion of Ru(H)$_2$(H$_2$)$_2$(PCy$_3$)$_2$ Ru-11a to Ru-6a and Ru-5 in Freons (mixtures of CDCl$_3$, CDFCl$_2$, and CDF$_2$Cl) and in neat CDCl$_3$. In sharp contrast, Ru-6b undergoes complete decomposition to paramagnetic products in CH$_2$Cl$_2$ over 16 h, while Ru-7 is stable.

In a more direct probe of the relative susceptibility of Ru-6 and Ru-7 to decomposition under conditions related to catalysis, we subjected all four complexes to thermolysis in benzene and methylene chloride under 1 atm H$_2$ (Figure 2.3). Again, the high stability of the carbonyl complexes is notable, little or no decomposition being evident in either solvent.
The dihydrogen complexes are less robust: after just one hour at 55 °C in benzene, the integration due to Ru-6a decreases by ca. 30% (Figure 2.3a). New $^{31}\text{P}\{^1\text{H}\}$ NMR signals are present for free PCy$_3$ and an unidentified species at ca. 63 ppm (6%), but the balance of material is either paramagnetic or devoid of $^{31}\text{P}$ nuclei. For Ru-6b, ca. 60% decomposition occurs over this time, and no new $^{31}\text{P}\{^1\text{H}\}$ NMR signals are apparent (Figure 2.4).

**Figure 2.3.** Thermolytic stability of Ru-6 and Ru-7 under 1 atm H$_2$, as indicated by $^{31}\text{P}\{^1\text{H}\}$ NMR integration vs. Ph$_3$P=O as internal standard. (a) After 1 h in C$_6$D$_6$ at 55 °C. (b) In refluxing CH$_2$Cl$_2$. Dashed lines, L = PCy$_3$; solid lines, L = IMes. Data represent average of two independent runs (±3%).

**Figure 2.4.** $^{31}\text{P}\{^1\text{H}\}$ NMR spectra for thermolysis of RuHCl(H$_2$)(IMes)(PCy$_3$) Ru-6b. Conditions: C$_6$D$_6$, 55 °C.
In refluxing CH$_2$Cl$_2$, **Ru-6a** is completely consumed after 24 h (Figure 2.3b), and **Ru-5** is the only $^{31}$P-containing product observed (70%). The coordinative saturation of **Ru-5** appears to confer some protection against more extensive decomposition. When formation of **Ru-5** is suppressed by repeating this reaction in the presence of NEt$_3$, the only species observed by $^{31}$P{$^1$H} NMR is an unidentified product of singlet multiplicity at 36 ppm, which integrates to ca. 40%. Consistent with the generally greater vulnerability described above, **Ru-6b** undergoes near-total conversion to paramagnetic species within 2.5 h in refluxing CH$_2$Cl$_2$ (Figure 2.3b). Unexpectedly, however, a small signal for **Ru-6a** is observed within 15 min, which disappears over the next 2 h. A very small signal at 91 ppm (<5% integration, **Ru-5**) is also observable. Formation of **Ru-6a** signifies that **Ru-6b** undergoes some disproportionation under these conditions, as also reported by Mol for thermolysis of related benzylidene in MeOH at 80 °C.$^{12}$ Thermolysis of **Ru-6a** shows good first-order kinetics (Figure 2.5); fewer data-points are obtained for **Ru-6b** ($k = 0.089$ s$^{-1}$ and 1.4 s$^{-1}$, respectively).

![Figure 2.5](image_url)  

**Figure 2.5.** First-order plot for thermolysis of **Ru-6a/b**.
2.3 Conclusions

The foregoing describes a clean, high-yield synthetic route to RuHCl(H$_2$)(IMes)(PCy$_3$)Ru-6b by ligand exchange reactions of RuHCl(H$_2$)(PCy$_3$)$_2$ Ru-6a, though attempts to develop a route to Ru-6a itself from RuHCl(PPh$_3$)$_3$ Ru-9 were unsuccessful. Comparison of the olefin hydrogenation activity of Ru-6 with the corresponding carbonyl complexes Ru-7 demonstrates that replacing the H$_2$ ligand by CO improves hydrogenation efficiency. Thermolysis experiments suggest that this reflects a positive influence on catalyst lifetime associated with the low lability of the CO ligand, as complexes Ru-7 are much more stable than their dihydrogen analogues Ru-6. The $\pi$-acidity of the carbonyl group may also play a part: while this will hamper catalyst initiation via ligand loss, as well as oxidative addition of H$_2$, it will also decrease the susceptibility of the complex to nucleophilic attack. The significantly greater robustness of the CO complexes appears to compensate for their lower activity, by maintaining higher concentrations of active catalyst over the timescale of hydrogenation.

2.4 Experimental

2.4.1 General Procedures.

Reactions were carried out at room temperature (23 °C) under argon, using standard Schlenk or glovebox techniques, unless otherwise stated. Dry, oxygen-free solvents were obtained using a Glass Contour solvent purification system, and stored over Linde 4Å molecular sieves. CDCl$_3$ and C$_6$D$_6$ were degassed by consecutive freeze/pump/thaw cycles and dried over activated sieves (Linde 4Å). [RuCl$_2$(COD)]$_n$, RuHCl(PPh$_3$)$_3$ Ru-9, RuHCl(CO)(PCy$_3$)$_2$ Ru-7a, RuHCl(CO)(IMes)(PCy$_3$) Ru-7b, IMes, and substrates S3, S4, S5 were prepared according to literature methods. H$_2$ (UHP grade) was obtained...
from BOC Gases and used as received. Styrene and allylbenzene (Aldrich) were distilled from CaH₂ under vacuum, and stored at -35 °C under Ar in the dark. Tetrahydronaphthalene was distilled from Na metal, freeze-pump-thaw degassed, and stored over Linde 4Å molecular sieves under Ar. Ethylbenzene (Aldrich) and PCy₃ (Strem) were used as received. NMR spectra were recorded on a Bruker Avance 300 or Avance 500 spectrometer at 298 K, unless otherwise specified. ¹H and ¹³C NMR spectra were referenced to the residual proton and carbon signals of the deuterated solvent. Peaks are reported in ppm, relative to TMS (¹H, ¹³C) or 85% H₃PO₄ (³¹P) at 0 ppm. IR spectra were measured on a Bomem MB100 IR spectrometer. Microanalysis was carried out by Guelph Chemical Laboratories Ltd., Guelph, Ontario.

2.4.2 Synthesis of RuHCl(H₂)(PCy₃)₂ Ru-6a.

In a modification of a literature method,³⁰ a suspension consisting of [RuCl₂(COD)]ₙ (400 mg, 1.43 mmol), PCy₃ (850 mg, 3.0 mmol), NEt₃ (199 mL, 1.43 mmol) and 2-propanol (20 mL) was stirred at 200 psi H₂ and 80 °C for 40 h. The resulting orange precipitate was filtered off, washed with EtOH (3 × 3 mL) then cold hexanes (5 × 4 mL), and dissolved in 15 mL CH₂Cl₂ under H₂. A bright orange solid was obtained by filtering through Celite to remove a dark, insoluble impurity, concentrating to 0.2 mL and adding 5 mL cold hexanes under 1 atm H₂. The precipitate was filtered off, washed with hexanes (3 × 3 mL), and reprecipitated from a minimum volume of toluene by adding hexanes under H₂ and chilling at -35 °C for an hour, then dried under vacuum. Yield: 0.511 g (73%). ³¹P{¹H} NMR (C₆D₆, Ar): δ 54.2 (s). ¹H NMR (C₆D₆, Ar): δ 2.3–0.9 (m, 66 H, Cy), -16.3 (br s, 3H, RuH(H₂)). Under N₂, ca. 10% RuHCl(N₂)(PCy₃)₂ Ru-12a is observed: δ₂₃ 43.7 (s).³⁵ δ_H -27.26 (t, 1H, RuH, J_HP = 18.3 Hz).
2.4.3 Synthesis of RuHCl(H₂)(IMes)(PCy₃)_2 Ru-6b.

Solid IMes (46 mg, 0.15 mmol) was added to orange RuHCl(H₂)(PCy₃)_2 Ru-6a (100 mg, 0.142 mmol) in 5 mL benzene. No color change is apparent, but $^{31}$P{¹H} NMR monitoring indicated complete reaction at 1.5 h at 23 °C: only signals for free phosphine and Ru-6b (integration 1:1) were observed in an aliquot removed at this time. The solvent was stripped off, and hexanes (2 mL) added. An orange powder was obtained on cooling to −35 °C overnight. This was filtered off, washed with cold hexanes (3 x 3 mL) and dried under vacuum. Yield 73 mg (71%; limited by partial solubility in hexanes). $^{31}$P{¹H} NMR (C₆D₆, Ar): 56.4 (s, PCy₃). ¹H NMR: 6.82 (s, 4H, Mes m-CH), 6.16 (s, 2H, NCH=CHN), 2.37 (s, 12H, o-CH₃), 2.14 (s, 6H, p-CH₃), 1.88-1.10 (m, 33H, PCy₃), −16.44 (s, 3H, RuH(H₂)).

Hydride $T_{1(min)}$: 36.6 ms (C₇D₈, 253 K, 300 MHz; corresponds to a H-H distance of 1.03 Å).

$^{13}$C{¹H} NMR: 196.0 (d, JCP = 100 Hz, NCN), 138.1 (s, Mes p-C), 137.1 (s, Mes i-C), 136.5 (s, Mes o-C), 129.1 (s, Mes m-C), 121.4 (s, NC=CN), 35.3 (d, JCP = 17 Hz, Cy), 30.6 (d, JCP = 2 Hz, Cy), 28.0 (d, JCP = 10 Hz, Cy), 26.9 (s, Cy), 21.1 (s, p-CH₃), 19.0 (s, o-CH₃). IR (Nujol): v(Ru-H) 2047 cm⁻¹. Anal. Calcd. for C₃⁹H₆₂ClN₂PRu: C, 64.66 %; H, 8.35 %; N, 3.87 %. Found: C, 64.63 %; H, 7.98 %; N, 3.70 %. NMR spectra under N₂ (24 h) show ca. 70% RuHCl(N₂)(IMes)(PCy₃) Ru-12b: δp 45.1 (s, PCy₃). δH −27.63 ppm (d, RuH, JHP = 21.4 Hz).

2.4.4 Attempted Synthesis of RuHCl(H₂)(PCy₃)_2 Ru-6a from RuHCl(PPh₃)_3 Ru-9: partial formation of RuHCl(PCy₃)(PPh₃)_2 Ru-10.

Solid PCy₃ (31 mg, 0.11 mmol) was added to purple Ru-9 (50 mg, 0.054 mmol) in 10 mL C₆H₆, and H₂ was bubbled through the suspension. No color change was observed after 3 h, but integration of the ¹H NMR signals against the quartet for Ru-9 at −17.5 ppm indicates
70% unreacted Ru-9 in the soluble portion. Complete conversion was hampered by competing decomposition of the product over a further 20 h reaction. $^{31}$P{$^1$H} NMR for Ru-10 (C$_6$D$_6$): 74.0 (d, $^2$J$_{PP}$ = 118 Hz, 2P, PPh$_3$), 28.9 (t, $^2$J$_{PP}$ = 118 Hz, 1P, PCy$_3$). Key $^1$H NMR for Ru-10 (C$_6$D$_6$): –18.1 (td, $^2$J$_{HP}$ = 29 and 18 Hz). $^1$H-$^{31}$P HMBC correlations between the $^{31}$P{$^1$H} NMR doublet at 74.0 ppm and the aromatic $^1$H NMR signals support identification of Ru-10 as a bis(PPh$_3$) complex.

2.4.5 Hydrogenation Reactions.

(a) Representative procedure for hydrogenation of molecular substrates. Solid RuHCl(H$_2$)(PCy$_3$)$_2$ Ru-6a (14 mg, 0.0198 mmol) was added to a glass-lined Parr autoclave containing a solution of styrene (2.083 g, 0.020 mol, 1.0 M) with 1,2,3,4-tetrahydronaphthalene (THN) as internal standard (1.322 g, 0.010 mol) in 20 mL C$_6$H$_6$ in the glovebox. The autoclave was sealed, removed from the drybox, purged with H$_2$, and pressurized to 1000 psi H$_2$ at 23 °C. Samples were analyzed by GC-FID. Kinetic runs on S1 were monitored by removing 1 mL samples at set time intervals using the sampler tube. The first 0.5 mL was discarded; from the second half, a 5 mL aliquot was removed, diluted to 1.00 mL with CH$_2$Cl$_2$ and analyzed (GC-FID). Reactions of other substrates were carried out at a bath temperature of 55 °C. Reactions of S3 were analyzed by GC-FID; of S2, by $^1$H NMR.

(b) Representative procedure for hydrogenation of polymer substrates. A solution of S4 (183 mg, 0.722 mmol, 1.0 M in CH$_2$Cl$_2$) with 1,3,5-trimethoxybenzene (51 mg, 0.30 mmol, 0.2 M in CH$_2$Cl$_2$) as internal standard was subjected to hydrogenation as above (1000 psi H$_2$, 55 °C). Following reaction, volatiles were removed under reduced pressure and the residues were dissolved in CDCl$_3$ for $^1$H NMR analysis. Conversions were determined through
comparison of integrals between olefinic signals (S4: br m, 5.58 ppm) and the methoxy singlet of trimethoxybenzene (3.77 ppm). For S5, conversions were quantified by comparing the integrated intensity of the olefinic + galactopyranose CH signals at 5.60-5.30 ppm with the galactopyranose C5 CH multiplet at 4.59 ppm.

2.4.6 Thermolysis of Ru-6 and Ru-7.

In a representative procedure, a solution of Ru-6a (8 mg, 0.011 mmol) and Ph3P=O (4 mg, 0.014 mmol) was dissolved in CH2Cl2 (0.75 mL, with a 50 µL spike of C6D6 as deuterium lock for shimming) in a J. Young NMR tube. An initial 31P{1H} NMR spectrum was measured to establish the Ru-6a: Ph3P=O integration ratio at t0. The NMR sample was then freeze-pump-thaw degassed, backfilled with H2 (1 atm), and heated to 55 °C in an oil bath.
2.5 References.


Chapter 3. Hydrogenolysis versus Methanolysis as a Means of Effecting Transformation of Grubbs Metathesis Catalysts into Ru Hydrides.*

3.1 Introduction.

Tandem ROMP-hydrogenation (ROMP = ring-opening metathesis polymerization) offers powerful routes to functionalized polyolefins inaccessible by direct polymerization of \( \alpha \)-olefins.\(^1\) Hydrogenation extends the range of applications for unsaturated ROMP polymers, reducing their susceptibility to oxidative, thermal, and chemical degradation.\(^2\) The reduced materials are used in demanding applications ranging from tissue engineering\(^3\) to separations science,\(^4,6\) on-bead chemical synthesis,\(^7\) and electronic and optical contexts,\(^8\) among others; they also form the basis of specialty polymer products such as "perfect polyethylene",\(^9,10\) alternating copolymers of ethylene with CO\(_2\) or polar vinyl monomers,\(^11,12\) and polymeric antioxidants.\(^13\)

Hydrogenation of unsaturated polymers is much more challenging than hydrogenation of structurally similar molecular olefins, and the forcing conditions commonly required sets a high bar for catalyst lifetime and/or loadings, resulting in poor performance for highly active but fragile catalysts. Thus, limited efficiency has been reported in reduction of ROMP polymers via classical hydrogenation catalysts such as the Wilkinson or Crabtree catalysts (RhCl(PPPh\(_3\))\(_3\) or [Ir(COD)(PCy\(_3\))(py)]PF\(_6\), respectively), or using supported palladium catalysts, despite their often outstanding performance in reduction of molecular olefins at relatively low H\(_2\) pressures.\(^14\) The best results to date are achieved via tandem ROMP-hydrogenation, which enables efficient reduction of ROMP polyoctenes at 50-60 °C and as

little as 1 atm of H\textsubscript{2}.\textsuperscript{15} Hydrogenation of polynorbornenes, particularly those bearing bulky substituents, is considerably more demanding. Hydrogen pressures of up to 1000 psi can be required for efficient reduction at these moderate temperatures (high pressures are preferable to use of higher temperatures, which can trigger competitive thermal cross-linking of the unsaturated polymers).\textsuperscript{15} Our group recently reported an advanced methodology for tandem ROMP-hydrogenation, which integrates the high activity and molecular weight precision of the "third-generation" Grubbs catalyst RuCl\textsubscript{2}(IMes)(py)(CHPh) \textbf{Ru-1d} with the robust hydrogenation activity of RuHCl(CO)(IMes)(PCy\textsubscript{3}) \textbf{Ru-7b}.\textsuperscript{3,16}

A number of methods have been successfully used to transform metathesis-active Ru-alkylidene complexes into hydrogenation catalysts.\textsuperscript{12,15-25} In tandem ROMP-hydrogenation, the efficiency of the hydrogenation step depends both on the catalytic activity of the Ru-hydride species generated (see Chapter 2), and on the rate, selectivity, and efficiency of the alkylidene-to-hydride transformation (examined in this Chapter). Two protocols are compared. The first adopts the most recent methodologies developed by our group, and builds on the inorganic chemistry already established: that is, the early observation that reaction of the Grubbs catalyst \textbf{Ru-1a} with H\textsubscript{2} in CH\textsubscript{2}Cl\textsubscript{2} affords solely dihydride Ru(H)\textsubscript{2}Cl\textsubscript{2}(PCy\textsubscript{3})\textsubscript{2} \textbf{Ru-5} (a feeble hydrogenation catalyst);\textsuperscript{15} that addition of base enables clean conversion to RuHCl(H\textsubscript{2})(PCy\textsubscript{3}) (L = PCy\textsubscript{3}, \textbf{Ru-6a}; see Scheme 3.1);\textsuperscript{17} and finally, that use of methanol as co-solvent affords RuHCl(CO)(PCy\textsubscript{3})\textsubscript{2} \textbf{Ru-7a}\textsuperscript{17} (a more robust, productive hydrogenation catalyst; see Chapter 2).\textsuperscript{26,27} The second method draws on subsequent work from the Mol and Grubbs groups, which described direct formation of complexes of type \textbf{Ru-7} (L = PCy\textsubscript{3}, H\textsubscript{2}IMes, H\textsubscript{2}IPr; H\textsubscript{2}IMes = N,N'-bis-(2,4,6-trimethylphenyl)imidazolin-2-ylidene, H\textsubscript{2}IPr = N,N'-bis-(2,6-diisopropylphenyl)imidazolin-
on treatment of the corresponding benzylidene catalysts with base and alcohol in
the absence of H₂.22,28-30 These and other20,31,33 direct, H₂-free routes from Ru-1 to Ru-7 could
be of keen interest for tandem metathesis-functionalization, as they would eliminate the risk
of competing olefin hydrogenation.

The present study was thus aimed at improving our fundamental understanding of the non-
metathetical reactivity of the Grubbs catalysts, by establishing the relative kinetics of
hydrogenolysis vs. methanolysis. As well, motivated by the potential to further enhance
efficiency in tandem catalysis reactions mediated by Ru-1 and Ru-7, we wished to establish
whether the Ru-1→Ru-7 transformation is induced more efficiently by the two-step process
– that is, by hydrogenolysis of the alkylidene Ru-1, followed by carbonylation of the
hydrogenolysis product Ru-6 (Scheme 3.1, paths (a) + (b)) – or by direct methanolysis of
Ru-1 (Scheme 3.1, path (c)). This Chapter presents a systematic comparison of rates,
speciation, and efficiency for each of these reaction manifolds, utilizing both first-generation
and second-generation Grubbs catalysts Ru-1a/b (L = PCy₃, IMes), and their hydride
derivatives Ru-6a/b. Unanticipated differences in behaviour emerge, which highlight the
need for "generation-specific" protocols for transforming Ru-1. It should be noted that this
study excluded the commercially available H₂IMes complex 1b', because the latter was
found to exhibit unexpectedly low activity in tandem ROMP-hydrogenation by Dr. Debbie
Mitra of the Fogg group. The origins of this difference are not yet clear, and have not been
systematically studied.
Scheme 3.1. Reaction manifolds targeted. (a) Hydrogenolysis of Ru-1 (1000 psi H\textsubscript{2}, 3 NEt\textsubscript{3}, CH\textsubscript{2}Cl\textsubscript{2}). (b) Carbonylation of Ru-6 (Ar, 3 NEt\textsubscript{3}, 4:1 CH\textsubscript{2}Cl\textsubscript{2}-MeOH). (c) Methanolysis of Ru-1 (conditions as in (b)). For byproducts, see text and Table 3.1. All reactions carried out at a bath temperature of 60 °C and a ruthenium concentration of 15 mM.

3.2 Results and Discussion.

In all experiments, reaction rates were assessed from the rate of disappearance of the \textsuperscript{31}P{\textsuperscript{1}H} NMR signal for the ruthenium precursor relative to Ph\textsubscript{3}P=O as internal standard. Excellent agreement was found for yields determined in situ, vs. samples stripped and redissolved in C\textsubscript{6}D\textsubscript{6}. \textsuperscript{1}H NMR analysis of the latter was used to quantify phosphine-free products, again by integration against an internal standard added prior to reaction. 1,3,5-Trimethoxybenzene (TMB) was chosen as the internal standard for its low volatility (b.p. 255 °C), which aids in reproducibility, and for the convenient location of its \textsuperscript{1}H NMR singlets in regions rarely populated by other groups (CH\textsubscript{3}: 3.30 ppm; CH: 6.25 ppm). Table 3.1 summarizes in situ yields of complexes Ru-6 and Ru-7 observed under the reaction conditions of Scheme 3.1. Chemical shifts of key complexes appear in Table 3.2.
Table 3.1. In situ distribution of products observed in reactions of Scheme 3.1.\(^a\)

<table>
<thead>
<tr>
<th>Entry</th>
<th>Reaction</th>
<th>time (h)</th>
<th>Ru-6 (%)</th>
<th>Ru-7 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>a  b  c</td>
<td>a  b  c</td>
<td></td>
</tr>
<tr>
<td>1a</td>
<td>Ru-1a + H(_2), NEt(_3)</td>
<td>0.5</td>
<td>75  –  –</td>
<td>–  –  –</td>
</tr>
<tr>
<td>1b</td>
<td>Ru-1b + H(_2), NEt(_3)</td>
<td>1</td>
<td>10  61  7</td>
<td>–  –  –</td>
</tr>
<tr>
<td>2a</td>
<td>Ru-6a + MeOH, NEt(_3)</td>
<td>2</td>
<td>–  –  96</td>
<td>–  –  –</td>
</tr>
<tr>
<td>2b</td>
<td>Ru-6b + MeOH, NEt(_3)</td>
<td>2.5</td>
<td>2  –  14</td>
<td>65  –  –</td>
</tr>
<tr>
<td>3a</td>
<td>Ru-1a + MeOH, NEt(_3)</td>
<td>8</td>
<td>–  –  58</td>
<td>–  –  –</td>
</tr>
<tr>
<td>3b</td>
<td>Ru-1b + MeOH, NEt(_3)</td>
<td>4</td>
<td>–  –  83</td>
<td>–  –  –</td>
</tr>
</tbody>
</table>

*Entry numbers correspond to the reactions of Scheme 3.1. Time corresponds to that required for consumption of the starting Ru species. NMR yields; agreement <±3% in replicate runs. Structures for all complexes are shown in Scheme 3.1, with the exception of Ru-6c, RuHCl(H\(_2\))(IMes).*

Table 3.2. NMR chemical shifts for key complexes described in this Chapter.\(^a\)

<table>
<thead>
<tr>
<th>Complex</th>
<th>4:1 CH(_2)Cl(_2)-MeOH</th>
<th>C(_6)D(_6)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(^{31})P {(^1)H}</td>
<td>(^{31})P {(^1)H}</td>
</tr>
<tr>
<td>RuCl(_2)(PCy(_3))(_2)(=CHPh) Ru-1a</td>
<td>37.2</td>
<td>36.9</td>
</tr>
<tr>
<td>RuCl(_2)(IMes)(PCy(_3)) (=CHPh) Ru-1b</td>
<td>32.3</td>
<td>32.1</td>
</tr>
<tr>
<td>RuHCl(H(_2))(PCy(_3))(_2) Ru-6a</td>
<td>53.4</td>
<td>54.2</td>
</tr>
<tr>
<td>RuHCl(H(_2))(IMes)(PCy(_3)) Ru-6b</td>
<td>55.4</td>
<td>56.3</td>
</tr>
<tr>
<td>RuHCl(H(_2))(IMes)(_2) Ru-6c</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>RuHCl(CO)(PCy(_3))(_2) Ru-7a</td>
<td>46.2</td>
<td>46.9</td>
</tr>
<tr>
<td>RuHCl(CO)(IMes)(PCy(_3)) Ru-7b</td>
<td>47.7</td>
<td>47.8</td>
</tr>
<tr>
<td>RuHCl(CO)(IMes)(_2) Ru-7c</td>
<td>–</td>
<td>–</td>
</tr>
</tbody>
</table>

*Values at 298 K, 300 or 500 MHz. \(^b\) Position of Ru=CH (Ru-1) or Ru-H (Ru-6, Ru-7) signal. IMes = N,N'-bis-(2,4,6-trimethylphenyl)imidazol-2-ylidene.*

3.2.1 Two-step hydridocarbonylation, Step 1: hydrogenolysis of Ru-1.

In a preliminary assay of the minimum conditions required for hydrogenolysis, consumption of Ru-1a was found to proceed very slowly (2.5 d) at 1 atm H\(_2\) and room temperature (ca. 23 °C). At 1000 psi H\(_2\), the required reaction time decreased to 6 h. In comparison, hydrogenolysis of Ru-1b was incomplete even after 1 week at 1 atm H\(_2\), or after 24 h at 1000 psi H\(_2\). Hydrogenolysis of the "third-generation" Grubbs catalyst RuCl\(_2\)(IMes)(py)\(_2\)(=CHPh) Ru-1d under the same conditions is complete within 2 h, but affords negligible amounts of hydride species (4% vs internal standard), consistent with the
poor performance of this catalyst in ROMP-hydrogenation. In the case of Ru-1a, added PCy₃ inhibits reaction, indicating that hydrogenolysis (like metathesis reactions promoted by these alkylidene complexes) proceeds via a dissociative pathway. In the present case, incoming dihydrogen presumably replaces a phosphine ligand.

The slower reaction of Ru-1b relative to Ru-1a is thus consistent with the lower lability of the phosphine ligand in the "second-generation" NHC catalysts. This difference in activity is amplified at ambient temperatures, elevated temperatures being required to gain access to the highly reactive 14-electron intermediate RuCl₂(IMes)(=CHPh).

The reactivity above sheds light on the efficiency of Ru-1a in effecting hydrogenation of polyoctenes under as little as 1 atm H₂, where elevated temperatures (50-60 °C) are used. Functionalized polynorbornenes are more challenging, as noted above, and require use of higher hydrogen pressures. The experiments below were designed to probe efficiency and selectivity under conditions that reflect the current state of the art in tandem ROMP-hydrogenation of sterically encumbered polynorbornenes: thus, in CH₂Cl₂ (required to maintain solubility of the saturated polymers) with 3 equiv NEt₃, at 60 °C under 1000 psi H₂.

Under these conditions, disappearance of Ru-1a was complete within 30 min (Figure 3.1a). Selectivity for Ru-6a was high, if less so than under our original conditions: integration relative to internal standards indicated that 75% Ru-6a was formed from Ru-1a (Table 3.1, Entry 1a). Minor amounts of two unidentified phosphine-containing species were evident (<5% each). We assign one of these as a coordinatively saturated mono-phosphine complex, RuHCl(PCy₃)L₃, on the basis of the upfield location and multiplicity of the hydride
signal (-7.45 ppm; $^2J_{HP} = 51.3$ Hz; correlates (HMBC) with a $^{31}P\{^1H\}$ NMR singlet at 62.9 ppm). Free PCy$_3$ was observed in similar amounts. No other phosphorus-containing species were apparent. A 20% decrease in total $^{31}P\{^1H\}$ NMR integration is thus evident, suggesting formation of paramagnetic Ru(III) species (possibly via solvent-induced chlorination). The paramagnetic nature of the byproducts was confirmed by EPR analysis; see below.

**Figure 3.1.** Rates of hydrogenolysis of first- and second-generation Grubbs catalysts under 1000 psi H$_2$ (CH$_2$Cl$_2$, 60 °C; 3 equiv NEt$_3$, [Ru]= 15 mM). (a) Transformation of Ru-1a into Ru-6a. (b) Transformation of Ru-1b into Ru-6b and (via disproportionation) Ru-6a and Ru-6c. Agreement between replicate runs ±3%.

Hydrogenolysis of Ru-1b was slower, as expected, requiring 1 h for complete reaction (Figure 3.1b). Good first-order kinetics are evident from the plot of Figure 3.2, with a first-order rate constant of $k = 3.3 \text{ s}^{-1}$. (The corresponding analysis was not undertaken for Ru-1a because the much faster reaction limited the number of data points; see Figure 3.1a). Of note, $^{31}P\{^1H\}$ NMR analysis in C$_6$D$_6$ showed a singlet for Ru-6a (10% based on mol Ru; 20% of total integration) accompanying that expected for Ru-6b (61%; see Table 3.1, Entry 1b). The implied disproportionation of Ru-6b (Scheme 3.2, top) is confirmed by observation of $^1H$ NMR signals for RuHCl(H$_2$)(IMes)$_2$ (Ru-6c, 7%), assignment of which was
established by independent synthesis as described below. Disproportionation of Ru-6b obviously necessitates loss and recoordination of both the PCy₃ and the IMes ligands in Ru-6b. The observation of near-equimolar amounts of Ru-6a and Ru-6c indicate minimal scavenging of free IMes, despite the established susceptibility of IMes to reaction with chlorinated solvents. Disproportionation of Ru-6b occurs independent of the presence of methanol, although it is slow at room temperature (10% after 24 h in C₆D₆). A similar process of loss and re-uptake of PCy₃ presumably also occurs for Ru-6a, but goes undiagnosed in the absence of a mixed-ligand "marker" to reveal its operation.

**Figure 3.2.** First-order log plot for hydrogenolysis of Ru-1b. $k = 3.3 \text{ s}^{-1}$.

**Scheme 3.2.** Reactions of hydrogenolysis products Ru-6 with methanol.
3.2.2 Step 2: Carbonylation of dihydrogen complexes Ru-6.

Figure 3.3a depicts the rate profile measured for the reaction of Ru-6a with methanol in the presence of base. Carbonylation is complete in 2 h at 60 °C, with near-quantitative selectivity for Ru-7a (Table 3.1, Entry 2a); no other products are observable by \(^1\)H or \(^{31}\)P\(^{1}\)H\} NMR analysis. The rate of reaction is essentially independent of added PCy\(_3\), suggesting that the mechanism is not dissociative in phosphine. Good first-order dependence on [Ru-6a] is evident from Figure 3.4. Observation of extensive effervescence immediately on immersing the vessel in the preheated bath indicates loss of the dihydrogen ligand: given the absence of extensive C-H activation of the cyclohexyl rings,\(^{37,38}\) methanol is presumed to rapidly take up the vacated site.

**Figure 3.3.** Rates of carbonylation of dihydrogen complexes by methanol (Ar, 3 NEt\(_3\), 4:1 CH\(_2\)Cl\(_2\)-MeOH, 60 °C, [Ru] = 15 mM). (a) Transformation of Ru-6a into Ru-7a. (b) Transformation of Ru-6b into Ru-7b and Ru-7a, and disproportionation product Ru-6a. Agreement between replicate runs ±3%.
Figure 3.4. First-order log plot for carbonylation of Ru-6. Ru-6a: $k = 1.5 \text{s}^{-1}$; Ru-6b: $k = 2.3 \text{s}^{-1}$.

Consumption of Ru-6b occurs at a rate comparable to Ru-6a (Figure 3.3b), again in a process that appears to follow good first-order kinetics in terms of the loss of the starting complex (Figure 3.4). Yields of Ru-7b are considerably lower, however, at 65% (Table 3.1, Entry 2b). Complexes Ru-6a (2%) and Ru-6c (7%) are also generated, reflecting the susceptibility of the parent complex to disproportionation, as noted above. The bis-phosphine carbonyl complex Ru-7a is also observed (14%). We attribute formation of the latter to carbonylation of Ru-6a (Scheme 3.2, bottom), rather than disproportionation of the carbonyl complex Ru-7b, given that no disproportionation is observed on thermolysis of isolated Ru-7b.\textsuperscript{27} The absence of Ru-7c is notable. It is unclear whether this reflects slower reaction of Ru-6c with methanol, or interception of the free carbene by CH\textsubscript{2}Cl\textsubscript{2}-induced decomposition. Relevant in the latter context is the longer timescale of carbonylation, relative to hydrogenolysis. Scavenging of free IMes by methanol\textsuperscript{22} is probably less likely, given the general tolerance of these carbenes toward alcohols,\textsuperscript{39} and the proposed reversibility with which their alcohol adducts are formed.\textsuperscript{40,41} However, adduct formation could prolong the residence of the metal-free IMes species in solution, and thereby facilitate
its decomposition by CH₂Cl₂. Irrespective of the specific decomposition pathways involved, transformation of **Ru-6** into **Ru-7** is considerably less clean and efficient for **Ru-6b** than **Ru-6a**. This translates into a higher net yield for the **Ru-1a→Ru-6a→Ru-7a** transformation (ca. 75%, as compared to <40% for **Ru-1b→Ru-6b→Ru-7b**).

3.2.3 One-step hydridocarbonylation: methanolysis of benzyldienes **Ru-1a/b**.

Independent reports from the Mol and Grubbs groups have described the formation of products of type **Ru-7**, accompanied by varying amounts of decomposition, on reaction of Grubbs-class catalysts with primary alcohols.²²,²⁸,³⁰ Dinger and Mol noted that addition of base increased in situ yields for the **Ru-1a→Ru-7a** transformation to 85% over 24 h,²⁸ but that hydridocarbonylation of **RuCl₂(H₂IMes)(PCy₃)(=CHPh)** Ru-1b' was limited to 30-40% yield by disproportionation and other side-reactions.²² We find that methanolysis is much slower than hydrogenolysis for the benzyldiene complexes **Ru-1a/b**, as evident from comparing Figures 3.1 and 3.5. Further, and consistent with the Mol report,²² **Ru-1a** reacts more slowly than its NHC analogue (cf. Figures 3.5a and 3.5b).

In contrast with the behaviour reported for the H₂IMes complex **Ru-1b'**, however, we observe no disproportionation during methanolysis of **Ru-1b** (Table 3.1, Entry 3b), as indeed expected from the low lability of the PCy₃ ligand in both starting **Ru-1b**⁴² and the carbonyl-containing product **Ru-7b** (vide supra). In consequence, the yield of **Ru-7b** (ca. 85%) is much improved in direct hydridocarbonylation of **Ru-1b**, relative to the two-step hydrogenolysis-carbonylation process, in which **Ru-6b** functioned as a vector for decomposition. The difference is unexpected, but may account for the poor performance observed on attempted use of **Ru-1b'** in tandem ROMP-hydrogenation noted above.
Figure 3.5. Methanolysis of the first- and second-generation Grubbs catalysts under the conditions of Scheme 3.1c (Ar, 3 equiv NEt₃, 4:1 CH₂Cl₂-MeOH, 60 °C, present, [Ru] = 15 mM). (a) Transformation of Ru-1a into Ru-7a. (b) Transformation of Ru-1b into Ru-7b. Agreement between replicate runs ±3%.

For Ru-1a, in comparison, methanolysis is less satisfactory as a route to Ru-7a, the latter being formed in only ca. 60% yield (Table 3.1, Entry 3a). Decomposition is unsurprising given the longer reaction time, the lability of the PCy₃ ligand in Ru-1a, relative to Ru-1b, and the susceptibility of this basic phosphine to reaction with the chlorinated solvent, which will impede its re-uptake. A $^{31}$P{$^{1}$H} NMR signal is indeed observed in the region typical for phosphonium salts (34.7 ppm; cf. values of 34.5 ppm (C₆D₆)₄ for MePCy₃•Cl and of 33.8 ppm (CD₃OD)₄ for HPCy₃•Cl), which integrates to ca. 11% vs. the original proportion of Ru-1a. The importance of PCy₃ re-uptake in limiting decomposition of RuCl₂(L)(=CHR) was demonstrated by our earlier study documenting the instability of the highly labile catalyst RuCl₂(IMes)(py)(=CHPh) Ru-1d.¹⁶ Finally, it should be noted that consumption of Ru-1a/b does not show a clean first-order dependence on ruthenium (Figure 3.6), suggesting that multiple competing pathways contribute. This contrasts sharply with the behaviour of the dihydrogen complexes Ru-6a/b, and may point toward a vulnerability specific to the
benzylidene moiety. We speculate that decomposition of Ru-1 could occur via direct attack by methanol on the benzylidene functionality, as well as via a pathway dissociative in phosphine.

Figure 3.6. First-order plot for methanolysis of Ru-1. Ru-1a: $k = 0.42 \text{ s}^{-1}$; Ru-1b: $k = 0.76 \text{ s}^{-1}$.

EPR analysis of the crude products obtained following methanolysis of Ru-1a and Ru-1b confirmed the presence of paramagnetic species (Figure 3.7). In both cases, a signal is observed at a Landé $g$ factor of ca. 2.07 (Ru-1a: 2.0704 ($\omega_{1/2} = 111 \text{ G}$); Ru-1b: $g = 2.0779$ ($\omega_{1/2} = 88 \text{ G}$)), suggesting formation of analogous products. The breadth of these signals is consistent with residence of an unpaired electron on a transition-metal center, and the $g$ factors are similar to that observed for [Ru$^{III}$(C$_6$H$_5$NO)$_3$]•MeOH ($g = 2.074$). A second inorganic radical species is formed from Ru-1a, which gives rise to a higher-energy signal ($g = 1.9630$; $\omega_{1/2} = 38 \text{ G}$). An organic radical is also generated, as indicated by observation of a singlet at $g = 1.9996$, very near the organic-radical benchmark value of $g = 2.000$.45
Figure 3.7. EPR spectra of products formed following methanolysis of (a) Ru-1a and (b) Ru-1b.

The much faster reaction of Ru-1b, vs. Ru-1a, is of interest. This may reflect the poor charge-donor capacity of the IMes ligand relative to PCy₃, which would render the Ru center in Ru-1b more electropositive, thus enhancing electrostatic attraction of the Lewis basic alcohol donor. In experimental and theoretical studies of the Grubbs catalysts Ru-1a and Ru-1b', the Kennepohl group noted the poor charge-donor capacity of the related H₂IMes ligand.⁴⁷ This perspective was supported by a recent theoretical study by Carbo and Poblet utilizing extended charge decomposition analysis to quantify the donor-acceptor properties of the phosphine and NHC ligands in the same catalysts.⁴⁸
The reason for the slower reaction of the benzylidene complexes with methanol, relative to hydrogen, is not obvious. We initially speculated that this behaviour might reflect the greater steric conflict incurred by approach of MeOH to five-coordinate Ru-1 within an associative pathway. This would also account for the slower reaction of Ru-1a, relative to Ru-1b, access to the former being retarded by the three-dimensional bulk associated with the two PCy₃ ligands. However, we find that the rate of methanolysis is inhibited by added PCy₃, consistent with a mechanism that is dissociative in phosphine.⁴⁹ As the putative four-coordinate intermediate RuCl₂(L)(=CHR) (L = PCy₃, IMes) is unlikely to exert significant steric discrimination in the approach of H₂, vs. MeOH, the slower reaction with methanol is presumably electronic in origin. Computational studies now under way are directed at clarifying the mechanisms of both reactions. Even at this stage, however, the trends in activity and the effect of added phosphine suggest very different pathways for the two reactions.

3.2.4 Synthesis of RuHCl(H₂)(IMes)₂ Ru-6c.

Assignment of the NMR signals for Ru-6c was confirmed by independent synthesis of this complex via reaction of Ru-6a with IMes (Eqn 3.1). Use of hexanes as solvent limits solubility and hence disproportionation, this enabling clean conversion to Ru-6c over 4 days. The complex was isolated in >80% yield. Its identity was confirmed by NMR, infrared, and elemental analysis. IR analysis reveals a weak band, tentatively assigned to the \( \nu(\text{Ru-H}) \) vibration, at 2037 cm⁻¹. The hydride and \( \eta^2-\text{H}_2 \) ligands appear as a broad \( ^1\text{H} \) singlet at -16.58 ppm in C₆D₆ (-16.63 ppm in C₇D₈), which did not decoalesce down to -90 °C. Integration against these signals indicates the presence of two IMes ligands. Efforts to
measure \(^1J_{\text{HD}}\) values to obtain insight into the H-H bond distance were complicated by rapid exchange, as is also the case for Ru-6a, for which no H-D coupling was reportedly observable.\(^{51}\) Of note is the long \(T_{1(\text{min})}\) value for the hydride signal (64.5 ms at 300 MHz, 250 K, C\(_7\)D\(_8\)), corresponding to an H-H distance of 1.13 Å for fast-spinning H\(_2\).\(^{50}\) While long relaxation times are characteristic of \(\eta^2\)-H\(_2\) perturbed by interaction with cis-hydride,\(^{50b}\) this value is significantly longer than those reported for Ru-6a (30 ms at 243 K, 250 MHz, CD\(_2\)Cl\(_2\);\(^{51}\) corrected to 36 ms at 300 MHz) or Ru-6b (36.6 ms at 300 MHz, 253 K, C\(_7\)D\(_8\)).\(^{27}\)

Elongation of the H-H distance may reflect increased donation from the H-H bond to the electropositive Ru center in this bis(NHC) complex. The poor charge-donor capacity of the NHC ligand, relative to PCy\(_3\),\(^{47,48}\) was noted above.

\[
\text{Ru-6a} \quad \xrightarrow{\text{2.1 IMes, 23 °C, 4 d hexanes}} \quad \text{Ru-6c}
\]

\[\text{(3.1)}\]

3.2.5 Synthesis of RuHCl(CO)(IMes)$_2$ Ru-7c.

Assignment of the NMR signals for Ru-7c was confirmed by independent synthesis of this complex via reaction of the known complex RuHCl(CO)(IMes)(PPh\(_3\)) Ru-13b with IMes (Eqn 3.2; 81% yield). While this work was in progress, synthesis of Ru-7c and related bis-NHC complexes was independently reported by the groups of Whittlesey\(^{52}\) and Gunnoe.\(^{53}\) The literature routes involved, respectively, thermolysis of Ru(H\(_2\))(CO)(AsPh\(_3\))\(_3\) Ru-14 with an excess of the NHC ligand, followed by addition of CH\(_2\)Cl\(_2\) (yield reported as moderate to high), or thermolysis of [RuCl\(_2\)(CO)\(_2\)]\(_n\) with excess IMes, followed by addition of methanol (32% yield). Alternatively, Ru-7c can be isolated in quantitative yields under very mild
conditions, by exposure of the hydroxy hydride complex RuH(OH)(CO)(IMes)$_2$, Ru-15 to CH$_2$Cl$_2$ at ambient temperature.$^{52}$

\[
\begin{align*}
\text{Imes} & \quad \text{Ru} & \quad \text{CO} & \quad \text{PPh}_3 \\
\text{Cl} & \quad & & \\
\text{Ru-13b} & \quad \text{H} & \quad 70^\circ\text{C}, 40\text{ h toluene} & \quad \text{Ru-7c} & \quad \text{H} & \quad \text{CO} \quad (3.2)
\end{align*}
\]

3.3 Conclusions.

The foregoing reveals unexpected reactivity differences between the first- and second-generation Grubbs complexes, which have striking implications for tandem catalysis processes mediated by these important metathesis catalysts. Direct interrogation of the inorganic transformations involved reveals that the protocols optimal for the Ru-1a $\rightarrow$ Ru-6a transformation are poorly suited to the Ru-1b $\rightarrow$ Ru-7b transformation. Thus, hydrogenolysis of Ru-1a is an efficient route to dihydrogen complex Ru-6a, which can in turn be converted into Ru-7a in high yields by reaction with methanol. Direct methanolysis of Ru-1a, however, occurs only over a timescale of hours, and decomposition therefore competes. Conversely, methanolysis is significantly more efficient than the hydrogenolysis-carbonylation sequence in converting Ru-1b to Ru-7b, with yields approaching 85%. The susceptibility of the dihydrogen complex Ru-6b to disproportionation is a major impediment to both hydrogenolysis of Ru-1b and carbonylation of Ru-6b. This difference in the behaviour of the first- and second-generation Grubbs catalysts indicates that surprisingly different experimental methodologies are required to attain maximum productivity in tandem ROMP-hydrogenation using either catalyst. Work currently under way is directed at elucidating whether similar behavioural differences exist for the corresponding methyldiene complexes that represent the resting states in ring-closing metathesis (RCM) and cross-
metathesis (CM). This point is expected to be central to the development of efficient RCM-functionalization and CM-functionalization methodologies that exploit the catalytic versatility of complexes **Ru-7**.

### 3.4 Experimental.

**3.4.1 General procedures.**

Reactions were carried out at room temperature (23 °C) under argon, using standard Schlenk or glovebox techniques, unless otherwise stated. Dry, oxygen-free solvents were obtained using a Glass Contour solvent purification system, and stored over Linde 4Å molecular sieves. Methanol was distilled from Mg(OCH$_3$)$_2$ under argon and stored over molecular sieves (Linde 4Å). Triethylamine and C$_6$D$_6$ were distilled from CaH$_2$, degassed by consecutive freeze/pump/thaw cycles, and stored over molecular sieves (Linde 4Å). The Grubbs catalysts **Ru-1a**$^{54}$ and **Ru-1b**$^{42c}$ and the dihydrogen complexes **Ru-6a**$^{15}$ and **Ru-6b**$^{27}$ were prepared according to literature procedures. Triphenylphosphine oxide and 1,3,5-trimethoxybenzene were purchased from Aldrich and used as received. Hydrogen (UHP Grade) was purchased from BOC Gases and used without purification. NMR spectra were recorded on a Bruker Avance 300 or Bruker AMX-500 spectrometer at 298 K. $^1$H and $^{13}$C{$^1$H} NMR spectra were referenced to the residual proton and carbon signals of the deuterated solvent. Peaks are reported in ppm, relative to TMS ($^1$H, $^{13}$C) or external 85% H$_3$PO$_4$ ($^{31}$P) at 0 ppm. EPR spectra were acquired on a JEOL FA-100 X-band EPR spectrometer equipped with a JEOL ES-UCX2 cylindrical cavity. These spectra were kindly run by Mr. Paul Billone of the Scaiano group; spectrometer access provided by Prof. J.C. Scaiano. IR spectra were measured on a Bomem MB100 IR spectrometer. Microanalysis was carried out by Guelph Chemical Laboratories Ltd., Guelph, Ontario.
3.4.2 Synthesis of RuHCl(H\(_2\))(IMes)\(_2\) Ru-6c.

Solid IMes (179 mg, 0.588 mmol) was added to an orange suspension of RuHCl(H\(_2\))(PC\(_\text{y}_3\))\(_2\) Ru-6a (200 mg, 0.283 mmol) in hexanes (10 mL). The reaction mixture was stirred for 4 d at 23 °C, concentrated to ~2 mL, and cooled to -35°C for 2 h. The precipitate was filtered off, washed with cold hexanes (3 x 3 mL), and dried under vacuum to yield Ru-6c as an orange powder. Yield: 187 mg (88%).

\(^1\)H (300 MHz, C\(_6\)D\(_6\)): δ 6.80 (s, 8H, Mes \(m\)-CH), 6.09 (s, 4H, NCH=CHN), 2.34 (s, 12H, \(p\)-CH\(_3\)), 2.07 (s, 24H, \(o\)-CH\(_3\)), -16.58 (br s, 3H, Ru-HCl(H\(_2\))). \(^{13}\)C{\(^1\)H} NMR (75.5 MHz, C\(_6\)D\(_6\)): δ 199.6 (s, NCN), 137.8 (s, Mes \(p\)-C), 136.7 (s, Mes \(i\)-C), 136.4 (s, Mes \(o\)-C), 128.8 (s, Mes \(m\)-C), 120.7 (s, NC=CN), 21.3 (s, \(p\)-CH\(_3\)), 18.8 (s, \(o\)-CH\(_3\)). IR (Nujol, cm\(^{-1}\)): ν(Ru-H) 2037 (w). Anal. Calcd. for C\(_{42}\)H\(_{51}\)ClN\(_4\)Ru: C, 67.40 %; H, 6.87 %; N, 7.49 %. Found: C, 67.16 %; H, 7.04 %; N, 7.39 %.

3.4.3 Synthesis of RuHCl(CO)(IMes)\(_2\) Ru-7c.

Solid IMes (83 mg, 0.27 mmol) was added to a solution of RuHCl(CO)(IMes)(PPh\(_3\)) Ru-13b (100 mg, 0.14 mmol) in 3 mL toluene. The yellow solution was heated at 70 °C for 40 h, over which time conversions were monitored by NMR analysis. Once reaction was complete, the solution was concentrated, treated with hexanes, and chilled to -35 °C to precipitate a yellow-orange microcrystalline product. The solid was filtered off, washed with hexane (3 x 3 mL), and dried under vacuum. Yield: 85 mg (81%). Spectroscopic data are in good agreement with the values reported.\(^{52,53}\) \(^1\)H NMR (C\(_6\)D\(_6\)): δ 6.82 (s, 4H, Mes \(m\)-CH), 6.78 (s, 4H, Mes \(m\)-CH), 6.16 (s, 4H, NCH=CHN), 2.32 (s, 12H, \(p\)-CH\(_3\)), 2.17 (s, 12H, \(o\)-CH\(_3\)), 2.05 (br s, 12H, \(o\)-CH\(_3\)), -25.39 (s, 1H, RuH). \(^{13}\)C{\(^1\)H} NMR (C\(_6\)D\(_6\)): δ 202.1 (s, CO), 195.2 (s, NCN), 137.3 (br s, Mes \(m\)-C), 137.0 (s, Mes \(p\)-C), 136.3 (br s, Mes \(o\)-C), 129.0 (s,
Mes m-C), 121.6 (s, NC=CN), 21.3 (s, Mes p-CH₃), 19.0 (br s, Mes o-CH₃) 18.9 (br s, Mes o-CH₃). IR (Nujol, cm⁻¹): ν(CO) 1883 (s), ν(Ru-H) 1839 (w).

3.4.4 Representative procedure for hydrogenolysis of benzylidene complexes Ru-1.

To a solution of Ru-1a or Ru-1b (100 mg, 0.12 mmol) was added NEt₃ (50 µL, 0.36 mmol; 3 equiv), 1,3,5-trimethoxybenzene (TMB; 20 mg, 0.12 mmol, 1 equiv) and Ph₃P=O (34 mg, 0.12 mmol, 1 equiv) in CH₂Cl₂ (20 mL). Aliquots of this stock solution (2.0 mL each) were distributed to five glass-lined autoclaves. These were purged with H₂ (3 × 250 psi), pressurized to 1000 psi and stirred at 60 °C (oil bath; 10 min allowed to reach temperature). At appropriate times, the autoclaves were vented to 50 psi, cooled for 10 min (ice bath), purged with Ar (250 psi), dried externally (acetone, CH₂Cl₂), and returned to the glovebox. The contents of each autoclave were evaporated to dryness and taken up in C₆D₆ for NMR analysis. Conversions were determined by monitoring the decrease in the integration of the ¹H NMR singlet for Ru-1a (20.6 ppm) or Ru-1b (19.9 ppm), and the increase in integration of a broad singlet for Ru-6a, or for Ru-6a/b (-16.45 ppm, 3H), relative to the methyl proton singlet for TMB (3.3 ppm, 9H). These conversions were confirmed by ³¹P{¹H} NMR analysis, by integrating the singlets for Ru-1a (36.9 ppm) or Ru-1b (32.1 ppm) and Ru-6a (54.2 ppm) or Ru-6b (56.3 ppm) relative to that of Ph₃P=O (25.5 ppm).

For reactions at room temperature, aliquots were removed at regular intervals inside a glovebox, stripped, and redissolved in C₆D₆ for NMR analysis. Hydrogenolysis of Ru-1b was very slow: at 24 h, 35% unreacted Ru-1b, 8% Ru-6b, and 7% Ru-6a.
3.4.5 Representative procedure for methanolysis of benzylidene complexes Ru-1.

To a solution of Ru-1a or Ru-1b (10 mg, 0.012 mmol) and Ph₃P=O (6 mg, 0.02 mmol) in CH₂Cl₂ (0.59 mL) in a thick-walled J. Young NMR tube was added MeOH (0.16 mL). C₆D₆ (50 µL) was added as deuterium lock, and a zero-time (t₀) ³¹P{¹H} NMR spectrum was acquired. Addition of NEt₃ (5.0 µL, 0.036 mmol) and subsequent heating (oil bath, 60 °C) initiated the reaction, which was monitored by ³¹P{¹H} NMR analysis. Conversions were determined by measuring the integration of the singlets due to Ru-1a (37.2 ppm) or Ru-1b (32.3 ppm) and Ru-7a (46.2 ppm) or Ru-7b (47.7 ppm) relative to that for Ph₃P=O (32.8 ppm). The chemical shift for Ru-1a is shifted slightly downfield from its value in neat CD₂Cl₂ (36.6 ppm; cf. 36.9 in C₆D₆).
3.5 References.


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(40) Schmidt, M. A.; Muller, P.; Movassaghi, M. *Tet. Lett.* **2008**, 49, 4316-4318.
(49) Consistent with the thermal requirement for phosphine dissociation, this effect is not observed during the room-temperature reaction of Ru-1b with methanolic methoxide (Chapter 4).


Chapter 4: Rapid Extinction of the Grubbs Catalysts with Methoxide Ion: Formation of Novel Methoxyhydride Complexes

4.1 Introduction

The Grubbs metathesis catalysts RuCl\(_2\)(L)(PCy\(_3\))(-CHPh) (e.g., Ru-1a: L = PCy\(_3\); Ru-1b: L = IMes, \(N,N'\)-bis(mesityl)imidazol-2-ylidene) are now widely recognized as powerful agents for further, non-metathetical transformations.\(^{1,2}\) In some cases, this expanded reactivity is due to the action of Ru-1 and its alkylidene and/or methylidene derivatives: in others, it reflects the operation of further ruthenium catalysts generated in situ, whether by chance or design.\(^3\) While a greater understanding of the underlying inorganic transformations of these important complexes would clearly be advantageous, overwhelming interest in their organic applications has tended to overshadow their inorganic reaction chemistry. Many of their fundamental reactivity patterns thus remain obscure, studies of the transformation of Ru-1 into the catalytically important hydrides RuHCl(CO)(L)(PCy\(_3\)) Ru-7 (particularly Ru-7a; L = PCy\(_3\)) notwithstanding.\(^4,5\)

A potentially important example of this obscurity is found in the reactions of the Grubbs catalysts with alkoxides. Schmidt has demonstrated that post-metathesis treatment of Ru-1a with isopropanol and NaOH (5-10 equiv vs. Ru) yields efficient catalysts for double-bond isomerization. Primary alcohols, however, were strikingly less effective.\(^6\) While metal hydrides are formed in either case, one obvious difference lies in the resistance of secondary alkoxides to Ru-mediated decarbonylation. In contrast, Mol and co-workers\(^4a\) have shown that treating Ru-1a with one equivalent of methoxide at 70-75 °C yields the carbonyl adduct Ru-7a, among other Ru species (ca. 50% Ru-7a; we suspected that the unidentified co-products might arise from thermolytic degradation of Ru-1a). Given that complexes Ru-
7a/b are high-productivity catalysts in the mechanistically-related context of olefin hydrogenation, we hypothesized that the poor isomerization activity associated with primary alcohols might be due to formation of deactivated polycarbonyl species in the presence of excess alkoxide.

Within part of a broader program of study directed at evaluating the behaviour of Ru-alkylidene complexes with reactive [ER] / HER species, we thus wished to clarify the reactivity of Ru-1a and Ru-1b toward excess methoxide (>2 equiv) in the presence of methanol. We chose to explore this chemistry at ambient temperatures, both to intercept the relevant Ru species (rather than "downstream" products arising from extraneous thermal decomposition pathways), and to gain a clearer picture of the minimum conditions required for loss of the benzylidene functionality. Here we report strikingly different outcomes for the first- and second-generation Grubbs catalysts. While Ru-1a is immediately converted into RuH(OMe)(CO)2(PCy3)2 Ru-18a and RuH(OMe)(H2)(PCy3)2 Ru-17a at 23 °C, complex Ru-1b undergoes much slower transformation into a rare, unexpectedly stable five-coordinate methoxyhydride species, RuH(OMe)(CO)(IMes)(PCy3) Ru-16b, with no sign of the expected Ru-17b/Ru-18b. Routes to the new complexes Ru-16b and Ru-18a/b from convenient hydride precursors were developed to confirm the identities of observed products (Ru-16b, Ru-18a), and the absence of expected products (Ru-18b).

4.2 Results and Discussion

4.2.1 Reactions of Grubbs catalysts with methoxide ion.

Addition of excess methanolic NaOMe to a solution of Ru-1a in CH2Cl2 (Scheme 4.1a) caused an instant color change from purple to pale yellow, evolution of small bubbles
presumed to be H₂, and complete loss of the NMR signals for Ru-1a within 5 minutes, without need for elevated temperatures. No evidence was seen of methoxyhydride RuH(OMe)(CO)(PCy₃)₂ Ru-16a, an intermediate inferred from the corresponding, slower reaction of Ru-1b discussed below (Scheme 4.1b). Instead, the sole Ru products observed were RuH(OMe)(CO)₂(PCy₃)₂ Ru-18a and RuH(OMe)(CO)(H₂)(PCy₃)₂ Ru-17a, formed in ca. 2:1 ratio. Formaldehyde and free PCy₃ were also detected (ca. 10% each), as well as toluene, although quantification of the latter was hampered by interfering signals from the cyclohexyl groups or the internal standard Ph₃PO. Co-formation of ca. 25% paramagnetic material is indicated by integration against Ph₃PO; vide infra.

The distribution of Ru products did not change on longer reaction (4 h), but stripping off the solvent and redissolving the residue in C₆D₆ effected transformation of Ru-17a into Ru-18a, via uptake of a further equivalent of methanol (see mechanistic section). Traces of known⁸ dihydride Ru(H)₂(CO)₂(PCy₃)₂ Ru-19a (<5%) were also formed. The identity of Ru-18a was confirmed by independent synthesis from hydride precursors; dihydrogen adduct Ru-17a was characterized by in situ NMR analysis, including T₁(min) measurements. Facile β-elimination from methoxide, discussed in more detail below, disfavors formation of stable bis(alkoxide) or deprotonated carbyne products, as formed in the corresponding reactions of Ru-1a with excess tert-butoxide⁹ or phenoxides.¹⁰-¹²
Scheme 4.1. Products observed following reaction of Grubbs catalysts with excess methoxide. Reactions at 23 °C in CH₂Cl₂-MeOH. PCy₃, toluene, and formaldehyde also observed; see text. The trans-disposition of the hydride and CO ligands in Ru-17a (favored by donor-acceptor push-pull interactions) is suggested by analogy to the structure of Ru-18a.

Consumption of Ru-1b, in comparison, required several hours even at relatively high proportions of methoxide (4 h at 20 equiv). As shown in Scheme 4.1b, reaction also halted at an earlier stage, yielding five-coordinate RuH(OMe)(CO)(IMes)(PCy₃) Ru-16b (a rare example of a coordinatively unsaturated alkoxyhydride complex),¹³ rather than Ru-18b and/or Ru-17b. Addition of excess PCy₃ had no effect on the rate of transformation of Ru-1b into Ru-16b, although such treatment retarded consumption of the first-generation catalyst Ru-1a. We attribute the difference to the much higher lability of the PCy₃ ligand in Ru-1a, which gives equilibrium access to four-coordinate RuCl₂(PCy₃)(=CHPh) Ru-1a' in solution. Salt metathesis via this sterically accessible species (see Path II, Scheme 4.2) is sufficiently faster that the corresponding reaction of the parent Ru-1a (Path I) does not compete. The slow salt metathesis of Ru-1b, as well as the resistance of Ru-16b to further reaction, are consistent with the very low room-temperature lability of the PCy₃ ligand in these IMes complexes,¹⁶ which significantly increases the steric impediment to reaction. The strong binding characteristic of phosphine ligands trans to an NHC ligand is known to retard
dissociative reaction pathways in catalysis, particularly at ambient temperatures. Such 
behaviour has been documented in hydrogenation and isomerization via the hydride 
complex Ru-7b, and in metathesis via Ru-1b.

A proposed mechanism for the transformation of Ru-1 into Ru-16 thus involves initial 
reaction of Ru-1 via exchange of both chloride ligands, followed by proton transfer from 
bound methoxide to benzylidene (see A/A'; Scheme 4.2), and coordination of formaldehyde 
to give Ru-benzyl intermediate B/B'. Deinsertion of CO and liberation of the benzyl group 
as toluene (and recoordination of PCy₃, in the case of Ru-16a') would then generate Ru-
16a/b. Labeling evidence consistent with such a pathway was reported by Dinger and Mol
in the transformation of Ru-1a into Ru-7a with a single equivalent of methoxide. For details 
(including the key CO deinsertion step), the reader is referred to the mechanism shown in 
Chapter 1 (Scheme 1.27). More recently, Leung and co-workers invoked the analogous 
attack by bound methoxide on benzylidene on treatment of RuCl[N((iPr₂PS)₂(PCy₃)(=CHPh) 
with NaOMe. These reactions fall into a broader class of proton migrations onto 
benzylidene from E-R groups on an adjacent ligand (notwithstanding the moderately 
electrophilic character inferred computationally for Ru=CH₂ systems). Proton migration 
need not be restricted to β- or α-E-H groups: Owen and co-workers recently reported attack 
on benzylidene by a γ-dihydroborate moiety in a scorpionate derivative of Ru-1a, underscoring the point that ligand flexibility, in conjunction with a reactive E-H bond, can 
expand the scope of this alkylidene transformation pathway. Ru-NHC derivatives show 
substantially higher tolerance toward adjacent N-H functionalities than first-generation 
complexes, perhaps indicating that migration proceeds via a dissociative pathway (vide infra).
Scheme 4.2. Proposed pathways for transformation of Ru-1a/b into five-coordinate Ru-16a/b. Product is isolable only for Ru-16b (L = IMes). For ensuing reactions of Ru-16a/Ru-16a', see text. For L = PCy₃, both of the pathways depicted are feasible, but Path II is kinetically dominant. For L = IMes, only Path I is available, and reaction is slow.

Conversion of the intermediate Ru-16a (or, more probably, Ru-16a') into methoxydicarbonyl Ru-18a necessitates installation of a further equivalent of methoxide via reaction with methanol. The fact that Ru-16b does *not* evolve indicates that the associative pathway is not productive in this case. Scheme 4.3 depicts a plausible pathway for Ru-16a, involving coordination of methanol and α-metathesis²⁵ of the O-H and Ru-hydride bonds, followed by β-hydride elimination and CO deinsertion as before. Scavenging of H₂ by unreacted Ru-16a would account for the competitive formation of dihydrogen adduct Ru-17a. Reversible binding of dihydrogen enables release and recycling of Ru-16a, as indicated
by the conversion of Ru-17a into Ru-18a on workup noted above. Transient signals assigned to Ru-16a are observed by in situ NMR analysis, at shifts very similar to those for Ru-16b, on freeze-pump-thaw degassing solutions of Ru-17a. Hydrogen-bonding interactions between incoming methanol and the hydride and/or methoxide ligands may account for the dramatically faster reaction of methanol with Ru-16a, vs. the benzylidene complex Ru-1a (the latter reaction requires hours even at 60 °C).\(^5\)

Scheme 4.3. Proposed pathway for transformation of Ru-16a into six-coordinate Ru-18a and Ru-17a.

An anticipated competing pathway involves direct \(\beta\)-elimination and deinsertion from Ru-16a/b to afford dihydrides Ru(H)\(_2\)(CO)\(_2\)(L)(PCy\(_3\))\(_2\) Ru-19a/b. While traces of Ru-19a and Ru-19b form on workup, this pathway is clearly a minor one. The minimal formation of Ru-19a is probably due to the rapid conversion of Ru-16a into Ru-18a and Ru-17a, reflecting the abundance and non-innocence of the methanol cosolvent. Importantly, however, the resistance of Ru-16b to transformation into Ru-19b implies that \(\beta\)-elimination again requires phosphine loss, despite the formal coordinative unsaturation of Ru-16b.
Finally, it may be noted that the inhibited methanolysis of Ru-16b, relative to Ru-16a, contrasts with the behaviour earlier established for the corresponding dihydrogen complexes RuHCl(H\(_2\))(L)(PCy\(_3\)) Ru-6a/b. The IMes derivative of the latter reacted only marginally more slowly with methanol and NEt\(_3\) than did its PCy\(_3\) analog.\(^{5}\) The difference may be due to the lability of the H\(_2\) ligand (although this will be attenuated by the cis-hydride effect),\(^{26}\) which circumvents the requirement for phosphine loss found in the present chemistry. Alternatively, an associative pathway involving outer-sphere, \(\sigma\)-bond metathesis of methanol may be enabled by the acidity of bound H\(_2\).\(^{27}\) Either is consistent with the reported [PCy\(_3\)]-independence of the reaction.\(^{5}\)

### 4.2.2 Paramagnetic byproducts.

A common challenge in organometallic chemistry is the formation of paramagnetic products that go undetected by direct NMR methods. In the work above, observation of free PCy\(_3\) led us to suspect the presence of such co-products. We quantified the proportion of paramagnetic Ru by integration against Ph\(_3\)PO as an internal standard. A ca. 25% decrease in total integration was evident for the reactions of both Ru-1a and Ru-1b: we attribute this to the formation of paramagnetic species, rather than fluxional diamagnetic products, as low-temperature \(^{31}\)P\({^{1}\text{H}}\) NMR analysis revealed no additional signals. Notably, however, Ru-18a can be prepared in 85% isolated yield from a non-benzylidene precursor (see below), tending to implicate the benzylidene functionality in the Ru(II) to Ru(III) oxidation. It is unclear whether C-H activation of the PCy\(_3\) and/or IMes ligands also contributes: both are well precedented.\(^{28,29}\) The four-coordinate species generated by phosphine loss is almost certainly a key vector for decomposition, as suggested by parallel experiments with the labile, phosphine-free "third-generation" Grubbs catalyst RuCl\(_2\)(IMes)(py)\(_2\)(=CHPh) Ru-1d.
This complex was completely consumed within 15 min of treating with methoxide, but only ca. 15% of a hydride product was observed, which itself disappears within 1 h.

4.2.3 Preparation of Five-Coordinate Methoxyhydride RuH(OMe)(CO)(IMes)(PCy₃) Ru-16b.

To confirm the identity of Ru-16b, we undertook its synthesis on preparative scale from the well-behaved hydride precursors Ru-7b. Addition of methanolic NaOMe (20 equiv; Scheme 4.4) to a solution of Ru-7b in CH₂Cl₂ at 23 °C caused an immediate color change from orange-yellow to red-orange. NMR analysis revealed complete conversion to the new methoxyhydride species RuH(OMe)(CO)(IMes)(PCy₃) Ru-16b within 15 minutes. Quantitative conversion was confirmed in separate NMR-scale experiments by integration against Ph₃PO as internal standard, as noted above. Isolation of Ru-16b was frustrated by formation of traces of Ru-18b and Ru-19b on concentrating to dryness, but detailed NMR analysis supports the proposed structure. In particular, the upfield location and doublet multiplicity of the hydride signal (-23.61 ppm; ²JHP = 22 Hz; Table 4.1; cf. the very similar data for chloride analogue Ru-7b) provide unequivocal evidence for a square-pyramidal complex in which an apical hydride ligand lies cis to a single basal phosphine. The latter gives rise to a ³¹P{¹H} singlet at 50.2 ppm. The hydride signal correlates (HMBC) with the IMes carbene carbon (δc 193.9 ppm, d, ²JCP = 103.2 Hz) and a single carbonyl ligand (δc 204.7 ppm, d, ²JCP = 8.7 Hz), although not with the broad OCH₃ signal (63.5 ppm, "0.5 25 Hz). Assignment of the latter was confirmed by a DEPT-135 experiment (−30 °C, C₇D₈) and HMQC correlation with the methoxy proton singlet (4.22 ppm). ¹H NOESY-NMR analysis reveals a through-space interaction between the methoxy protons and hydride. Rapid rotation about the Ru-C₇Mes bond in Ru-16b is indicated by the equivalence of the IMes
"backbone" protons, as well as the mesityl p-Me nuclei, despite the difference in environment above and below the basal plane of the square pyramid.\(^\text{30}\)

\[
\begin{align*}
\text{Ru-7b} & \quad \xrightarrow{\text{Cl} \quad \text{Ru} \quad \text{PCy}_3} \quad \text{Ru-16b} \\
\text{H} & \quad \text{CO} & \quad \text{20 NaOMe} & \quad \text{CH}_2\text{Cl}_2\text{-MeOH} & \quad \text{RT, 15 min} & \quad \text{H} & \quad \text{CO} \\
\text{IMes} & \quad \text{Ru} & \quad \text{PCy}_3 & \quad \text{MeO} & \quad \text{Me} & \quad \text{Ru} & \quad \text{PCy}_3
\end{align*}
\]

\textbf{Scheme 4.4.} Synthesis of five-coordinate methoxyhydride complex \textbf{Ru-16b}.

4.2.4 \textit{Synthesis of six-coordinate} \textit{RuH(OMe)(CO)}_{\text{2}}(\text{L})(\text{PCy}_3) \textbf{Ru-18a/b} and \textit{Ru(H)}_{\text{2}}(\text{CO})_{\text{2}}(\text{IMes})(\text{PCy}_3) \textbf{Ru-19b} from \textit{RuH(OTf)(CO)}_{\text{2}}(\text{L})(\text{PCy}_3) \textbf{Ru-21a/b}.

High-yield routes to \textbf{Ru-18a/b} and \textbf{Ru-19b} were devised to support characterization of these previously unreported complexes (Scheme 4.5). We initially envisaged synthesis of \textbf{Ru-18} from the known\(^8\) bis(carbonyl) complex \textit{RuHCl(CO)}_{\text{2}}(\text{PCy}_3)_{\text{2}} \textbf{Ru-20a} and its IMes analogue \textbf{Ru-20b}. Complexes \textbf{Ru-20} were conveniently prepared in ca. 85\% isolated yield via reaction of \textbf{Ru-7a/b} with CO. Reactions of \textbf{Ru-20a} with methanolic NaOMe in THF proved slow (<20\% in 4 h), however. We therefore converted \textbf{Ru-20a/b} into their more reactive triflates \textit{RuH(OTf)(CO)}_{\text{2}}(\text{L})(\text{PCy}_3) \textbf{Ru-21a/b} by reaction with AgOTf in THF (\textbf{Ru-21a}: 70\%; \textbf{Ru-21b}: 83\%). Treatment of \textbf{Ru-21a/b} with NaOMe/MeOH in THF effected complete conversion to yellow \textit{RuH(OMe)(CO)}_{\text{2}}(\text{L})(\text{PCy}_3) \textbf{Ru-18a/b} within 30 min.\(^3\)

Sodium triflate was removed by stripping the reaction mixture to dryness, extracting with \text{CH}_2\text{Cl}_2, and filtering through Celite. Reprecipitation with hexanes afforded \textbf{Ru-18a/b} as light yellow powders in excellent yields (ca. 85\% each).

A convenient route to \textit{Ru(H)}_{\text{2}}(\text{CO})_{\text{2}}(\text{IMes})(\text{PCy}_3) \textbf{Ru-19b} from \textbf{Ru-21b} was also developed, via reaction with excess NaH at 50 °C in THF. Reaction was complete within 45 min. While high solubility in hexanes and diethyl ether frustrated reprecipitation, crude \textbf{Ru-}}
19b exhibits spectroscopic features closely similar to those reported for Ru-19a (originally prepared by the Chaudret group by treating Ru(H)_2(H_2)(PCy_3)_2 with CO; data are provided in Table 4.1).^8

![Scheme 4.5. Synthetic routes to Ru-18a/b and Ru-19b from Ru-7a/b.](image)

The structures of the new complexes Ru-18a/b, Ru-19b, Ru-20b, and Ru-21a/b were established by one- and two-dimensional NMR experiments, supported by IR spectroscopy,^32 and by elemental analysis for all but Ru-19b, which proved highly sensitive toward decomposition even in the solid state. Coordinative saturation in each is indicated by the downfield location of the hydride signal (between −4 and −8 ppm; Table 4.1), the triplet or doublet multiplicities of which indicate retention of the PCy_3 ligand(s) originally present. Trans-disposition of the two PCy_3 groups, or of the PCy_3 and IMes groups, is confirmed from the singlet multiplicity of the 31P NMR signal (for Ru-18a, Ru-21a), or from the magnitude of 2J_{CP} coupling to the carbene carbon (Ru-18b: 96 Hz; Ru-19b: 70 Hz; Ru-20b: 88 Hz; Ru-21b: 84 Hz). In contrast with Ru-19b, the symmetry of which results in equivalent carbonyl carbon (and hydride) signals, complexes Ru-18a/b, Ru-20a/b, and Ru-21a/b contain inequivalent carbonyl groups. Each appears as a 13C{^1H} NMR doublet or
triplet, the $^{2}J_{cp}$ values for which (6-15 Hz) confirm cis-disposition relative to the PCy$_3$ ligand(s). The expected HMBC correlations are seen between the hydride and the carbonyl and carbene ligands. For methoxides Ru-18a/b, assignment of the methoxy carbons (ca. 67 ppm) is confirmed by DEPT-135 analysis and HMQC correlation with the methoxy methyl singlet at ca. 4.0 ppm. A NOESY correlation between the latter and the hydride signal confirms the cis-disposition of these ligands. Finally, the triflate CF$_3$ groups in Ru-21a/b exhibit essentially identical NMR values (a $^{13}$C{$^{1}$H} quartet at ca. 120 ppm ($^{1}J_{cp} = 319$ Hz), and a $^{19}$F{$^{1}$H} singlet at -77 ppm).
### Table 4.1. Key NMR chemical shifts (ppm), coupling constants (Hz), and IR bands (cm$^{-1}$) for hydride complexes discussed in this Chapter.

<table>
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<th>Complex</th>
<th>NMR solvent</th>
<th>$\delta_p$</th>
<th>$\delta_H$ (Ru-X)</th>
<th>$\delta_{CO}$</th>
<th>IR (v)</th>
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<td></td>
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<td>$H (^2J_{HP})$</td>
<td>$^2J_{CP}$</td>
<td>CO</td>
<td>Ru-H</td>
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<td>(d, 23)</td>
<td>196.7 (d, 6)</td>
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$^a$NMR chemical shifts in ppm; coupling constants in Hz; IR bands in cm$^{-1}$. Values at 23 °C unless otherwise noted. NMR samples in 10:1 CH$_2$Cl$_2$-MeOH were spiked with C$_6$D$_6$ as a deuterium lock. References are given to literature values in the solvents indicated. $^b$ This work. $^c$ Cf. values for transient species Ru-16a at −30 °C in C$_7$D$_8$: $\delta_H$ 47.8 ppm (s); $\delta_H$ −22.94 (d, 19 Hz). At 23 °C in C$_6$D$_6$, $\delta_H$ −22.81 (br t, $^2J_{HP}$ = 17.4 Hz). $^d$ Measurement of IR and $^{13}$C NMR data was hampered by the low proportion of these species.
4.3 Conclusions

The foregoing describes the rapid reaction of the first-generation Grubbs catalyst \textbf{Ru-1a} with excess methoxide and methanol at room temperature. Major products are the coordinatively saturated methoxyhydride complexes \( \text{RuH(OMe)(CO)}_2(\text{PCy}_3)_2 \) \textbf{Ru-18a} and \( \text{RuH(OMe)(CO)(H}_2)(\text{PCy}_3)_2 \) \textbf{Ru-17a}. Formation of such species may account for the poor isomerization activity found when an excess of primary alkoxides is used to trigger C=C isomerization following \textbf{Ru-1a}-mediated metathesis. Reaction of the second-generation catalyst \textbf{Ru-1b} with methanolic methoxide is much slower, and terminates at the five-coordinate methoxyhydride complex \( \text{RuH(OMe)(CO)(IMes)(PCy}_3)_2 \) \textbf{Ru-16b}. The identities of the new complexes \textbf{Ru-16b} and \textbf{Ru-18a/b} were confirmed by independent synthesis from \( \text{RuHCl(CO)(IMes)(PCy}_3)_2 \) \textbf{Ru-7b} or hydridotriflates \( \text{RuH(OTf)(CO)}_2(L)(\text{PCy}_3) \) \textbf{Ru-21a/b}, respectively; isolation of \( \text{RuH(OMe)(CO)(PCy}_3)_2 \) \textbf{Ru-16a} is hampered by its much higher reactivity. The slower rate of formation of \textbf{Ru-16b} at room temperature, and its stability once formed, reflect the low lability characteristic of phosphine ligands trans to an N-heterocyclic carbene. This constrains salt metathesis to a non-dissociative pathway for \textbf{Ru-1b}, rather than (as with \textbf{Ru-1a}) proceeding via a sterically accessible four-coordinate species formed by equilibrium loss of \text{PCy}_3. The stability of \textbf{Ru-16b} toward reaction with methanol indicates that for this subsequent reaction, the associative pathway is either inaccessible or prohibitively slow. Precipitation of NaCl from solution (in which the proportion of \text{CH}_2\text{Cl}_2 dominates by 10:1 over MeOH) contributes to the greater driving force of the initial salt metathesis reaction.

Notable in this chemistry is the facility with which these "robust" benzylidene complexes decompose into hydride species under exceptionally mild conditions. Consumption of \textbf{Ru-}
1a by alkoxide occurs within minutes at room temperature; loss of Ru-1b – while slower – is complete within a few hours. Reaction conditions that can give rise to adventitious alkoxides, particularly in the presence of methanol co-solvent (a favored reaction medium for olefin metathesis reactions of biologically relevant substrates)\textsuperscript{34} should thus be recognized as profoundly detrimental to catalytic performance.

4.4 Experimental

4.4.1 General Procedures.

Reactions were carried out at room temperature (23 °C) under argon using standard Schlenk or glovebox techniques, unless otherwise stated. Dry, oxygen-free solvents were obtained using a Glass Contour solvent purification system, and stored over Linde 4Å molecular sieves. C\textsubscript{6}D\textsubscript{6} was degassed by consecutive freeze/pump/thaw cycles and dried over molecular sieves (Linde 4Å). Methanol was distilled from Mg(OMe)\textsubscript{2} under Ar and stored over molecular sieves (Linde 3Å). Sodium methoxide solutions were prepared by digesting Na metal in methanol immediately before use. RuCl\textsubscript{2}(PCy\textsubscript{3})\textsubscript{2}(=CHPh) Ru-1a,\textsuperscript{35} RuCl\textsubscript{2}(IMes)(PCy\textsubscript{3})(=CHPh) Ru-1b,\textsuperscript{36,37} and RuHCl(CO)(L)(PCy\textsubscript{3}) (Ru-7a: L = PCy\textsubscript{3}, Ru-7b: L = IMes)\textsuperscript{33} were prepared according to literature procedures. NMR spectra were recorded on a Bruker Avance 300 or Avance 500 spectrometer, at 298 K unless otherwise specified. Chemical shifts are reported relative to TMS (\textsuperscript{13}C, \textsuperscript{1}H), 85% external H\textsubscript{3}PO\textsubscript{4} (\textsuperscript{31}P), or CFCl\textsubscript{3} (\textsuperscript{19}F) at 0 ppm. \textsuperscript{1}H and \textsuperscript{13}C NMR spectra were referenced to the carbon or residual proton signal of the deuterated solvent, \textsuperscript{19}F spectra to CF\textsubscript{3}CO\textsubscript{2}H at -76.55 ppm. In the NMR assignments of IMes derivatives given below, a/b labels indicate corresponding, inequivalent nuclei on the same mesityl ring, as indicated by HMQC or HMBC correlations. IR spectra were measured as Nujol mulls between NaCl plates using a Bomem MB100
spectrometer, or as powders using a Varian 640-IR reflectance IR spectrometer. Microanalyses were carried out by Guelph Chemical Laboratories Ltd., Guelph, Ontario.

4.4.2 NMR-scale reactions of Grubbs catalysts with methoxide.

In a representative reaction, a solution of Ru-1a (10 mg, 0.012 mmol) was dissolved in CH₂Cl₂ (0.7 mL, with a 50 µL spike of C₆D₆) in a J. Young NMR tube. To this was added NaOMe as a solution in MeOH (9.7 µL of a 3.75 M solution, 3 equiv), and the reactions were monitored by NMR analysis (in some cases with Ph₃PO added as an internal standard for integration). No solvent suppression was used for the ¹H NMR spectra, as the alkylidene and hydride regions (10 to 30 ppm and 0 to -30 ppm, respectively) could be viewed without interference.

4.4.3 RuCl₂(PCy₃)₂(=CHPh) Ru-1a + methoxide: observation of Ru-18a and Ru-17a.

The solution changed color from deep purple to pale yellow over 5 min. ³¹P{¹H} NMR (CH₂Cl₂-MeOH-C₆D₆): 52.1 (s, Ru-18a, 48%), 72.0 (s, Ru-17a, 19%); 11.1 (s, PCy₃, 13%); the deficit is attributed to paramagnetic material (see text). ¹H NMR (CH₂Cl₂-MeOH-C₆D₆; hydride region): -4.59 (Ru-18a), -7.45 (Ru-17a). For the synthesis and full characterization of Ru-18a, see below.

4.4.4 RuCl₂(IMes)(PCy₃)(=CHPh) Ru-1b + methoxide: observation of Ru-16b.

A color change from red to pale orange-yellow occurred over 4 h. ³¹P{¹H} NMR (CH₂Cl₂-MeOH-C₆D₆): 49.6 (Ru-16b, 73%), 11.1 (s, PCy₃, 10%); the deficit is attributed to paramagnetic material (see text). ¹H NMR (CH₂Cl₂-MeOH-C₆D₆; hydride region): -25.02 ppm (Ru-16b). For the synthesis of Ru-16b using 20 equiv NaOMe, with full details of NMR characterization, see below.
4.4.5 In Situ Observation of RuH(OMe)(CO)(H₂)(PCy₃)₂ Ru-17a.

Complex Ru-17a was generated in situ (as a 2:1 mixture of Ru-18a and Ru-17a) as described above. Sweeping the atmosphere with Ar resulted in partial transformation of Ru-17a into Ru-16a (ca. 15% vs. the original Ru-1a). This was readily reversed by freeze-pump-thaw degassing (3×) and backfilling with H₂. NMR data for Ru-17a: ³¹P{¹H} NMR (121.5 MHz, 10:1 CH₂Cl₂-MeOH): δ 72.0 (s). ¹H NMR (300.1 MHz, 10:1 CH₂Cl₂-MeOH): -7.45 (br s). Hydride T₁(min) (C₇D₈, H₂, 263 K, 500.1 MHz): 37.5 ms (d₁-₁ = 0.95 Å for fast-spinning H₂). Decoalescence was not observed down to -90 °C in C₇D₈.


Adding a solution of NaOMe in methanol (300 µL, 2.75 M, 0.83 mmol, 20 equiv) to a vigorously-stirred solution of RuHCl(CO)(IMes)(PCy₃) Ru-7b (31 mg, 0.041 mmol) in 3 mL CH₂Cl₂ caused a color change from orange-yellow to red-orange over 15 min. In situ ³¹P{¹H} NMR analysis indicated solely Ru-16b. The solvent was stripped off, and the residue was redissolved in benzene, filtered through Celite, and stripped to dryness. Yield 24 mg (78%). ³¹P{¹H} NMR analysis of the residue revealed, in addition to Ru-16b, small amounts of Ru(H)₂(CO)₂(IMes)(PCy₃) Ru-19b (5%), RuH(OMe)(CO)₂(IMes)(PCy₃) Ru-18b (2%), and free PCy₃ (5%), which impede microanalysis. Data for Ru-16b: ³¹P{¹H} NMR (121.5 MHz, C₇D₈): δ 50.2 (s). ¹H NMR (300.1 MHz, C₇D₈): δ 6.85 (s, 2H, Mes m-CH₂) 6.83 (s, 2H, =CHN), 4.22 (s, 3H, OCH₃), 2.42-2.38 (two overlapping s, 12H, Mes o-CH₃), 2.14 (s, 6H, Mes p-CH₃), 2.2-1.1 (m, Cy; accurate integration impeded by overlap with Cy signals for Ru-18b, Ru-19b), -23.61 (d, ²J₉H = 22.2 Hz, 1H, RuH). ¹³C{¹H} NMR (125.8 MHz, C₇D₈, 243 K): δ 204.7 (d, ²J₉C = 8.7 Hz, CO), 193.9 (d, ²J₉C = 103.2 Hz, NCN), 138.3 (s, Mes p-C), 138.0 (br, Mes o-C), 137.3 (br, Mes o-
C), 136.4 (s, Mes i-C), 129.0 (s, Mes m-CH), 122.1 (s, =CHN), 63.5 (br s, $\omega_{0.5}$ 25 Hz, OCH$_3$), 34.2 (d, $^1J_{CP} = 16.6$ Hz, C1 of Cy), 31.1 (s, Cy), 30.2 (s, Cy) 28.6 (m, Cy), 27.4 (s, Cy), 21.5 (s, Mes p-CH$_3$), 19.3 (s, Mes o-CH$_3$). IR (Nujol, cm$^{-1}$): ν(CO) 1875 (s); ν(Ru-H) 1890 (w).

4.4.7 Preparation of RuH(OMe)(CO)$_2$L(PCy$_3$) Ru-18a/b. $L = PCy$, Ru-18a.

Addition of NaOMe as a solution in methanol (49 µL, 3.58 M, 0.18 mmol) to RuH(OSO$_2$CF$_3$)(CO)$_2$(PCy$_3$)$_2$ Ru-21a (150 mg, 0.173 mmol) in THF (5 mL), with stirring, caused a color change from pale brown to yellow over 30 min, and deposition of a white precipitate. The reaction mixture was stripped to dryness, and the residue was taken up in CH$_2$Cl$_2$ (15 mL). The mixture was filtered through Celite, concentrated to ca. 0.5 mL, treated with hexanes (5 mL), and chilled to -35 ºC. A light yellow powder deposited, which was filtered off, washed with cold hexanes (3 × 2 mL) and dried under vacuum. Yield: 110 mg (85%). $^{31}$P{$^1$H} (121.5 MHz, C$_6$D$_6$): δ 53.8 (s). $^1$H NMR (300.1 MHz, C$_6$D$_6$): δ 4.10 (s, 3H, OCH$_3$), 2.3–1.2 (m, 66H, Cy), −4.25 (t, $^2J_{HP} = 20.2$ Hz, 1H, RuH). $^{13}$C{$^1$H} (125.8 MHz, C$_6$D$_6$): δ 203.7 (t, $^2J_{CP} = 6.6$ Hz, CO), 201.4 (t, $^2J_{CP} = 11.6$ Hz, CO), 66.4 (s, OCH$_3$), 34.4 (vt, $^1J_{CP} = 10$ Hz, C1 of Cy), 29.8 (d, $J_{CP} = 2.6$ Hz (or two overlapping s), Cy), 28.3 (overlapping m, Cy), 27.1 (s, C4 of Cy). IR (Nujol, cm$^{-1}$): ν(CO) 2006 (s), 1891 (s); ν(Ru-H) 1939 (w).


$L = IMes$, Ru-18b.

The light yellow powder was prepared as for Ru-18a, from RuH(OSO$_2$CF$_3$)(CO)$_2$(IMes)(PCy$_3$) Ru-21b (154 mg, 0.173 mmol). Yield: 115 mg (86%). $^{31}$P{$^1$H} NMR (121.5 MHz, C$_6$D$_6$): δ 54.0 (s). $^1$H NMR (300.1 MHz, C$_6$D$_6$): δ 6.91 (s, 2H,
Mes \( m\text{-CH}^\beta \), 6.89 (s, 2H, Mes \( m\text{-CH}^\beta \)), 6.32 (s, 2H, \( =\text{CHN} \)), 3.96 (s, 3H, OCH\(_3\)), 2.37 (s, 6H, Mes \( o\text{-CH}^\delta \)), 2.30 (s, 6H, Mes \( o\text{-CH}^\alpha \)), 2.20 (s, 6H, Mes \( p\text{-CH}^\delta \)), 2.2-1.0 (m, 33H, Cy), -4.18 (d, \(^2J_{\text{HP}} = 25.3\) Hz, 1H, Ru\( H \)). \(^{13}\text{C}\{^1\text{H}\} \) NMR (125.8 MHz, C\(_6\)D\(_6\)): \( \delta \) 202.9 (d, \(^2J_{\text{CP}} = 12.4\) Hz, CO), 199.5 (d, \(^2J_{\text{CP}} = 6.9\) Hz, CO), 187.5 (d, \(^2J_{\text{CP}} = 95.6\) Hz, NCN), 139.4 (s, Mes \( i\text{-C} \)), 138.2 (s, Mes \( p\text{-C} \)), 137.4 (s, Mes \( o\text{-C}^\alpha \)), 136.2 (s, Mes \( o\text{-C}^\delta \)), 129.2 (s, Mes \( m\text{-CH}^\beta \)), 128.9 (s, Mes \( m\text{-CH}^\beta \)), 122.3 (m, \( =\text{CHN} \)), 67.4 (s, OCH\(_3\)), 34.1 (d, \(^1J_{\text{CP}} = 18.8\) Hz, C1 of Cy), 29.4 (d, \(^1J_{\text{CP}} = 6.9\) Hz (or two overlapping s), Cy), 28.3 (d, \(^3J_{\text{CP}} = 9.9\) Hz, Cy), 28.3 (d, \(^3J_{\text{CP}} = 10.1\) Hz, Cy), 27.0 (s, C4 of Cy), 21.2 (s, Mes \( p\text{-CH}^\delta \)), 18.4 (overlapping s, Mes \( o\text{-CH}^\delta \)). IR (powder, cm\(^{-1}\)): \( \nu(\text{CO}) \) 2013 (s), 1896 (s); \( \nu(\text{Ru-H}) \) 1948 (w). Anal. Calcd. for C\(_{42}\)H\(_{62}\)N\(_2\)O\(_3\)PRu: C, 65.09; H, 8.06; N, 3.61. Found: C, 64.76; H, 7.96; N, 3.67.

4.4.8 Preparation of Ru(\( H \))\(_2\)(CO)\(_2\)(IMes)(PCy\(_3\)) \( \text{Ru-19b} \).

Solid NaH (30 mg, 1.3 mmol) was added to a solution of RuH(OSO\(_2\)CF\(_3\))(CO)\(_2\)(IMes)(PCy\(_3\)) \( \text{Ru-21b} \) (110 mg, 0.123 mmol) in THF (1.0 mL), and the reaction mixture was heated to 50 °C. A color change from pale brown to light yellow occurred over 45 min, accompanied by complete transformation to \( \text{Ru-19b} \). The solvent was stripped off, and the residue taken up in benzene (5 mL) and filtered through Celite. Additional, unassigned NMR signals (<5% total integration) were observed when the filtrate was stripped to dryness and redissolved in C\(_6\)D\(_6\). Attempts to obtain pure \( \text{Ru-19b} \) by reprecipitation from benzene-hexanes, benzene-diethyl ether, or neat hexanes were frustrated by high solubility, and satisfactory microanalysis could not be obtained. \(^{31}\text{P}\{^1\text{H}\} \) NMR (121.5 MHz, C\(_6\)D\(_6\)): \( \delta \) 68.9 (s). \(^1\text{H}\) NMR (300.1 MHz, C\(_6\)D\(_6\)): \( \delta \) 6.88 (s, 4H, Mes \( m\text{-CH} \)), 6.28 (s, 2H, \( =\text{CHN} \)), 2.24 (s, 12H, Mes \( o\text{-CH}^\delta \)), 2.19 (s, 6H, Mes \( p\text{-CH}^\delta \)), 2.0-1.1 (m, 33H, Cy), -7.37 (d, \(^2J_{\text{HP}} = 24.9\) Hz, 2H, Ru\( H \)). \(^{13}\text{C}\{^1\text{H}\} \) NMR (125.8 MHz, C\(_6\)D\(_6\)): \( \delta \) 204.7 (d,
\( ^2J_{CP} = 7.7 \text{ Hz, CO} \), 190.1 (d, \( ^2J_{CP} = 69.8 \text{ Hz, NCN} \)), 139.6 (s, Mes \( i-C \)), 138.0 (s, Mes \( p-C \)), 136.1 (s, Mes \( o-C \)), 129.2 (s, Mes \( m-CH \)), 121.5 (s, =CHN), 37.9 (d, \( ^1J_{CP} = 20.9 \text{ Hz, C1 of Cy} \)), 30.1 (s, Cy), 28.1 (d, \( J_{CP} = 10.1 \text{ Hz, Cy} \)), 27.0 (s, C4 of Cy), 21.2 (s, Mes \( p-CH_3 \)), 18.6 (s, Mes \( o-CH_3 \)). IR (Nujol, cm\(^{-1}\)): \( \nu (\text{CO}) \) 1995 (s), 1951 (s); \( \nu (\text{Ru-H}) \) 1898 (w).

4.4.9 Preparation of RuHCl(CO)\(_2\)(IMes)(PCy\(_3\)) \textbf{Ru-20b}.

(Known\(^8\) \textbf{Ru-20a} was prepared similarly, in 84\% yield). An orange-yellow solution of RuHCl(CO)(IMes)(PCy\(_3\)) \textbf{Ru-7b} (320 mg, 0.546 mmol) in benzene (5 mL) was stirred under 1 atm CO for 1 h, after which the colorless solution was concentrated (ca. 0.5 mL) and hexanes added to precipitate the white product. This was reprecipitated from benzene-hexanes, filtered off, washed with cold hexanes (3 \( \times \) 2 mL) and dried under vacuum. Yield: 270 mg (81\%). \(^{31}\)P\{\(^1\)H\} NMR (121.5 MHz, C\(_6\)D\(_6\)): \( \delta \) 48.2 (s). \(^1\)H NMR (300.1 MHz, C\(_6\)D\(_6\)): \( \delta \) 6.87 (s, 2H, Mes \( m-CH \)), 6.84 (s, 2H, Mes \( m-CH \)), 6.28 (s, 2H, =CHN), 2.36 (s, 6H, Mes \( o-CH_3 \)), 2.34 (s, 6H, Mes \( o-CH_3 \)), 2.21 (s, 6H, Mes \( p-CH_3 \)), 2.3.1 (m, 33H, Cy), -4.77 (d, \( ^2J_{HP} = 22.8 \text{ Hz, 1H, RuH} \)). \(^{13}\)C\{\(^1\)H\} NMR (125.8 MHz, C\(_6\)D\(_6\)): \( \delta \) 202.3 (d, \( ^2J_{CP} = 12.6 \text{ Hz, CO} \)), 197.2 (d, \( ^2J_{CP} = 6.6 \text{ Hz, CO} \)), 184.6 (d, \( ^2J_{CP} = 88.4 \text{ Hz, NCN} \)), 139.4 (m, Mes \( i-C \)), 138.5 (s, Mes \( p-C \)), 136.9 (m, Mes \( o-C \)), 136.6 (m, Mes \( o-C \)), 129.4 (m, Mes \( m-CH \)), 122.7 (overlapping s, =CHN), 34.5 (d, \( J_{CP} = 20.0 \text{ Hz, C1 of Cy} \)), 29.3 (d, \( J = 12.4 \text{ Hz (or overlapping s), Cy} \)), 28.0 (d, \( J_{CP} = 9.0 \text{ Hz, Cy} \)), 27.9 (d, \( J_{CP} = 9.0 \text{ Hz, Cy} \)), 26.8 (s, C4 of Cy), 21.2 (s, Mes \( p-CH_3 \)), 18.8 (s, Mes \( o-CH_3 \)), 18.7 (s, Mes \( o-CH_3 \)). IR (powder, cm\(^{-1}\)): \( \nu (\text{CO}) \) 2035 (s), 1913 (s); \( \nu (\text{Ru-H}) \) 1954 (w). Anal. Calcd. for C\(_{41}\)H\(_{59}\)ClN\(_2\)O\(_2\)PRu: C, 63.18; H, 7.63; N, 3.59. Found: C, 63.09; H, 7.53; N, 3.63.
4.4.10 Preparation of \( \text{RuH(O}_{2}\text{CF}_3)(\text{CO})_2(L)(\text{PCy}_3) \) \( \text{Ru-21a/b} \). \( L = \text{PCy}_3 \), \( \text{Ru-21a} \).

Solid \( \text{AgOSO}_2\text{CF}_3 \) (90 mg, 0.35 mmol) was added to \( \text{RuHCl(CO)}_2(\text{PCy}_3)_2 \) \( \text{Ru-20a} \) (250 mg, 0.35 mmol) in THF (15 mL) in a foil-wrapped vessel, and stirred for 1 h. The solvent was stripped off under vacuum, and the residue extracted with \( \text{CH}_2\text{Cl}_2 \) (3 × 5 mL). The combined extracts were filtered through Celite, concentrated (ca. 0.5 mL), and treated with hexanes to precipitate the pale beige powder. This was chilled (-35 °C), filtered off, washed with cold hexanes (3 × 2 mL), and dried under vacuum. Yield: 200 mg (70%).

\( ^{31}\text{P}\{^1\text{H}\} \) NMR (121.5 MHz, \( \text{C}_6\text{D}_6 \)): \( \delta 53.7 \) (s).

\( ^1\text{H} \) NMR (300.1 MHz, \( \text{C}_6\text{D}_6 \)): \( \delta 2.4-1.0 \) (m, 66H, Cy), -4.02 (t, \( ^2J_{HP} = 18.8 \) Hz, 1H, RuH). \( ^{13}\text{C}\{^1\text{H}\} \) NMR (125.8 MHz, \( \text{C}_6\text{D}_6 \)): \( \delta 202.7 \) (t, \( ^2J_{CP} = 13.5 \) Hz, CO), 201.7 (t, \( ^2J_{CP} = 7.0 \) Hz, CO), 119.8 (q, \( ^1J_{CF} = 319.2 \) Hz, \( \text{OSO}_2\text{CF}_3 \)), 34.7 (br s, C1 of Cy), 29.7 (d, \( J_{CP} = 12.2 \) Hz (or overlapping s), Cy), 27.7 (m, Cy), 26.8 (s, C4 of Cy). \( ^{19}\text{F}\{^1\text{H}\} \) NMR (282.4 MHz, \( \text{C}_6\text{D}_6 \)): \( \delta -77.2 \) (s, \( \text{CF}_3 \)). IR (powder, cm\(^{-1}\)): \( \nu(\text{CO}) \) 2046 (s), 1966 (s); \( \nu(\text{Ru-H}) \) 1917 (w). Anal. Calcd. for \( \text{C}_{39}\text{H}_{67}\text{F}_3\text{O}_5\text{P}_2\text{RuS} \): C, 53.96; H, 7.78. Found: C, 54.22; H, 8.20.

\( L = \text{IMes}, \text{Ru-21b} \).

Reaction as for \( \text{Ru-21a} \), using \( \text{RuHCl(CO)}_2(\text{IMes})(\text{PCy}_3)_2 \) \( \text{Ru-20b} \) (250 mg, 0.321 mmol) as precursor. Yield of the pale beige powder: 190 mg (83%). In the NMR assignments, \( a/b \) labels indicate corresponding, inequivalent nuclei on the same mesityl ring, as indicated by HMQC or HMBC correlations; a prime label is used to differentiate the two Mes rings.

\( ^{31}\text{P}\{^1\text{H}\} \) NMR (121.5 MHz, \( \text{C}_6\text{D}_6 \)): \( \delta 51.3 \) (s). \( ^1\text{H} \) NMR (300.1 MHz, \( \text{C}_6\text{D}_6 \)): \( \delta 6.94 \) (s, 1H, Mes \( m\text{-CH}^+ \)), 6.89 (s, 1H, Mes \( m\text{-CH}^+ \)), 6.84 (s, 1H, Mes \( m\text{-CH}^+ \)), 6.73 (s, 1H, Mes \( m\text{-CH}^+ \)), 6.32 (s, 1H, \( =\text{CHN} \)), 6.22 (s, 1H, \( =\text{CHN} \)), 2.57 (s, 3H, Mes \( o\text{-CH}_3^{a*} \)), 2.34 (s, 3H, Mes \( o\text{-CH}_3^{a*} \)), 2.19 (s, 3H, Mes \( p\text{-CH}_3 \)), 2.12 (s, 3H, Mes \( p\text{-CH}_3 \)), 2.02 (overlapping s; 6H, 99
Mes $o$-$CH_3$, $o$-$CH_3$), 2.2-1.0 (m, 33H, Cy), -4.07 (d, $^2J_{CH} = 23.1$ Hz, 1H, RuH). $^{13}$C\{\H\} NMR (125.8 MHz, C$_6$D$_6$): $\delta$ 204.4 (d, $^2J_{CP} = 13.9$ Hz, CO), 196.7 (d, $^2J_{CP} = 5.5$ Hz, CO), 182.3 (d, $^2J_{CP} = 83.8$ Hz, NCN), 139.9 (s, Mes $i$-C), 139.7 (s, Mes $p$-C'), 138.3 (s, Mes $p$-C), 138.1 (s, Mes $o$-$C''$), 137.5 (s, Mes $o$-$C''$), 137.3 (s, Mes $i$-C'), 135.3-135.2 (overlapping s, Mes $o$-$C'$, $o$-$C''$), 130.4 (s, Mes $m$-$CH^{a'}$), 129.4 (s, Mes $m$-$CH^{a'}$), 129.1 (s, Mes $m$-$CH^{b'}$), 128.5 (s, Mes $m$-$CH^{b'}$), 123.5 (s, $=CH$), 119.9 (q, $^1J_{CF} = 320.4$ Hz, OSO$_2$CF$_3$), 34.2 (d, $^1J_{CP} = 15.7$ Hz, C1 of Cy), 29.3 (overlapping s, Cy), 27.8 (d, $J_{CP} = 10.2$ Hz, Cy), 27.7 (d, $J_{CP} = 10.4$ Hz, Cy), 26.7 (s, C4 of Cy), 21.0 (coincident s, Mes $p$-$CH_3$, $p$-$CH_i'$), 19.1 (s, Mes $o$-$CH_3$), 18.4-18.3 (overlapping s, Mes $o$-$CH_3$). $^{19}$F\{\H\} NMR (282.4 MHz, C$_6$D$_6$): $\delta$ -77.1 (s, CF$_3$). IR (powder, cm$^{-1}$): v(CO) 2049 (s), 1935 (s); v(Ru-H) 1972 (w). Anal. Calcd. for C$_42$H$_{59}$F$_3$N$_2$O$_5$PRuS: C, 56.49; H, 6.66; N, 3.14. Found: C, 56.65; H, 6.68; N, 3.10.
4.5 References.


(19) In striking contrast, attack of bound phenoxide on the alkylidene proton results in α-elimination of phenol and formation of a ruthenium carbyne (see above, and refs. 10-12).


(25) Both σ-bond metathesis and σ-complex-assisted metathesis are plausible: we favor the latter, given the evidence for a dissociative pathway. See: Perutz, R. N.; Sabo-Etienne, S. Angew. Chem., Int. Ed. **2007**, *46*, 2578-2592.


(31) Related chemistry was suggested by a referee as an alternative route to Ru-16a/b, via reaction of Ru-7a/b with AgOTf, then NaOMe. This was explored for Ru-7b, but is thwarted by the rapid decomposition of Ru-7b in the presence of AgOTf.

(32) Two strong $\nu$(CO) bands, and one weak $\nu$(Ru-H) band, were observed in the IR spectrum for each of Ru-18a/b, Ru-20a/b, and Ru-21a/b.


Chapter 5. Generating RuHCl(CO)(L)(PCy$_3$) from the Initiating, Resting, and Quenched States of First- and Second-Generation Grubbs Catalysts

5.1 Introduction.

Recent advances in tandem catalysis involving (R)CM-functionalization were discussed in Chapter 1. Because these approaches are typically product-oriented, the identity of the second catalyst species is often a matter of conjecture. By extension, so are the optimal reaction protocols used to generate it from the metathesis catalyst. Our group has demonstrated the advantages of a mechanistic approach to optimization in ROMP-hydrogenation (see Chapter 1).$^{1,2}$ The protocols developed to efficiently transform Ru-alkylidenes into hydridocarbonyl Ru-7 may hold unexploited promise for other tandem catalysis methodologies, of which tandem (R)CM-isomerization is one obvious candidate.

In Ru-catalyzed RCM and CM, however, the resting state is normally a methyldiene species such as RuCl$_2$(L)(PCy$_3$)(=CH$_2$) Ru-2. A key question thus centers on whether the [Ru]=CH$_2$ entity differs in its reaction chemistry from its better-studied [Ru]=CHPh parent. Despite the central importance of methyldiene complexes in RCM$^3$ and CM$^4$ reactions, their organometallic chemistry remains almost wholly unexamined. While one report suggests that the behaviour of Ru-2a parallels that of its benzylidene parent, at least for hydrogenolysis at ambient temperatures,$^5$ we suspected that thermal stability might emerge as an important distinction. Methyldiene complexes are notoriously fragile. The first-generation complex Ru-2a, for example, has a half-life of 40 min in C$_6$D$_6$ at 55 °C,$^6$ vs. 8 days for the benzylidene parent. Further, fundamental differences between the benzylidene and methyldiene functionalities are suggested by the report that Ru-2a decomposes via a unimolecular pathway, but Ru-1a via a bimolecular pathway.$^7$ A clearer understanding of
the conditions under which such species can be efficiently transformed into other catalysts could greatly benefit tandem metathesis methodologies that begin with RCM or CM.

Of corresponding interest is the behaviour of the Fischer carbene products formed by the common practice of quenching Ru metathesis catalysts with ethyl vinyl ether. Such heteroatom-functionalized alkylidenes (as well as [Ru]=CHC(O)R analogues), are less robust than their benzylidene parents: in some cases, they undergo decomposition faster than metathesis. The [Ru]=CHCO\(_2\)Me entity, for example, is too unstable to detect at room temperature.\(^9\),\(^10\) Similarly, Renata Nunes of this research group\(^1\) noted that the [Ru]=CHC(O)Me moiety formed from Ru-2a or the "third-generation" Grubbs catalyst Ru-1d is readily displaced by pyridine at 50 °C. One product identified in the latter reaction is shown in Scheme 5.1. Several groups have reported that Fischer carbenes readily decompose to liberate Ru-7 (Scheme 5.2, path (a)); indeed, Arisawa and co-workers report that the TMS derivative Ru-23b' affords Ru-7b' quantitatively.\(^12\) The latter finding is particularly promising from the perspective of tandem catalysis, provided that the Fischer carbene can be efficiently generated from the methylidene resting-state species.

\[\text{Scheme 5.1. Facile displacement of the keto-alkylidene moiety by pyridine.}^{11}\]
Scheme 5.2. Methods studied for transforming Ru metathesis catalysts into hydride Ru-7: (a) CM-thermolysis;\(^8,12\) (b) hydrogenolysis,\(^5,13,14\) followed by carbonylation;\(^13,15\) (c) base-assisted methanolysis.\(^16-18\)

This Chapter evaluates the efficiency with which first- and second-generation Grubbs methylidenes can be transformed into the versatile catalyst Ru-7, either directly or via in situ formation of their Fischer carbenes by cross-metathesis (Scheme 5.2). The behaviour of the benzylidene complexes, some of which was described in Chapter 3, is included here for comparison. Three of the most promising methodologies are selected for examination: CM-thermolysis, hydrogenolysis-carbonylation, or methanolysis. A question of added fundamental interest is whether the behaviour of Ru-2 and Ru-22 would replicate the "generation gap" observed for Ru-1 in Chapter 3: that is, whether the protocol of Path (b) would prove superior for transformation of the first-generation catalyst into its hydridocarbonyl derivative Ru-7a, vs. that of Path (c) for the second-generation analogue.

In situ NMR chemical shifts for all compounds surveyed are tabulated at the end of the Experimental section.
5.2 Results and Discussion.

5.2.1 Preparation of RuCl$_2$(IMes)(PCy$_3$)(=CH$_2$) Ru-2b.

The literature route to first-generation methylidene Ru-2a involves CM of benzylidene Ru-1a with ethylene (1 atm C$_2$H$_4$, 15 min, CH$_2$Cl$_2$). While quantitative yields were reported, we found that this procedure resulted in persistent contamination by small amounts of Ru-1a (as indeed expected from the equilibrium formation of Ru-2a; Eqn 5.1. Justin Lummiss of this research group improved the synthesis by isolating the Ru-2a product and washing it with pentane to remove styrene, then resubjecting the clean material to ethylene. This afforded Ru-2a free of Ru-1a in 85% yield. From clean Ru-2a, he developed a high-yield, high-purity route to the second-generation analogue Ru-2b', previously accessible in <40% yield with limited purity, via ligand exchange of Ru-2a with free H$_2$IMes.

\[
\begin{align*}
\text{Ru-1a} & \xrightarrow{\text{C}_2\text{H}_4} \text{Ru-2a} \\
\text{Cy}_3\text{P} \cdots \text{Cl} & \text{Ru} \cdots \text{PCy}_3 \\
\text{Cl} & \text{Ph} \\
\end{align*}
\]

The same method was used to prepare IMes analogue Ru-2b. Thus, on stirring methylidene Ru-2a with 1 equiv IMes at 60 °C in C$_6$H$_6$ (Eqn. 5.2), complete conversion was observed at 1 h by $^{31}$P{$^1$H} NMR analysis, accompanied by a color change from red to orange. Reprecipitation from C$_6$H$_6$-hexanes afforded Ru-2b as an orange powder in 78% yield. (Future experiments should be undertaken to determine whether the reaction is complete in shorter time, as this could potentially improve the yield). The identity of Ru-2a is supported by NMR and elemental analysis. The methylidene protons appear as a singlet at 18.74 ppm (2H, cf. Ru-2b': $\delta_H$ 18.41), and the corresponding carbon as a $^{13}$C{$^1$H} NMR doublet at 295.3 ppm ($^2$J$_{CP}$ = 7.9 Hz; cf. Ru-2b': $\delta_C$ 294.8, $^2$J$_{CP}$ = 10 Hz). The $^{31}$P{$^1$H} NMR
singlet is likewise very near that for Ru-2b' (δp 41.1, vs. 38.6 ppm). As with related complexes,20 restricted rotation about the N–C_{Mes} bond is evident from the inequivalent mesityl C–H and ortho-methyl groups.

5.2.2 Thermolysis of Fischer carbenes RuCl₂(L)(PCy₃)(=CHOR) Ru-22/23.

As noted in the Introduction, ethyl vinyl ether is potentially attractive as a vector for transformation of metathesis catalysts into Ru-7, provided that formation and deinsertion of the Fischer carbenes (Scheme 5.3) is rapid and efficient. We also explored use of CH₂=CHOTMS, which appeared highly promising from Arisawa's work12 (see above).

![Scheme 5.3](image-url)

Scheme 5.3. CM-thermolysis of Ru-2 (R = H) and Ru-1 (R = Ph) with (a) CH₂=CHOEt and (c) CH₂=CHOTMS (a, L = PCy₃; b, L = IMes).

5.2.2.1 Optimizing formation of Fischer carbenes by CM with CH₂=CHOEt (EVE)

Reactions of methylidenes Ru-2a/b with a tenfold excess of ethyl vinyl ether (EVE) in CH₂Cl₂ or C₆H₆ were assessed at ambient and elevated temperatures (Table 5.1). At these proportions of EVE, formation of the Fischer carbene is slow at RT even for the first-generation methylidene Ru-2a (91% conversion only after 13 h in CH₂Cl₂, with 83% net
yield of Ru-22a and the ultimate target Ru-7a; cf. complete CM of benzylidene Ru-1a within 0.5 h). In refluxing C₆H₆, 20% Ru-7a is observed once loss of Ru-2a is complete, indicating that deinsertion competes with CM at 80 °C. At 40 °C, consumption of Ru-2a requires 3 h (in CH₂Cl₂ or C₆H₆); at 60 °C in C₆H₆, the reaction time can be reduced to 0.5 h, but yields drop to ca. 50%. Justin Lummiss of this research group has observed a sharp onset of thermal decomposition for Ru-2a at 50 °C (t₁/₂ ca. 40 min) in C₆D₆.

For Ru-2b, methyldiene exchange with EVE is much slower at 23 °C (again as expected from the trend in PCy₃ lability),¹⁹ with no change after 24 h. Even for the benzylidene analogue Ru-1b, reaction is slow at RT (5% conversion at 1 h: in quenching of metathesis reactions, this may be overcome by use of larger excesses of EVE). High temperatures are evidently essential to overcome the low lability of the PCy₃ ligand in these second-generation complexes. In refluxing C₆H₆, CM of Ru-2b is complete in 8 h, vs. three days at 60 °C (cf. 15 min for benzylidene Ru-1b). At this temperature, benzylidene Ru-1b yields Ru-22b quantitatively. In contrast, the greater fragility of the methyldiene complex results in substantial decomposition to unknown byproducts,⁶,²¹ with just 55% of the Ru targets (30% Ru-22b, 24% Ru-7b). Also observed is 22% MePCy₃Cl, a marker for methyldiene decomposition (the methyl group of this phosphonium salt originates in the methyldiene ligand). This species emerges in both methylene chloride and benzene. This salt was observed by Piers and co-workers during thermal decomposition (70 °C, CH₃CHCl₂) of his phosphonium-alkylidene complexes,²² and by the Grubbs group during thermal decomposition (55 °C, C₆D₆) of Ru-2a²¹ and its H₂IMes analogue Ru-2b'.²³
Table 5.1. Ligand exchange by reaction of Ru-2 or Ru-1 with CH₂=CHOEt (10 equiv).a

<table>
<thead>
<tr>
<th>Starting complex</th>
<th>Solvent</th>
<th>T (°C)</th>
<th>Time</th>
<th>Conv. (%)</th>
<th>Ru-22 (%)</th>
<th>Ru-7 (%)</th>
<th>MePCy₃Cl (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ru-2a</td>
<td>CH₂Cl₂</td>
<td>23</td>
<td>13 h</td>
<td>91</td>
<td>80</td>
<td>3</td>
<td>5</td>
</tr>
<tr>
<td></td>
<td>CH₂Cl₂</td>
<td>40</td>
<td>3 h</td>
<td>100</td>
<td>79</td>
<td>4</td>
<td>10</td>
</tr>
<tr>
<td></td>
<td>C₆H₆</td>
<td>40</td>
<td>3 h</td>
<td>100</td>
<td>79</td>
<td>3</td>
<td>5</td>
</tr>
<tr>
<td></td>
<td>C₆H₆</td>
<td>60</td>
<td>0.5 h</td>
<td>100</td>
<td>43</td>
<td>8</td>
<td>8</td>
</tr>
<tr>
<td>Ru-1a</td>
<td>CH₂Cl₂</td>
<td>23</td>
<td>20 min</td>
<td>100</td>
<td>100</td>
<td>0</td>
<td>–</td>
</tr>
<tr>
<td></td>
<td>C₆H₆</td>
<td>23</td>
<td>0.5 h</td>
<td>100</td>
<td>100</td>
<td>0</td>
<td>–</td>
</tr>
<tr>
<td></td>
<td>CH₂Cl₂</td>
<td>40</td>
<td>5 min</td>
<td>100</td>
<td>100</td>
<td>0</td>
<td>–</td>
</tr>
<tr>
<td></td>
<td>C₆H₆</td>
<td>80</td>
<td>5 min</td>
<td>100</td>
<td>80</td>
<td>20</td>
<td>–</td>
</tr>
<tr>
<td>Ru-2b</td>
<td>CH₂Cl₂</td>
<td>23</td>
<td>24 h</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>C₆H₆</td>
<td>60</td>
<td>3 d</td>
<td>96</td>
<td>43</td>
<td>10</td>
<td>15</td>
</tr>
<tr>
<td></td>
<td>C₆H₆</td>
<td>80</td>
<td>8 h</td>
<td>100</td>
<td>31</td>
<td>24</td>
<td>22</td>
</tr>
<tr>
<td>Ru-1b</td>
<td>CH₂Cl₂</td>
<td>23</td>
<td>1 h</td>
<td>5</td>
<td>5</td>
<td>0</td>
<td>–</td>
</tr>
<tr>
<td></td>
<td>C₆H₆</td>
<td>23</td>
<td>1 h</td>
<td>5</td>
<td>5</td>
<td>0</td>
<td>–</td>
</tr>
<tr>
<td></td>
<td>CH₂Cl₂</td>
<td>40</td>
<td>8 h</td>
<td>100</td>
<td>100</td>
<td>0</td>
<td>–</td>
</tr>
<tr>
<td></td>
<td>C₆H₆</td>
<td>80</td>
<td>15 min</td>
<td>100</td>
<td>100</td>
<td>0</td>
<td>–</td>
</tr>
</tbody>
</table>

a Conditions: [Ru] = 17 mM. Reaction subjected to NMR analysis at 30 min intervals. Time is that required to consume the proportion of starting complex indicated, as determined from kinetic profiles for all reactions except those complete at 5 min. Optimal conditions for the key methylidene complexes indicated in bold face.

5.2.2.2 Optimizing yields of Ru-7 from thermolysis of Ru-22.

Data for thermolysis of Ru-22a/b are summarized in Table 5.2. In refluxing CH₂Cl₂, reaction is slow for first-generation Ru-22a (45% unreacted after 16 h), but is complete within 6 h at 60 °C, with 96% selectivity for Ru-7a. More forcing conditions are required for Ru-22b (2 days at 60 °C in CH₂Cl₂), but selectivity for Ru-7b is again nearly 95%. Thermolysis is much slower in C₆H₆, requiring over a month for consumption of Ru-22b at 60 °C, though this is reduced to 2 days at reflux.

These data indicate that thermolysis is highly selective for the hydridocarbonyls Ru-7, and can be completed in <2 h for the first-generation ethoxylidene Ru-22a in refluxing C₆H₆. In contrast, the second-generation complex Ru-22b shows high thermal stability, and its decomposition into Ru-7b is inconveniently slow.
Table 5.2. Yields of Ru-7 from thermolysis of Ru-22.

<table>
<thead>
<tr>
<th>Starting complex</th>
<th>Solvent</th>
<th>T (°C)</th>
<th>Time</th>
<th>Conv. (%)</th>
<th>Ru-7 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ru-22a</td>
<td>CH₂Cl₂</td>
<td>40</td>
<td>16 h</td>
<td>55</td>
<td>55</td>
</tr>
<tr>
<td></td>
<td>CH₂Cl₂</td>
<td>60</td>
<td>6 h</td>
<td>100</td>
<td>96b</td>
</tr>
<tr>
<td></td>
<td>C₆H₆</td>
<td>80</td>
<td>1.5 h</td>
<td>100</td>
<td>92b</td>
</tr>
<tr>
<td>Ru-22b</td>
<td>CH₂Cl₂</td>
<td>60</td>
<td>51 h</td>
<td>100</td>
<td>86c</td>
</tr>
<tr>
<td></td>
<td>C₆H₆</td>
<td>60</td>
<td>35 d</td>
<td>100</td>
<td>78</td>
</tr>
<tr>
<td></td>
<td>C₆H₆</td>
<td>80</td>
<td>46 h</td>
<td>100</td>
<td>93b</td>
</tr>
</tbody>
</table>

* Conditions: [Ru] = 17 mM. Time is that required for complete consumption of Ru-22a/b, unless otherwise stated. Byproducts observed: a 5% RuCl₂(CO)(PCy₃)₂ Ru-27a. b 12% Ru-27b.

A minor side-product (ca. 5%) in these reactions is dichloride RuCl₂(CO)(L)(PCy₃) Ru-27 (a: L = PCy₃, 35.7 ppm in CH₂Cl₂; 36.7 ppm in C₆D₆; b: L = IMes, 34.6 ppm in CH₂Cl₂; 34.2 ppm in C₆D₆). The bis-PCy₃ species is known;²⁴,²⁵ the identity of the IMes analogue was confirmed by its independent synthesis (Scheme 5.4). These species are formed in C₆H₆, as well as chlorinated solvents. They may arise from elimination of ethane from a Ru(IV)-formyl intermediate RuCl₂(Et)(C(O)H)(L). This does not appear to significantly compete with reductive elimination of EtCl, however (cf. thermolysis of Ru(OC(O)CF₃)₂(PPh₃)₂(=CHOBn) Ru-24).²⁶ An unknown byproduct (δp 46.3 ppm) is also observed for the IMes derivatives.

Scheme 5.4. Formation of Ru-27a/b from Ru-7a at 23 °C.

5.2.2.3 CM-thermolysis of Ru-2 and Ru-1 with CH₂=CHOEt.

The conditions optimized above for the individual CM and thermolysis steps were combined (Table 5.3). Thus, CM was carried out in C₆H₆ with 10 CH₂=CHOEt. The thermal
sensitivity of the first-generation methylidene Ru-2a\textsuperscript{21,23} necessitated CM at 40 °C, then thermolysis at 80 °C; for Ru-2b and Ru-1a/b, both reactions were performed at 80 °C.

For the first-generation methylidene Ru-2a, CM-thermolysis afforded Ru-7a in 69% overall yield, with 10% of a PCy\textsubscript{3} byproduct. (In comparison, benzylidene Ru-1a affords Ru-7a in 80% yield after 2 h). For second-generation methylidene Ru-2b, conversion of Ru-22b into Ru-7b was complete after 28 h (faster than the 8 + 46 h period expected from the independent reactions), but proceeded in only 45% overall yield. Trace amounts (5%) of the dichloride Ru-27b were also observed.

In comparison, CM of benzylidene Ru-1b is rapid (15 min) but, somewhat unexpectedly, thermolysis of the Ru-22b product is even slower, requiring 80 h to reach completion (cf. half that for isolated Ru-22b). Selectivity for Ru-7b was also lower than that observed during thermolysis of isolated Ru-22b (70%, vs. 100%). The excess CH\textsubscript{2}=CHOEt present may inhibit deinsertion by binding to ruthenium. Relevant in this context is the high affinity of second-generation complexes for olefins\textsuperscript{19}.

Despite the reasonable selectivities for Ru-7a/b found on CM-thermolysis of Ru-1 and Ru-2 with CH\textsubscript{2}=CHOEt, the lengthy thermolysis required is inconvenient. An alternative is suggested by Arisawa's report of the fast formation and decomposition of vinylsiloxy species described in the Introduction. Of particular interest was the rapid reaction of Ru-1b' with CH\textsubscript{2}=CHOTMS at 50 °C (toluene), and the quantitative formation of Ru-7b' within 1 h\textsuperscript{12}. The utility of the vinylsiloxy route to Ru-7a/b from Ru-2a/b and Ru-1a/b was therefore examined.
Table 5.3. Formation of Ru-7 by CM-thermolysis of Ru-2 and Ru-1 with CH₂=CHOEt.⁶

<table>
<thead>
<tr>
<th>Starting complex</th>
<th>Time</th>
<th>Ru-7 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ru-2a</td>
<td>3 h (40 °C)</td>
<td>69⁹</td>
</tr>
<tr>
<td>Ru-1a</td>
<td>5 min</td>
<td>80</td>
</tr>
<tr>
<td>Ru-2b</td>
<td>8 h</td>
<td>46⁷</td>
</tr>
<tr>
<td>Ru-1b</td>
<td>15 min</td>
<td>70</td>
</tr>
</tbody>
</table>

⁶ General conditions: [Ru] = 17 mM, C₆H₆, 10 equiv CH₂=CHOEt, 80 °C bath temperature unless otherwise stated. Time is that required for complete loss of starting Ru-1 or Ru-2. Byproducts observed: ⁹ 10% MePCy₃Cl. ⁷ 20% MePCy₃Cl, 5% Ru-27b.

5.2.2.4 CM-thermolysis of Ru-2 and Ru-1 with CH₂=CHOTMS.

Decomposition of [Ru]=CHOR is much faster for R = SiMe₃ than R = Et. We find that RuCl₂(PCy₃)₂(=CHOTMS) Ru-23a converts to Ru-7a almost immediately once formed. At room temperature, no more than 5% Ru-23a was evident at any time. Even at 0 °C, no remaining Ru-23a was observed by the time that Ru-1a was completely consumed (12 h; 50 equiv CH₂=CHOTMS). The TMSCl co-product was observed as a ¹H NMR singlet at δ₁₁ 0.15 ppm.

Rates of CM between methylidenes Ru-2a/b and benzylidenes Ru-1a/b and 10 equiv CH₂=CHOTMS (Table 5.3) are similar to those observed with CH₂=CHOEt. That is, CM requires hours for methylidenes Ru-2a and Ru-2b (3 or 8 h, respectively), vs. minutes for benzylidenes Ru-1a and Ru-1b (5 or 15 min). For Ru-23a/b, rapid deinsertion eliminates the need for thermolysis. While enabling much faster formation of Ru-7, in comparison to the EVE route, selectivities for Ru-7 were lower by ca. 10% for the first-generation systems, though only by 5% for the IMes analogue (Table 5.4 vs. 5.3). This is probably due to liberation of TMSCl during deinsertion,²⁶ and attack of the silyl chloride on the hydride ligand in Ru-7a/b to form dichlorides Ru-27a/b. This is particularly problematic during the
lengthy CM-thermolysis of **Ru-2b**, which results in 30% **Ru-27b**. Addition of base may be advantageous in preventing consumption of this catalyst species by liberated TMSCl.

**Table 5.4.** Yields of **Ru-7** from CM-thermolysis with CH$_2$=CHOTMS (10 equiv).$^a$ For duration of CM, see Table 5.3.

<table>
<thead>
<tr>
<th>Starting complex</th>
<th>Time</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Ru-2a</strong></td>
<td>3 h</td>
</tr>
<tr>
<td><strong>Ru-1a</strong></td>
<td>5 min</td>
</tr>
<tr>
<td><strong>Ru-2b</strong></td>
<td>8 h</td>
</tr>
<tr>
<td><strong>Ru-1b</strong></td>
<td>15 min</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>solvent</th>
<th>T (°C)</th>
<th>Ru-7 (%)</th>
<th>Key byproducts</th>
</tr>
</thead>
<tbody>
<tr>
<td>C$_6$H$_6$</td>
<td>40</td>
<td>60</td>
<td>10% MePCy$_3$Cl, 5% PCy$_3$</td>
</tr>
<tr>
<td></td>
<td>80</td>
<td>90</td>
<td>5% <strong>Ru-27a</strong></td>
</tr>
<tr>
<td></td>
<td>80</td>
<td>40</td>
<td>30% <strong>Ru-27b</strong>, 25% MePCy$_3$Cl</td>
</tr>
<tr>
<td></td>
<td>80</td>
<td>75</td>
<td>5% <strong>Ru-27a</strong></td>
</tr>
</tbody>
</table>

$^a$ General conditions: [Ru] = 17 mM. Time shown is that required for complete consumption of starting complex.

The diminished metathesis activity of the methylidenes **Ru-2a/b** means that these key resting-state species undergo slower, less selective formation of **Ru-7a/b** during CM-thermolysis than is suggested by model studies of benzylidenes **Ru-1a/b**. Use of CH$_2$=CHOTMS (and base, to take up the TMSCl co-product) is likely to aid in reducing the timescale required for transformation into **Ru-7**.

5.2.3 Hydrogenolysis of **Ru-2** and **Ru-22**.

While hydrogenolysis offers a less versatile entry point to **Ru-7** for tandem metathesis-functionalization, it may be useful where competing olefin hydrogenation is slow. We were also curious to see if the "generation gap" noted for benzylidenes **Ru-1a/b** in Chapter 3$^{13}$ would carry over to the methylidenes **Ru-2a/b** and ethoxylidenes **Ru-22a/b**. Reactions with H$_2$ were therefore carried out under the same conditions (at 60 °C in CH$_2$Cl$_2$ in the presence of NEt$_3$; 1000 psi H$_2$; Table 5.5). Data from the analogous reactions of benzylidenes **Ru-1a/b** are included for comparison.

Hydrogenolysis of **Ru-2a** generated hydride **Ru-6a** in near-quantitative yield within 30
min (Scheme 5.5), accompanied by a color change from pale red to bright orange. Selectivity for Ru-6a is substantially higher than was the case for benzylidene Ru-1a, perhaps due to the greater steric accessibility of Ru-2a. An intriguing alternative possibility, however, is that the methylidene ligand of Ru-2a is *displaced* by incoming H₂, as it is by pyridine.²¹ We were unable to confirm formation of the hydrogenolysis product CH₄ under these conditions, as any of this volatile species was lost when the autoclave is opened.

The first-generation ethoxylidene RuCl₂(PCy₃)₂(=CHOEt) Ru-22a is likewise converted within 30 min. Selectivity for Ru-6a is only 83%, in part due to competing deinsertion of Ru-22a to afford Ru-7a (10%). The total yield of catalytically-relevant hydrides is again impressive, however, approaching 95%. As discussed in Chapter 3, Ru-6a can be converted into Ru-7a in 96% yield by treatment with methanol and NEt₃ at 60 °C in CH₂Cl₂.

Table 5.5. Proportion of Ru-6 present after complete hydrogenolysis of Ru-2 and Ru-22.a

<table>
<thead>
<tr>
<th>Starting complex</th>
<th>Time (h)</th>
<th>Ru-6 (%)</th>
<th>Byproducts</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ru-2a</td>
<td>0.5</td>
<td>95</td>
<td></td>
</tr>
<tr>
<td>Ru-22a</td>
<td>0.5</td>
<td>83</td>
<td>10% Ru-7a</td>
</tr>
<tr>
<td>Ru-1a b</td>
<td>0.5</td>
<td>80</td>
<td></td>
</tr>
<tr>
<td>Ru-2b</td>
<td>66</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Ru-22b</td>
<td>12</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Ru-1b b</td>
<td>1</td>
<td>60</td>
<td>10% Ru-6a, 7% Ru-6c</td>
</tr>
</tbody>
</table>

a Conditions: [Ru] = 17 mM, CH₂Cl₂, H₂ (1000 psi), 3 equiv NEt₃, 60 °C bath temperature. Time corresponds to that required for complete consumption of starting complex. b Data from Section 3.2.1.

Scheme 5.5. Hydrogenolysis of first-generation Ru-2a (R = H) and Ru-22a (R = OEt).
The second-generation methyldiene Ru-2b and ethoxylidene Ru-22b underwent extremely slow hydrogenolysis, with complete consumption of starting material requiring 66 h and 12 h, respectively (vs. 1 h for benzylidene Ru-1b). In remarkable contrast with its first-generation counterpart, methyldiene Ru-2b undergoes substantial decomposition (27% MePCy₃Cl), yielding low proportions of four unidentified species (ca. 5% each; $^{31}$P{$^1$H} NMR singlets between 70 and 65 ppm).

Identical Ru species form in hydrogenolysis of Ru-22b, with larger amounts of a fifth species ($\delta_p$ 70.0 ppm, br; 25%). Only traces of Ru-6b form (ca. 5% after 8 h). None is observed once reaction is complete (12 h), owing to its low thermal stability (Section 2.2.3). No Ru-7b is observed, indicating that reaction with H₂ is rapid compared to β-ethyl elimination. Broad, overlapping hydride multiplets centered around -11.5 ppm integrate to 25% (Ru-2b) and 80% (Ru-22b) relative to the starting material, although their breadth ($\omega_{0.5}$ >100 Hz) limits the reliability of integration, and prevents correlation with $^{31}$P{$^1$H} NMR signals. The high proportion of “missing” (i.e. NMR-invisible) material during these reactions indicates formation of paramagnetic byproducts, as for thermolysis and carbonylation of Ru-6b (Sections 2.2.3 and 3.2.2).

Clearly, these second-generation systems exhibit the same vulnerability during hydrogenolysis observed for benzylidene Ru-1b (Section 3.2.1), and are indeed even more susceptible. This reflects their lower lability, which retards hydrogenolysis, enabling decomposition of Ru-6b to compete with its formation. Thus, the "generation gap" is maintained: while hydrogenolysis-carbonylation is a viable route to hydridocarbonyl Ru-7a
from the first-generation methylidene and ethoxylidene, this transformation is incompatible with second-generation systems.

### 5.2.4 Methanolysis of Ru-2, Ru-22, and Ru-1.

Reactions of Ru-2b and Ru-22b with methanolic methoxide were considered promising, given the rapidity of these reactions with Ru-1a (cf. Section 4.2.1). Use of methanol and NEt₃ was also explored for its potential relevance to state-of-the-art ROMP-hydrogenation protocols (cf. Section 3.2.3).¹²⁸

#### 5.2.4.1 Reactions of Ru-2, Ru-22 and Ru-1 with methoxide and methanol.

Solutions of the Ru species in CH₂Cl₂ were treated with equimolar amounts of NaOMe, as a ca. 0.2 M solution in MeOH, and heated to 60 °C (Scheme 5.6; Table 5.6). Under these conditions, the first-generation methylidene Ru-2a was consumed in 30 min, but Ru-7a is obtained in only 30% yield, while decomposition is significant. Transformation of ethoxylidene Ru-22a is slower (3 h), but generates Ru-7a product in 80% yield. Formation of the six-coordinate methoxyhydride complex RuH(OMe)(CO)₂(PCy₃)₂ Ru-18a (5%) indicates abstraction of the second chloride ligand. Unexpectedly, Ru-1a is only 80% converted at the same stage. Abstraction of the second chloride ligand results in coordinatively saturated dihydride and methoxyhydride species (Chapter 4). An unidentified RuHCl(PCy₃)L₃ product was also formed (5% yield), as noted in Section 3.2.3.¹³

The corresponding reaction of second-generation methylidene Ru-2b is complete in 2 h, and likewise gives Ru-7b in low (25%) yield. Competing decomposition and disproportionation are observed, behaviour not seen for Ru-22b. The latter complex generates 78% Ru-7b in 1 h, with small amounts of coordinatively saturated
methoxyhydride Ru-18b (11%) and dihydride Ru-19b (5%). Benzylidene Ru-1b was also efficiently transformed into Ru-7b (83%; 30 min) under these conditions. The absence of disproportionation or dihydrides renders this treatment the most efficient route to hydridocarbonyl Ru-7b for this benzylidene species. For the key methylidene species Ru-2a/b, however, competing decomposition undermines yields of Ru-7a/b. Use of the weaker base Cs₂CO₃ was explored in the hope of circumventing the side-reactions found with NaOMe.

Scheme 5.6. Reactions of Ru complexes (Ru-2, Ru-22, Ru-1) with methanolic methoxide.
Table 5.6. Formation of Ru-7 during NaOMe-assisted methanolysis of Ru-2, Ru-22 and Ru-1.\textsuperscript{a}

<table>
<thead>
<tr>
<th>Starting complex</th>
<th>Time (h)</th>
<th>Ru-7 (%)</th>
<th>Key byproducts</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ru-2a</td>
<td>0.75</td>
<td>30</td>
<td>25% MePCy, Cl</td>
</tr>
<tr>
<td>Ru-22a</td>
<td>3</td>
<td>80</td>
<td>5% Ru-18a</td>
</tr>
<tr>
<td>Ru-1a</td>
<td>0.5</td>
<td>40</td>
<td></td>
</tr>
<tr>
<td>Ru-2b</td>
<td>2</td>
<td>25</td>
<td>20% MePCy, Cl</td>
</tr>
<tr>
<td>Ru-22b</td>
<td>1</td>
<td>78</td>
<td>12% Ru-7a, 3% Ru-7c, 11% Ru-18b, 5% Ru-19b</td>
</tr>
<tr>
<td>Ru-1b</td>
<td>0.5</td>
<td>83</td>
<td></td>
</tr>
</tbody>
</table>

\textsuperscript{a} Conditions: [Ru] = 17 mM, 10 CH\textsubscript{2}Cl\textsubscript{2} : 1 MeOH, 1 equiv NaOMe (0.20 M in MeOH), 60 °C bath temperature. Time corresponds to that required for complete consumption of starting complex, except for Ru-1a, which remains 20% unreacted.

5.2.4.2 Cs\textsubscript{2}CO\textsubscript{3}-assisted methanolysis of Ru-2, Ru-22 and Ru-1.

Mol and coworkers reported formation of Ru-7a via reaction of Ru-1a with 0.5 equiv K\textsubscript{2}CO\textsubscript{3} and methanol.\textsuperscript{16} In reactions of Ru-2a/b, Ru-22a/b and Ru-1a/b with Cs\textsubscript{2}CO\textsubscript{3} and methanol (Scheme 5.7; Table 5.7), THF solvent was used to maximize the solubility of Cs\textsubscript{2}CO\textsubscript{3}. Given the diprotic nature of the conjugate acid H\textsubscript{2}CO\textsubscript{3}, initial reactions employed 0.5 equiv of Cs\textsubscript{2}CO\textsubscript{3}.

Methanolysis was complete in 0.5 h for Ru-2a, but yields of Ru-7a were limited to 30%. A similar proportion of methylcarbonatohydride Ru-28a was formed (for characterization data, see next Section). For Ru-22a and Ru-1a, reaction was slower (3 or 6 h, respectively) but gave ca. 55% Ru-7a with 10% Ru-28a.

The second-generation complexes are consumed within 1.5-3 h, and afford ca. 60% Ru-7b, with 10% Ru-28b. On doubling the proportion of Cs\textsubscript{2}CO\textsubscript{3} (1 equiv per Ru), thermolysis is complete in 15 min, probably owing to the higher basicity of carbonate, vs. bicarbonate.
(pKₐ 6.35, vs. 10.33)²⁹ and the efficiency with which chloride is abstracted by the twofold excess of Cs⁺ (2 equiv per Ru). The hydridocarbonyls Ru-7a/b were not observed, presumably due to abstraction of both chloride ligands by Cs⁺, and subsequent coordination of CO₃²⁻; the methylcarbonatohydrides Ru-28a/b were formed in moderate yield (45%). A common byproduct (5% from Ru-1a; 20% from Ru-1b) is tentatively identified as the bicarbonatohydride RuH(κ²-OC(O)OH)(CO)(L)(PCy₃) Ru-29a/b based on the similarity of its NMR shifts to Ru-28a/b, respectively (see next Section).

As with NaOMe, Cs₂CO₃ effects rapid methanolysis of methylenes and ethoxylidenes (as well as benzylidenes), but results in poor selectivity for Ru-7a/b. Neither of these methodologies is thus useful in the present context.

![Scheme 5.7. Cs₂CO₃-assisted methanolysis of Ru-1.](image-url)
Table 5.7. Yield of hydrides following reactions of Ru-2, Ru-22 and Ru-1 with methanol and Cs₂CO₃. 

<table>
<thead>
<tr>
<th>Starting complex</th>
<th>Equiv. Cs₂CO₃</th>
<th>Time (h)</th>
<th>Ru-7 (%)</th>
<th>Ru-28 (%)</th>
<th>Ru-29 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ru-2a</td>
<td>0.5</td>
<td>0.5</td>
<td>30</td>
<td>30</td>
<td>-</td>
</tr>
<tr>
<td>Ru-22a</td>
<td>0.5</td>
<td>3</td>
<td>52</td>
<td>10</td>
<td>-</td>
</tr>
<tr>
<td>Ru-1a</td>
<td>0.5</td>
<td>6</td>
<td>55</td>
<td>10</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>1</td>
<td>0.25</td>
<td>0</td>
<td>45</td>
<td>20</td>
</tr>
<tr>
<td>Ru-2b</td>
<td>0.5</td>
<td>1.5</td>
<td>62</td>
<td>10</td>
<td>-</td>
</tr>
<tr>
<td>Ru-22b</td>
<td>0.5</td>
<td>2</td>
<td>55</td>
<td>15</td>
<td>-</td>
</tr>
<tr>
<td>Ru-1b</td>
<td>0.5</td>
<td>3</td>
<td>57</td>
<td>10</td>
<td>-</td>
</tr>
</tbody>
</table>

Conditions: [Ru] = 17 mM, 10 THF : 1 MeOH, 60 °C bath temperature. Time is that required for complete consumption of starting complex. [Cs₂CO₃] = 8.5 mM (0.5 equiv), 17 mM (1.0 equiv).

Salt metathesis of Ru-7 with the CsHCO₃ byproduct is presumed to form Ru-29 (Scheme 5.8). In turn, this methoxycarbonatohydride species may be converted into Ru-28 by nucleophilic attack at the bicarbonate carbon by MeOH, followed by proton transfer and elimination of water.


5.2.4.3 Preparation of RuH(κ²-OC(O)OME)(CO)(L)(PCy₃) Ru-28.

Stirring the hydridocarbonyl complexes Ru-7a/b with equimolar methanolic Cs₂CO₃ in THF resulted in their complete consumption within 15 min at 23 °C (NMR analysis). The solvent was stripped off and the residue redissolved in C₆H₆, and filtered through Celite. The crude product was contaminated by 5% of side-products tentatively identified as the
bicarbonatohydrides Ru-29a/b. The major products are suggested to be Ru-28a/b on the basis of NMR analysis (Scheme 5.9).

![Scheme 5.9. Formation of Ru-28 via reaction of Ru-7 with methanolic Cs$_2$CO$_3$ (a, L = PCy$_3$; b, L = IMes).](image)

The hydride signals for Ru-28a/b appear at $-17.58$ (t, $^2J_{HP} = 19.2$ Hz) and $-17.96$ ppm (d, $^2J_{HP} = 22.3$ Hz), which correlate (HMBC) to $^{31}$P{^1}H singlets at 45.7 and 46.8 ppm, respectively. These multiplicities, and the $^2J_{HP}$ values, indicate the presence of two or one cis-PCy$_3$ ligands, respectively. The hydride shifts suggest coordinative unsaturation; a nearly identical shift ($\delta_H$ $-18.49$; C$_6$D$_6$) was reported for RuH($\kappa^2$-OC(O)C$_5$H$_4$N)(CO)(IMes)$_2$ Ru-30, in which $\kappa^2$-$O,O$-coordination mode of the isonicotinate ligand was indicated by X-ray analysis.$^{30}$ ($\kappa^2$-$O,O$-coordination of the methylcarbonato ligands in Ru-28a/b is consistent with the small frequency difference between the symmetric (1608 and 1607 cm$^{-1}$) and asymmetric OCO stretching bands (1445 and 1448 cm$^{-1}$), respectively).$^{31-33}$ The methoxy protons of Ru-28a/b appear as sharp $^1$H NMR singlets at 3.64 and 3.50 ppm, respectively, which integrate 3:1 relative to hydride and exhibit HMQC correlations to $^{13}$C{^1}H NMR singlets at 53.1 and 52.6 ppm, respectively. The latter are assigned to methyl groups by $^{13}$C DEPT analysis. The methoxy $^1$H signals also correlate (HMBC) to $^{13}$C{^1}H singlets for the carbonate carbons at 159.1 and 158.9 ppm, respectively (cf. $\delta_C$ 160.3 for RuH($\kappa^2$-OC(O)OH)(CO)(IMes)$_2$ Ru-29c).$^{30}$ An HMBC correlation was also observed between the hydride $^1$H doublet and the singlet for the carbonate carbon for Ru-28b. Finally, the
presence of single carbonyl ligands is confirmed for Ru-28a and Ru-28b by HMBC correlations between the hydride multiplets and $^{13}$C{^1H} signals at 202.2 (t, $^2J_{CP} = 12.8$ Hz) and 208.0 ppm (d, $^2J_{CP} = 5.7$ Hz), respectively.

Other byproducts noted above were tentatively identified as the bicarbonatohydride complexes RuH($\kappa^2$-OC(O)OH)(CO)(L)(PCy$_3$) Ru-29a/b based on NMR analysis. These give rise to hydride multiplets at -16.54 (t, $^2J_{HP} = 19.8$ Hz) and -16.73 ppm (d, $^2J_{HP} = 23.9$ Hz), which correlate (HMBC) with $^{31}$P{^1H} NMR singlets at 46.0 and 47.1 ppm, respectively. Broad $^1$H NMR singlets at 7.98 and 8.51 ppm (integrating 1:1 vs. hydride) are assigned to the carbonate OH proton; cf. 8.80 ppm for RuH($\kappa^2$-OC(O)OH)(CO)(IMes)$_2$ Ru-29c. Low yield and rapid decomposition impeded more detailed analysis.

5.2.4.4 Reaction of Ru-2 and Ru-22 with methanol and NEt$_3$

The relatively efficient conversion of Ru-1b into Ru-7b on treatment with methanol and NEt$_3$ (83% in 4 h in CH$_2$Cl$_2$-MeOH at 60 °C; Section 3.2.3) led us to hope that similar behaviour might apply to Ru-2b and Ru-22b. As well, we wished to see if the behaviour of the benzylidene complexes accurately modeled that of the methylidene or Fischer carbene derivatives. These reactions are summarized in Scheme 5.10 and Table 5.8.

Methylidenes Ru-2a/b are converted more rapidly than the benzylidenes Ru-1a/b. Their NMR signals disappear within 15 min or 1.5 h, respectively, accompanied by a color change from pale red (Ru-2a) or dark orange (Ru-2b) to yellow-orange. A $^1$H NMR singlet at 0.24 ppm$^4$ confirms reduction of the methylidene ligand to CH$_4$ in both cases. For Ru-2a, the yield of Ru-7a was 65%; for Ru-2b, unexpectedly, it dropped below 50%, owing to
competing disproportionation and decomposition (the latter being indicated by the formation of substantial MePCy₃Cl; Ru-2a: 25%; Ru-2b: 15%).

Methanolysis of ethoxylidenes required hours (4 h for Ru-22a; 1.5 h for Ru-22b) but afforded hydridocarbonyls Ru-7a/b in 91% and 80% yield, respectively. No disproportionation of Ru-22b is evident. The faster reaction of Ru-2b relative to Ru-1b (1.5 vs. 4 h) is consistent with the mechanism discussed in Chapter 3: that is, stronger binding of MeOH to the more electropositive NHC-bound Ru center. Computational work suggests a more positive Ru center for methylidenes Ru-2a and Ru-2b than benzylidene analogues Ru-1a and Ru-1b (Δq$_{Ru}$ = ca. 0.30 e$^-$ for the non-truncated complexes).

Thus, while methanolysis of the first-generation methylidene Ru-2a is fast and moderately selective for Ru-7a, the second-generation Ru-2b suffers from disproportionation. The quenched Fischer carbenes Ru-22a/b exhibited excellent to good selectivity for Ru-7a/b, and hence may offer the most useful route, albeit offset by slow formation of Ru-22 from the [Ru]=CH$_2$ resting states.

Table 5.8. Formation of Ru-7 by treating Ru-2, Ru-22 and Ru-1 with methanol and NEt$_3$.$^a$

<table>
<thead>
<tr>
<th>Starting complex</th>
<th>Time (h)</th>
<th>Ru-7 (%)</th>
<th>Key byproducts</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ru-2a</td>
<td>0.25</td>
<td>65</td>
<td>MePCy$_3$Cl (25%)</td>
</tr>
<tr>
<td>Ru-22a</td>
<td>4</td>
<td>91</td>
<td>Ru-27a ($&lt;$2%)</td>
</tr>
<tr>
<td>Ru-1a</td>
<td>8</td>
<td>60$^b$</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ru-2b</td>
<td>1.5</td>
<td>47$^d$</td>
<td>Ru-7a (15%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Ru-7c (3%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>MePCy$_3$Cl (15%)</td>
</tr>
<tr>
<td>Ru-22b</td>
<td>1.5</td>
<td>80</td>
<td>-</td>
</tr>
<tr>
<td>Ru-1b</td>
<td>4</td>
<td>85$^b$</td>
<td>-</td>
</tr>
</tbody>
</table>

$^a$ Conditions: [Ru] = 17 mM, 4:1 CH$_2$Cl$_2$-MeOH, 3 equiv NEt$_3$, 60 °C. Time corresponds to that required for complete consumption of starting complex. $^b$ Data from Section 3.2.3.
Scheme 5.10. Reactions of [Ru]=CHR species with methanol and NEt$_3$. Ru-2 (R = H) and Ru-22 (R = OEt): L, L’ = a, (PCy$_3$)$_2$; b, (IMes)(PCy$_3$)$_2$; c, (IMes)$_2$.

5.3 Conclusions.

This chapter explored methods by which first- and second-generation Grubbs metathesis catalysts can be converted into the versatile hydridocarbonyl catalyst Ru-7. The reaction chemistry of benzylidenes, methyldene, and selected Fischer carbenes is compared. Table 5.9 summarizes the routes that give efficient access to Ru-7 (arbitrarily defined as yields ≥60%, within 8 h). For the first-generation catalysts Ru-1a and Ru-2a, the most attractive route involves CM with ethyl vinyl ether or vinyloxytrimethylsilane, followed by thermolytic degradation. Hydrogenolysis, followed by reaction with methanol and NEt$_3$, is efficient for both these complexes and for the Fischer carbene Ru-22a. However, the high H$_2$ pressures are problematic if tandem (R)CM-functionalization is the goal, as competing olefin hydrogenation may occur.

Transformation of the second-generation methyldiene Ru-2b into Ru-7b is of particular interest, given the central importance of Ru-NHC catalysts in RCM and CM. Few methods work well, however. Hydrogenolysis is generally problematic for the second-generation systems, because the dihydrogen adducts formed are susceptible to ligand disproportionation. The Fischer carbene route is slow: the CM step alone requires 8 h, and yields significant byproducts. The reaction with vinyloxytrimethylsilane is more promising: it offers fast conversion, and the yield of Ru-7b can reach 70% where formation of the
byproduct RuCl$_2$(CO)(IMes)(PCy$_3$)$_2$ 27b is inhibited by (e.g.) carrying out the reaction in the presence of a sacrificial base such as NEt$_3$. Otherwise, the best route involves reaction with methanol in the presence of Cs$_2$CO$_3$.

Table 5.9. Efficient* routes to Ru-7 from Grubbs benzylidenes, methyldienes and ethoxylidenes.

<table>
<thead>
<tr>
<th>Triggers</th>
<th>Complex</th>
<th>time (h)</th>
<th>Ru-7 (%)</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>(i) CH$_2$=CHOEt (ii) heat (Table 5.3)</td>
<td>Ru-1a</td>
<td>2</td>
<td>80</td>
<td>Compatible with first-generation catalysts only</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Ru-2a</td>
<td>5</td>
<td>69</td>
<td></td>
</tr>
<tr>
<td>CH$_2$=CHOTMS (Table 5.4)</td>
<td>Ru-1a</td>
<td>5 min</td>
<td>90</td>
<td>Compatible with first-generation catalysts and second-generation precatalyst</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Ru-2a</td>
<td>3</td>
<td>60</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Ru-1b</td>
<td>0.25</td>
<td>75</td>
<td></td>
</tr>
<tr>
<td>(i) H$_2$, NEt$_3$ (ii) MeOH, NEt$_3$ (Table 5.5)</td>
<td>Ru-1a</td>
<td>3</td>
<td>77</td>
<td>Compatible with first-generation catalysts (but requires high H$_2$ pressures; risk of competing hydrogenation)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Ru-2a</td>
<td>3</td>
<td>90</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Ru-22a</td>
<td>3</td>
<td>90</td>
<td></td>
</tr>
<tr>
<td>MeOH, NaOMe (Table 5.6)</td>
<td>Ru-22a</td>
<td>3</td>
<td>80</td>
<td>Compatible with quenched Fischer carbenes and second-generation precatalyst. Poor stoichiometric control; may yield byproducts.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Ru-22b</td>
<td>1</td>
<td>78</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Ru-1b</td>
<td>0.5</td>
<td>83</td>
<td></td>
</tr>
<tr>
<td>MeOH, Cs$_2$CO$_3$ (Table 5.7)</td>
<td>Ru-2b</td>
<td>1.5</td>
<td>62</td>
<td>Compatible with second-generation methylidene</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MeOH, NEt$_3$ (Table 5.8)</td>
<td>Ru-1a</td>
<td>8</td>
<td>60</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Ru-2a</td>
<td>0.25</td>
<td>65</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Ru-22a</td>
<td>4</td>
<td>91</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Ru-1b</td>
<td>4</td>
<td>85</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Ru-22b</td>
<td>1.5</td>
<td>80</td>
<td></td>
</tr>
</tbody>
</table>

*Defined as methods that generate Ru-7 in ≥60% yield within 8 h.
Table 5.10. Optimal methods for production of Ru-7 from Ru metathesis catalysts for various tandem catalysis procedures.

<table>
<thead>
<tr>
<th>Targeted procedure</th>
<th>First-generation</th>
<th>Second-generation</th>
</tr>
</thead>
<tbody>
<tr>
<td>ROMP, RCM, or CM-hydrogenation</td>
<td>(i) H₂ + 3 NEt₃,</td>
<td>1 NaOMe + MeOH</td>
</tr>
<tr>
<td></td>
<td>(ii) MeOH</td>
<td>or 0.5 Cs₂CO₃ + MeOH</td>
</tr>
<tr>
<td>ROMP-functionalization</td>
<td>10 CH₂=CHOTMS</td>
<td>10 CH₂=CHOTMS</td>
</tr>
<tr>
<td>RCM/CM-functionalization</td>
<td>3 NEt₃ + MeOH</td>
<td>0.5 Cs₂CO₃ + MeOH</td>
</tr>
<tr>
<td></td>
<td></td>
<td>or 1 NaOMe + MeOH</td>
</tr>
</tbody>
</table>

5.4 Experimental.

5.4.1 General Procedures:

See Chapter 2; other aspects are given here. In situ NMR chemical shifts for all compounds surveyed are presented in Table 5.11 below. Triethylamine was distilled from CaH₂ and stored under Ar. Methanol was distilled from Mg(OCH₃)₂ under Ar and stored over molecular sieves (Linde 3Å). Literature procedures were used to prepare Ru-1a,⁴ Ru-1b,³⁶,³⁷ Ru-2a,⁴ Ru-22a/b,⁸ and Ru-27a.²⁴,²⁵ In NMR assignments of IMes derivatives, a/b labels indicate nuclei that correlate via HMQC or HMBC experiments. IR spectra of powdered compounds were measured on a Varian 640-IR reflectance FTIR spectrometer. NMR-scale reactions were performed in protio solvents with C₆D₆ (5% v/v) added as a deuterium source for locking and shimming. Conversions were quantified by integration against Ph₃P=O (³¹P) and 1,3,5-trimethoxybenzene (TMB, ¹H) as internal standards. Reactions at 60 °C in CH₂Cl₂ were carried out in thick-walled J Young NMR tubes. The anticipated vapor pressure of the solvent at this temperature is 28.4 psi (see: Chemical Engineering Research Information Center (CERIC)).
5.4.2 Synthesis of RuCl₂(IMes)(PCy₃)(=CH₂) \textit{Ru-2b}.

In the glovebox, solid white IMes (62 mg, 0.203 mmol) was added to a stirred solution of \textit{Ru-2a} (150 mg, 0.200 mmol) in C₆H₆ (15 mL). The Schlenk tube was removed to a vacuum line and heated to 60 °C for 45 min under Ar. Over 1 h at 60 °C, a color change from red to orange was observed. The solution was concentrated to ca. 1 mL, treated with hexanes (10 mL), and chilled to -35 °C. The resulting orange powder was filtered off, washed with cold hexanes (3×2 mL), and dried under vacuum. Yield: 120 mg (78%). Spectroscopic data are in good agreement with those obtained for \textit{Ru-2b}'.

\[ ^{31}P\{^1H\} \text{NMR (202.5 MHz, C}_6\text{D}_6\}: \delta \text{ 40.9 ppm (s, PCy}.\text{)} \]

1H NMR (500.1 MHz, C₆D₆): \( \delta \text{ 18.77 (s, 2H, Ru=CCH)} \), 2.90 (s, 2H, Mes \( \text{m-CH} \)) \( \), 2.37 (s, 6H, \text{o-CH}_3 \)), 2.44-2.30 (m, 3H, Cy) \( \), 2.19 (s, 3H, \text{p-CH}_3 \)), 1.77-1.47 (m, 15H, Cy) \( \), 1.30-1.01 (m, 15H, Cy). \( ^{13}C\{^1H\} \text{NMR (125.8 MHz, C}_6\text{D}_6\}: \delta \text{ 294.5 (d, } ^2J_{PC} = 12 \text{ Hz, Ru=CCH}, 191.6 (d, } ^2J_{PC} = 79 \text{ Hz, NCN}) \), 139.6, 139.0, 138.4, 137.4, 137.0, 135.6, 129.8, 129.4, 124.1 (d, \( ^4J_{PC} = 3 \text{ Hz, NCH=}) \), 123.6 (s, NCH=), 30.9 (d, \( J_{PC} = 19 \text{ Hz, Cy} \)), 29.4 (Cy), 28.2 (d, \( J_{PC} = 10 \text{ Hz, Cy} \)), 26.8 (Cy), 21.34 (p-CH₃), 21.32 (p-CH₃), 19.8 (o-CH₃), 18.9 (o-CH₃). Anal. Calcd. for \( \text{C}_{40}\text{H}_{60}\text{Cl}_2\text{N}_2\text{PRu} \): C, 62.16%; H, 7.96%; N, 3.62%. Found: C, 62.46%; H, 7.59%; N, 3.62%.

5.4.3 NMR-Scale Observation of RuCl₂(CO)(IMes)(PCy₃) \textit{Ru-27b}.

Solid IMes (5 mg, 0.016 mmol) was added to a solution of RuCl₂(CO)(PCy₃)₂ (8.6 mg, 0.011 mmol) in C₆D₆ (0.75 mL) and stirred at 23 °C for 2 h. \( ^{31}P\{^1H\} \text{NMR analysis revealed} \)

\textit{Ru-27b} (\( \delta_p \text{ 34.6}) \) and \textit{Ru-27a} (\( \delta_p \text{ 36.6}) \); integration 2:1; molar ratio 1:1. Also present was free PCy₃ (\( \delta_p \text{ 11.1}) \); 1:1 vs. \textit{Ru-27b}. An unknown signal at \( \delta_p \text{ 46.3} \) was also present, which
grew as the reaction continued. Consumption of **Ru-27a** was complete after 6 h, with **Ru-27b** (85%), free PCy₃ (100%), and δₚ 46.3 (ca. 10%).

5.4.4 NMR-Scale Preparation of RuH(κ²-OC(O)OMe)(CO)(L)(PCy₃) **Ru-28**.

L = PCy₃, **Ru-28a**.

A solution of Cs₂CO₃ in MeOH (86 µL, 0.16 M, 0.014 mmol) to an orange solution of RuHCl(CO)(PCy₃)₂ **Ru-7a** (10 mg, 0.014 mmol) in THF (0.6 mL) and C₆D₆ (50 µL). After stirring for 15 min at 23 °C, a colour change from orange-yellow to pale yellow was observed and a white precipitate formed. NMR analysis confirmed conversion of **Ru-7a** to **Ru-28a** (with ca. 5% of bicarbonatohydride **Ru-29a** at δ₁H –16.54 (t, ²J_HP = 19.8) and δₚ 45.8 (s)). The reaction mixture was stripped of solvent, taken up in C₆H₆, filtered through Celite, and stripped again, then redissolved in C₆D₆ for NMR analysis. ¹H NMR (300.1 MHz, C₆D₆): δ 3.64 (s, 3H, OC(O)OC₃H₃), 2.6–1.1 (m, Cy), –17.58 (t, ²J_HP = 19.2 Hz, 1H, RuH). ³¹P{¹H} NMR (121.5 MHz, C₆D₆): δ 45.7 (s, PCy₃). ¹³C{¹H} NMR (75.5 MHz, C₆D₆): δ 202.2 (t, ²J_CP = 12.8 Hz, CO), 159.1 (s, OC(O)OCH₃), 53.1 (s, OC(O)OCH₃), 34.9 (t, ²J_CP = 9.6 Hz, Cy), 31.2 (s, Cy), 30.3 (s, Cy), 28.1 (m, Cy), 27.0 (s, Cy). IR (cm⁻¹): ν(Ru–H) 2037, ν(CO) 1897, ν(OCO) 1608, ν(OCO) 1445, ν(COC) 1323.

L = IMes, **Ru-28b**.

Preparation as for **Ru-28a**, from RuHCl(CO)(L)(PCy₃) **Ru-7b** (10 mg, 0.014 mmol). A small amount (ca. 5%) of bicarbonatohydride **Ru-29b**, appearing at δ₁H –16.73 (d, ²J_HP = 23.9) and δₚ 47.1 (s) is also formed. ¹H NMR (500.1 MHz, C₆D₆): δ 6.85 (s, 1H, Mes m-CH₃), 6.83 (s, 1H, Mes m-CH₃), 6.66 (s, 2H, Mes m-CH₃), 6.23 (s, 2H, HC=CH), 3.50 (s, 3H, OC(O)OCH₃), 2.33 (s, 6H, Mes o-CH₃), 2.27 (s, 6H, Mes o-CH₃), 2.13 (s, 6H, Mes p-
$\text{CH}_3$, 2.6–1.1 (m, Cy), –17.96 (d, $^2J_{HP} = 22.3$ Hz, 1H, RuH). $^{31}\text{P}\{^1\text{H}\}$ NMR (121.5 MHz, C$_6$D$_6$): δ 46.8 (s, PCy$_3$). $^{13}\text{C}\{^1\text{H}\}$ NMR (75.5 MHz, C$_6$D$_6$): δ 208.0 (d, $^2J_{CP} = 5.7$ Hz, CO), 190.8 (d, $^2J_{CP} = 92.0$ Hz, NCN), 158.9 (s, OC(O)OCH$_3$), 138.1 (s, Mes $i$-C), 137.8 (s, Mes $p$-C), 136.7 (s, Mes $o$-C), 136.0 (s, Mes $o$-C$^b$), 129.2 (s, Mes $m$-CH$^a$), 129.0 (s, Mes $m$-CH$^b$), 122.5 (m, NC=CN), 52.6 (s, OC(O)OCH$_3$), 34.6 (d, $^2J_{PC} = 16.7$ Hz, Cy), 30.2 (s, Cy), 29.4 (s, Cy), 28.3 (d, $^2J_{CP} = 9.0$ Hz, Cy), 28.2 (d, $^2J_{CP} = 10.2$ Hz, Cy), 27.0 (s, Cy), 21.1 (s, Mes $p$-CH$_3$), 18.5 (s, Mes $o$-CH$_3$), 18.4 (s, Mes $o$-CH$_3$). IR (cm$^{-1}$): ν(Ru–H) 2031, ν(CO) 1908, ν(OCO) 1607, ν(OCO) 1448, ν(COC) 1324.

5.4.5 General protocol for in situ NMR monitoring of methanolysis, thermolysis, and hydrogenolysis reactions.

In a representative procedure, a solid mixture of Ru-2a (9.0 mg, 0.012 mmol), 1,3,5-trimethoxybenzene (1 mg, 0.01 mmol) and Ph$_3$P=O (6 mg, 0.02 mmol) was dissolved in CH$_2$Cl$_2$ (520 μL), MeOH (130 μL), and C$_6$D$_6$ (50 μL, added as deuterium source for shimming) in a J. Young NMR tube. Initial $^1$H and $^{31}\text{P}\{^1\text{H}\}$ NMR spectra were acquired to establish the Ru-2a:Ph$_3$P=O integration ratio at $t_o$. NEt$_3$ (5.0 μL, 0.036 mmol) was then added to the sample and the tube heated in an oil bath (60 °C). At various times, the sample tube was cooled and subjected to $^1$H and $^{31}\text{P}\{^1\text{H}\}$ NMR analysis in order to assess the reaction progress. MeO / MeOH made use of methanolic solutions of NaOMe, prepared by digestion of Na metal in MeOH (64 μL, 0.20 M). Cs$_2$CO$_3$-assisted methanolyses were performed in THF using methanolic solutions of Cs$_2$CO$_3$ (64 μL, 0.10 M).

Thermolysis and CM-thermolysis reactions were performed as above using CH$_2$Cl$_2$ or C$_6$H$_6$ (0.65 mL) and C$_6$D$_6$ (50 μL) as reaction solvent. Vinyl ethers CH$_2$=CHOEt (1.2 μL,
0.013 mmol) or CH₂=CHOTMS (1.9 µL, 0.013 mmol) were added following acquisition of t₀ NMR spectra, and the ensuing reaction monitored by ¹H and ³¹P{¹H} NMR analysis.

Hydrogenolysis reactions utilized stock solutions of Ru starting material with internal standards. Thus, Ru-22a (18 mg, 0.023 mmol), 1,3,5-trimethoxybenzene (2 mg, 0.01 mmol) and Ph₃P=O (12 mg, 0.043 mmol) were dissolved in CH₂Cl₂ (1.340 mL). A 670 µL aliquot of this stock solution was transferred to a J Young NMR tube, and t₀ data were acquired as above. Another 670 µL aliquot was transferred to a screw-cap vial equipped with a stirbar, and NEt₃ (4.5 µL, 0.033 mmol) was added. The vial was then loosely capped and transferred to a Parr autoclave, which was purged with H₂ (3 × 250 psi), pressurized to 1000 psi, and heated to 60 °C (oil bath). After 30 min, the reactor was vented (ca. 50 psi), cooled in an ice bath, purged with Ar (3 × 250 psi) and brought into a glovebox to transfer the reaction mixture to a J Young NMR tube. A C₆D₆ spike (50 µL) was added for NMR analysis.
Table 5.11. In situ NMR chemical shifts of key complexes discussed in this chapter.\(^a\)

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<tr>
<th>Complex</th>
<th>solvent</th>
<th>(\delta_p) (ppm)</th>
<th>(\delta_H) (ppm)</th>
<th>(^{2}J_{HP}) (Hz)</th>
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<tr>
<td>(\text{RuCl}_2(\text{PCy}_3)_2(=\text{CH}_3)) Ru-2a</td>
<td>(\text{C}_6\text{H}_6)</td>
<td>43.6 (s)</td>
<td>19.40 (s)</td>
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<td>19.02 (s)</td>
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<td>14.76 (s)</td>
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<td>15.58 (s)</td>
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<td>(\text{C}_6\text{H}_6)</td>
<td>33.3 (s)</td>
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<td>50.5 (s)</td>
<td>–5.30 (t)</td>
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<td>(\text{RuH(OMe)(CO)}_2(\text{IMes})(\text{PCy}_3)_2) Ru-18b</td>
<td>(\text{CH}_2\text{Cl}_2)-MeOH</td>
<td>55.9 (s)</td>
<td>–4.99 (d)</td>
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<tr>
<td>(\text{Ru(H}_2\text{(CO)}_2(\text{IMes})(\text{PCy}_3)_2) Ru-19b</td>
<td>(\text{CH}_2\text{Cl}_2)-MeOH</td>
<td>68.2 (s)</td>
<td>–7.68 (d)</td>
<td>25</td>
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<td>(10:1)</td>
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</tr>
<tr>
<td>(\text{RuH(κ^2-OC(O)OMe)(CO)(PCy}_3)_2) Ru-28a</td>
<td>(\text{CH}_2\text{Cl}_2)-MeOH</td>
<td>45.5 (s)</td>
<td>–18.07 (t)</td>
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<td>47.1 (s)</td>
<td>–16.73 (d)</td>
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</table>

\(^a\) \text{C}_6\text{D}_6\) added as deuterium source for locking and shimming. \(^b\) \text{H} NMR values given for alkylidene or hydride signals observed on solvent suppression. All reactions of methylidenes \(\text{Ru-2a/b}\) displayed the methylphosphonium salt \(\text{MePCy}_3\text{Cl}\) (s, \(\delta_p\) 34.5 in \(\text{C}_6\text{D}_6\), 34.6 in \(\text{CH}_2\text{Cl}_2\)). \(^b\) Formed in situ from \(\text{Ru-1} + 10 \text{CH}_2\text{=CHOTMS}\) at 23 °C.
5.5 References

6 Conclusions and Future Work

The focus of this thesis work was the potential opportunities presented by tandem catalysis within the context of olefin metathesis. Coupling of metathesis manifolds with olefin hydrogenation or functionalization was reviewed in Chapter 1. The key step involves transformation of the spent, uninitiated, or resting-state metathesis catalyst into a second catalyst species. To maximize the efficiency of this transformation – and hence to maximize the efficiency with which the second catalytic cycle can operate – a clearer mechanistic and practical understanding of the chemistry is essential. Similarly desirable is identification of the most appropriate structure for catalysis in the second cycle.

Chapter 2 of this thesis presents a comparative study of the hydrogenation activity and lifetime of hydride catalysts accessible from benzylidene complexes. Specifically, hydridodihydrogen complexes were compared to their hydridocarbonyl analogues: the superior hydrogenation performance of the latter was demonstrated, and was related to their exceptionally long lifetime under typical hydrogenation conditions.

A mechanistic study follows (Chapter 3), which gives insight into the factors controlling the efficiency with which the catalytically most productive hydridocarbonyl complexes can be generated via state-of-the-art procedures for tandem ROMP-hydrogenation. The Grubbs benzyldiene precatalysts were used as proxies for the alkylidene complexes that represent the propagating species in ROMP. A "generation gap" was observed, in which the first-generation catalyst was found to be most efficiently transformed into the RuHCl(CO)(L)(PCy₃) target Ru-7 by a two-step reaction with H₂ and base, then methanol and base, but the second-generation catalyst was much more efficiently transformed via the H₂-free reaction with methanol and base. This study demonstrates that catalyst-specific
tailoring is essential, even for such closely related catalyst species, and thus carries profound implications for the design of successful tandem catalysis protocols.

A cautionary study follows (Chapter 4), in which use of excess methoxide in methanol to trigger formation of the target hydride has unexpected consequences. Reactions of this promiscuous reagent with the benzyldiene precatalysts (used as a proxy for the alkylidene resting state) yields unanticipated methoxyhydride derivatives, rather than Ru-7. The implications are clear: knowledge of the fundamental inorganic reaction pathways is essential to the development of efficient tandem catalysis protocols.

Finally, Chapter 5 examines the validity of using [Ru]=CHPh precatalysts as a proxy for [Ru]=CH₂ and [Ru]=CHOR species. A specific question was the efficiency with which catalytically-versatile Ru-7 could be obtained from methyldienes (resting-state species in RCM and CM), or from Fischer carbenes (such as those formed on quenching metathesis). Efficient routes for such transformations could improvement of established methodologies, and development of new methodologies for tandem (R)CM-functionalization. The first-generation benzylidene, methylidene and ethoxylidene complexes were found to be transformed into Ru-7a most efficiently via hydrogenolysis, followed by treatment with methanol and NEt₃. In cases where olefin saturation is not wanted, CM with vinyloxytrimethylsilane, followed by degradation of the resulting trimethylsiloxylidene, gives yields of Ru-7a from benzyldiene Ru-1a, while methylidene Ru-2a and ethoxylidene are most compatible with H₂-free methanolysis. Hydrogenolysis cannot be used for the second-generation systems, because it triggers disproportionation and decomposition. Instead, H₂-free methanolysis proved optimal, as with the benzyldiene complex described in Chapter 3. Thus, while the second-generation benzylidene serves as an excellent proxy for
its methylidene and ethoxylidene analogues, the first-generation benzylidene exhibits an optimal $\text{H}_2$-free pathway to $\text{Ru-7a}$ that is dissimilar to that of its methylidene and ethoxylidene analogues.

The latter studies, in particular, set the stage for tandem (R)CM-functionalization processes based on $\text{Ru-7}$. Future studies should include examination of the activity of first- and second-generation $\text{Ru-7a/b}$ for olefin functionalization. Attractive candidates for preliminary catalytic studies include hydroamination and alkene-amine coupling, given the proliferation of nitrogenous compounds in natural products and pharmaceuticals.

Structural characterization and isolation of the paramagnetic byproducts, formed during all reactions of Grubbs-type complexes described in this thesis, would enable elucidation of their olefin functionalization activity. Use of optimized olefin functionalization protocols could then be matched to appropriate metathesis transformations, using the optimized trigger protocols outlined in this thesis, thereby providing a versatile toolkit for the efficient, economical synthesis of challenging organic targets via tandem metathesis-functionalization.

The relative thermal stability of the IMes- and $\text{H}_2\text{IMes}$-substituted catalyst systems should be examined, in hopes of explaining our observation of lower post-ROMP hydrogenation activity of the $\text{H}_2\text{IMes}$ systems. Of particular interest is the possibility that saturation of the imidazole backbond leads to fundamental differences in reactivity.
Appendices:

A.1: NMR Spectra

Figure A.1.1. $^1$H spectrum of Ru-6b ($C_6D_6$).

Figure A.1.2. $^{31}$P{$^1$H} spectrum of Ru-6b ($C_6D_6$).
Figure A.1.3. $^{13}$C($^1$H) spectrum of Ru-6b ($C_6D_6$).

Figure A.1.4. $^1$H spectrum for Ru-6b under N$_2$, 24 h ($C_6D_6$).
Figure A.1.5. $^{31}\text{P}\{^1\text{H}\}$ spectrum for Ru-6b under N$_2$, 24 h (C$_6$D$_6$).

Figure A.1.6. $^{31}\text{P}\{^1\text{H}\}$ spectra for Ru-6a thermolysis. [Ru-6a] = 14 mM, CH$_2$Cl$_2$, H$_2$ (1 atm), 55 °C.
Figure A.1.7. $^{31}\text{P}^{1\text{H}}$ spectra for Ru-6b thermolysis. [Ru-6b] = 14 mM, CH$_2$Cl$_2$, H$_2$ (1 atm), 55 °C.

Figure A.1.8. $^{31}\text{P}^{1\text{H}}$ spectra for Ru-7a thermolysis. [Ru-7a] = 14 mM, CH$_2$Cl$_2$, H$_2$ (1 atm), 55 °C.
Figure A.1.9. $^{31}\text{P}_{\{^1\text{H}\}}$ spectra for Ru-7b thermolysis. [Ru-7b] = 14 mM, CH$_2$Cl$_2$, H$_2$ (1 atm), 55 °C.

Figure A.1.10. $^1\text{H}$ spectrum of isolated Ru-6c (C$_6$D$_6$).
Figure A.1.11. $^{13}\text{C}\{^1\text{H}\}$ spectrum of isolated Ru-6c ($\text{C}_6\text{D}_6$).

Figure A.1.12. $^1\text{H}$ spectra for Ru-1a hydrogenolysis ($\text{C}_6\text{D}_6$). Left: alkylidene region; right: hydride region.
Figure A.1.13. $^{31}\text{P}$-$^{1}\text{H}$ spectra for Ru-1a hydrogenolysis (C$_6$D$_6$).

Figure A.1.14. $^1\text{H}$ spectra for Ru-1b hydrogenolysis (C$_6$D$_6$). Left: alkylidene region; right: hydride region.
Figure A.1.15. $^{31}\text{P}^{\{^1\text{H}\}}$ spectra for Ru-1b hydrogenolysis ($\text{C}_6\text{D}_6$).

Figure A.1.16. $^{31}\text{P}^{\{^1\text{H}\}}$ spectra for Ru-6a carbonylation (4:1 $\text{CH}_2\text{Cl}_2$-$\text{MeOH}$, $\text{C}_6\text{D}_6$ lock).
Figure A.1.17. $^{31}$P/$^1$H spectra for Ru-6b carbonylation (4:1 CH$_2$Cl$_2$-MeOH, C$_6$D$_6$ lock).

Figure A.1.18. $^{31}$P/$^1$H spectra for Ru-1a methanolysis (4:1 CH$_2$Cl$_2$-MeOH, C$_6$D$_6$ lock).
Figure A.1.19. $^1$H-$^{31}$P HMBC spectrum of Ru-1a methanolysis reaction mixture ($C_6D_6$).

Figure A.1.20. $^{31}$P{$^1$H} spectra for Ru-1b methanolysis (4:1 CH$_2$Cl$_2$-MeOH, C$_6$D$_6$ lock).
Figure A.1.21. $^1$H spectrum of Ru-18a (C$_6$D$_6$).

Figure A.1.22. $^{31}$P{$^1$H} spectrum of Ru-18a (C$_6$D$_6$).
Figure A.1.23. $^{13}$C($^1$H) spectrum of Ru-18a (C$_6$D$_6$).

Figure A.1.24. $^{13}$C DEPT spectrum of Ru-18a (C$_6$D$_6$).
Figure A.1.25. $^1$H-$^{13}$C HMBC spectrum of Ru-18a (C$_6$D$_6$).

Figure A.1.26. $^1$H NOESY spectrum of Ru-18a ($\tau_{\text{mix}} = 345$ ms).
Figure A.1.27. $^1$H spectrum of Ru-18b (C$_6$D$_6$).

Figure A.1.28. $^{31}$P($^1$H) spectrum of Ru-18b (C$_6$D$_6$).
Figure A.1.29. $^{13}$C\{\textsuperscript{1}H\} spectrum of Ru-18b (C\textsubscript{6}D\textsubscript{6}).

Figure A.1.30. $^{13}$C DEPT spectrum of Ru-18b (C\textsubscript{6}D\textsubscript{6}).
Figure A.1.31. $^1$H-$^{13}$C HMBC spectrum of Ru-18b (C$_6$D$_6$).

Figure A.1.32. $^1$H NOESY spectrum of Ru-18b (C$_6$D$_6$, $\tau_{\text{mix}} = 1$ s).
Figure A.1.33. $^1$H spectrum of crude Ru-17a ($C_7D_8$, 243 K).

Figure A.1.34. $^{31}P^{(1}H\)}$ spectrum of crude Ru-17a ($C_6D_6$).
Figure A.1.35. $^{13}$C-$^1$H spectrum of crude Ru-17a (C$_7$D$_8$, 243 K).

Figure A.1.36. $^1$H-$^{13}$C HMQC of crude Ru-17a (C$_7$D$_8$, 243 K).
Figure A.1.37. $^1$H spectrum of crude Ru-17b (C₆D₆).

Figure A.1.38. $^{31}$P{$^1$H} spectrum of crude Ru-17b (C₇D₈).
Figure A.1.39. $^{13}\text{C}_{1}{^1\text{H}}$ spectrum of crude Ru-17b (C$_7$D$_8$, 243 K).

Figure A.1.40. $^{13}\text{C}$-DEPT spectrum of crude Ru-17b (C$_7$D$_8$, 243 K).
Figure A.1.41. $^1$H NOESY of crude Ru-17b ($C_6D_6$, $\tau_{\text{mix}} = 1$ s).

Figure A.1.42. $^1$H spectrum of crude Ru($H)_2$(CO)$_2$(IMes)(PCy$_3$) Ru-19b ($C_6D_6$).
Figure A.1.43. $^{31}\text{P}^1\text{H}$ spectrum of crude $\text{Ru}(\text{H})_2(\text{CO})_2(\text{IMes})(\text{PCy}_3)$ Ru-19b ($\text{C}_6\text{D}_6$).

Figure A.1.44. $^{13}\text{C}^1\text{H}$ spectrum of crude $\text{Ru}(\text{H})_2(\text{CO})_2(\text{IMes})(\text{PCy}_3)$ Ru-19b ($\text{C}_6\text{D}_6$).
Figure A.1.45. $^1$H spectrum of RuHCl(CO)$_2$(IMes)(PCy$_3$) Ru-20b (C$_6$D$_6$).

Figure A.1.46. $^{31}$P {$_1^1$H} spectrum of RuHCl(CO)$_2$(IMes)(PCy$_3$) Ru-20b (C$_6$D$_6$).
Figure A.1.47. $^{13}$C{$^1$H} spectrum of RuHCl(CO)$_2$(IMes)(PCy$_3$)$_2$ Ru-20b (C$_6$D$_6$).

Figure A.1.48. $^1$H spectrum of RuH(OSO$_2$CF$_3$)(CO)$_2$(PCy$_3$)$_2$ Ru-21a (C$_6$D$_6$).
Figure A.1.49. $^{31}$P$^1$$^1$H spectrum of RuH(OSO$_2$CF$_3$)(CO)$_2$(PCy$_3$)$_2$ Ru-21a (C$_6$D$_6$).

Figure A.1.50. $^{13}$C$^1$H spectrum of RuH(OSO$_2$CF$_3$)(CO)$_2$(PCy$_3$)$_2$ Ru-21a (C$_6$D$_6$).
Figure A.1.51. $^{19}$F$^{1}$H spectrum of RuH(OSO$_2$CF$_3$)(CO)$_2$(PCy$_3$)$_2$ Ru-21a (C$_6$D$_6$).

Figure A.1.52. $^1$H spectrum for RuH(OSO$_2$CF$_3$)(CO)$_2$(IMes)(PCy$_3$) Ru-21b (C$_6$D$_6$).
Figure A.1.53. $^{31}$P($^1$H) spectrum for RuH(OSO$_2$CF$_3$)(CO)$_2$(IMes)(PCy$_3$) Ru-21b (C$_6$D$_6$).

Figure A.1.54. $^{13}$C($^1$H) spectrum of RuH(OSO$_2$CF$_3$)(CO)$_2$(IMes)(PCy$_3$) Ru-21b (C$_6$D$_6$).
Figure A.1.55. $^{19}F\{^1H\}$ spectrum for RuH(OSO$_2$CF$_3$)(CO)$_2$(IMes)(PCy$_3$) Ru-21b (C$_6$D$_6$).

Figure A.1.56. $^1$H spectrum for RuCl$_2$(IMes)(PCy$_3$)(=CH$_2$) Ru-2b (C$_6$D$_6$).
Figure A.1.57. $^{31}\text{P} \{^1\text{H}\}$ spectrum for RuCl$_2$(IMes)(PCy$_3$)(=CH$_2$) Ru-2b (C$_6$D$_6$).

Figure A.1.58. $^{13}\text{C} \{^1\text{H}\}$ spectrum for RuCl$_2$(IMes)(PCy$_3$)(=CH$_2$) Ru-2b (C$_6$D$_6$).
A.2: Reaction plots illustrating PCy₃-dependence of Ru-1 consumption during Ru hydride production processes.

**Figure A.2.1.** Inhibition of NEt-assisted Ru-1a hydrogenolysis by added PCy₃. Solid lines: no PCy₃ added. Dashed lines: 3 equiv PCy₃ added. Conditions: CH₂Cl₂, 60 °C; 3 equiv NEt₃, 1000 psi H₂, [Ru]= 15 mM.

**Figure A.2.2.** Inhibition of NEt₃-assisted Ru-6a carbonylation by PCy₃. Solid lines: no PCy₃ added. Dashed lines: 3 equiv PCy₃ added. Conditions: 10:1 CH₂Cl₂-MeOH, 60 °C; 3 equiv NEt₃, [Ru]= 15 mM.
**Figure A.2.3.** Inhibition of NEt$_3$-assisted Ru-1a methanolysis by PCy$_3$. Solid lines: no PCy$_3$ added. Dashed lines: 3 equiv PCy$_3$ added. Conditions: 10:1 CH$_2$Cl$_2$-MeOH, 60 °C; 3 equiv NEt$_3$, [Ru]= 15 mM.

**Figure A.2.4.** Inhibition of NaOMe-assisted Ru-1a methanolysis by PCy$_3$. Solid lines: no PCy$_3$ added. Dashed lines: 5 equiv PCy$_3$ added. Conditions: 10:1 CH$_2$Cl$_2$-MeOH, 60 °C; 3 equiv NaOMe, [Ru]= 15 mM.
Figure A.2.5. Tolerance of NaOMe-assisted Ru-1b methanolysis towards added PCy₃. Solid lines: no PCy₃ added. Dashed lines: 5 equiv PCy₃ added. Conditions: 10:1 CH₂Cl₂-MeOH, 60 °C; 20 equiv NaOMe, [Ru]= 15 mM.