

New Directions in Catalyst Design and Interrogation: Applications in Dinitrogen Activation and Olefin Metathesis

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Abstract

A major driving force for development of new catalyst systems is the need for more efficient synthesis of chemical compounds essential to modern life. Catalysts having superior performance offer significant environmental and economic advantages, but their discovery is not trivial. Well-defined, homogeneous catalysts can offer unparalleled understanding of ligand effects, which proves invaluable in directing redesign strategies. This thesis work focuses on the design of ruthenium complexes for applications in dinitrogen activation and olefin metathesis. The complexes developed create new directions in small-molecule activation and asymmetric catalysis by late-metal complexes.

Also examined are the dual challenges, ubiquitous in catalysis, of adequate interrogation of catalyst structure and performance. Insight into both is essential to enable correlation of ligand properties with catalyst activity and/or selectivity. Improved methods for accelerated assessment of catalyst performance are described, which expand high-throughput catalyst screening to encompass parallel acquisition of kinetic data. A final aspect focuses on direct examination of metal complexes, both as isolated species, and under catalytic conditions. Applications of charge-transfer MALDI mass spectrometry to structural elucidation in organometallic chemistry is described, and the technique is employed to gain insight into catalyst decomposition pathways under operating conditions.

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Abbreviations

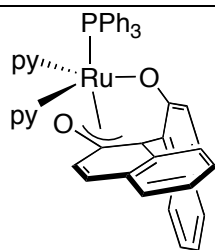
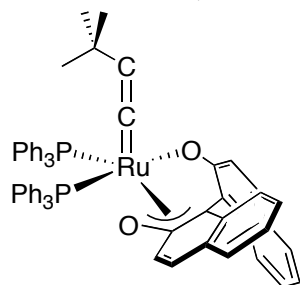
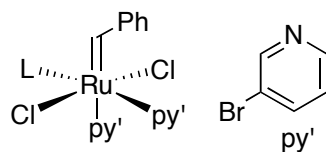
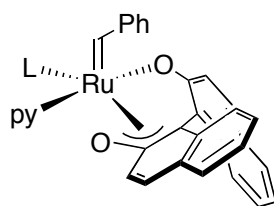
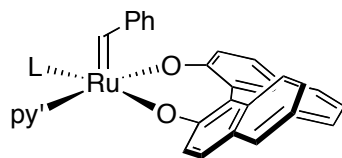
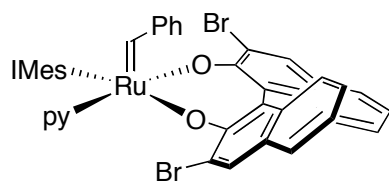
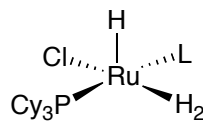
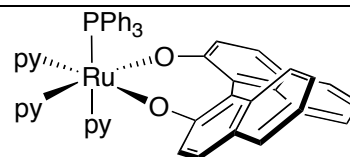
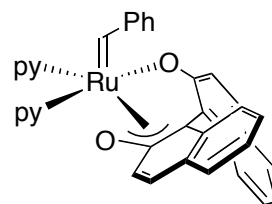
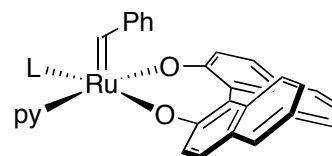
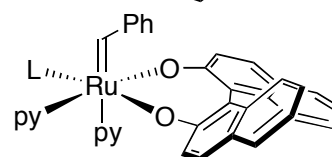
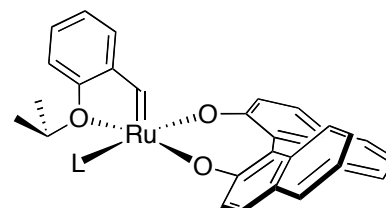
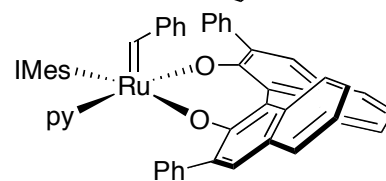
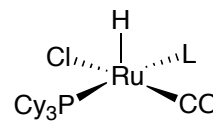
ADMET	Acyclic diene metathesis
ARCM	Asymmetric ring closing metathesis
B3LYP	Becke, three-parameter, Lee-Yang-Parr
BAr ^F ₄	tetrakis[3,5-bis(trifluoromethyl)phenyl]borate
9-BBN	9-borabicyclononane
BHT	2,6-di-(tert)-butyl-4-methyl-phenol
BINAP	2,2'-bis(diphenylphosphanyl)-1,1'-binaphthyl
BINO	1,1'-binaphthyl-2,2'-diolate
BINOL	1,1'-binaphthyl-2,2'-diol
BINOP	2-diphenylphosphanyl-1,1'-binaphthyl-2'-olate
BIPHEP	2,2'-bis(diphenylphosphino)-1,1'-biphenyl
CD	Circular dichroism
CHCA	α -Cyano-4-hydroxycinnamic acid
CM	Cross metathesis
COD	Cycloocta-1,5-diene
COSY	Correlation spectroscopy
Cp	Cyclopentadienyl
CT	Charge-transfer
2D	Two-dimensional
DCE	1,2-dichloroethane
DCTB	(<i>E</i>)-2-(3-(4-Tertbutylphenyl))-2-methylallylidenemalonitrile
depe	1,2-bis(diethylphosphanyl)ethane
DFT	Density functional theory
DHB	2,5-dihydroxybenzoic acid
DMSO	Dimethylsulfoxide
EN	<i>N,N'</i> -dibenzylethylenediamine
equiv	equivalents
ESI	Electrospray ionization
EtOAc	Ethyl acetate
EXSY	Exchange spectroscopy

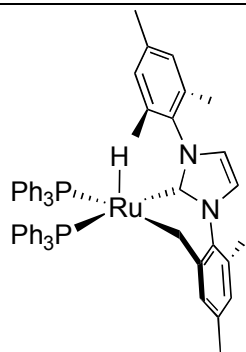
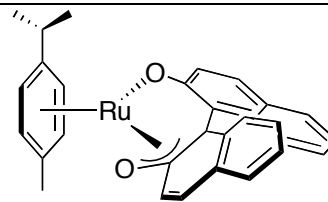
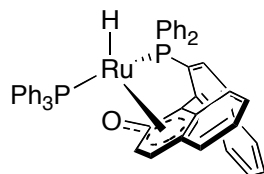
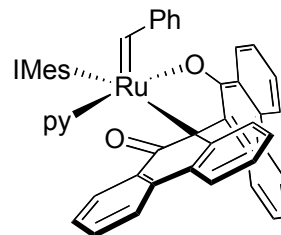
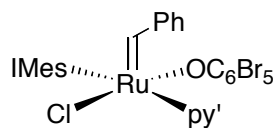
EYCM	Enyne cross metathesis
FAB	Fast atom bombardment
FMO	Fragment molecular orbital
GC-FID	Gas chromatography flame ionization detection
HBD	Hydrogen-bond donor
H ₂ IMes	1,3-bis-(2,4,6-trimethylphenyl)imidazolin-2-ylidene
H ₂ ITol	1,3-bis-(2-methylphenyl)imidazolin-2-ylidene
HMBC	Heteronuclear multiple bond correlation
HMQC	Heteronuclear multiple quantum coherence
HOFO	Highest occupied fragment orbital
HPLC	High performance liquid chromatography
HSQC	Heteronuclear single quantum coherence
HTE	High-throughput experimentation
HTS	High-throughput screening
Hz	Hertz
IMes	1,3-bis-(2,4,6-trimethylphenyl)imidazol-2-ylidene
IP	Ionization potential
IPr	1,3-bis-(2,6-diisopropylphenyl)imidazol-2-ylidene
IR	Infrared
LDI	Laser desorption ionization
LUFO	Lowest unoccupied fragment orbital
Lut	Lutidinium or 2,6-dimethylpyridinium
M	Molecular ion
MALDI-TOF	Matrix assisted laser desorption ionization-time of flight
Me ₂ BINO	3,3'-dimethyl-1,1'-binaphth-2,2'-olate
MeCN	Acetonitrile
Mes	Mesityl
MIM	1-Methylimidazole
MS	Mass spectrometry
NBE	Norbornene
NHC	<i>N</i> -heterocyclic carbene

NMR	Nuclear magnetic resonance
OAr	Aryloxiide
ORTEP	Oak ridge thermal ellipsoid plot program
OTf	Trifluoroacetate
P	Product
PAH	Polyaromatic hydrocarbon
PhMe	Toluene
ppm	Parts per million ($\mu\text{g/g}$)
py	Pyridine
py'	3-Bromopyridine
pyr	Pyrene
Q	Quenching agent
RCM	Ring closing metathesis
RCEYM	Ring closing enyne metathesis
ROM/CM	Ring opening metathesis/cross metathesis
ROMP	Ring opening metathesis polymerization
S	Substrate
SA	Sinapinic acid
SFC	Supercritical fluid chromatography
THF	Tetrahydrofuran
THN	1,2,3,4-Tetrahydronaphthalene
TMB	1,3,5-Trimethoxybenzene
TLC	Thin layer chromatography
TOF	Turnover frequency
TON	Turnover number
Tp	Hydrotris(pyrazolyl)borate
Ts	Toluene sulfonate
UV-vis	Ultraviolet-visible
XRD	X-ray diffraction

List of compounds

Ruthenium complexes			
#	Compound	#	Compound
	L: a = PCy ₃ b = IMes c = H ₂ IMes d = IPr e = H ₂ ITol		# = η^1, η^1 -BINO #' = η^3, η^1 -BINO #'' = η^3, η^3 -BINO (with the exception of Ru-8)
Ru-1		Ru-2	
Ru-3		Ru-4	
Ru-5		Ru-6	
Ru-7		Ru-8: X = H; X' = Cl	
		Ru-8': X, X' = H	
		Ru-8'': X, X' = H	
Ru-9		Ru-10	
Ru-11''		Ru-11'	
Ru-12'		Ru-13	

Ru-14'**Ru-16'****Ru-18****Ru-19'****Ru-21****Ru-23****Ru-25****Ru-15****Ru-17'****Ru-19****Ru-20****Ru-22****Ru-24****Ru-26**

Ru-27**Ru-28****Ru-29****Ru-30****Ru-31**

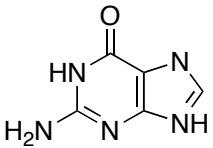
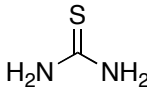
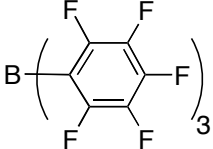
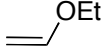
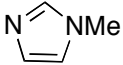
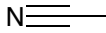
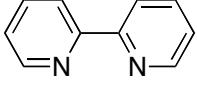
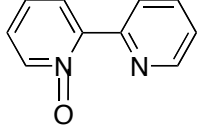
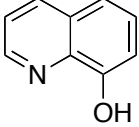
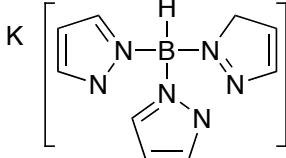
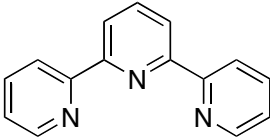
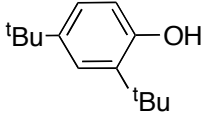
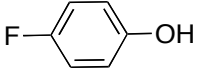
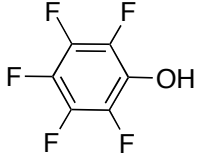
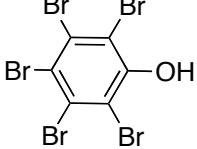
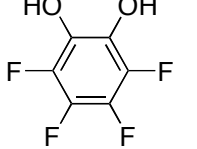
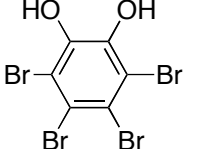
Substrates and products

#	Compound	#	Compound
1		1'	
2		2'	
3		3'	
exo-4		5	
6		6'	
7		7'	

8		8'	
8''		9	
9'		10a	
10b		11a	
11b		12	
12'		12''	
13		13'	

Additives

#	Compound	#	Compound
14		15	
16		17	
18		19	
20		21	

22		23	
24		25	
26		27	
28		29	
30		31	
32		33	
34		35	
36		37	
38			

Chapter 1. Introduction

1.1 Motivation.

An increasing body of evidence points toward dramatic changes to the biosphere over the approximately 250 years since the industrial revolution began. According to the International Panel on Climate Change, global temperatures have steadily risen, while atmospheric concentrations of CO₂ have increased by 36%.¹ Much current effort is directed at increasing utilization of renewable energy sources and feedstocks, and reducing the amount of waste generated in industrial and domestic practice, in the hope of attenuating or retarding these negative anthropogenic effects.

While environmental problems are global in impact, they are local in origin. Green Chemistry targets better control at the local level, in the context of sustainable chemical practice.²⁻⁴ Its Twelve Principles set forth guidelines for environmentally more benign processes, centered on atom economy, waste reduction, and the use of catalysis to improve efficiency in the utilization of energy and materials. Atom economy, as one quantitative measure of reaction efficiency, simply divides the molecular weight of products by the summed molecular weights of reactants. The inefficiency associated with use of stoichiometric reagents is thereby cast into high relief. This overlooks, however, the contribution of solvents, additives, and workup reagents, and thus provides a limited perspective on total waste generation. The environmental or E-factor, a metric now nearly 30 years old, was developed to address this deficiency.⁵ The E-factor is assessed by dividing the total mass of waste generated throughout an entire process by the mass of isolated product. In fine-chemicals and pharmaceutical manufacturing, E-factors range from 5-100, owing in large part to a long-standing reliance on wasteful stoichiometric methodologies. Sheldon has usefully discussed the merits and limitations of this analysis.⁵

1.2 Catalysis.

Replacing stoichiometric by catalytic methodologies has the potential to significantly reduce total materials and energy consumption, and in some cases to dramatically reduce the number of synthetic steps required for the synthesis of a given target compound.^{2,6} In a conventional chemical reaction, energy is added to reagents **A** and **B** to overcome the activation barrier to their conversion into products **C** and **D** (Figure 1.1 a, b).⁶ The activation barrier (E_a) can in some cases be reduced by use of stoichiometric reagents, but this contributes to waste. Use of a catalyst to interact with and activate **A** (and/or **B**) facilitates reaction, by affording access to a low-energy pathway (Figure 1.1b). Liberation of product regenerates the catalyst, which takes up substrate again, and the cycle is then re-engaged (Figure 1.1c). The process of substrate transformation is terminated by catalyst decomposition, and one measure of catalyst efficiency is the number of cycles that it is able to complete prior to decomposition. This value defines the turnover number (TON). The *rate* at which the catalyst operates is defined by the turnover frequency (TOF): that is, the number of turnovers per unit of time. For quantitative conversion of starting materials to products, catalyst lifetimes must be adequate: less robust catalysts will require higher loadings, and will themselves contribute to waste both through catalyst decomposition, and through the need to remove spent catalyst from the desired product stream.

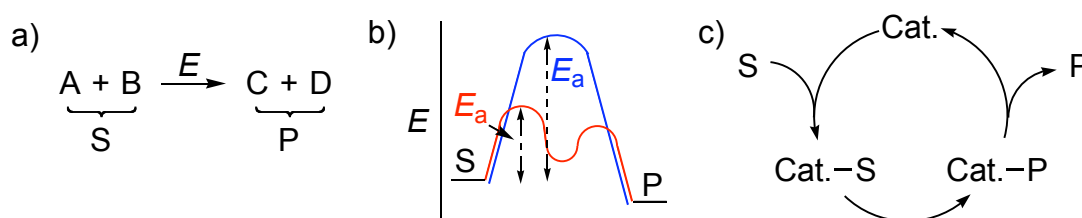


Figure 1.1. A simplified chemical reaction. a) Uncatalyzed conversion of substrate to product where the reaction is promoted by energy (E) input; b) energy barriers for an uncatalyzed (blue) and a catalyzed reaction (red); c) a simplified catalytic cycle showing turnover of the catalyst.

A further challenge is that of selectivity. Where a mixture of products is obtained (i.e. **C**, **D**; Figure 1.1a), separation requirements impose new needs in terms of energy, materials, and solvent expenditures. Where only one product is desired, mass yields also suffer. Selective

catalyst systems, which favor formation of solely the desired product, are advantageous for their capacity to maximize yields, and also to reduce purification requirements, which are frequently very solvent-intensive. Ongoing research in homogeneous and heterogeneous catalysis are aimed at improving the efficiency of many transformations through catalyst design and reaction optimization. The first part of this thesis describes the development and assessment of homogeneous ruthenium complexes relevant to dinitrogen activation and olefin metathesis. A second theme centers on the development and use of new methodologies to aid in the synthesis, deployment, and interrogation of these and other complexes in catalysis.

1.3 Dinitrogen Activation.

The Haber-Bosch process, which reduces dinitrogen to ammonia, is an example of a catalytic system that yields a product central to modernity. Much of the ammonia is converted into nitrogenous fertilizers, and thus plays an essential role in sustaining global food production. The reaction is highly demanding given the great strength of the $\text{N}\equiv\text{N}$ bond ($225 \text{ kcal mol}^{-1}$), and the activation barrier is very high even in the presence of the catalyst. High pressures and temperatures (200 atm , $400 \text{ }^{\circ}\text{C}$)⁷ are therefore required, to the extent that this simple process consumes 1% of the world's annual energy budget.⁸ The past hundred years have seen very few improvements on the Haber-Bosch catalysts: product demand and pricing is sufficient to defend current process economics, and despite much effort, chemists have so far been unsuccessful in significantly improving the working catalyst. To date, a single homogeneous catalyst has been found to promote the selective formation of NH_3 : astonishingly, this system is operative *at room temperature and one atmosphere of N_2* , although its performance is limited by low turnover numbers and the need for a specialized proton source.^{7,9-11} While the higher sensitivity generally characteristic of homogeneous, vs. heterogeneous, catalysts presents a challenge in large-scale, commodity chemical processes, the greater ease of acquiring mechanistic insight is likely to facilitate development of lower-energy N_2 reduction catalysts. New directions in N_2 activation by more robust, late-metal complexes will be discussed in Chapter 3.

1.4 Olefin Metathesis.

Methods for the assembly of carbon skeletons are a central theme in organic synthesis. One of the most powerful such reactions in current use is olefin metathesis,^{12,13} in which carbon atoms of two olefinic units switch their bonding partners (Figure 1.2a). Cross-metathesis of two styrene molecules, for example, produces one equivalent of ethylene and a mixture of *cis*- and *trans*-stilbene (Figure 1.2b). A major breakthrough in this area was Chauvin's 1971 proposal of a mechanism involving the [2+2]-cycloaddition of a metal alkylidene and an olefin (Figure 1.2c).^{14,15} The process is reversible, but expulsion of volatile ethylene as a side-product favours the forward reaction.¹⁶ Depending on the nature of the starting olefin, a variety of transformations can be induced: cross-metathesis (CM), ring-closing metathesis (RCM), ring-opening metathesis coupled with cross-metathesis (ROM/CM), ring-opening metathesis polymerization (ROMP), and ring-closing enyne metathesis (RCEYM) (Figure 1.3). The first three manifolds generate ethylene, if the usual vinylic substrates are used, while ROMP and RCEYM are wholly atom-economical, being driven (respectively) by relief of ring strain and by conjugative stabilization of the diene product. A key issue is the nature of the resting state or propagating species. For RCM and CM reactions, the metal-alkylidene precatalyst is typically transformed into a methylidene species after a single turnover (Figure 1.2d). Reactions that begin with an internal olefin (e.g. a ROMP monomer) will instead generate an alkylidene species (Figure 1.2d). The behaviour, sensitivity, and lifetime of these species will emerge as central to the work discussed in Chapters 4-6.

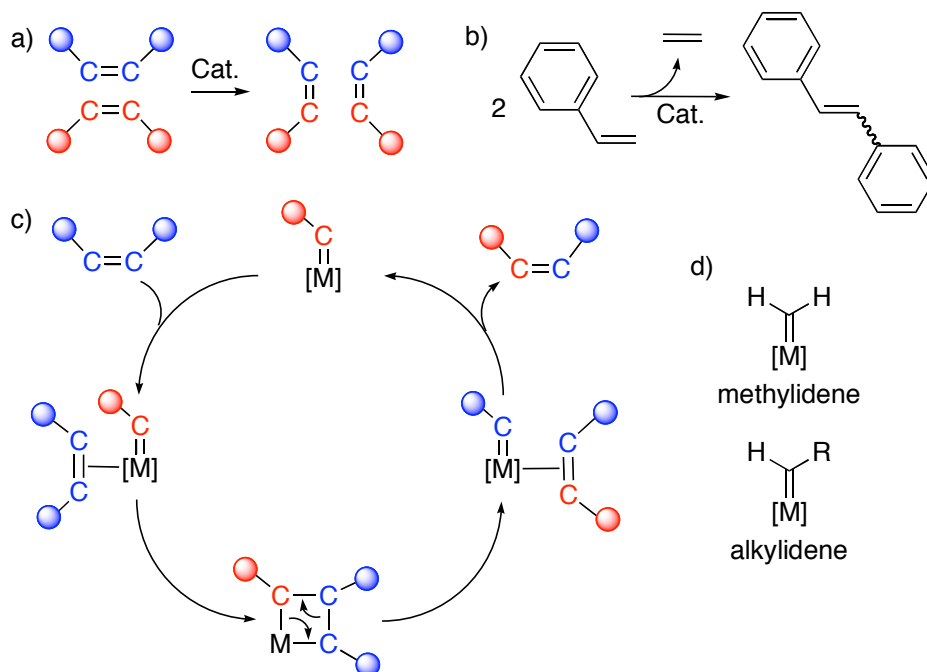


Figure 1.2. The Chauvin mechanism for olefin metathesis.

Elucidation of the mechanism for olefin metathesis was rapidly followed by the rational synthesis of "well-defined" catalysts containing the essential metal-alkylidene functionality. Most important of the catalyst classes reported to date are the Mo-imido complexes developed by Schrock,¹⁷ and the ruthenium complexes first reported by Grubbs (Chart 1.1, **Mo-1** and **Ru-1a**).^{18,19} The molybdenum catalysts demonstrate exceptional, highly tunable metathesis activity, and in some cases remarkable selectivity. Their thermal stability is poor, however, and they are highly sensitive toward decomposition by air, water, and protic groups, as well as aldehydes and carboxylic acids.^{17,20} The greater challenges involved in handling these complexes, coupled with the emergence of competing, more robust ruthenium systems, has significantly limited uptake of the molybdenum catalysts by the organic community.²¹

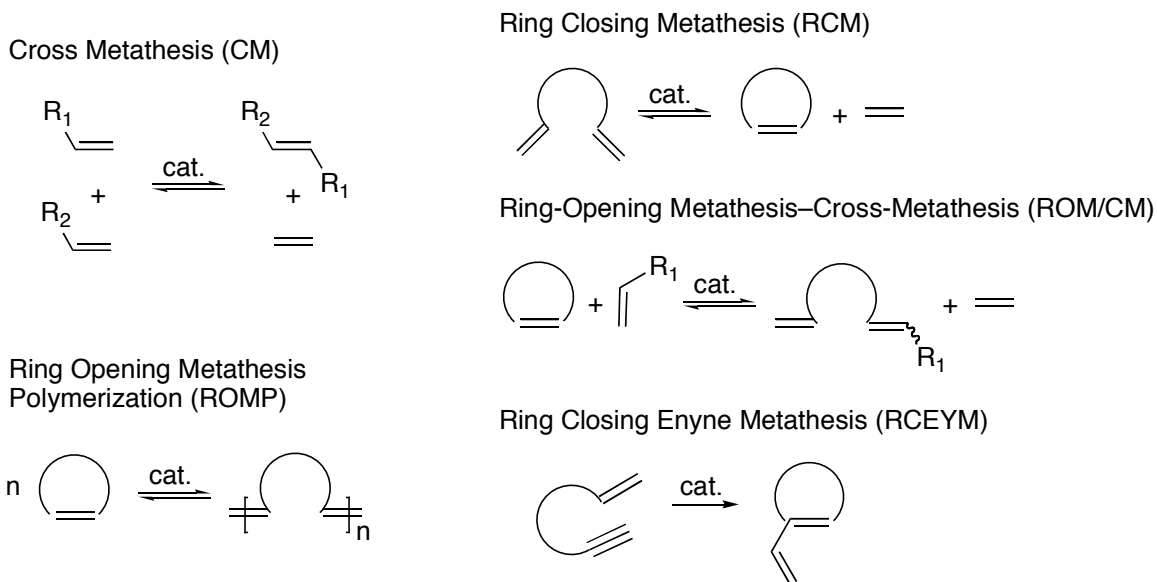


Figure 1.3. Common olefin metathesis transformations.

The ruthenium systems are much more tolerant toward traces of air and water, and toward some functional groups, but exhibit lower metathesis activity.^{18,19} The breakthrough ruthenium complex now known as the first-generation Grubbs catalyst is shown as **Ru-1a** (Chart 1.1). Subsequent substitution of one PCy₃ ligand by an *N*-heterocyclic carbene (NHC), reported nearly simultaneously by Grubbs,²² Nolan,²³ and Furstner and Herrmann,²⁴ greatly increased the activity and scope of these catalysts. These second-generation catalysts (see, e.g., **Ru-1b**, **Ru-1c**) were found to display higher thermal stability than **Ru-1a**, and are widely believed to show greater tolerance toward alcohols, aldehydes and carboxylic acids.¹² The distinction between the behaviour of the precatalyst and that of the active catalyst, unrecognized in the early reports, is discussed below; it should also be recognized that robustness depends strongly on the relative kinetics of decomposition vs. metathesis, and that much "evidence" for functional-group tolerance is biased by the use of highly reactive RCM or ROMP substrates.

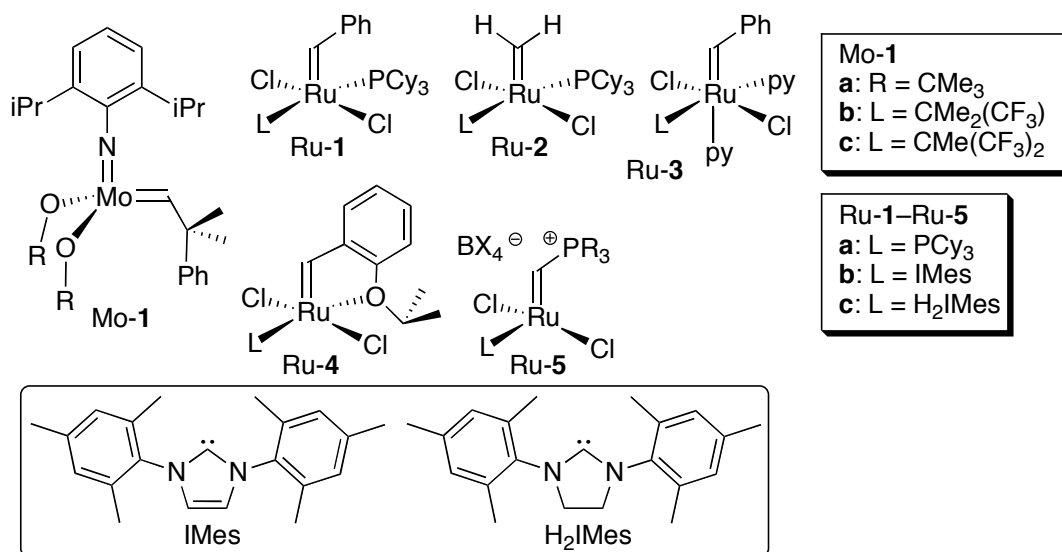
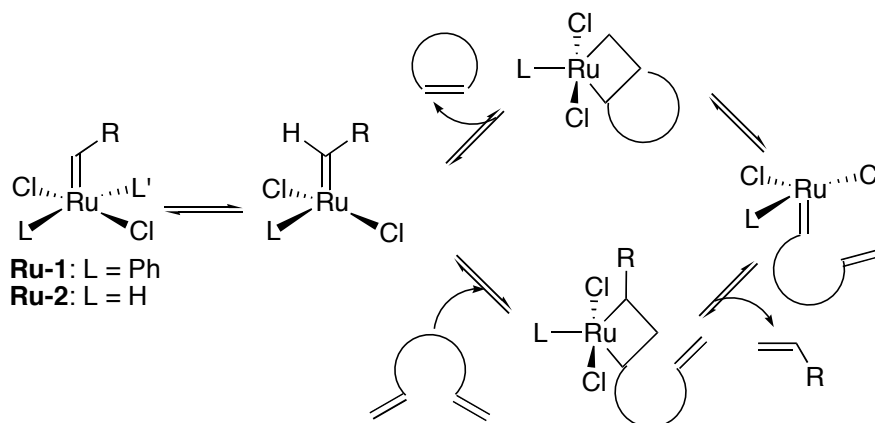


Chart 1.1. Common Mo and Ru olefin metathesis catalysts.

For these Ru catalysts, a large body of experimental and computational work supports the mechanism shown in Scheme 1.1: one neutral L-donor ligand remains bound to the metal throughout the catalytic cycle, while the second dissociates to generate a 14-electron intermediate as the active catalyst.²⁵ For the second-generation systems, the strong σ -donor NHC remains bound, while PCy₃ acts as the labile ligand. The active catalyst, in either case, binds olefin and undergoes [2+2] cycloaddition to form the metallocyclobutane intermediate. A competing equilibrium involves reversible recapture of PCy₃ to generate the 16-electron methylidene complex **Ru-2** as the resting state.



Scheme 1.1. The dissociative mechanism for olefin metathesis via the dominant, square pyramidal ruthenium catalysts.

Dozens of variants on the parent ruthenium catalyst **Ru-1** have now been reported, of which most common are examples containing various NHC ligands.^{26,27} In other important examples, the remaining PCy₃ ligand is replaced by one or two pyridine groups (see **Ru-3**, the "third-generation" Grubbs catalyst),^{28,29} or a chelating ether pendant on the benzyldiene functionality (**Ru-4**, the Hoveyda catalyst);³⁰⁻³² in the Piers system, the second L-donor ligand is removed altogether, and a phosphonium substituent is present on the alkylidene (**Ru-5**).^{33,34} Replacement of the chloride ligands has received less attention,³⁵ but leading examples include complexes containing other halides,²⁵ Schiff bases,³⁶⁻³⁹ and aryloxide ligands.⁴⁰⁻⁴³ As with any versatile catalytic transformation, no single catalyst proves ideal for all applications.^{44,45} Most commonly used in organic synthesis, however – owing in large part to their commercial availability – are **Ru-1a**, **Ru-1c** and **Ru-4c**, while **Ru-1a** and **Ru-3c** are now dominant in materials synthesis. As this breadth of contexts suggests, leading-edge applications of olefin metathesis are very wide-ranging: they include the construction of specialty polymers by ROMP,⁴⁶ and key intermediates in natural product synthesis by RCM and CM.^{12,47-49} In the latter two reaction manifolds, however, catalyst loadings of 5-10 mol%, and occasionally as high as 50 mol%, are common, resulting in considerable purification problems and limiting the industrial viability of these methodologies.

1.5 Asymmetric Olefin Metathesis.

Much effort has also focused on applications of olefin metathesis in asymmetric catalysis.⁵⁰⁻⁵² Asymmetric metathesis involves the simultaneous construction of new C=C bonds and establishing one (or many) chiral centres in a single catalytic event. Both Mo and Ru catalysts have been developed for this purpose, and the general trends in stability and reactivity established in achiral systems are maintained.⁴⁹ Catalysts are typically assessed by either of two manifolds; ROM/CM or ARCM. The latter requires catalysts of higher activity: conversely, attenuated activity is essential for ROM/CM reactions, to inhibit competing ROMP pathways. The absence of an agreed-on benchmark reaction and conditions hampers direct comparison of catalysts. The counter-argument can be made, however, that the key point is not the maximum enantioselectivity attainable for each catalyst under some arbitrary set of conditions, but the best performance under conditions optimized for each unique catalyst system. The considerable experimental demands associated with the large numbers of experiments required in the latter case are discussed below.

In ruthenium systems, the chiral element is typically sited within a monodentate or bidentate NHC ligand. Unsymmetrical substitution of the imidazole ring in monodentate NHCs is used to direct, or "gear", the conformation of the *N*-substituents (Chart 1.2a and b). The Grubbs group has exploited this effect using C_2 -symmetric imidazolinidene ligands (Chart 1.2a);⁵³⁻⁵⁵ in the more successful variants, only one side of the aryl ring is substituted (i.e. $R_2, R_3 = H$).⁵⁴ High enantioselectivities generally require substitution of iodide for chloride (usually in situ), which diminishes reactivity.⁵³⁻⁵⁵ Inspired by the potential of the gearing effect, and by the unsymmetrical imidazolinidene ligand previously reported by Blechert,⁵⁶ Collins developed C_1 -symmetric NHCs in which one nitrogen bears an alkyl group, the other an aryl group (Chart 1.2b).⁵⁷⁻⁵⁹ These catalysts permit high enantioselectivity without the need to replace chloride by iodide. A catalyst containing a C_1 -symmetric NHC ligand, reported by Blechert, exhibits only moderate activity, but a remarkable, 30:1 selectivity for *E* over *Z* olefins (Chart 1.2b).⁶⁰ In general, the C_1 -symmetric monodentate NHCs appear more promising than the C_2 -symmetric ligands developed by Grubbs.

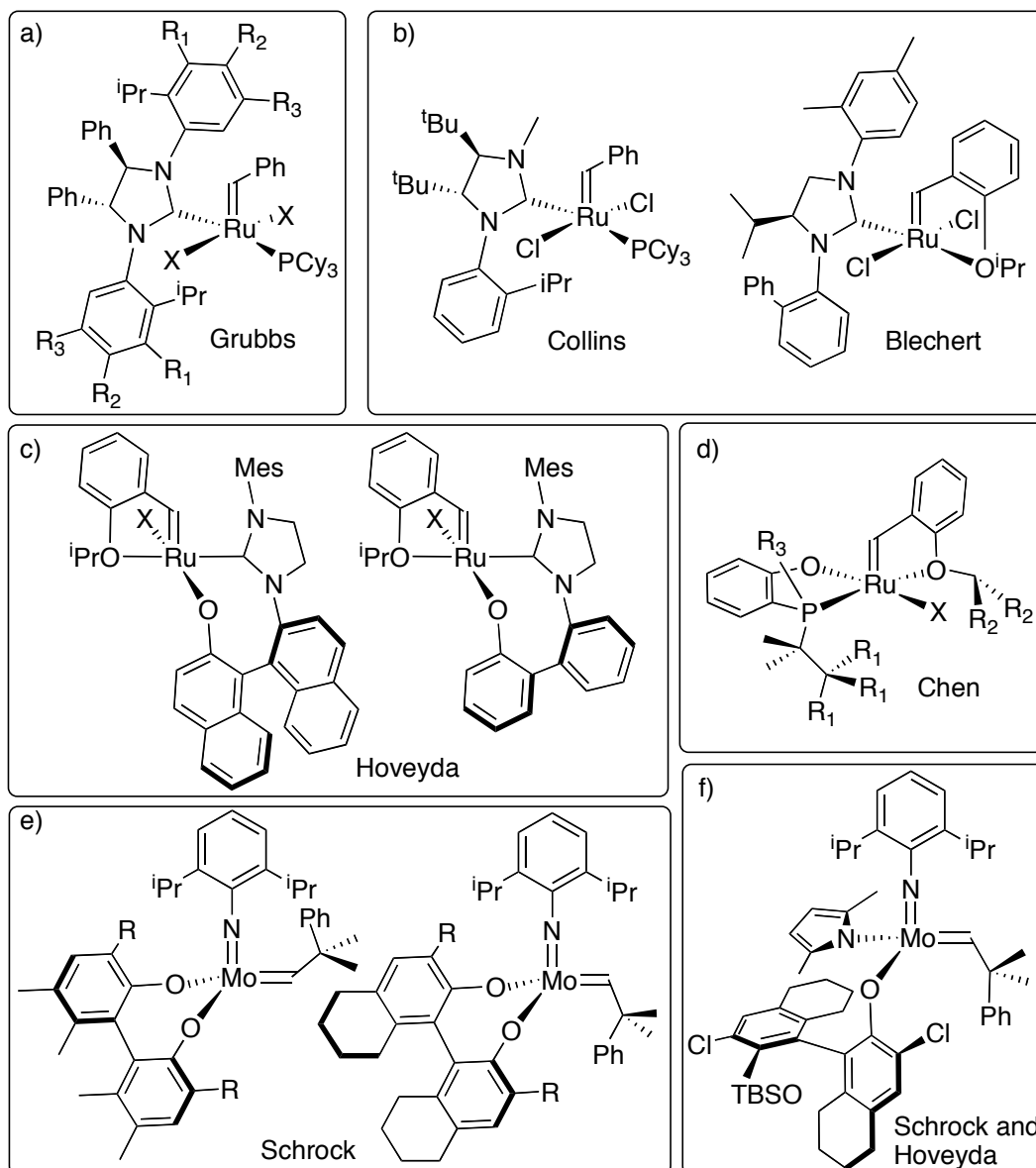


Chart 1.3. Chiral ruthenium and molybdenum olefin metathesis catalysts. Sources of chirality: a) A C_2 -symmetric NHC; b) a C_1 -symmetric NHC; c) a bidentate, atropisomeric NHC; d) a chiral phosphine; e) bidentate, atropisomeric biphenolate or binaphtholate; f) a stereogenic Mo center.

Atropisomeric NHCs in which one nitrogen ligand bears a pendant binaphtholate or biphenolate moiety were explored by Hoveyda (Chart 1.2c).⁶¹⁻⁶⁴ High enantioselectivities are possible but, as with the Grubbs catalysts, exchange of chloride for iodide is required. The lower activity of these catalysts relative to the complexes containing monodentate NHCs

makes them best suited for ROM/CM applications. A promising catalyst developed by Chen contains a chiral phosphine derived from catechol (Chart 1.2d).⁶⁵⁻⁶⁷ Not yet employed for asymmetric metathesis (it may lack the reactivity for RCM, but ROM-CM applications could be possible), this catalyst exhibited excellent selectivity in the alternating ROMP copolymerization of norbornene and cyclooctene. A further chiral catalyst was prepared (not shown) by incorporating a binaphtholate moiety into the benzyldiene functionality within a Hoveyda-type structural motif,⁶⁸ but this approach can be expected to be of limited efficacy, given that benzyldiene is converted to methyldiene following one catalyst turn-over in RCM or CM. Unsurprisingly, zero enantioinduction was observed in ARCM of a triene using this catalyst. In summary, none of the ruthenium systems developed to date combine high activity and high enantioselectivity; moreover, the range and "tunability" of the chiral elements remains restricted, relative to the Group 6 catalysts.

In molybdenum systems, the principal source of chirality arises from binaphtholate or biphenolate ligands.^{20,51,69} Key to high, tunable enantioselectivities is the incorporation of a range of large substituents (i.e. R = *t*-butyl, mesityl, 2,4,6-triisopropylphenyl) at the 3,3'-positions of the ligands (Chart 1.2e). The superior performance of these catalysts is apparent from, inter alia, ARCM reactions exhibiting high conversions *and* enantioselectivities, at lower catalyst loadings and temperatures⁵¹ relative to ruthenium systems.^{59,62} (It may be noted, however, that the milder operating conditions are essential, given the poor thermal stability characteristic of the catalyst class).

A breakthrough in catalyst design was achieved by Schrock and Hoveyda with a new class of monoalkoxide monopyrrolide (MAP) catalysts (Chart 1.2f).^{70,71} Not only is the level of activity and selectivity unrivaled, but these species can be assembled in situ from achiral bis-pyrrolide alkylidene complexes, with no detrimental effect on catalyst performance.⁷² Moreover, MAP catalysts afford a selectivity for *Z*-olefins (ROM/CM and CM reactions) unattainable using known ruthenium systems.^{72,73} Chapter 4 of this thesis will discuss a new class of chiral ruthenium metathesis catalysts that integrates some of the key advantages of the Schrock and Grubbs-type systems.

1.6 High-Throughput Experimentation.

The need to compare catalyst activity and selectivity under conditions optimal for (ideally) each catalyst system, alluded to above, emphasizes the bottleneck that catalyst screening can represent, as well as the materials-intensive nature of screening programs. While the complexity of catalyst structure-selectivity relationships makes this a particularly challenging problem in asymmetric catalysis, the issue is of course very general. As a specific instance relevant to the industrial uptake of (achiral) olefin metathesis, extensive optimization is required to adapt RCM to the economic stringencies of chemical manufacturing. A Boehringer-Ingelheim campaign directed at the synthesis of a Hepatitis C protease inhibitor, which utilizes RCM as a key step,⁷⁴⁻⁷⁶ has been subjected to intensive optimization efforts over the last five years. Over this period, the catalyst loadings required were reduced from 5 mol%⁷⁴ to 0.05-0.1 mol%,⁷⁵ and the E-factor for the process from 370 to 52,⁷⁵ but time-to-market constraints make this kind of extended study a luxury.

In other areas of homogeneous catalysis, such as hydrogenation⁷⁷⁻⁷⁹ and polymerization⁸⁰, high-throughput experimentation (HTE) has significantly accelerated catalyst discovery and reaction optimization.^{6,77,81} The overall time required from catalyst discovery to scale-up to kg quantities can be dramatically reduced: an astonishing recent example from DSM reports an example of a 25-day campaign for a specific hydrogenation process,⁷⁹ as compared to a conventional timescale of years. Decreasing reaction scale and performing many reactions in parallel expands the scope of the systems that can be tested, while reducing materials costs and waste for each system screened. Simultaneous advances in serial and, to a lesser extent, parallel analytical methodologies, facilitate rapid screening of reaction arrays.^{82,83} Olefin metathesis could benefit greatly from the use of such methods to optimize, assay, and discover improved catalyst systems. Application of HTE to ruthenium-catalyzed olefin metathesis will be discussed in Chapter 5 of this thesis.

1.7 Structure Elucidation in Catalyst Synthesis and Decomposition.

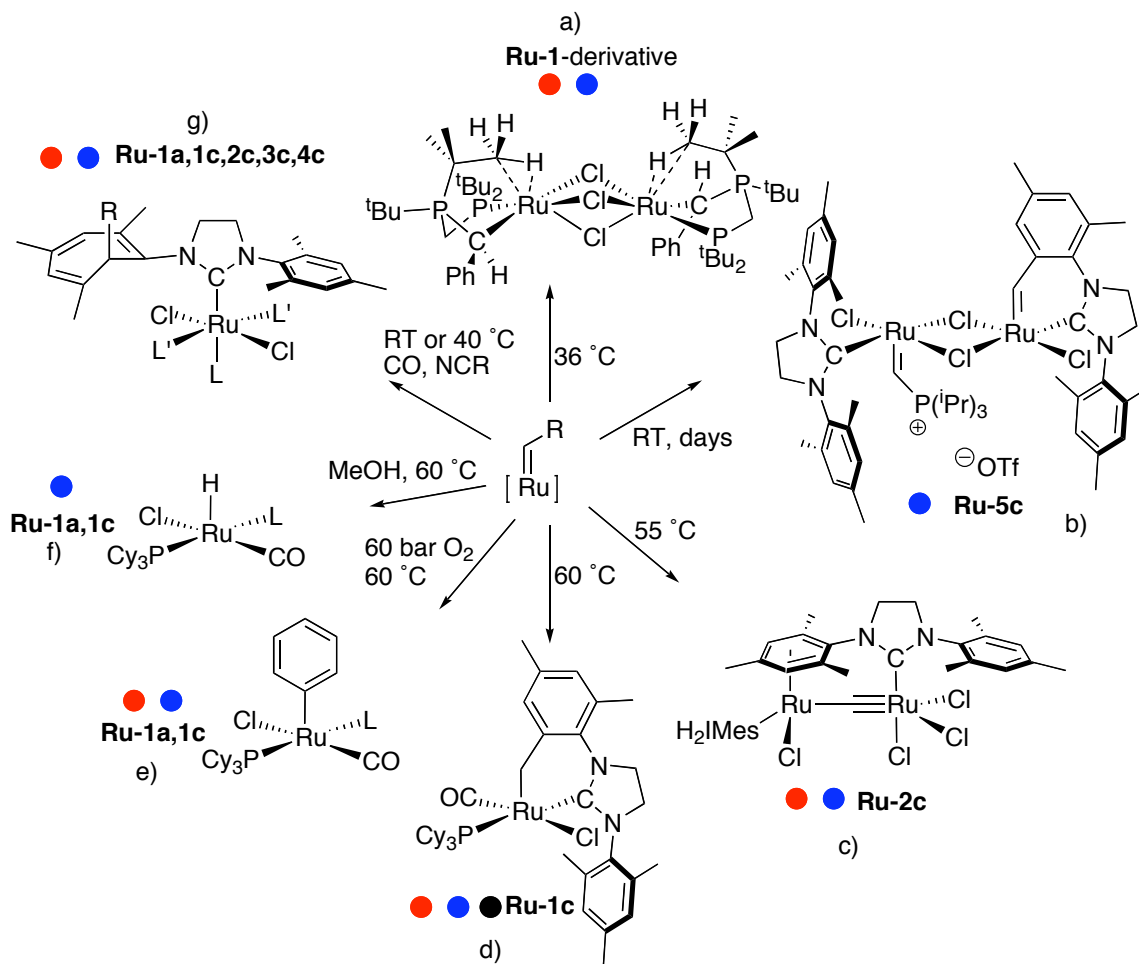
Faster optimization has the potential to expand industrial uptake of olefin metathesis methodologies. Still needed, however, are more robust catalysts that could circumvent those

aspects of optimization directed at increasing turnover numbers. One of the most time-consuming steps in organometallic synthesis, however, is elucidation of the structure of the product. Identification of structures of decomposition products is even more demanding, although clearly central to understanding decomposition pathways and hence catalyst redesign. Complicating the latter, in metathesis as with other catalytic contexts, is the large excess of substrate normally present in catalytic reactions, which hampers (e.g.) NMR elucidation of structures for catalyst resting states, as well as decomposition products.⁶ A final major aspect of this thesis work therefore focuses on the application of "organometallic-friendly" conditions for MALDI-TOF mass spectrometric analysis of isolated organometallic complexes, including highly reactive catalysts, and of catalysts at work (MALDI = matrix-assisted laser desorption-ionization; TOF = time-of-flight). MALDI-MS analysis gives direct insight into "global" molecular composition, unlike all spectroscopic methods, each of which reports on a separate piece of the molecule, but not on the integrated whole.

Of particular interest is the capacity of this methodology to circumvent a common situation, which can be described as "adapting the problem to the method". Decomposition of organometallic catalysts, for example, is frequently assessed under NMR-friendly model conditions: in the absence of substrate, under a subset of (usually thermal) conditions, occasionally in the presence of suspected hazards or additives, such as dioxygen or alcohols (Scheme 1.2). Alternatively, serendipitous crystallization of decomposition products can permit X-ray analysis. The causal relationship is unclear in the latter case, while considerable discrepancies exist between conditions of assessment and operation, in the former. Nevertheless, the products thus identified can point toward decomposition pathways relevant to catalysis. In the context of olefin metathesis, formation of chloride-bridged dimers was invoked as a decomposition pathway for vinylalkylidene,⁸⁴ vinylidene,⁸⁵ and benzylidene systems,⁸⁶ and later emerged in studies of phosphonium alkylidene⁸⁷ and methyldiene⁸⁸ species (Scheme 1.2a-c). Unimolecular deactivation, proposed as a dominant feature for the methyldiene species,⁸⁹ may involve C-H activation of the ortho-methyl group of an IMes or H₂IMes ligand, resulting in loss of the alkylidene functionality (Scheme 1.2d).⁹⁰ On exposure to air in solution, all of these Ru(II) complexes undergo oxidation to Ru(III) species (notwithstanding their comparative robustness in the solid state). The rate of oxidation,

unsurprisingly, was found to increase on use of O₂ pressure for **Ru-1a** and **Ru-1c**^{91,92} (Scheme 1.2e). Primary alcohols attack the alkylidene functionality, eliminating the corresponding alkane and forming a ruthenium hydride (Scheme 1.2f) species.^{90,91} Diver has shown that π -acids (i.e. CO, NCR) induce a Buchner insertion of the benzylidene or methylidene into the NHC *N*-aryl group, followed by ring expansion (Scheme 1.2g).⁹³⁻⁹⁵ This behaviour was attributed to the increased electrophilicity of the carbene carbon. Reaction of the first-generation catalyst **Ru-1a** with CO or isocyanide ligands triggers insertion of the benzylidene into a Ru-P bond and formation of the phosphonium cation [PhCHPCy₃]⁺.⁹⁶

Most striking from these studies is the rapidity with which the benzylidene and, particularly, the methylidene species decompose even at relatively low temperatures. This is particularly important as metathesis reactions are commonly carried out at 80 °C or higher: the above suggests that the effective catalyst charge under such conditions will decline very rapidly.

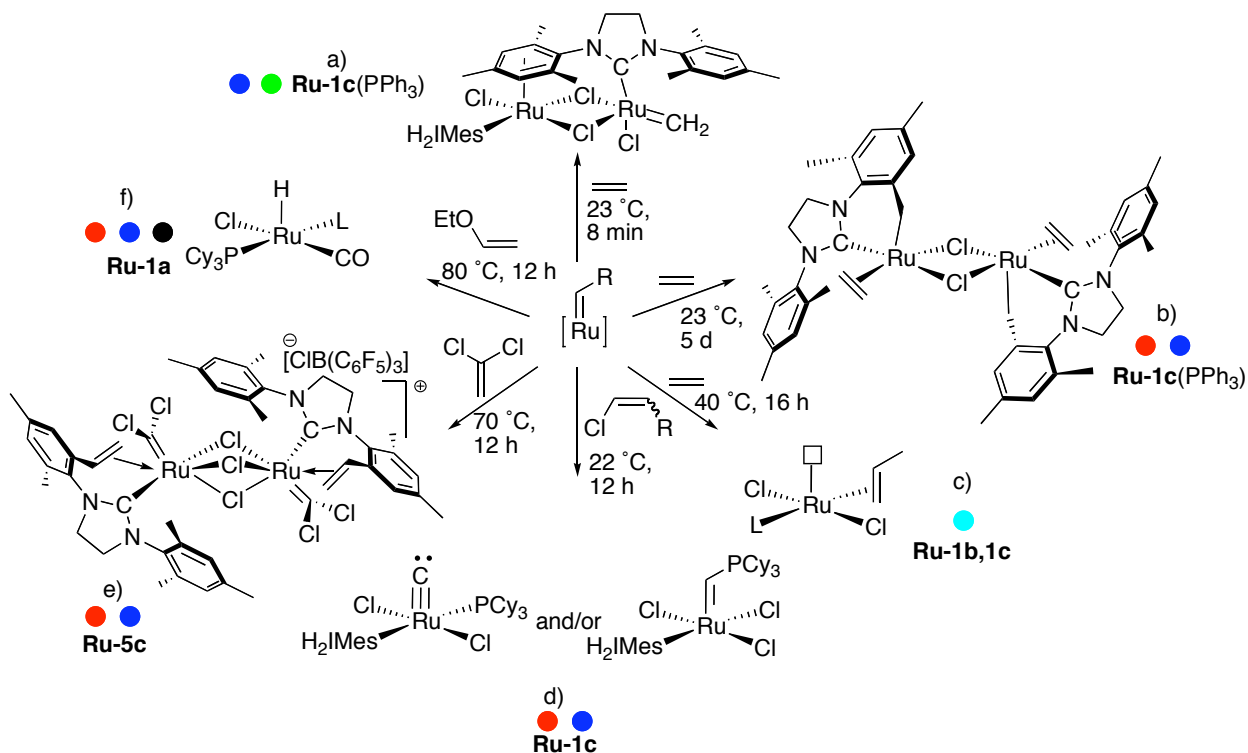


Scheme 1.2. Decomposition of ruthenium alkylidene precursors in the absence of an olefin. Compound numbers represent the starting ruthenium complex in the decomposition reaction. References are provided in the text. Coloured dots represent the analytical detection method: ●, NMR; ●, XRD; ●, IR.

As well as model conditions, model substrates are often employed in attempts to identify decomposition products under more catalytically relevant conditions. Ethylene is one such substrate of choice in metathesis, as it is gaseous and thus easily removed, and is also a coproduct of RCM and CM reactions. As a model for other olefins, however, it is limited in its steric and electronic relevance to typical metathesis substrates.⁹⁷ Catalyst turnover with ethylene affords a methyldene species that subsequently decomposes into dimers (Scheme 1.3a and b).⁹⁸ Interestingly, the observed products are different from the dimer that results from thermal decomposition of the methyldene (Scheme 1.2c). On the basis of DFT

calculations, the Sasol group suggested that reaction with ethylene can result in β -hydride elimination from the metallocyclobutane (Scheme 1.3c).⁹⁹ Experimental evidence supported propene formation, but no metal product was identified. Piers and co-workers have observed (NMR) in situ transformation of catalyst **Ru-5c** into the metallocyclobutane intermediate on reaction with ethylene or a cycloolefin.¹⁰⁰¹⁰¹ While low-temperature NMR studies provided insight into the nature of the intermediate and activation barriers associated with its reactivity, decomposition products were not elucidated; the differences between the experimental conditions and those operative during catalysis are also considerable.

Alternative "model" substrates are the vinyl halides: while these have been successfully subjected to cross-metathesis with sufficiently reactive coupling partners,¹⁰² they otherwise give low yields.¹⁰³ This is thought to be due to generation of a Fischer carbene intermediate which decomposes to ruthenium carbide or phosphonium-alkylidene products (Scheme 1.3d).¹⁰⁴ In other studies, C-H activation by the phosphonium alkylidene at 70 °C was proposed to account for an extra carbon in the mesityl groups, observed after trapping the reactive species with a vinyl halide to generate a chloride-bridged dimer (Scheme 1.3e)⁸⁷ or a ruthenium hydride complex (Scheme 1.3f).¹⁰⁵ While these studies provide valuable evidence for substrate-induced decomposition pathways, the relevance to more common substrates and conditions is unclear. Chapter 6 of this thesis will address methodologies that enable direct monitoring of ruthenium olefin metathesis catalysts with substrates of broader relevance, and under catalytic conditions.



Scheme 1.3. Decomposition of ruthenium alkylidene precursors in the presence of an olefin. Compound numbers represent the starting ruthenium complex in the decomposition reaction. References are provided in the text. Coloured dots represent the analytical detection method: ●, NMR; ●, XRD; ●, IR; ●, MS; ●, DFT (supporting evidence for low energy pathway).

1.8 Scope of This Thesis Work.

This thesis examines new methodologies for interrogation of catalyst performance and structure, as well as synthetic routes to new catalyst species. Chapter 3 will discuss the synthesis of a ruthenium complex with an unexpectedly strong bond to dinitrogen. Key structural features responsible for the unprecedentedly low lability of the N₂ ligand are discussed, and implications for dinitrogen activation. Synthesis of new Ru-binaphtholate catalysts for asymmetric olefin metathesis, which form a bridge between existing important molybdenum and ruthenium systems, are the focus of Chapter 4. Chapters 5 and 6 establish methods for catalyst interrogation from complementary perspectives: in Chapter 5, high-throughput experimentation protocols are adapted to support parallel interrogation of activity and selectivity over time, and several case studies are presented. Finally, Chapter 6 describes

the development of MALDI-TOF mass spectrometry as an exceptionally powerful tool for structural elucidation in organometallic chemistry, and use of these methodologies to create a new window on the operation of transition-metal catalysts under operating catalytic conditions.

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Chapter 2. Experimental Methods

2.1 General Procedures.

2.1.1 Reaction Conditions.

Reactions were carried out at room temperature under an N₂ atmosphere, using standard Schlenk techniques (23 °C), or glovebox techniques (ca. 23-25 °C). Temperature fluctuations in the glovebox were associated with circulating the atmosphere through the catalyst unit, in consequence of heat generated via the fan blower. Circulation was turned off when solvents were in use (i.e. open to the glovebox atmosphere); once the vessels containing them were sealed to minimize escape, the atmosphere was purged for 15 min before turning circulation on again. Glassware was cleaned by rinsing and scrubbing with solvents suitable to remove trace compounds present (usually with CH₂Cl₂, MeOH then acetone), then soaking overnight in a base bath (0.64 M KOH in ⁱPrOH with 5% v/v H₂O). The residual base was rinsed off with water, after which the glassware was passed through an acid bath (5%_{v/v} nitric acid solution in H₂O), rinsed with water, then acetone, and oven-dried (110 °C). Glass frits were not subjected to the base bath, but were rinsed with an appropriate solvent, and treated with a small amount of aqua regia, if required, to remove decomposed metal.

2.1.2 Reagents.

The following compounds were prepared according to literature procedures: RuHCl(PPh₃)₃ **Ru-6**,¹ RuCl₂(PPh₃)₃ **Ru-7**,² 1,3-bis-(2,4,6-trimethylphenyl)imidazol-2-ylidene (IMes),³ 1,3-bis-(2,4,6-trimethylphenyl)imidazolin-2-ylidene (H₂IMes),⁴ 1,3-bis-(2-methylphenyl)imidazolin-2-ylidene hydrochloride (H₂ITol•HCl),⁵ lutidinium BAr^F₄ (BAr^F₄ = 2,6-dimethylpyridinium tetrakis(bis-3,5-trifluoromethylphenyl)borate),⁶ diethyl 2,2-bis(2-methylallyl)malonate **2**,⁷ *N,N*-diallyl-*p*-toluene sulfonamide **3**,⁸ (1-allyloxy)-3-butenylbenzene **6**,⁹ (2-allyloxy)but-3-yn-2-ylbenzene **7**,¹⁰ hexa-5-enyl undec-10-enolate **8** (synthesized by Sebastien Monfette of this research group),¹¹ (1-(2-methylallyloxy)prop-2-yne-1,1-diyl)dibenzene **9** (synthesized by Jay Conrad of this research group), K₂(BINO),¹² 3,3'-dibromo-1,1'-binaphtholate,¹³ 3,3'-diphenyl-1,1'-binaphtholate,¹³ phenyldiazomethane,¹⁴ RuCl₂(PCy₃)₂(=CHPh) **Ru-1a**,¹⁵ RuCl₂(PCy₃)₂(=CH₂) **Ru-2a**,¹⁵ RuCl₂(PCy₃)(IMes)(=CHPh)

Ru-1b,¹⁶ $\text{RuCl}_2(\text{PCy}_3)(\text{H}_2\text{IMes})(=\text{CHPh})$ **Ru-1c**,⁴ $\text{RuCl}_2(\text{IPr})(\text{PCy}_3)(=\text{CHPh})$ **Ru-1d** (synthesized by Matthew Kotyk of this research group),¹⁷ $\text{RuCl}_2(\text{IMes})(\text{py})_2(=\text{CHPh})$ **Ru-3b**,¹⁸ $\text{RuCl}_2(\text{H}_2\text{IMes})(\text{py})_2(=\text{CHPh})$ **Ru-3c**,¹⁹ $\text{RuCl}_2(\text{PCy}_3)(\text{py})_2(=\text{CHPh})$ **Ru-3a**,²⁰ $\text{RuCl}_2(\text{H}_2\text{IMes})(=\text{CH}(\text{O}^i\text{Pr})\text{C}_6\text{H}_4)$ **Ru-4c**.²¹

Hydrated ruthenium chloride was obtained from Strem Chemicals, as was tricyclohexylphosphine (97%); the latter is highly air-sensitive, and the quality of PCy_3 purchased from Aldrich was very unreliable. The following reagents were purchased from Aldrich: diethyl diallylmalonate **1** (98%), anthracene (99%), 2,2'-bipyridyl **28** (>98%), 9-borabicyclononane (9-BBN; 98%), chlorocatechol borane **14** (97%), triphenylborane **15** (<2% H_2O),* *cis*-5-norbornene-*exo*-2,3-dicarboxylic anhydride **4** (95%), 1-adamantylamine **21** (97%), thiourea **23** (99%), tris(pentafluorophenyl)borane **24** (95%), ethylvinyl ether **25** (99%), diallylether **12** (99%), 2,2'-dipyridyl-*N*-oxide **29** (98%), lithium bis(trimethylsilyl)amide (97%), 1-methylimidazole **26** (99%), pentafluorophenol **35** (99%), pentabromophenol **36** (96%), 4-fluorophenol **34** (99%), 3,4,5,6-tetrabromobenzene-1,2-diol **38** (96%), potassium *tert*-butoxide (95%), pyrene (99%), silver triflate (>99%), sodium hydride (95%), styrene (>99%), terpyridine (>98.5%), *tert*-butylacetylene (98%), tetrahydronaphthalene (99%), thallium ethoxide (98%), 1,3,5-trimethoxybenzene (>99%). Other commercial reagents included: 1,1'-binaphtholate **19** (racemic BINOL, 99%; Alfa Aesar) and (*R*)-(+)-BINOL (99% optical purity; Strem), (*S*)-(–)-BINOL (99% optical purity; Strem), 3,3'-di-*tert*-butyl-5,5',6,6'-tetramethylbiphenyl-2,2'-diol **20** (99%, Strem), 3,4,5,6-tetrafluorobenzene-1,2-diol **37** (97%, Matrix Scientific), bis(cyclopentadienyl)cobalt (II) (98%, Acros), 3-bromopyridine (99%, Acros), CO (BOC Gases), D_2 (99.8%, CIL), $^{15}\text{N}_2$ (98%, CIL), potassium hydrotris(pyrazol-1-yl)borate **31** (98%, Strem),

2.1.3 Solvents.

All solvents used were reagent grade, with the exception of dichloromethane (manufacturers of the solvent purification system recommend use of HPLC grade CH_2Cl_2). Benzene, hexanes, dichloromethane, and tetrahydrofuran (unstabilized) were freed from oxygen and water using a Glass Contour solvent purification system, diethyl ether using an Anhydrous

* The purity of this reagent was not otherwise specified.

Engineering solvent purification system. Other solvents were purified and degassed by standard distillation:²² pyridine from CaH₂, methanol from fresh-cut sodium; pentane from sodium benzophenone ketyl. All solvents were stored over Linde 4 Å molecular sieves in the glovebox under N₂.

2.1.4 Deuterated Solvents.

Deuterated solvents were purchased from Cambridge Isotope Laboratories Ltd. or Aldrich. For analysis of organometallic complexes or catalytic reactions monitored by NMR spectroscopy, anhydrous ampoules of CD₂Cl₂, C₆D₆, toluene-*d*₈ and THF-*d*₈ were used as received. For larger-volume ampoules, where not all of the solvent was used at once, the remainder was stored over Linde 4 Å molecular sieves. CDCl₃ was distilled from CaH₂ and stored over activated Linde 4 Å molecular sieves under N₂. Before deuterated solvents were opened in the glovebox, the atmosphere was purged for at least 5 minutes to remove solvent vapours that could contaminate the NMR solvent.

2.1.5 NMR Spectroscopy.

¹H (300 or 500 MHz), ³¹P (121 or 202 MHz), ¹⁵N (30 MHz), ¹¹B (160 MHz) and ¹³C (126 MHz) NMR spectra were recorded at 296 K, unless otherwise stated. VT-NMR experiments were permitted to equilibrate at each temperature for at least 5 minutes prior to acquiring spectra. ¹H and ¹³C NMR spectra acquired for structural characterization (as opposed to reaction monitoring), as well as ¹¹B experiments, were recorded on a Bruker Avance 500 MHz instrument; all other spectra were recorded on a Bruker Avance 300 MHz spectrometer. The following chemical shift windows were used for routine acquisition: ¹H, +25 to –35 ppm; ¹³C, +200 to 0; ³¹P, +250 to –50 ppm; ¹⁵N, +500 to –100 ppm. For 2D ¹H-¹³C correlation experiments, a window of +320 to 0 ppm was used, and the number of acquisition slices in the F1 domain (TD: data acquisition size) were increased from 256 to 1024 to maximize resolution along the ¹³C axis. ¹H-¹⁵N HMQC experiments were optimized for 8 Hz coupling. Chemical shifts (δ) are reported in ppm relative to TMS (¹H, ¹³C), 85% H₃PO₄ (³¹P), BF₃•OEt₂ (¹¹B), or nitromethane (¹⁵N) at 0 ppm. Coupling constants are reported as absolute values in Hz. Acquisition parameters for quantitative ³¹P NMR analysis were set for prolonged acquisition times and recycle delays (aq = 2 sec and d1 = 6 sec), to permit

complete relaxation of **Ru-11'** between pulses. This compensates for the slow room temperature relaxation of **Ru-11'** (measured ($T_1 = 1.4$ sec at 300 MHz, 23 °C).

2.1.6 Gas Chromatography.

Conversion values for catalytic reactions were determined by gas chromatography (GC) using an Agilent 6850 Series II GC equipped with an flame ionization detector (FID), and a Agilent HP-1 methylsiloxane column. Analysis of reactions with 16-lactone **8** were carried out on an Agilent 6890 series GC instrument, again with FID detection, but using a Varian CP-Wax 52 CB Carbowax column to improve separation. Asymmetric induction, in asymmetric metathesis reactions, was assessed from the enantiomeric excess (% e.e. = $(R-S)/(R+S)*100$) measured for the products by GC-FID analysis, using an Agilent 6850 Series II GC with a chiral Astec B-DM column.

2.1.7 High-Throughput Experimentation.

These experiments were carried out using the High-Throughput Facility of the University of Ottawa's Centre for Catalysis Research & Innovation (CCRI). High-throughput screening reactions were set up using a Symyx Technologies Core Module, consisting of a Cavo MSP-9500 liquid-handling robot controlled by the Symyx Epoch software, and housed in an mBraun glovebox under N₂. Experimental libraries were constructed using the Symyx Library Studio software. The temperature was controlled by a Julabo Presto system. High-pressure reaction plates were sealed in reactor blocks rated to 1500 psi. Blocks were pressurized and placed in a Heated Orbital Shaker System for the duration of reaction. In accordance with safe handling practices, the maximum pressure (at operating temperatures) was maintained below 2/3 of the rated pressure maximum for the rupture disk assembly. When necessary, solvent was evaporated from a reaction plate with a Genevac EZ-2 Plus Vacuum Concentrator.

2.1.8 MALDI-TOF Mass Spectrometry.

Spectra were measured using a Bruker Daltonics Omnistar benchtop MALDI-TOF mass spectrometer interfaced to an mBraun glovebox, as described in Chapter 6. MALDI-TOF mass spectra were collected in positive reflectron mode, with the accelerating voltage held at 20 kV for all experiments. The laser power was maintained at the minimum required to

detect analyte signals. Matrix (pyrene or anthracene) solutions were prepared in CH_2Cl_2 , C_6H_6 or THF, at concentrations of 20 mg/mL. The concentration of analyte solutions varied depending on the experiment; values are tabulated in Section 2.13. These matrix and analyte solutions were mixed (typically using a five- to ten-fold excess by volume of the former; * for exact volumetric and molar ratios, see Section 2.13) and spotted in 1-3 μL aliquots on the target plate. Given the volatility of the solvents used, this can be regarded as an accelerated version of the dried-droplet method. The mass spectrometer was calibrated externally before each use with *trans*- $\text{RuCl}_2(\text{dppe})_2$, using the linear fit method. The two dominant signals, for $[\text{M}]^+$ and $[\text{M}-\text{Cl}]^+$ (m/z 968.11 and 933.14 Da, respectively), are within the mass window of interest. For all samples, 300-400 laser shots were collected and averaged.

2.1.9 UV-vis and CD Spectroscopy.

Stock solutions (2.5 mM) for each complex were prepared in an N_2 -filled glovebox by accurately weighing ca. 10 mg of the complex and dissolving the sample in an appropriate solvent using a gas-tight syringe. Fluctuations in mass accuracy were only observed in the fourth decimal point, particularly if the following precautions were taken: the circulation was turned off, a static eliminator was placed beside the balance and aluminum weigh-boats were used to minimize static (glass vials created greater fluctuations). Serial dilution into volumetric flasks afforded solutions of 10^{-4} or 10^{-5} M,** which were loaded into quartz cuvettes, fitted with a rubber septum, and sealed with Parafilm before bringing them out of the box and rapidly measuring their spectra. Complex **Ru-11''/11'** proved too air-sensitive for this method, but was satisfactorily analyzed using screw-cap quartz cuvettes borrowed from Prof. J.C. Scaiano of this department.

Electronic absorption and circular dichroism (CD) spectra were recorded on a Cary 100 spectrophotometer and a Jasco J-810 spectropolarimeter, respectively, access to which was graciously provided by Prof. J.C. Scaiano of this department. Minimum UV-vis absorbance values were determined by running a background spectrum without a cuvette, and maximum

* A preferable protocol would involve mixture of matrix and analyte in standard *molar* ratios. A molar excess of 100:1 (matrix to analyte) would be appropriate.

** The accuracy of these concentrations would be more reliable if the initial stock solution was also prepared in a volumetric flask instead of by dilution with a microlitre syringe.

absorbance values by blocking the beam. The absorbance due to the analyte was evaluated for both absorption and CD spectra by subtracting the absorbance due to the solvent, measured sequentially in spectroscopically-matched cuvettes.

2.1.10 Other Instrumentation.

IR spectra were measured on a Bomem MB100 IR spectrometer, access to which was kindly provided by Prof. S. Gambarotta of this department, using NaCl salt plates. Samples were analyzed as Nujol mulls. In the case of the dinitrogen complex described in Chapter 3, IR analyses were also performed on a Varian 640-IR FT-IR equipped with an attenuated total reflectance probe, and using a diamond-anvil Cell. Access to which was kindly provided by Prof. R.T. Baker of this department and Serge Briere of the RCMP Forensics Laboratory, respectively.

Combustion analyses (C, H, N) were carried out by Guelph Chemical Laboratories of Guelph, Ontario.

X-ray analyses were carried out by Dr. Robert McDonald of the University of Alberta X-Ray Crystallography Laboratory, or by Dr. Scott Dalgarno of the School of Engineering and Physical Sciences - Chemistry, Heriot-Watt University, Scotland. Crystallographic collection parameters and data are summarized in Appendix D.

DFT calculations were performed by Dr. Serge Gorelsky of the UO Centre for Catalysis Research & Innovation (CCRI), using the Gaussian 03 software package.²³ Stationary points on the potential-energy surface were obtained using the B3LYP hybrid density functional method.²⁴ Geometry optimizations were performed using the DZVP basis set²⁵ for all atoms. Tight SCF convergence criteria were used for all calculations. The converged wave functions were tested to confirm that they correspond to the ground-state surface. The second-order derivative of the energy with respect to nuclear positions was evaluated to determine the nature of the stationary points. Vibrational zero point energies (ZPE) and thermal corrections were included in the calculation of Gibbs free energies at 298K and 1 atm. Analysis of

molecular orbitals in terms of fragment orbital contributions were carried out using the AOMix program.²⁶

2.2 Ligand Synthesis.

2.2.1 Synthesis of Na₂(BINO).

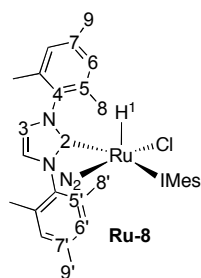
Addition of a suspension of NaH (38 mg, 1.58 mmol) Et₂O (2 mL) to a suspension of BINOL (204 mg, 0.713 mmol) in Et₂O (ca. 2 mL) caused immediate evolution of H₂ gas, and formation of a colourless suspension which was stirred for 45 min. A white powder was filtered off, washed with Et₂O (3 × 1 mL), and dried. Yield: 227 mg (98%).

2.2.2 Representative Procedure for the Synthesis of Tl Salts: Synthesis of Tl₂(BINO).

To a solution of TlOEt (967 mg, 3.88 mmol) and Et₂O (10 mL) in a disposable 20 mL vial was added solid, racemic BINOL (505 mg, 1.77 mmol). The resulting suspension was stirred for 18 h. A yellow solid was filtered off and washed with Et₂O (2 mL). Yield: 1.06 g (87%). Warning: Thallium is extremely toxic²⁷, and must be handled using secondary-containment procedures. Soaking contaminated glassware in hot water (or, if residues persists, with aqua regia) aids in removing thallium residues; both are disposed of (after neutralization if required) with the other thallium-contaminated solution and solid wastes.

2.3 Synthesis and Reaction Chemistry of Metal Complexes.

2.3.1 Synthesis of RuHCl(IMes)₂(N₂) **Ru-8**.



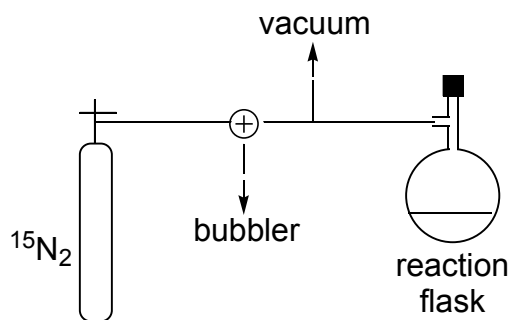
Solid IMes (359 mg, 1.812 mmol, 2.2 equiv) was added to a stirred suspension of clean **Ru-6** (496 mg, 0.537 mmol) in THF (9 mL) under N₂. Solid residues were washed down using a further 5-mL aliquot of THF. A colour change from pink-red to orange occurred over 20 h. ³¹P{¹H} NMR analysis after this time revealed only free PPh₃. The dark orange solution was filtered through Celite, and the filtrate was stripped to dryness and

taken up in hexanes (6 mL). The resulting suspension was chilled (−35 °C) and filtered. The orange solid was washed with cold hexanes (3 mL) and 3:1 hexanes:Et₂O (3 × 1 mL), and dried under vacuum. Yield: 309 mg (74%). It is important to note that starting **Ru-6** must be free of contaminating PPh₃. Extraction of residual phosphine from solid **Ru-8** by washing

with hexanes severely reduces isolated yields, owing to the partial solubility of **Ru-8** in hexanes. ^1H NMR (C_6D_6 , 500 MHz): δ 6.84 (s, H^6 , 4H), 6.82 (s, H^6 , 4H), 6.25 (s, H^3 , 4H), 2.34 (s, H^9 , 12H), 2.14-2.08 (br, H^8 , 24H), -28.03 (s, H^1 , 1H). At 203K, the signals for the mesityl CH protons (H^6) resolve fully into two singlets, and those for methyl groups (H^8 and H^9) into six singlets. $^{13}\text{C}\{^1\text{H}\}$ NMR (C_6D_6 , 126 MHz): δ 198.4 (s, C^2), 150.3 (s, C^4), 136.9 (s, C^7), 129.1 (s, C^6), 128.4 (s, C^5), 121.7 (s, C^3), 21.3 (s, C^9), 19.0 (br s, C^8). IR (Nujol): $\nu(\text{Ru-H})$, $\nu(\text{N}_2)$ 2041 cm^{-1} . CT-MALDI MS (pyrene), m/z : Calcd $[\text{M}+\text{H}]^+$ 775.3, Found 775.1; Calcd $[\text{M}-\text{N}_2-\text{H}_2]^+$ 744.3, Found, 744.3. Anal. Calcd. for $\text{C}_{42}\text{H}_{49}\text{ClN}_6\text{Ru}$: C, 65.14; H, 6.38; N, 10.85. Found: C, 65.22; H, 6.27; N, 10.78.

2.3.2 Synthesis of $\text{RuHCl}(\text{IMes})_2(^{15}\text{N}_2)$ (**Ru-8- $^{15}\text{N}_2$**).

The procedure above was followed with respect to concentrations, reagent proportions, and reaction times. The synthesis was carried out using 300 mg (0.325 mmol) of **Ru-6** in a thick-walled Kontes flask fitted with a Teflon valve. The suspension of **Ru-6** in THF was degassed by eight freeze-pump-thaw cycles to ensure complete removal of $^{14}\text{N}_2$. The flask was then attached to a T-joint with one arm leading to the vacuum line, and the second to a T-joint fitted with an oil bubbler and a lecture bottle of $^{15}\text{N}_2$ (Scheme 2.1). The line connecting the lecture bottle to the reaction flask was evacuated, the flask filled to 1 atm with $^{15}\text{N}_2$ (oil-bubbler control), and the solution was chilled to -131°C in a N_2 -pentane slush bath, to draw in a maximum amount of the isotopically-labeled gas. The flask was sealed and the solution stirred at 23°C for 20 h, prior to isolating the product as above. Yield: 132 mg (52%). ^1H NMR (C_6D_6 , 300 MHz): δ 6.85 (s, Ar- H , 4H), 6.82 (s, Ar- H , 4H), 6.25 (s, NCHCHN , 4H), 2.34 (s, $p\text{-CH}_3$, 12H), 2.16-2.08 (br m, $o\text{-CH}_3$, 24 H), -28.03 (d, $^2J_{\text{HN}} = 4$ Hz). $^{15}\text{N}\{^1\text{H}\}$ NMR (C_6D_6 , 30 MHz): δ -55.8 (d, $^1J_{\text{NN}} = 5$ Hz, N_β), -72.6 (d, $^1J_{\text{NN}} = 5$ Hz, N_α). IR (Nujol): $\nu(\text{Ru-H})$ 2039 cm^{-1} , $\nu(^{15}\text{N}\equiv^{15}\text{N})$ 1972 cm^{-1} . Note: We cannot exclude the possibility that the band at 2039 cm^{-1} reflects formation of **Ru-8** due to minor impurities of $^{14}\text{N}_2$ in the enriched gas (98%). Attempts to confirm assignment of $\nu(\text{Ru-H})$ by deuterium labeling were unsuccessful, but the DFT-calculated $\nu(\text{Ru-H})$ and $\nu(\text{N}\equiv\text{N})$ values are very close, at 2187 and 2174 cm^{-1} , respectively. (Such trends in calculated IR frequencies – that is relative values – are significant, although *absolute* values should be treated with caution, given the limited precision of current DFT methods for vibrational analyses.)²⁸

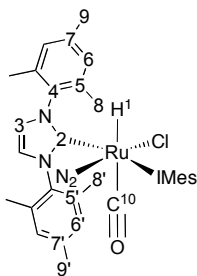


Scheme 2.1. Schematic of the set-up employed in the synthesis of **Ru-8-¹⁵N₂**.

2.3.3 Synthesis of **Ru-8** by Reaction of RuHCl(H₂)(IMes)₂ with N₂.

Solid, orange RuHCl(H₂)(IMes)₂ (8 mg, 0.011 mmol) was dissolved in C₆D₆ (0.75 mL) and stirred for 10 min in an N₂-filled glovebox. The vial was capped and the solution allowed to stir overnight. No colour change was observed, but analysis by ¹H NMR and CT-MALDI MS provided unequivocal evidence for complete conversion to **Ru-8**. (Reaction carried out by Nicholas Beach of this research group).

2.3.4 Synthesis of RuHCl(CO)(IMes)₂(N₂) **Ru-9**.



A solution of **Ru-8** (70 mg, 0.090 mmol) in C₆H₆ (2 mL) was degassed by three consecutive freeze-pump-thaw cycles, and allowed to thaw under an atmosphere of CO at room temperature. A colour change from orange to pale yellow was complete within 5 minutes. The solvent was stripped off to obtain a pale yellow solid. Yield 66 mg (90%). ¹H NMR (C₆D₆, 500 MHz): δ 6.77 (s, H⁶ or H^{6'}, 4H), 6.75 (s, H⁶ or H^{6'}, 4H), 6.13 (s, H³, 4H), 2.24 (s, H⁹, 6H), 2.15 (s, H⁸ or H^{8'}, 6H), 2.13 (s, H⁸ or H^{8'}, 6H), -3.26 (s, H¹, 1H). ¹³C{¹H} NMR (C₆D₆, 126 MHz): δ 195.0 (s, C¹⁰), 187.7 (s, C²), 139.4 (s, C⁴), 137.2 (s, C⁷), 136.7 (s, C⁵ or C^{5'}), 136.4 (s, C⁵ or C^{5'}), 129.43 (s, C⁶ or C^{6'}), 129.37 (s, C⁶ or C^{6'}), 123.2 (s, C³), 21.3 (s, C⁹), 18.81 (s, C⁸ or C^{8'}), 18.74 (s, C⁸ or C^{8'}). ¹³C NMR: 195.0 (d, ²J_{CH} = 49 Hz, CO), 187.7 (d, ²J_{CH} = 5 Hz, RuC_{NHC}). IR (Nujol): ν(N≡N), 2118 cm⁻¹; ν(Ru-H), 2039 cm⁻¹; ν(C≡O), 2005 cm⁻¹. Microanalysis is consistently poor, owing to the presence of RuHCl(CO)₂(IMes)₂ **Ru-10** in minor amounts (ca. 5%), and ligand loss on extended exposure to vacuum to remove trace solvent. Attempts to purify by reprecipitation were consistently contaminated with **Ru-10**.

2.3.5 In Situ Formation of $\text{RuHCl}(\text{CO})(\text{IMes})_2(\text{N}_2)$ **Ru-9** and $\text{RuHCl}(\text{CO})_2(\text{IMes})_2$ **Ru-10** from $\text{RuHCl}(\text{IMes})_2(\text{N}_2)$ **Ru-8**.

A solution of **Ru-8** (ca. 10 mg) in C_6D_6 (0.7 mL) was added to an NMR tube equipped with a J. Young valve under an atmosphere of N_2 . The tube was degassed by three consecutive freeze-pump-thaw cycles, and allowed to thaw under an atmosphere of CO. Upon shaking, the solution immediately turned light yellow from orange. ^1H NMR analysis (C_6D_6 , 300 MHz): **Ru-9** (95%), **Ru-10** (5%) (initial values measured at 23 °C; no change after 1 h). After 1.5 h at 65 °C: **Ru-9** (35%), **Ru-10** (65%).

2.3.6 Attempted Reduction of the N_2 Ligand in $\text{RuHCl}(\text{IMes})_2(\text{N}_2)$ **Ru-8** with Lutidinium BAr^{F}_4 and CoCp_2 .

In a glovebox, C_6H_6 (0.5 mL) was added to a mixture of solid CoCp_2 (15 mg, 80 μmol , 3.5 equiv) and lutidinium BAr^{F}_4 (79 mg, 81 μmol , 3.5 equiv) in a round-bottomed flask fitted with a vertically-mounted Teflon valve, and a side-arm terminating in a 24/40 ground-glass joint. To the flask was added a solution of **Ru-8** (18 mg, 23 μmol) in THF (0.5 mL), followed by an additional portion of THF (0.5 mL) to wash the solution from the side arm; the flask was then quickly sealed, transferred to an oil bath set to 50 °C, and stirred for 20 h. Reaction volatiles were then vacuum-transferred to a collection flask held at -131 °C (N_2 -pentane). To the collection flask had previously been added a commercial solution of HCl in dioxane (4 M), which was diluted with Et_2O to 1 M. The frozen contents of the collection flask were allowed to warm to 0 °C by replacing the slush bath with an ice bath, and the melted solution was stirred for at least 30 minutes to promote reaction between any NH_3 product, and HCl. To the sealed reaction flask was concurrently added KO^tBu (9 mg, 80 μmol , 3.5 equiv) in THF (0.5 mL), to cleave any metal-bound NH_3 ; this mixture was stirred for 10 minutes at 23 °C, after which the vacuum-transfer step was repeated. A known amount of trimethoxybenzene (TMB, used as internal standard; 400 μL of a 56.6 mM solution in THF) was then added to the collection flask, and the solvent was removed under vacuum. (Addition of the internal standard at this stage was chosen to avoid inaccuracies due to the anticipated inefficiency in its vacuum-transfer from the reaction flask; TMB boils at 255 °C). The residue was dissolved in $\text{DMSO}-d_6$ and analyzed by ^1H NMR spectroscopy. No evidence

of NH_4Cl formation was observed (δ DMSO: 7.48 ppm),²⁹ in two separate trials, nor in a third reaction carried out with **Ru-8**- $^{15}\text{N}_2$.

2.3.7 Attempted Protonation of the N_2 Ligand with Lutidinium BAr_4^{F} .

To a solution of lutidinium BAr_4^{F} (123 mg, 0.129 mmol) in C_6H_6 (4 mL) was added **Ru-8** (98 mg, 0.129 mmol), followed by 4 mL C_6H_6 . The solution was stirred for 3 h at 25 °C. Analysis of an NMR-scale reaction carried out under identical conditions indicated a shift in the hydride signal to -28.26 ppm, and a decrease in integration (total 73% relative to internal standard). Losses were assigned to paramagnetic decomposition. The product was isolated by stripping off the solvent, dissolving the residue in THF (0.5 mL) and adding hexanes (1 mL). The isolated orange solid was identical to starting **Ru-8**, exhibiting a hydride signal in the ^1H NMR spectrum at -28.05 ppm (C_6D_6), and an IR stretch for $\nu(\text{N}\equiv\text{N})$ at 2039 cm^{-1} (Nujol). ^1H - ^{15}N HMQC experiments showed only correlations due to **Ru-8**.

2.3.8 Attempted Formation of a Lewis Acid-Base Adduct with $\text{RuHCl}(\text{IMes})_2(\text{N}_2)$ **Ru-8** and $\text{B}(\text{C}_6\text{F}_5)_3$ in C_6D_6 .

Solid **Ru-8** (10 mg, 0.0129 mmol) was added to $\text{B}(\text{C}_6\text{F}_5)_3$ (13 mg, 0.0258 mmol, 2 equiv) in C_6D_6 (0.6 mL). An additional ca. 0.2 mL C_6D_6 were added to wash down solid from the sides of the NMR tube. The solution was left to stand for 45 minutes, after which a two-phase system was observed, consisting of a brown layer of greater density, and larger amounts of a dark yellow solution. ^1H NMR (C_6D_6): -8.88 (s, Ru-H). $^{11}\text{B}\{^1\text{H}\}$ NMR (C_6D_6): null signal, indicating that the unidentified boron-containing product is present in the shallow bottom layer, below the zone of the NMR observation coil. (The starting $\text{B}(\text{C}_6\text{F}_5)_3$ is benzene-soluble, and gives a broad ^{11}B NMR signal at 59.6 ppm). ^1H - ^{15}N HMQC: one hydride correlation, to the imidazol nitrogens. ^1H - ^{13}C HMBC: one hydride correlation, to the carbene carbon (187.7 ppm). IR (Nujol, cm^{-1}): 1644 (s).

2.3.9 Attempted Formation of a Lewis Acid-Base Adduct with $\text{RuHCl}(\text{IMes})_2(\text{N}_2)$ **Ru-8** and $\text{B}(\text{C}_6\text{F}_5)_3$ in CD_2Cl_2 .

Dissolution of **Ru-8** (20 mg, 0.0258 mmol) and $\text{B}(\text{C}_6\text{F}_5)_3$ (26 mg, 0.0516 mmol, 2 equiv) in CD_2Cl_2 (0.7 mL) afforded a dark brown solution. Immediate ^1H NMR analysis (new signals only): δ 2.38 (s, 3H, Mes *p*-Me), 2.11 (s, 6H, Mes *o*-Me) ppm (cf. values for **3** in CD_2Cl_2 :

2.47, *p*-Me; 1.75, *o*-Me). No new hydride signal was observed below 0 ppm. $^{11}\text{B}\{^1\text{H}\}$ NMR: δ -0.83 ppm (br). IR (Nujol): 2212 (w), 2163 (s), 1645 (s). IR (Nujol): 1644 (s), 1606 (w).

2.3.10 Attempted Hydroboration of the N_2 Ligand in $\text{RuHCl}(\text{IMes})_2(\text{N}_2)$ **Ru-8** with 9-BBN.

A solution of **Ru-8** (8.4 mg, 0.011 mmol) and TMB (1.0 mg, 0.0059 mmol) was prepared in C_6D_6 (0.7 mL), and a t_0 NMR spectrum was obtained. To this solution was added 0.5 equivalents of the 9-BBN dimer (2.6 mg, 0.00532 mmol), and the reaction was analyzed (^1H NMR) at 2 and 24 h. No new product, nor consumption of the starting hydride, was observed, and $^{11}\text{B}\{^1\text{H}\}$ NMR analysis was therefore not undertaken.

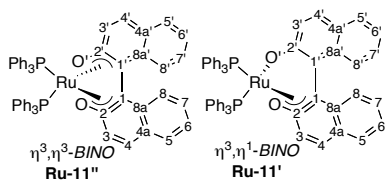
2.3.11 Attempted Reduction of $\text{RuHCl}(\text{IMes})_2(\text{N}_2)$ **Ru-8** with NaH.

To a stirred solution of NaH (2.0 mg, 0.078 mmol) in THF (0.5 mL) was added orange **Ru-8** (20.0 mg, 0.0258 mmol). An additional portion of THF (0.5 mL) was added to wash solid residues down the flask walls. No color change was observed either at this point, or over the ensuing 24 h at 25 °C. After this time, the solution was passed through a plug of glass-fiber filter paper to remove any salts present. The orange filtrate was stripped of solvent, and the residue redissolved in C_6D_6 . ^1H NMR (C_6D_6): only signals for **Ru-8** were observed. Formation of a paramagnetic products was deemed unlikely based on the excellent S/N ratio.

2.3.12 Attempted Nucleophilic Attack of $\text{RuHCl}(\text{IMes})_2(\text{N}_2)$ **Ru-8** with Succinyl Chloride.

A solution of **Ru-8** (10 mg, 0.0129 mmol) and TMB (0.2 mg, 1.4 μmol) was prepared in C_6D_6 (0.7 mL) and a t_0 NMR spectrum was obtained. Succinyl chloride (4 mg, 0.0258 mmol, 2 equiv) was added, and washed down with ca. 0.1 mL C_6D_6 . ^1H NMR analysis over 24 h: no new signals, but the integrated intensity of the hydride signal decreased (1 h, 96%; 4 h, 89%; 24 h, 79%), implying decomposition.

2.3.13 Synthesis of $\text{Ru}(\eta^3, \eta^3\text{-BINO})(\text{PPh}_3)_2$ **Ru-11''** and $\text{Ru}(\eta^3, \eta^1\text{-BINO})(\text{PPh}_3)_2$ **Ru-11'**.

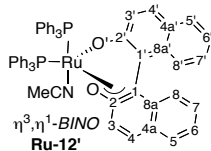


To a 50 mL Schlenk flask was added solid (*S*)- Ti_2BINO (326 mg, 0.470 mmol), $\text{RuCl}_2(\text{PPh}_3)_3$ **Ru-7** (450 mg, 0.470 mmol), and THF (6 mL). An additional portion of THF (6 mL) was added to wash down the walls of the flask. The

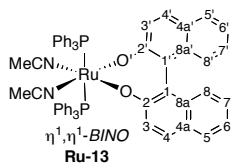
reaction was stirred for 1 h at 25 °C, during which time a colour change from purple to pink was observed. The suspensions in THF were very fine, impeding removal of TiCl₄. The solvent was therefore stripped to dryness, and the solid taken up in benzene. The suspension was filtered through Celite, then a glass-fiber plug, to remove thallium salts; product residues were washed through with additional C₆H₆ until the washings were clear. The combined washings were stripped to dryness and redissolved in a minimum volume of THF (ca. 0.5 mL). Addition of hexanes (6 mL) precipitated a reddish-pink solid, which was cooled (–35 °C), filtered off, washed with cold hexanes (3 mL) and cold 3:1 hexanes:Et₂O (3 × 1 mL), and dried. The product was identified as two isomers, η^3, η^3 -*BINO Ru-11''* and η^3, η^1 -*BINO Ru-11'*. Yield: 351 mg (82%). η^3, η^3 -*BINO Ru-11''*: ¹H NMR (CD₂Cl₂, 500 MHz): δ 7.38 (m, H⁵ and H⁶, 4H), 7.34 (d, ³J_{H₄H₃} = 9.3 Hz, H⁴, 2H), 7.26 (m, H⁷, 2H), 7.22–7.06 (m, P(C₆H₅)₃), 6.91 (m, H⁸ and P(C₆H₅)₃), 6.44 (d, ³J_{H₃H₄} = 9.3 Hz, H³, 2H). ¹³C{¹H} NMR (CD₂Cl₂, 126 MHz): δ 144.7 (s, C²), 137.8 (s, C^{8a}), 137.4 (s, C⁴), 134.6 (d, J_{CP} = 10 Hz, P(C₆H₅)₃), 134.1 (br, P(C₆H₅)₃), 133.8 (d, J_{CP} = 10 Hz, P(C₆H₅)₃), 132.3 (d, J_{CP} = 10 Hz, P(C₆H₅)₃), 132.2 (d, J_{CP} = 4 Hz, P(C₆H₅)₃), 130.9 (s, C^{4a}), 130.2 (d, J_{CP} = 1 Hz, P(C₆H₅)₃), 129.4 (s, C⁵), 129.2 (br, P(C₆H₅)₃), 128.1 (d, J_{CP} = 6 Hz, P(C₆H₅)₃), 128.0 (d, J_{CP} = 6 Hz, P(C₆H₅)₃), 127.4 (s, C⁷), 127.3 (m, P(C₆H₅)₃), 124.9 (s, C⁸), 124.5 (s, C⁶), 124.3 (s, C³), 93.2 (t, ²J_{CIP} = 4 Hz, C¹). ³¹P{¹H} NMR (CD₂Cl₂ 121 MHz): δ 56.9 (s).

η^3, η^1 -*BINO Ru-11'*: ¹H NMR (CD₂Cl₂, 500 MHz): δ 8.17 (d, ³J_{H₄H₃} = 9 Hz, H⁴), 7.89 (d, ³J_{H₅H₆} = 8 Hz, H⁵), 7.55 (H⁵), 7.29 (H³), 7.45 (H⁴), 7.27 (H⁶), 6.88 (H³), 6.86 (H⁶), 6.70 (H⁷ and H⁷), 6.57 (H⁸), 5.96 (d, ³J_{H₈H₇} = 9 Hz, H⁸). ¹³C{¹H} NMR (CD₂Cl₂, 126 MHz): δ 170.4 (d, ³J_{CP} = 5 Hz, C²), 143.1 (s, C²), 141.3 (d, ³J_{CP} = 3 Hz, C^{8a}), 135.1 (s, C⁴), 134.6 (s, C^{8a}), 129.6 (s, C⁸), 128.9 (s, C⁴), 128.8 (s, C^{4a}), 128.6 (s, C⁵), 128.2 (s, C⁵), 127.4 (s, C⁷), 127.2 (s, C^{4a}), 124.9 (s, C⁷), 124.6 (s, C⁶), 124.4 (s, C³), 124.2 (s, C⁸), 123.9 (s, C³), 119.8 (s, C⁶), 114.2 (d, ³J_{CP} = 2 Hz, C¹), 109.1 (d, ³J_{CP} = 16 Hz, C¹). ³¹P{¹H} NMR (CD₂Cl₂ 121 MHz): δ 43.5 (s); at 288 K, 43.7, 43.3 (AB, ²J_{pp} = 19 Hz).

CT-MALDI MS (pyrene), *m/z*: Calcd [M]⁺ 910.2, Found 910.2; Calcd [M-PPh₃]⁺ 648.1, Found 648.2. Anal. Calcd. for C₅₆H₄₂O₂P₂Ru: C, 73.92; H, 4.65. Found: C, 74.23; H, 4.38.

2.3.14 Synthesis of $\text{Ru}(\eta^3, \eta^1\text{-BINO})(\text{MeCN})(\text{PPh}_3)_2$ **Ru-12'**.

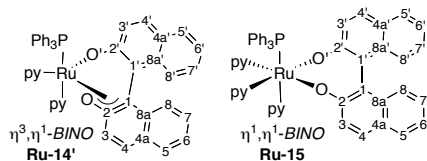
Addition of acetonitrile (0.5 mL) to solid **Ru-11'**/**11''** (151 mg, 0.166 mmol) did not completely dissolve the sample, but resulted in an immediate colour change from red to orange. Parallel analysis of **Ru-11'**/**11''** in 3:1 $\text{C}_6\text{D}_6\text{-CD}_3\text{CN}$ (low solubility precluded analysis in neat CD_3CN) revealed complete conversion to bis-nitrile, $\eta^1, \eta^1\text{-BINO}$ complex **Ru-13**; as the proportion of CD_3CN decreased, signals for the mono-acetonitrile adduct **Ru-12'** emerged. The suspension was stirred for 5 minutes, after which the solvent was stripped off under vacuum. The residue was stirred with cold hexanes (2 mL) and chilled to -35°C , after which the supernatant was removed by pipette and the solid was dried under vacuum. Work-up conditions for this reaction were kindly optimized by Carolyn Higman of this research group. Yield: 120.5 mg (76%). ^1H NMR (CD_2Cl_2 , 500 MHz): δ 8.00 (d, $J_{\text{H}_4\text{H}_3} = 9.5$ Hz, H^4 , 1H), 7.81 (d, $J_{\text{H}_5\text{H}_6} = 7.5$ Hz, H^5 , 1H), 7.57-7.51 (m, $\text{H}^{5'}$ and PPh_3 , 8H), 7.40 (d, $J_{\text{H}^4\text{H}^{3'}} = 8.5$ Hz, $\text{H}^{4'}$, 1H), 7.28-7.25 (m, 3H), 7.19 (d, $J_{\text{H}_3\text{H}_4} = 9.0$ Hz, H^3 , 1H), 7.17 (m, H^6 , 1H), 7.14-7.11 (m, PPh_3 , 10H), 6.92-6.89 (m, $\text{H}^{3'}$ and PPh_3 , 7H), 6.80 (m, H^6 , 1H), 6.66 (m, $\text{H}^{7'}$, 1H), 6.62 (m, H^7 , 1H), 6.58 (d, $^3J_{\text{H}_8\text{H}^7} = 5.0$ Hz, H^8 , 1H), 6.55-6.51 (m, PPh_3 , 6H), 5.91 (d, $J_{\text{H}_8\text{H}^{7'}} = 8.5$ Hz, $\text{H}^{8'}$, 1H), 1.37 (s, CH_3CN , 3H). $^{13}\text{C}\{^1\text{H}\}$ NMR (CD_2Cl_2 , 126 MHz): δ 172.1 (d, $J_{\text{CP}} = 5$ Hz, $\text{C}^{2'}$), 143.3 (d, $J_{\text{CP}} = 2$ Hz, C^2), 142.3 (d, $J_{\text{CP}} = 2$ Hz, C^{8a}), 134.8 (s, $\text{C}^{8a'}$), 134.65 (d, $J_{\text{CP}} = 8.8$ Hz, PPh_3), 133.8 (d, $J_{\text{CP}} = 10.0$ Hz, PPh_3), 133.1 (s, C^4), 129.9 (s, C^3), 129.4 (s, C^8), 128.8 (s, C^{4a}), 128.7 (s, $\text{C}^{4'}$), 128.3 (s, C^5), 127.9 (m, $\text{C}^{5'}$ and PPh_3), 126.9 (s, C^7), 126.8 (s, $\text{C}^{4a'}$), 124.6 (s, C^7), 124.5 (s, $\text{C}^{3'}$), 123.9 (s, $\text{C}^{8'}$), 123.3 (s, C^6), 120.3 (s, CH_3CN), 118.9 (s, C^6), 115.2 (d, $^2J_{\text{CP}} = 1$ Hz, $\text{C}^{1'}$, 1H), 106.4 (d, $^2J_{\text{CP}} = 15$ Hz, C^1 , 1H), 3.41 (s, CH_3CN). $^{31}\text{P}\{^1\text{H}\}$ NMR (CD_2Cl_2 , 121 MHz): δ 49.1 (d, $^2J_{\text{PP}} = 22$ Hz), 48.3 (d, $^2J_{\text{PP}} = 22$ Hz). IR (Nujol): $\nu(\text{C}\equiv\text{N})$ 2263 cm^{-1} (w). Anal. Calcd. for $\text{C}_{58}\text{H}_{45}\text{NO}_2\text{P}_2\text{Ru}$: C, 73.25; H, 4.77; N, 1.47. Found: C, 72.97; H, 4.61; N, 1.20.

2.3.15 In Situ Formation of $\text{Ru}(\eta^1, \eta^1\text{-BINO})(\text{MeCN})_2(\text{PPh}_3)_2$ **Ru-13**.

A solution of **Ru-11'**/**11''** (14.0 mg, 0.0154 mmol) and O=PPh_3 (2.0 mg, 7.69 μmol ; internal standard for ^{31}P NMR integration) in C_6D_6 (0.700 mL) was analyzed by ^1H and $^{31}\text{P}\{^1\text{H}\}$ NMR for t_0 integration values. Half the solution was placed in a 4 mL vial, to which MeCN (20 μL , 54

equiv) and additional C_6D_6 (0.350 mL) were added. (The second half of the solution was used for reaction with CO, which generated several unidentified products and was not further interrogated). The sample was analyzed by 1H and $^{31}P\{^1H\}$ NMR following addition of increasing amounts of MeCN. Consumption of **Ru-11'/11''** was complete within 5 min following addition of the first 20 μL aliquot of MeCN, resulting in a mixture of mono- and bis-nitrile adducts **Ru-12** and **Ru-13**. Relative proportions of **Ru-12** : **Ru-13** formed, as a function of the volume of added MeCN, are as follows: 20 μL , 3:1; 40 μL , 1.1:1; 80 μL , 1:1.3; 160 μL 1:2. In situ characterization of η^1, η^1 -*BINO* **Ru-13** is given in 30% v/v MeCN- d_3 in C_6D_6 , in which 10% of η^3, η^1 -*BINO* **Ru-12** is also present. 1H NMR (30% v/v MeCN- d_3 in C_6D_6 , 500 MHz): δ 7.56 (d, $^3J_{H_5H_6} = 8$ Hz, H^5 , 2H), 7.41 (m, PPh_3), 7.20 (d, $^3J_{H_4H_3} = 9$ Hz, H^4 , 2H), 7.00 (d, $^3J_{H_8H_7} = 8$ Hz, H^8 , 2H), 6.96 (m, PPh_3), 6.79 (m, H^7 , 2H), 6.90 (m, H^6 , 2H), 6.12 (d, $^3J_{H_3H_4} = 9$ Hz, H^3 , 2H), 1.35 (m, CH_3CN , 3H) $^{13}C\{^1H\}$ NMR (30% v/v MeCN- d_3 in C_6D_6 , 126 MHz): δ 168.9 (s, C^2), 135.9 (s, C^{8a}), 134.7 (m, PPh_3), 129.1 (s, C^3), 128.4-127.6 (overlap of residual C_6H_6 , PPh_3 , 128.3 (C^{4a}) and 127.6 (C^5); locations of the latter two were identified by correlation experiments), 127.4 (s, C^1), 126.8 (s), 125.4 (s, C^8), 125.0 (br s, C^4), 123.9 (s, C^7), 119.3 (s, C^6), 116.9 (s, CH_3CN), 0.3 (s, CH_3CN). $^{31}P\{^1H\}$ NMR (30% v/v MeCN- d_3 in C_6D_6 , 121 MHz): δ 47.0 (d, $^2J_{pp} = 22$ Hz), 45.8 (d, $^2J_{pp} = 22$ Hz) **Ru-12'**; 45.5 (s) **Ru-13**.

2.3.16 Synthesis of $Ru(\eta^3, \eta^1$ -*BINO*)(PPh_3)(py) $_2$ **Ru-14'** and $Ru(\eta^1, \eta^1$ -*BINO*)(PPh_3)(py) $_3$ **Ru-15**.



Addition of ca. 10 drops of pyridine (ca. 0.1 mL) to solid **Ru-11'/11''** (42 mg, 0.046 mmol) dissolved the complex and caused an immediate colour change from red to orange. (A parallel $^{31}P\{^1H\}$ NMR experiment in which

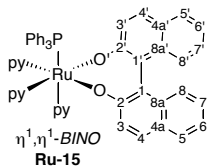
Ru-11'/11'' was analyzed in neat pyridine- d_5 indicated complete conversion to $Ru(\eta^1, \eta^1$ -*BINO*)(PPh_3)(py) $_3$ **Ru-15**). Pyridine was removed under vacuum to give an oily solid. Addition of hexanes (1 mL), with stirring, gave a suspension with an orange powder. Solvent was removed under vacuum in an attempt to remove any dissociated pyridine from the mixture. Pentane (1 mL) was added to give a fine suspension, which was filtered off and washed with cold pentane to give a bright orange solid (62 mg, 76%). Work-up conditions

were kindly optimized by Carolyn Higman of this research group. $^{31}\text{P}\{^1\text{H}\}$ NMR analysis indicated that the isolated solid consisted of **Ru-14'** and **Ru-15**, in a 4:1 ratio. Attempts to generate solely **Ru-14'** by repeated evaporation and precipitation to remove all free or labile pyridine consistently yielded **Ru-15**. However, X-ray analysis of crystals that deposited from the THF solution by vapour diffusion of Et_2O , revealed **Ru-14'** (Appendix D). Signals for the BINO ligand of **Ru-14'** could not be located by $^{13}\text{C}\{^1\text{H}\}$ NMR analysis at 23 °C, suggesting that the structure is fluxional in solution at this temperature. On cooling to –20 °C, considerable sharpening of the BINO signals was evident, but other signals remained broad: the latter are assigned to the pyridine ligands. On further cooling (–40 to –80 °C), signals emerged for a third species ($^{31}\text{P}\{^1\text{H}\}$ NMR: δ 48.3 ppm, s) which is assigned to $\text{Ru}(\eta^1, \eta^1\text{-BINO})(\text{PPh}_3)(\text{py})_2$ by analogy to the isomerization of $\eta^3, \eta^3\text{-BINO Ru-11'}$ to $\eta^3, \eta^1\text{-BINO Ru-11'}$ on cooling. To simplify this complex spectrum, characterization of **Ru-14'** was undertaken at –20 °C, i.e. with ca. 20% **Ru-15** present, but none of the $\text{Ru}(\eta^1, \eta^1\text{-BINO})(\text{PPh}_3)(\text{py})_2$ species. Characterization of $\eta^3, \eta^1\text{-BINO Ru-14'}$ and $\eta^1, \eta^1\text{-BINO Ru-15}$: ^1H NMR (CD_2Cl_2 , 500 MHz, 253 K): δ 8.93 (d, $^3J_{\text{HH}} = 5$ Hz, 1H), 8.75 (d, $^3J_{\text{HH}} = 6$ Hz, 1H), 8.58-8.57 (m, 3H), 8.15 (d, $^3J_{\text{HH}} = 5$ Hz, 1H), 7.92 (d, $^3J_{\text{HH}} = 4$ Hz, 2H), 7.67 (t, $^3J_{\text{HH}} = 8$ Hz, 2H), 7.61 (br s, 1H), 7.55-7.47 (m, including $\text{H}^{5'}$ and H^7 , 10H), 7.41 (d, $^3J_{\text{HH}} = 8$ Hz, **Ru-14'** H^4 , 1H), 7.36 (t, $J = 8$ Hz, 4H), 7.29-7.23 (m, 9H), 7.16-7.12 (m, 13H), 7.04-7.00 (m, including **Ru-14'** H^4 , 1.5H), 6.97 (d, $^3J_{\text{HH}} = 9$ Hz, **Ru-15** H^4 , 0.5H), 6.94-6.80 (m, including **Ru-14'** $\text{H}^{3'}$, **Ru-14'** $\text{H}^{6'}$ and **Ru-15** H^4 , 5H), 6.74-6.65 (m, including **Ru-14'** H^7 , 2H), 6.59 (t, $J = 7$ Hz, 2.2H), 6.54 (br s), 6.50-6.45 (m, 2H), 6.40 (br s), 6.24 (t, $^3J_{\text{HH}} = 6$ Hz, 0.6H), 6.09 (d, $^3J_{\text{H}^3\text{H}^4} = 9$ Hz, **Ru-14'** H^3 , 1H), 5.91 (br d, $^3J_{\text{H}^8\text{H}^7} = 9$ Hz, **Ru-14'** H^8 , 1H). $^{13}\text{C}\{^1\text{H}\}$ NMR (CD_2Cl_2 , 126 MHz, 253 K): δ 174.4 (d, $^3J_{\text{CP}} = 5$ Hz $\text{C}^{2'}$), 158.4 (s), 158.0 (s), 157.1 (s), 155.8 (s), 154.7 (br s), 152.8 (s), 149.9 (s), 143.5 (s, C^2), 142.0 (s, C^{8a}), 137.2 (s), 136.0 (s), 135.7 (s), 135.2 (s, $\text{C}^{8a'}$), 135.0 (s), 134.8 (s), 134.4 (d, $J_{\text{CP}} = 9$ Hz), 134.2-134.1 (m), 133.9 (s), 133.7 (d, $J_{\text{CP}} = 19$ Hz), 133.5 (s), 133.4 (s, C^4), 133.1 (s), 133.0 (s), 132.1 (s), 132.0 (s), 132.0 (s), 131.9 (s), 129.2 (s), 128.9 (s), 128.6 (d, $J_{\text{CP}} = 7$ Hz), 128.0-127.9 (m, including $\text{C}^{4'}$ and $\text{C}^{5'}$), 127.8 (s), 127.7 (s, $\text{C}^{5'}$), 127.6 (s), 127.4 (s), 127.2 (s), 126.8 (s, C^{4a}), 126.7 (s), 126.69 (s), 126.6 (s), 126.5 (s), 125.9 (s), 125.4 (s, C^3), 125.3 (s), 124.7 (s, C^7), 124.3 (d, $J_{\text{CP}} = 2$ Hz, $\text{C}^{3'}$), 124.2 (s), 123.8 (s), 123.7 (s), 123.6 (s), 123.5 (s), 123.1 (s), 123.0 (s), 122.6 (s, C^8), 122.2 (br s), 119.3 (s), 119.1 (s), 118.7 (s, C^6), 113.8 (s, $\text{C}^{1'}$), 97.6 (d, $^2J_{\text{CP}} = 19$ Hz, C^1).

$^{31}\text{P}\{^1\text{H}\}$ NMR (CH_2Cl_2 with 20 μL C_6D_6 for lock, 121 MHz, 296 K): δ 58.3 (br s). Anal. Calcd. for $\text{C}_{48}\text{H}_{37}\text{N}_2\text{O}_2\text{PRu}$; sample obtained by crushing and drying crystals grown from THF by diffusion of Et_2O : C, 71.54; H, 4.63; N, 3.48. Found: C, 71.26; H, 4.37; N, 3.15.

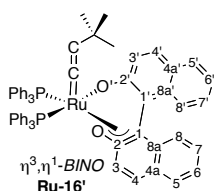
Diagnostic NMR signals for η^1, η^1 -*BINO* **Ru-15** in CD_2Cl_2 are given (see Section 2.4.5 for characterization in $\text{C}_5\text{D}_5\text{N}$): ^1H NMR (CD_2Cl_2 , 500 MHz, 296 K): δ 6.97 (H^4), 6.91 ($\text{H}^{4'}$); $^{13}\text{C}\{^1\text{H}\}$ NMR (CD_2Cl_2 , 126 MHz, 296 K): δ 169.8 (s, C^2), 168.7 (s, $\text{C}^{2'}$). $^{31}\text{P}\{^1\text{H}\}$ NMR (CH_2Cl_2 with 20 μL C_6D_6 for lock, 121 MHz, 296 K): δ 56.1 (s).

2.3.17 In Situ Formation of $\text{Ru}(\eta^1, \eta^1\text{-BINO})(\text{PPh}_3)(\text{py})_3$ **Ru-15**.



A solution of **Ru-11'**/**11''** (14 mg, 0.015 mmol) in pyridine- d_5 (0.7 mL), analyzed within 5 min, revealed complete conversion to **Ru-15** by $^{31}\text{P}\{^1\text{H}\}$ NMR analysis. Structural characterization was undertaken, but complete NMR assignment was hindered by overlapping signals due to residual protio-pyridine. Diagnostic values are given where assignment was possible. ^1H NMR ($\text{C}_5\text{D}_5\text{N}$, 500 MHz): δ 7.78-7.68 (m), 7.58 (br s), 7.50-7.42 (m), 7.38-7.34 (m, including H^4), 7.31-7.25 (m, including $\text{H}^{4'}$), 7.22 (br s), 7.20-7.04 (m), 6.97-6.83 (m, including H^3 and $\text{H}^{3'}$). $^{13}\text{C}\{^1\text{H}\}$ NMR ($\text{C}_5\text{D}_5\text{N}$, 126 MHz): δ 171.0 (s, C^2), 169.7 (s, $\text{C}^{2'}$), 137.9 (s), 137.8 (s), 136.9 (s), 136.3 (s), 136.0 (s), 135.9 (s), 135.1 (s), 134.9 (s), 134.8 (s), 134.2 (s), 134.1 (s), 132.4 (s), 132.3(s), 132.2 (s), 132.16 (s), 129.2 (s), 129.1 (s), 129.0 (s), 129.01 (s), 128.9 (s), 128.42-128.35 (m), 128.2 (s), 128.1 (s, C^1), 128.06 (s), 127.94-127.90 (m), 127.8 (s, $\text{C}^{1'}$), 127.6 (s), 127.5 (s, C^3), 127.1 (s), 126.1 (s), 126.0 (s), 125.8 (s), 125.6 (s), 124.1 (s), 123.9 (s), 123.8-123.3 (overlapping signals for residual $\text{C}_5\text{H}_5\text{N}$ and 123.5 (C^3); the latter located by correlation experiments), 123.1 (s), 119.8 (s), 119.5 (s); $^{31}\text{P}\{^1\text{H}\}$ NMR ($\text{C}_5\text{D}_5\text{N}$, 121 MHz): δ 57.3 (s).

2.3.18 Synthesis of $\text{Ru}(\eta^3, \eta^1\text{-BINO})(\text{PPh}_3)_2(\text{C}=\text{CH}^t\text{Bu})$ **Ru-16'**.



Slow, dropwise addition of a solution (16.6% v/v in C_6H_6) of tert-butylacetylene (2 equiv) to solution of **Ru-11'**/**11''** (46.5 mg, 0.051 mmol) in C_6H_6 (1 mL) caused an immediate color change from red to purple. The

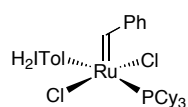
solution was stirred for 5 min, then stripped of volatiles. The residue was dissolved in THF (0.3 mL) and the purple product precipitated by addition of hexanes (4 mL). The reaction was cooled (-35°C), and the product was filtered off and washed with cold hexanes (3×0.3 mL). Low yields reflect the partial solubility of **Ru-16'** in hexanes and pentane even at -35°C . These optimized reaction conditions were kindly developed by Carolyn Higman of this research group. Yield: 23 mg (45%) ^1H NMR (CD_2Cl_2 , 500 MHz, 213 K): δ 8.53 (d, $^3J_{\text{H}3\text{H}4} = 9$ Hz, H^3), 8.01 (d, $^3J_{\text{H}4\text{H}3} = 9$ Hz, H^4), 7.90 (d, $^3J_{\text{H}5\text{H}6} = 8$ Hz, H^5), 7.66 (d, $^3J_{\text{H}5'\text{H}6'} = 8$ Hz, $\text{H}^{5'}$), 7.56 (d, $^3J_{\text{H}4'\text{H}3'} = 9$ Hz, $\text{H}^{4'}$), 7.45-7.30 (m, PPh_3), 7.35 (m, H^6), 7.12 (m, PPh_3), 7.00 (m, $\text{H}^{6'}$, H^7 , H^8 and $\text{H}^{8'}$), 6.91 (m, $\text{H}^{7'}$), 6.84 (m, $\text{H}^{3'}$ and PPh_3), 3.08 (br s, $\text{Ru}=\text{C}=\text{CHC}(\text{CH}_3)_3$), 1H) 0.72 (s, $\text{Ru}=\text{C}=\text{CHC}(\text{CH}_3)_3$), 9H). $^{13}\text{C}\{^1\text{H}\}$ NMR (CD_2Cl_2 , 126 MHz, 213 K): δ 347.2 ($\text{Ru}=\text{C}=\text{CHC}(\text{CH}_3)_3$), 162.0 (s, C^2), 148.0 (m, $J_{\text{CP}} = 3$ Hz, C^2), 135.3 (s, C^{8a}), 134.0-133.0 (m, PPh_3 , $\text{C}^{8a'}$), 132.7 (s, PPh_3), 132.3 (s, PPh_3), 130.8 (s, C^3), 130.2 (s, PPh_3), 129.1 (s), 128.8 (s, C^{4a}), 128.1 (s, PPh_3), 127.9 (s, C^4), 127.8 – 127.1 (C^8 , $\text{C}^{8'}$, C^5 , $\text{C}^{5'}$ and PPh_3), 126.6 (m, $\text{C}^{4'}$), 126.1 (s, $\text{C}^{4a'}$), 126.0 (s), 125.6 (m, $J_{\text{CP}} = 4$ Hz, C^1), 125.0 (s, C^7), 124.3 (s, C^7), 123.6 (s, C^3), 122.8 (s, C^6), 121.1 (s, $\text{Ru}=\text{C}=\text{CHC}(\text{CH}_3)_3$), 119.8 (s, C^6), 116.0 (s, $\text{C}^{1'}$), 67.6 (s, $\text{Ru}=\text{C}=\text{CHC}(\text{CH}_3)_3$), 30.9 (s, $\text{Ru}=\text{C}=\text{CHC}(\text{CH}_3)_3$). $^{31}\text{P}\{^1\text{H}\}$ NMR (CD_2Cl_2 , 121 MHz): δ 64.4 ($^2J_{\text{PP}} = 27$ Hz), 38.3 ($^2J_{\text{PP}} = 27$ Hz). IR: $\nu(\text{C}=\text{C})$ 1633 cm^{-1} . Anal. Calcd. for $\text{C}_{62}\text{H}_{52}\text{O}_2\text{P}_2\text{Ru}$: C, 75.06; H, 5.28. Found: C, 75.08; H, 5.41.

2.3.19 Optimized Synthesis of $\text{Ru}(\text{BINO})(\text{py})_2(=\text{CHPh})$ **Ru-17**.

To a stirred solution of red **Ru-11'/11''** (120 mg, 0.132 mmol) in 5 mL of 4:1 CH_2Cl_2 :pyridine was added, dropwise, a solution of phenyldiazomethane (34.36 mg, 0.29 mmol, 2.2 equiv) in CH_2Cl_2 (0.5 mL). A brown solution was observed after 5 minutes. $^{31}\text{P}\{^1\text{H}\}$ and ^1H NMR analysis indicated complete conversion to **Ru-17**. The reaction was stripped of solvent, and the residue redissolved in a minimum of THF (ca. 0.5 mL). Pentane (2 mL) was added to precipitate a brown solid, after filtering and washing with hexane (3×1 mL). Yield: 71.9 mg (86%). These optimized reaction conditions were kindly developed by Carolyn Higman of this research group.

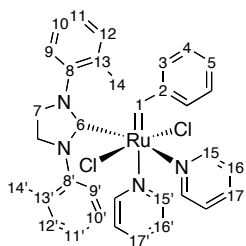
2.3.20 Synthesis of $\text{RuCl}_2(\text{IMes})(\text{py}')_2(=\text{CHPh})$ **Ru-18b**.

In a Schlenk flask, freshly distilled 3-bromopyridine (ca. 2 mL) was added to solid $\text{RuCl}_2(\text{IMes})(\text{PCy}_3)(=\text{CHPh})$ (2.966 g, 3.505 mmol). The solid residue mostly dissolved, and turned green almost immediately. Hexanes were added (20 mL) to precipitate the green solid. The suspension was cooled (-35°C), filtered, washed with hexanes (4×4 mL, then an additional 10 mL) and dried. Yield: 2.578 g (83%). ^1H NMR (CDCl_3 , 300 MHz): δ 19.33 (s, RuCHPh , 1H), 8.85 (br s, ArH , 1H), 8.71 (br s, ArH , 1H), 8.15 (s, ArH , 1H), 7.92 (br s, ArH , 1H), 7.74-7.72 (m, ArH , 3H), 7.49-7.44 (m, ArH , 3H), 7.09-7.05 (m, ArH , 6H), 6.72-6.70 (m, ArH , 3H), 3.35-2.21 (m, Ar-CH_3 , 12H).

2.3.21 Modified Synthesis of $\text{RuCl}_2(\text{H}_2\text{ITol})(\text{PCy}_3)(=\text{CHPh})$ **Ru-1e**.

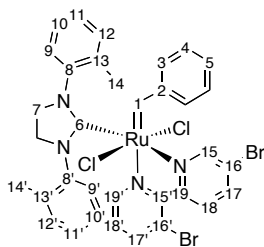
To a suspension of $\text{H}_2\text{ITol}\cdot\text{HCl}$ (1 g, 3.54 mmol, 1 equiv) and 50 mL C_6H_6 in a Schlenk flask was added KO^tBu (315 mg, 0.8 equiv) and $\text{LiN}(\text{SiMe}_3)_2$ (714 mg, 1.2 equiv). The suspension was stirred at 25°C for 30 minutes, until a clear yellow solution was formed, indicating that liberation of the free NHC was complete. This solution was added to a solution of **Ru-1a** (2.910 g, 3.54 mmol) in C_6H_6 (35 mL), and the reaction was stirred at 25°C for 22 h. At this time only 75% of **Ru-1a** was converted to **Ru-1e**. A second portion of the deprotected salt was prepared ($\text{H}_2\text{ITol}\cdot\text{HCl}$ 250 mg, 10 mL C_6H_6 , KO^tBu 35 mg, $\text{LiN}(\text{SiMe}_3)_2$ 175 mg) and added to the reaction to convert the 25% unreacted **Ru-1a**. The mixture was allowed to stir for an additional 2 days. The solvent volume was then reduced to a minimum (ca. 1 mL) by removal under vacuum; hexanes were added (50 mL), the suspension was chilled (-78°C), and a salmon-pink solid was filtered off and dried. Yield: 1.123 g (40 %). NMR data agree with values reported.⁵ ^1H NMR (CDCl_3): δ 19.06 ppm (s); $^{31}\text{P}\{^1\text{H}\}$ NMR (CDCl_3): δ 26.3 (s, **Ru-1e**), 34.5 ppm (unassigned; ratio 8:2); reprecipitation appears less effective than column chromatography⁵ for purification of **Ru-1e**. No further attempts to purify **Ru-1e** were made: the crude sample was used for synthesis of pyridine and 3-bromopyridine adducts **Ru-3e** and **Ru-18e**.

2.3.22 Synthesis of $\text{RuCl}_2(\text{H}_2\text{ITol})(\text{py})_2(=\text{CHPh})$ **Ru-3e**.



Addition of a minimum amount of pyridine (ca. 2 mL) to solid $\text{RuCl}_2(\text{H}_2\text{ITol})(\text{PPh}_3)(=\text{CHPh})$ **Ru-1e** (308 mg, 0.357 mmol) in a Schlenk flask caused an immediate colour change from pink to green. The solution was stirred for 5 minutes. Hexanes (5 mL) were added, the suspension was cooled (-35°C), and the green product was filtered off and washed with hexanes (5 mL). Yield: 185 mg (70%). ^1H NMR (C_6D_6 , 500 MHz): δ 19.31 (s, H^1 , 1H), 9.42 (d, $J = 10$ Hz, Tol-*H*, 1H), 8.51 (m, H^{15} , 2H), 7.92 (d, $J = 10$ Hz, H^3 , 2H), 7.54 (br s, Tol-*H*, 1H), 7.22-7.12 (m, H^5 and Tol-*H*, 5H), 7.06 (m, Tol-*H*, 1H), 6.92-6.88 (m, H^4 , 2H), 6.79 (br s, Tol-*H*, 1H), 6.50 (br m, H^{17} , 1H), 6.20 (m, H^{16} , 2H), 3.60 (m, $\text{H}^{7'}$, 1H), 3.50 (m, H^7 , 1H), 3.34 (m, $\text{H}^{7'}$, 1H), 3.21 (m, H^7 , 1H), 2.49 (s, H^{14} , 3H), 2.36 (br s, $\text{H}^{14'}$, 3H). ^{13}C NMR (C_6D_6 , 126 MHz): δ 153.4 (s, C^{15}), 151.8 (s, C^6), 142.0 (br s), 138.1 (br s, C^{13}), 136.9 (br s), 136.1 (br s, C^{17}), 132.4 (br s), 131.0 (s), 130.2 (s, C^3), 129.8 (s), 128.0 (C^4), 123.4 (s, C^{16}), 53.7 (s, C^7), 51.4 (br s, $\text{C}^{7'}$), 19.7 (s, C^{14}), 18.2 (s, $\text{C}^{14'}$). CT-MALDI MS (pyrene), m/z : Calcd $[\text{M}-2\text{py}]^{++}$ 512.0, Found 512.2; Calcd $[\text{M}-2\text{py}-\text{HCl}]^{++}$ 477.1, Found 476.2; Calcd $[\text{M}-2\text{py}-\text{HCl}-\text{Cl}]^+$ 442.1, Found 441.2; also significant aggregation.

2.3.23 Synthesis of $\text{RuCl}_2(\text{H}_2\text{ITol})(3\text{-Brpy})_2(=\text{CHPh})$ **Ru-18e**.



A minimum amount of 3-bromopyridine (ca. 1 mL) was added to solid $\text{RuCl}_2(\text{H}_2\text{ITol})(\text{PPh}_3)(=\text{CHPh})$ **Ru-18e** (255 mg, 0.250 mmol) in a Schlenk flask, causing an immediate colour change from green to dark green. The mixture was stirred for 5 minutes, then hexanes (5 mL) were added to precipitate the product. The suspension was cooled (-35°C), and the green product was filtered off and washed with hexanes (7×1 mL). Yield: 156 mg (60%). ^1H NMR (C_6D_6 , 500 MHz): δ 19.18 (s, H^1 , 1H), 9.36 (d, $J = 5$ Hz, H^{11} , 1H), 9.01 (br s, $\text{H}^{15'}$, 1H), 8.70 (br s, H^{15} , 1H), 8.28 (br s, H^{17} , 1H), 8.12 (br s, $\text{H}^{17'}$, 1H), 7.87 (d, $J = 5$ Hz, H^3 , 2H), 7.28 (m, H^{10} , 1H), 7.13-7.16 (m, H^{12} , H^5 and H^9 , 5H), 7.05 (m, H^{19} , 1H), 6.86-6.94 (m, H^4 , 2H), 6.78 (m, Ar-*H*, 1H), 6.62 (m, $\text{H}^{19'}$, 1H), 6.26 (br s, H^{18} , 1H), 5.77 (br s, $\text{H}^{18'}$, 1H), 3.17-3.58 (m, H^7 , 4H), 2.48 (s, H^{14} , 3H), 2.32 (br s, $\text{H}^{14'}$, 3H). $^{13}\text{C}\{^1\text{H}\}$ NMR (C_6D_6 , 126 MHz): δ 153.9 (s, $\text{C}^{15'}$), 152.2 (s, $\text{C}^{17'}$), 151.8 (s, C^2), 151.4 (s, C^{15}), 148.2 (s, C^{17}), 141.7 (s, C^8), 139.0 (s, C^{19}), 138.4 (s, C^{13}), 138.1 (s, $\text{C}^{19'}$), 132.7 (s, C^{12}), 130.1 (C^5), 129.9 (s,

C³), 128.9 (s, C¹¹), 128.5 (s, C⁴), 128.4 (s, C⁹), 128.0 (s, C¹⁰), 124.6 (s, C¹⁸), 124.5 (s, C¹⁸), 53.6 (s, C⁷), 51.2 (s, C⁷), 19.7 (s, C¹⁴), 18.2 (s, C¹⁴). CT-MALDI MS (pyrene), *m/z*: Calcd [M-2py]⁺ 512.0, Found 511.8; Calcd [M-2py-HCl]⁺ 477.1, Found 475.9; Calcd [M-2py-HCl-Cl]⁺ 442.1, Found 440.9; also significant aggregation.

2.3.24 Synthesis of RuCl₂(IPr)(py)₂(=CHPh) **Ru-3d**.

A solution of RuCl₂(IPr)(PCy₃)(=CHPh) **Ru-3d** (332 mg, 0.357 mmol) in a minimum volume of pyridine (ca. 1.2 mL). was stirred for about 10 min, over which time a colour change from pink to green was observed. Hexanes (12 mL) were added, and the suspension was cooled (−35 °C) to precipitate the product, which was filtered off, washed with hexanes (5 mL) and pentane (3 mL), and dried under vacuum. Yield: 233 mg (72%). ¹H NMR (CDCl₃, 300 MHz): δ 19.63 (s, H¹, 1H), 8.66 (d, ³J_{HH} = 4 Hz, 2H), 8.11 (d, ³J_{HH} = 5 Hz, 2H), 7.70 (t, ³J_{HH} = 7 Hz, 1H), 7.55-7.41 (m, 6H), 7.33-7.28 (m, 6H), 7.17 (br s, 2H), 7.03-6.95 (m, 3H), 3.25 (br m, CH(CH₃)₂, 4H), 1.34-1.13 (m, CH(CH₃)₂, 24H).

2.3.25 Attempted Synthesis of Ru(OC₆H₅)₂(IMes)(py)(=CHPh).

RuCl₂(IMes)(py)₂(=CHPh) **Ru-3b** (16.6 mg, 0.024 mmol) and TMB (0.8 mg, 0.005 mmol) were dissolved in C₆D₆ (1.4 mL) and a ¹H NMR spectrum was obtained for a *t*₀ measurement. The solution was divided into two equal portions (**A** and **B**). To each was added TiOPh (6.8 mg, 0.023 mmol), and the reactions were stirred at 25 °C. A color change from green to red was observed over 3 h. After 3 h (**A**) or 6 h (**B**), the samples were filtered through a glass-fiber plug to remove the TiCl byproduct. For each, ¹H NMR analysis revealed several new signals in the range of 4.5-5.5 ppm, indicating π-coordination of the phenoxide. Two isolated signals, designated **X** (5.26 ppm, d, *J*_{HH} = 5.2 Hz) and **Y** (5.26 ppm, d, *J*_{HH} = 5.2 Hz), were presumed to account for 1H each. Integrations were compared at the two time intervals, relative to internal standard. Sample **A** (3 h reaction): **Ru-3b**, 0%; **X**, 6%; **Y**, 25%. Sample **B** (6h): **Ru-3b**, 0%; **A**, 26%; **B**, 63%.

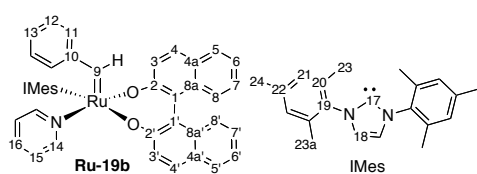
2.3.26 Representative Procedure for Probe Reactions of $\text{RuCl}_2(\text{L})(\text{L}')_2(=\text{CHPh})$ with A_2BINO ($\text{A} = \text{Ti}, \text{K}, \text{Na}$).

A solution of **Ru-3b** (40.6 mg, 0.055 mmol) and internal standard TMB (1.0 mg, 0.0059 mmol) in CDCl_3 (0.8 mL) was subjected to immediate ^1H NMR analysis to obtain a t_0 integration value. The solution was divided into $4 \times 200 \mu\text{L}$ portions (**A-D**) in 4 mL vials, of which **A** was topped up to 0.8 mL of CDCl_3 , and **B-D** were stripped of solvent and redissolved in, respectively, 0.8 mL of CH_2Cl_2 , THF, or C_6H_6 . To each was added $\text{Ti}_2(\text{BINO})$ (12 mg, 0.017, 1.2 equiv). Reactions were stirred at room temperature for 5 h, after which **B-D** were stripped of solvent and redissolved in CDCl_3 , and ^1H NMR spectra were recorded for **A-D**. Results for reactions **A-D** are summarized in Chapter 4 (Table 4.2, Entries 1-4). The results of other optimization reactions are summarized in Table 4.2, and Appendix B.

2.3.27 Representative Procedure for Probe Reactions of $\text{RuCl}_2(\text{L})(\text{L}')_2(=\text{CHPh})$ with K_2BINO and Silver Salt Additives.

Reactions were performed as above, except that solid AgOTf or AgPF_6 (1 equiv) was added to the reaction mixture. Conversion values are given in Appendix B.

2.3.28 Synthesis of $\text{Ru}(\eta^1, \eta^1\text{-BINO})(\text{IMes})(\text{py})(=\text{CHPh})$ **Ru-19b**.

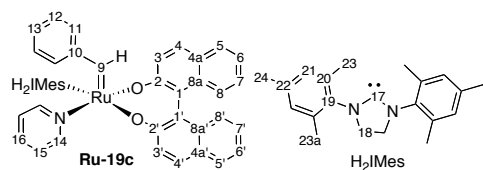


Addition of pyridine (1.5 mL) to **Ru-1b** (194 mg, 0.268 mmol) under N_2 caused an immediate colour change from pink to green. Solid $\text{K}_2(\text{BINO})$ (107 mg, 0.292 mmol) was added and washed down with

1 mL of pyridine, and stirring was continued at 25°C for 17 h. The solvent was then stripped off, using toluene (3 mL) to remove trace pyridine by azeotropic distillation. The residue was redissolved in THF (2 mL), filtered through Celite, washed through with THF (2×2 mL) and CH_2Cl_2 (2 mL), then concentrated to a minimum volume, precipitated with hexanes (5 mL), cooled to -35°C , and filtered. The brown powder was washed with hexanes (4 mL) and 3:1 hexanes: Et_2O (1 mL). A green powder was obtained by dissolving in CH_2Cl_2 (ca. 0.7 mL) and reprecipitating with hexanes (5 mL). Yield: 142 mg, 72%. ^1H NMR (CD_2Cl_2 , 500 MHz):

δ 19.18 (s, H⁹, 1H), 7.86 (d, $^3J_{\text{H14H15}} = 5.1$ Hz, H¹⁴, 2H), 7.82 (d, $^3J_{\text{H5H6}} = 7.9$ Hz, H⁵, 1H), 7.75 (d, $^3J_{\text{H4H3}} = 8.7$ Hz, H⁴, 1H), 7.46-7.43 (m, H^{5'}, H¹⁶, 2H), 7. (d, $^3J_{\text{H4'H3'}} = 9.0$ Hz, H^{4'}, 1H), 7.19 (t, $^3J_{\text{H13H12}} = 7.4$ Hz, H¹³, 1H), 7.11-7.10 (m, H³, H⁶, H¹¹, H¹⁸, 6H), 7.00-6.95 (m, H⁷, H²¹, 5H), 6.88-6.83 (m, H^{6'}, H¹², 3H), 6.81-6.75 (m, H^{7'}, H¹⁵, 3H), 6.71 (d, $^3J_{\text{H8H7}} = 8.4$ Hz, H⁸, 1H), 6.61 (d, $^3J_{\text{H3'H4'}} = 8.8$ Hz, H^{3'}, 1H), 6.53 (d, $^3J_{\text{H8'H7'}} = 8.7$ Hz, H^{8'}, 1H), 2.57 (s, ArCH₃, 6H), 2.08 (s, ArCH₃, 6H), 1.85 (br s, ArCH₃, 6H); $^{13}\text{C}\{^1\text{H}\}$ NMR (CD₂Cl₂, 126 MHz): δ 306.0 (s, C⁹), 185.9 (s, C¹⁷), 170.1 (s, C²), 164.0 (s, C²), 155.6 (s, C¹⁴), 154.0 (s, C¹⁰), 139.9 (s, C¹⁹, C²⁰ or C²²), 136.5 (s, C¹⁹, C²⁰ or C²²), 135.8 (s, C¹⁶), 135.7 (s, C^{8a}), 135.3 (s, C^{8a'}), 130.6 (s, C²¹), 129.7 (s, C¹⁹, C²⁰ or C²²), 128.5 (s, C¹²), 127.8 (s, C⁵, C^{5'} or C¹³), 127.74 (s, C⁵, C^{5'} or C¹³), 127.7 (s, C⁵, C^{5'} or C¹³), 127.5 (s, C¹⁸), 126.7 (s, C³, C⁴, C^{4'} or C¹¹), 126.66 (s, C³, C⁴, C^{4'} or C¹¹), 126.62 (s, C³, C⁴, C^{4'} or C¹¹), 126.58 (s, C³, C⁴, C^{4'} or C¹¹), 126.0 (s, C^{3'}), 125.5 (s, C⁸), 125.1 (s, C^{4a/4a'}), 124.7 (s, C^{8'}), 124.4 (s, C⁷), 124.2 (s, C¹), 123.94 (s, C^{7'}), 123.86 (s, C^{1'}), 123.7 (s, C¹⁵), 120.4 (s, C⁶), 120.0 (s, C^{6'}), 21.4 (s, C²³ or C²⁴), 20.8 (s, C²³ or C²⁴), 19.2 (s, C²³ or C²⁴), 18.2 (s, C²³ or C²⁴). CT-MALDI MS (pyrene), m/z : Calcd [M-py]⁺⁺ 780.2, Found 780.0. Anal. Calcd for C₅₃H₄₇N₃O₂Ru: C, 74.10; H, 5.51; N, 4.89. Found: C, 74.32; H, 5.66; N, 5.16.

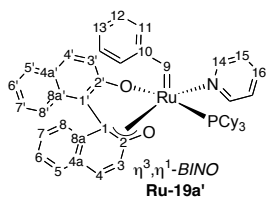
2.3.29 Synthesis of Ru(η^1, η^1 -BINO)(H₂IMes)(py)(=CHPh) Ru-19c.



Addition of pyridine (1 mL) to **Ru-1c** (300 mg, 0.354 mmol) under N₂ caused an immediate colour change from pink to green. Solid K₂(BINO) (141 mg, 0.389 mmol) was added, and washed down with 1 mL of pyridine. After stirring at 25 °C for 21 h, the solvent was stripped off. The residue was redissolved in THF (3 mL), filtered through Celite, and washed through with CH₂Cl₂ (15 mL). The filtrate was concentrated to a minimum volume (ca. 0.5 mL), treated with hexanes (3 mL) to precipitate the product, and cooled to −35 °C. The green product was filtered off, and washed with hexanes (3 mL) and 3:1 hexanes:Et₂O (1 mL), then additional hexanes (4 mL) and cold 3:1 hexanes:Et₂O (3 mL). Yield 85%. ^1H NMR (CD₂Cl₂, 500 MHz): δ 18.93 (s, H⁹, 1H), 7.86 (m, H¹⁴, 2H), 7.81 (d, $^3J_{\text{H5'H6'}} = 8.3$ Hz, H^{5'}, 1H), 7.71 (d, $^3J_{\text{H4'H3'}} = 8.5$ Hz, H^{4'}, 1H), 7.45 (m, H⁵, H¹⁶, 2H), 7.32 (d, $^3J_{\text{H4H3}} = 8.7$ Hz, H⁴, 1H), 7.15 (m, H⁷, 2H), 7.10 (m, H^{6'},

1H), 7.00-6.96 (m, H^{3'}, H⁷, H¹¹, H¹³, 5H), 6.87-6.80 (m, H⁶, H¹², H¹⁵, 5H), 6.74 (m, H⁷, 1H), 6.71 (d, ³J_{H⁸H⁷ = 8.3 Hz, H⁸, 1H), 6.68 (d, ³J_{H³H⁴ = 8.9 Hz, H³, 1H), 6.50 (d, ³J_{H⁸H⁷ = 8.7 Hz, H⁸, 1H), 4.02-3.94 (m, H¹⁸, 4H), 2.54 (s, Mes-CH₃, 6H), 2.21 (br s, Mes-CH₃, 6H). The remaining Mes-CH₃ singlet is broadened into the baseline.¹³C{¹H} NMR (CD₂Cl₂, 126 MHz): δ 307.1 (s, C⁹), 219.3 (s, C¹⁷), 170.3 (s, C²), 164.0 (s, C²), 156.3 (s, C¹⁶), 153.9 (s, C¹⁰), 139.4 (s, C²², C²⁰ or C^{20a}), 136.3 (s, C¹⁴), 135.9 (s, C^{8a'}), 135.5 (s, C^{8a}), 128.6 (s, C¹² or C¹⁵), 128.2 (s, C^{4a} or C^{4a'}), 128.1 (s, C²¹), 128.0 (s, C⁵), 127.9 (s, C⁵), 127.7 (s, C^{4a} or C^{4a'}), 127.0 (s, C¹³, C⁷ or C^{3'}), 126.8 (s, C⁴ or C^{4'}), 126.7 (s, C¹¹, C¹³, C⁷ or C^{3'}), 126.2 (s, C³), 125.6 (s, C⁸), 124.9 (s, C⁸), 124.8 (s, C¹³, C⁷ or C^{3'}), 124.5 (s, C⁷), 124.2 (s, C¹⁹), 124.1 (s, C¹² or C¹⁵), 123.94 (s, C¹ or C^{1'}), 123.87 (s, C¹ or C^{1'}), 120.5 (s, C^{6'}), 120.3 (s, C⁶), 68.3 (s, C¹⁸), 26.1 (s, C²³ or C²⁴), 21.6 (s, C²³ or C²⁴), 18.5 (s, C²³ or C²⁴). CT-MALDI MS (pyrene), *m/z*: Calcd [M-py]⁺ 782.2, Found 782.2. Anal. Calcd for C₅₃H₄₉N₃O₂Ru•CH₂Cl₂: C, 68.56; H, 5.43; N, 4.44. Found: C, 68.95; H, 5.39; N, 4.52.}}}

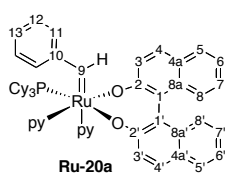
2.3.30 Synthesis of Ru(η³,η¹-BINO)(PCy₃)(py)(=CHPh) **Ru-19a'**.



Addition of pyridine (1.5 mL) to **Ru-1a** (460 mg, 0.559 mmol) under N₂ caused an immediate colour change from pink to green. Solid K₂(BINO) (180 mg, 0.686 mmol) was added and washed down with 2 mL of pyridine, causing a further colour change to brown. After stirring at 25 °C for 3 h, the solvent was removed under vacuum. The residue was redissolved in THF (20 mL), filtered through Celite and washed through with CH₂Cl₂ (5 mL). The filtrate was concentrated to a minimum, treated with hexanes to precipitate the product, cooled (−35 °C), and filtered. The product was washed with hexanes (10 mL), dissolved in THF (2.5 mL) and reprecipitated with hexanes (5 mL) to afford a greenish-brown solid. Yield 92%. ¹H NMR (CD₂Cl₂, 500 MHz): δ 17.55 (d, ³J_{H⁹p} = 5 Hz, H⁹, 1H), 7.89 (d, ³J_{H¹¹H¹²} = 7.6 Hz, H¹¹, 2H), 7.60 (d, ³J_{H⁵H⁶} = 7.9 Hz, H⁵, 1H), 7.55-7.52 (m, H¹⁴, H^{4'}, H¹⁶, 3H), 7.45 (tt, ³J_{H¹³H¹²} = 7.4 Hz, ³J_{H¹³H¹¹} = 1.1 Hz H¹³, 1H), 7.24 (d, ³J_{H⁵H⁶} = 7.9 Hz, H⁵, 1H), 7.21 (t, *J* = 8.0 Hz, H¹², 2H), 7.07 (dd, ³J_{H¹⁵H¹⁴} = 6.9 Hz and ³J_{H¹⁵H¹⁶} = 6.9 Hz H¹⁵, 2H), 6.99 (d, ³J_{H³H^{4'}} = 9.0 Hz, H^{3'}, 1H), 6.91 (m, H⁶, 1H), 6.85 (m, H^{6'}, 1H), 6.78 (d, ³J_{H⁴H³} = 9.2 Hz, H⁴, 1H), 6.72 (d, ³J_{H⁸H⁷} = 8.3 Hz, H⁸, 1H), 6.68 (m, H^{7'}, 1H), 6.53 (m, H⁷, 1H), 6.02 (d, ³J_{H³H⁴} = 9.2 Hz, H³, 1H), 5.95 (d, ³J_{H⁸H⁷}

= 8.6 Hz, H⁸, 1H), 2.28 (m, PCH, 3H), 1.88-1.43 (m, PCy-H, 30H). ¹³C{¹H} NMR (CD₂Cl₂, 126 MHz): δ 302.1 (s, C⁹), 174.1 (d, C^{2'}, ³J_{C2P} = 5 Hz), 155.3 (s, C^{8a'}), 154.3 (s, C¹⁰), 154.1 (d, C², ²J_{C2P} = 2.6 Hz), 141.2 (s, C^{8a}), 135.5 (s, C¹⁶), 135.3 (s, C^{4a'}), 134.2 (s, C⁴), 131.0 (s, C¹¹), 129.0 (s, C¹²), 128.8 (s, C¹³), 128.2 (s, C^{4'}), 127.84 (s, C^{5'}), 127.79 (s, C¹⁴), 127.5 (s, C³), 127.0 (s, C⁵), 126.7 (s, C⁸), 125.9 (s, C⁷), 125.4 (s, C^{4a}), 125.3 (s, C¹⁵), 124.8 (s, C^{7'}), 123.5 (s, C^{3'}), 123.2 (s, C^{8'}), 122.4 (s, C⁶), 119.6 (s, C^{6'}), 116.8 (s, C^{1'}), 95.6 (d, C¹, ²J_{C1P} = 11 Hz). ³¹P{¹H} NMR (CD₂Cl₂ 121 MHz): δ 46.8 (s). CT-MALDI MS (pyrene), *m/z*: Calcd [M-py]⁺ 756.3, Found 756.4. Anal. Calcd for C₅₀H₅₆NO₂PRu: C, 71.92; H, 6.76; N, 1.68. Found: C, 71.65; H, 6.59; N, 2.10.

2.3.31 In Situ Formation of Ru(η¹,η¹-BINO)(PCy₃)(py)₂(=CHPh) **Ru-20a**.



A solution of η³,η¹-BINO **Ru-19a'** (20 mg, 0.0239 mmol) was prepared in pyridine-*d*₅ (0.7 mL). ¹H NMR analysis indicated formation of Ru(η¹,η¹-BINO)(PCy₃)(py)₂(=CHPh) (93%) and an unidentified product at 20.67 ppm (s, 7%). ¹H NMR (C₅D₅N, 500 MHz): δ 20.46 (d, ³J_{H9P} = 11 Hz, H⁹, 1H), 8.75 (m, H¹¹, 2H), 8.13 (d, ³J_{H4H3} = 9 Hz, H⁴, 1H), 8.07 (d, ³J_{H5H6} = 8 Hz, H⁵, 1H), 7.81 (d, ³J_{H3H4} = 9 Hz, H³, 1H), 7.68 (m, H¹³, 1H), 7.52 (d, ³J_{H8'H7'} = 8 Hz, H^{8'}, 1H), 7.50 (d, ³J_{H5'H6'} = 8 Hz, H^{5'}, 1H), 7.47 (d, ³J_{H8H7} = 9 Hz, H⁸, 1H), 7.39 (m, H¹², 2H), 7.19 (m, H⁶), 7.05 (m, H^{6'}, 1H), 6.99-6.93 (m, H⁷ and H^{7'}), 6.71 (d, ³J_{H4'H3'} = 9 Hz, H^{4'}, 1H), 5.89 (d, ³J_{H3'H4'} = 9 Hz, H^{3'}, 1H). ¹³C{¹H} NMR (CD₂Cl₂, 126 MHz): δ 169.6 (d, ³J_{CP} = 3 Hz, C^{2'}), 167.9 (s, C²), 131.6 (s, C¹¹), 129.9 (s, C¹³), 129.3 (s, C¹²), 128.8 (s, C³), 128.2 (s, C⁵), 127.7 (s, C^{1'}), 127.7 (s, C^{5'}), 127.6 (s, C⁴), 127.5 (s, C^{3'}), 127.3 (s, C¹), 126.5 (s, C⁸), 126.4 (s, C^{8'}), 126.2 (s, C^{4'}), 124.1 (s, C⁷), 123.8 (s, C^{7'}), 119.9 (s, C^{6'}), 119.5 (s, C⁶).

2.3.32 Attempted Isolation of Ru(η¹,η¹-BINO)(PCy₃)(py)₂(=CHPh) **Ru-20a**.

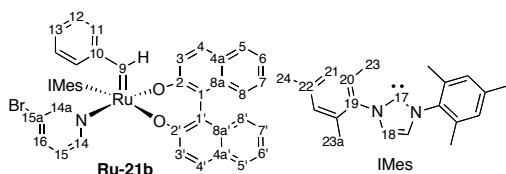
To a suspension of K₂BINO (25 mg, 0.093 mmol) in pyridine (0.5 mL) was added **Ru-3a** (59 mg, 0.072 mmol), which was washed down with an additional 0.5 mL of pyridine. The solution immediately turned from green to brown. The solution was allowed to stir at 25 °C for 2 h, then passed through a plug of glass-fiber filter paper, and washed through with pyridine (0.5 mL). Hexanes (2 mL) were added to the filtrate, and the solution was cooled (−35 °C) to precipitate a brown powder. This was filtered off, washed with hexanes (3 × 1

mL), and dried. ^1H NMR analysis (300 MHz, CDCl_3): η^3, η^1 -*BINO* **Ru-19a'** (72%); η^1, η^1 -*BINO* **Ru-20a** (8%); unidentified product (19.97, d, $^3J_{\text{HP}} = 11$ Hz; 20%).

2.3.33 Attempted Synthesis of $\text{Ru}(\eta^1, \eta^1\text{-BINO})(\text{IMes})(3\text{-Brpy})(=\text{CHPh})$ **Ru-21b** in 3-Bromopyridine.

3-Bromopyridine (1.0 mL) was added to **Ru-18b** (201 mg, 0.228 mmol), followed by solid $\text{K}_2(\text{BINO})$ (90 mg, 0.250 mmol) and 1.5 mL of 3-bromopyridine; the latter was used to wash solids down the sides of the flask. The solution turned a darker green on addition of these reagents, and was allowed to stir at 25 °C for 18 h. Formation of η^1, η^1 -*BINO* **Ru-21b** (18.74 ppm, 50%) and η^3, η^1 -*BINO* **Ru-21b'** (17.15 ppm, 11%) was confirmed by ^1H NMR analysis. These products are accompanied by a bis-Brpy analogue of **Ru-21b** (19.42 ppm, 23%) and two unknown species at 18.85 and 18.83 (16%). The solvent was stripped off, using toluene (2 mL) to remove trace pyridine as an azeotrope. The residue was redissolved in CH_2Cl_2 (2 mL), filtered through Celite, washed through with CH_2Cl_2 (3×1 mL), then concentrated. A brown solid was obtained following precipitation from THF (0.5 mL) and hexanes (8 mL), filtration and washing with hexanes (3×2 mL). Yield: 188 mg (88%). ^1H NMR analysis (CDCl_3 , 300 MHz): 19.32 (s, unknown, 50%), 18.73 (s, η^1, η^1 -*BINO* **Ru-21b**, 50%).

2.3.34 Synthesis of $\text{Ru}(\eta^1, \eta^1\text{-BINO})(\text{IMes})(3\text{-Brpy})(=\text{CHPh})$ **Ru-21b** in C_6H_6 .

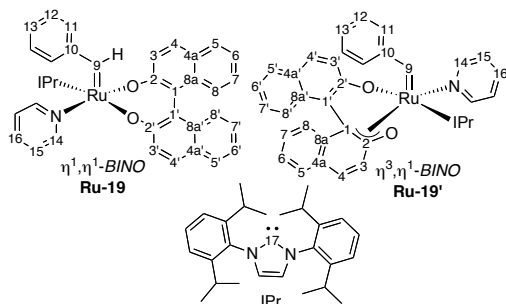


To a solution of **Ru-18b** (796 mg, 0.902 mmol) in C_6H_6 (80 mL) was added solid Ti_2BINO (750 mg, 1.08 mmol). The solution was stirred at reflux for 2 h, then stripped of solvent under vacuum. The

residue was redissolved in THF (25 mL), filtered through Celite, and washed through with THF (3 mL) and CH_2Cl_2 (10 mL). The filtrate was concentrated to ~1 mL; hexanes (20 mL) were added and the suspension was chilled (−35 °C). The resulting brown precipitate was filtered off and washed with cold hexanes: Et_2O (7:1, 8 mL) and cold pentane (8 mL). A green product was obtained following reprecipitation from C_6H_6 (10 mL). Yield 54%. ^1H NMR (CD_2Cl_2 , 500 MHz): δ 19.12 (s, H^9 , 1H), 8.22 (d, H^{16} , 1H), 7.83 (d, $J = 8.0$ Hz, H^5 , 1H), 7.77 (d, $J = 8.5$ Hz, H^4 , 1H), 7.58-7.56 (ov m, $\text{H}^{14/14a}$, 2H), 7.46 (d, $J = 8.0$ Hz, $\text{H}^{5'}$, 1H),

7.32 (d, $J = 9.0$ Hz, H^4 , 1H), 7.22 (m, H^{13} , 1H), 7.13-7.09 (ov m, H^3 , H^6 , H^{11} and H^{18} , 6H), 7.03 (br s, H^{21} , 4H), 6.97 (m, H^7 , 1H), 6.90-6.86 (ov m, H^6 and H^{12} , 3H), 6.76 (m, H^7 , 1H), 6.70 (d, $J = 8.5$ Hz, H^8 , 1H), 6.62 (d, $J = 8.5$ Hz, $H^{3'}$, 1H), 6.57 (dd, $J = 8.5$ Hz and $J = 6.0$ Hz, H^{15} , 1H), 6.52 (d, $J = 8.5$ Hz, H^8 , 1H); $^{13}\text{C}\{^1\text{H}\}$ NMR (CD_2Cl_2 , 126 MHz): δ 306.7 (s, C^9), 185.3 (s, C^{17}), 170.0 (s, C^2), 163.8 (s, C^2), 156.5 (s, C^{16}), 154.6 (s, C^{14} or C^{14a}), 154.0 (s, C^{10}), 140.2 (m, $\text{C}^{19/20/22}$), 138.2 (s, C^{14} or C^{14a}), 135.8 (s, C^{8a}), 135.4 (s, $\text{C}^{8a'}$), 130.8 (s, C^{21a} or C^{21b}), 129.7 (s, C^{21a} or C^{21b}), 128.7 (s, C^{12}), 128.23 (s, C^{4a}), 128.16 (s, C^{13}), 127.9 (s, C^{4a}), 127.8 (s, C^5), 127.6 (s, C^5), 126.9 (s, C^4), 126.71 (s, C^4), 126.68 (s, C^3 or C^{11}), 126.6 (C^3 or C^{11}), 126.0 ($\text{C}^{3'}$), 125.6 (s, C^8), 125.2 (s, $\text{C}^{18/18'}$), 124.8 (s, C^8), 124.5 (s, C^7), 124.2 (s, C^1), 124.14 (s, C^7), 124.08 (s, C^{15}), 123.8 (s, C^1), 120.6 (s, C^6), 120.2 (s, C^6), 119.7, 21.6 (s, C^{23} or C^{24}), 18.2 (s, C^{23} or C^{24}). CT-MALDI MS (pyrene) m/z : Calcd $[\text{M-py}]^+$ 780.2, Found 780.0. Anal. Calcd for $\text{C}_{53}\text{H}_{46}\text{BrN}_3\text{O}_2\text{Ru}$: C, 67.87; H, 4.94; N, 4.48. Found: C, 67.43; H, 5.25; N, 4.34.

2.3.35 Synthesis of $\text{Ru}(\eta^1, \eta^1\text{-BINO})(\text{IPr})(\text{py})(=\text{CHPh})$ **Ru-19d** and $\text{Ru}(\eta^3, \eta^1\text{-BINO})(\text{IPr})(\text{py})(=\text{CHPh})$ **Ru-19d'**.

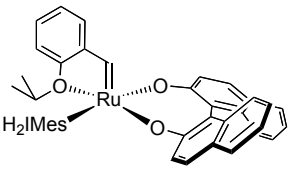
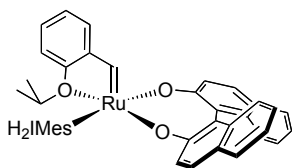


A suspension of $\text{K}_2(\text{BINO})$ (79 mg, 0.218 mmol) in pyridine (0.5 mL) was prepared. Solid **Ru-3d** (148 mg, 0.162 mmol) was added, followed by an additional portion of pyridine (1 mL) to wash the solid from the sides of the flask. The reaction was stirred at 25 °C for 22 h, then stripped of solvent.

The residue was redissolved in THF (1 mL), filtered through Celite, washed through with THF (3×1 mL), and concentrated under vacuum. Hexanes (5 mL) were added and the suspension was cooled (-35 °C). A green solid was filtered off and washed with hexanes (4 mL) and pentane (2 mL). Yield: 148 mg (95%). In all NMR solvents, both isomers **Ru-19** and **Ru-19'** were present. ^1H NMR (300 MHz): CDCl_3 , 17.74 ppm (**Ru-19**) and 17.65 ppm (**Ru-19'**), 1.7:1 ratio; C_6D_6 , 17.82 ppm (**Ru-19**) and 17.81 ppm (**Ru-19'**), 1:1.5 ratio; CD_2Cl_2 , 19.98 ppm (**Ru-19**) and 17.81 ppm (**Ru-19'**), 1.5:1. Characterization was undertaken in CD_2Cl_2 to eliminate interference with the signal for the residual protio solvent. The presence of both isomers (with overlapping resonances) prevented full assignment. The BINO

coordination modes in **Ru-19** and **Ru-19'** were elucidated from key ^1H and ^{13}C NMR signals listed below. Given that **Ru-19** and **Ru-19'** are present in nearly equal proportions and that not all signals could be assigned, the integration of an isolated signal for **Ru-19'** was set to 1, and integrations are reported with the observed, non-integer values. ^1H NMR (CD_2Cl_2 , 500 MHz): δ 17.98 (s, **Ru-19** H^9 , 1.5H), 17.81 (s, **Ru-19'** H^9 , 1H), 8.23-8.21 (m, 3.7H), 7.72-7.66 (m, 4.2H), 7.59 (d, $^3J_{\text{H}^4\text{H}^3} = 9$ Hz, **Ru-19** H^4 , 1.5H), 7.57-7.49 (m, 2.5H), 7.40 (d, $^3J_{\text{H}^4\text{H}^3} = 9$ Hz, **Ru-19** H^4 , 1.5H), 7.36-7.25 (m, 8H), 7.23-7.18 (m, includes **Ru-19'** H^7 , 4.3H), 7.14-7.11 (m, 3.2H), 7.08-6.82 (m, includes **Ru-19** H^3 , **Ru-19** $\text{H}^{3'}$ and **Ru-19'** $\text{H}^{3'}$, 19.6H), 6.76-6.68 (m, includes **Ru-19'** H^4 and $\text{H}^{4'}$, 8.2H), 6.36 (m, 1.9H), 5.93 (d, $^3J_{\text{H}^3\text{H}^4} = 9$ Hz, **Ru-19'** H^3 , 1H), 5.87 (d, $^3J_{\text{H}^8\text{H}^7} = 9$ Hz, **Ru-19'** H^8 , 1H), 4.36 (br m, **Ru-19'** $\text{CH}(\text{CH}_3)_2$, 1H), 3.69 (br m, **Ru-19'** $\text{CH}(\text{CH}_3)_2$, 1H), 2.29 (br m, **Ru-19** $\text{CH}(\text{CH}_3)_2$, 3H), 2.72 (br m, **Ru-19** $\text{CH}(\text{CH}_3)_2$, 3H), 2.39 (br m, **Ru-19'** $\text{CH}(\text{CH}_3)_2$, 1H), 2.08 (br m, **Ru-19'** $\text{CH}(\text{CH}_3)_2$, 1H), 1.28-0.78 (m, Ar- CH_3 , 57H). ^{13}C NMR (CD_2Cl_2 , 126 MHz): δ 303.7 (**Ru-19** C^9), 297.2 (**Ru-19'** C^9), 193.5 (s, **Ru-19'** C^{17}), 192.6 (s, **Ru-19** C^{17}), 167.7 (s, **Ru-19'** C^2), 166.7 (s, **Ru-19** $\text{C}^{2'}$), 166.4 (s, **Ru-19'** C^2), 156.6 (br s), 156.5, 154.8 (s), 153.1 (s, **Ru-19** C^{10}), 152.7 (s, **Ru-19** C^2), 152.5 (s), 151.2 (s, **Ru-19'** C^{10}), 147.2 (br s), 146.8 (br s), 145.8 (s), 145.5 (s), 145.2 (s), 144.3 (br s), 139.9 (br s), 136.8 (br s), 136.4 (s), 136.3 (s), 135.8 (s, **Ru-19'** C^{8a}), 135.6 (s), 135.4 (s, **Ru-19'** $\text{C}^{8a'}$), 134.7 (s), 134.6 (s), 134.5 (s), 132.5 (s), 130.4 (s), 130.0 (s), 129.9 (s), 129.4-129.3 (m), 129.2 (s, **Ru-19** C^{11}), 129.0 (s, **Ru-19** C^7), 128.9 (br s), 128.6 (s, **Ru-19'** C^{11}), 128.5 (s), 128.34 (s), 128.29 (s), 128.2-128.0 (m), 127.8 (s, **Ru-19'** C^5), 127.7 (s, **Ru-19'** C^5), 127.6-127.5 (m), 127.3 (s), 126.9 (s), 126.6 (s, **Ru-19'** C^4), 126.2-126.1 (m), 125.7 (s), 125.6 (s), 125.4 (s), 125.3 (s, **Ru-19'** C^4), 125.1 (s), 125.0 (s), 124.8 (s), 124.4 (br s), 124.2-124.0 (m), 123.8 (s), 123.1 (s), 123.0 (br s), 122.0 (s), 121.6 (s), 121.3 (s), 121.0 (br s), 120.1 (s), 119.83 (s), 119.76 (s), 115.6 (s, **Ru-19** $\text{C}^{1'}$), 29.8 (br s), 29.4 (s), 29.1 (s), 28.7 (br s), 28.6 (s), 28.1 (br m), 27.4 (br s), 27.1 (br s), 26.7 (s), 26.3 (s), 25.6 (s), 24.5 (s), 23.7 (s), 23.0-22.9 (m), 22.2 (s), 21.2 (br s), 20.3 (br s). Some ^1H resonances exhibit correlations to multiple ^{13}C signals. The number of signals in the aromatic region in some cases precluded precise location of correlated signals. For this reason, only ranges can be provided for the following diagnostic signals: 125.7-125.4 (**Ru-19** C^3), 128-121 (**Ru-19'** C^1 and $\text{C}^{1'}$).

2.3.36 Attempted Synthesis of Ru(BINO)(H₂IMes)(=CH(3-OⁱPr-C₆H₄)) **Ru-22c**.



To a vial containing a green solution of $\text{RuCl}_2(\text{H}_2\text{IMes})(\text{CHC}_6\text{H}_4^i\text{OPr})$ **Ru-4c** (40 mg, 0.0478 mmol) in pyridine (1 mL) was added AgOTf (13.5 mg, 0.0526 mmol) and K_2BINO (19 mg, 0.0526 mmol). The walls were washed down with additional pyridine (1 mL). Addition of AgOTf did not change the colour of the solution, but a colour change to brown followed addition of K_2BINO . The mixture was stirred at room temperature for 45 min, after which analysis of a reaction aliquot by ^1H NMR spectroscopy confirmed complete consumption of **Ru-4c** and conversion to **Ru-22c**. The reaction solvent was then removed under vacuum. The residue was redissolved in THF and filtered through Celite to remove salts. The resulting filtrate was concentrated to a minimum volume (~ 0.5 mL) and hexanes (2 mL) were added. The green suspension was cooled at -35°C overnight. The resulting green powder was filtered off and washed with hexanes (3×1 mL) and Et_2O (1 mL), then dried. Yield: 43 mg (80%). Decomposition was inferred from the presence of multiple alkylidene signals (^1H NMR).

2.3.37 Attempted Synthesis of Ru(3,3'-Br₂BINO)(IMes)(py)(=CHPh) **Ru-23b**.

Addition of solid $\text{Ti}_2(3,3'\text{Br}_2\text{BINO})$ (200 mg, 0.235 mmol) to a solution of **Ru-3b** (189 mg, 0.214 mmol) in C_6H_6 (4 mL) caused an immediate colour change from green to light green. this deepened to brown over 22 h at 25 °C. The solution was passed through Celite and washed through with C_6H_6 (3 mL) and THF (3 mL). The filtrate was concentrated (ca 0.5 mL), treated with hexanes (10 mL) to precipitate a brown product, and cooled (−35 °C). The brown product was filtered off, washed with cold 3:1 hexanes: Et_2O (2 × 3 mL) and cold pentane (3 mL), and dried. Three new alkylidene species were present. ^1H NMR (CDCl_3 , 300 MHz): δ 17.37 (16%), 17.34 (9%), 17.02 (74%).

2.3.38 Attempted Synthesis of Ru(3,3'-Ph₂BINO)(IMes)(py)(=CHPh) **Ru-24b**.

To a solution of **Ru-3b** (80 mg, 0.0946 mmol) in pyridine (0.5 mL) in a 4 mL scintillation vial was added solid $\text{Ti}_2(3,3'\text{Ph}_2\text{BINO})$ (88 mg, 0.104 mmol), which was washed down with an additional portion of pyridine (1 mL). The solution turned from green to reddish-brown

almost immediately. It was stirred for 17 h at 25 °C, then passed through Celite, washed through with CH₂Cl₂, and stripped of solvent. The residue was redissolved in CH₂Cl₂ (0.75 mL), treated with hexanes (3 mL), and cooled (−35 °C). A red solid was filtered off and washed with hexanes (5 × 1 mL). Four new alkylidene species were present. ¹H NMR (CDCl₃, 300 MHz): δ 19.09 (s, 62%), 18.31 (s, 14%), 16.86 (s, 19%), 16.03 (s, 6%).

2.4 Synthesis of Targeted Products of Catalysis.

2.4.1 Synthesis of ROM/CM Product **5**.

In a 250 mL Schlenk flask, *cis*-5-norbornene-*exo*-2,3-dicarboxylic anhydride **4** (200 mg, 1.22 mmol) was dissolved in THF (100 mL). Styrene (2.538 g, 24.4 mmol, 20 equiv) was added to the stirred solution, and washed down the sides of the flask with THF (5 mL). A solution of **Ru-19a'** (10 mg, 0.012 mmol, 1 mol%) in THF (2 mL) was then added. The vial that had contained the catalyst solution was rinsed with an additional portion of THF (3 mL), which was added to the reaction. A solution of chlorocatechol borane **14** (10 mg, 0.082 mmol, 5 mol%) in THF (10 mL) was added dropwise to the rapidly-stirred reaction to activate the catalyst (for discussion of additive effects, see Chapter 4, Section 4.3.5). During addition of the Lewis acid, the reaction solution slowly turned from a yellowish brown color to yellow. The flask was capped and stirred for 2 h at 25 °C. GC-FID analysis of a reaction aliquot at this point confirmed complete formation of **5**. The flask was removed from the glovebox and opened to air: ethylvinyl ether (1 mL) was added to quench the catalyst and cleave it from any ROMP side-product. The solution was stirred for 24 h under air to maximize catalyst decomposition and facilitate column chromatography. The solvent was stripped off, and MeOH was added. The mixture was cooled in an ice bath to precipitate any polymer side-product. The solution was filtered by gravity and stripped of solvent. The product was purified by column chromatography using a short silica column (ca. 5 cm). Unreacted styrene was collected by elution with 10% EtOAc in hexanes, and **5** was obtained by flushing the column with CH₂Cl₂. The product was subsequently passed through two silica plugs (ca. 1 cm in a glass pipette) with CH₂Cl₂ (ca. 15 mL each) to remove all ruthenium residues. The product was isolated by removal of CH₂Cl₂ solvent under vacuum. ¹H NMR chemical shifts matched literature values.³⁰

2.5 General Procedures for Catalytic Reactions.

Substrates were prepared according to literature procedures (see Section 2.1.2), and distilled prior to use. All catalytic reactions were carried out in an N₂-filled glovebox using dry, degassed solvents. Solids and liquids were weighed on a four-decimal analytical balance (see Section 2.1.9 for discussion of the accuracy of these measurements). Solvents were measured out with gas-tight syringes and added to stock solutions or reaction vials to achieve the target concentration. Catalyst stock solutions were prepared fresh for each catalytic run.

2.5.1 Parallel, Non-High-Throughput Catalytic Reactions.

Reactions were carried out in 4 mL vials loaded with Teflon-coated stir-bars. After addition of components, vials were sealed with screw-caps. Reactions at 25 °C were left to stir inside the glovebox. For reactions at elevated temperatures, the reaction vials were loaded into a preheated aluminum block outside the glovebox. The temperature of the block was pre-equilibrated to the desired temperature (monitored by a thermometer submerged in an oil-filled vial). After the desired reaction time, reactions were opened and analyzed immediately, or quenched with KTp for subsequent analysis.

2.5.2 High-Throughput Catalytic Reactions.

Stock solutions of substrates, catalysts and additives were prepared manually. The density of solids was ignored in calculating the solvent volume required to reach the desired molarity. The known density of commercially available additives or substrates was used in calculating the volume of solvent required to reach target concentrations. Liquid substrates of unknown density were assigned a value of 1 g/mL: higher precision can be attained by precisely weighing volumes measured out using (e.g.) a gas-tight microliter syringe. To ensure volumetric accuracy in aspirating solutions from 4 mL stock vials, an extra volume of 1.1 mL is required in the vial. This could be reduced if conical vials were employed. Reactions were carried out in 8 × 12 aluminum reaction blocks fitted with 7 × 40 or 7 × 30 mm glass vials (1.2 and 1.0 mL respectively), each containing a Parylene-coated stirbar. For high-pressure reactions, orbital shaking was employed rather than magnetic stirring; two glass beads were thus added to each vial in place of a stirbar. The backing solvent for the Cavo liquid-handling robots was toluene; the minimum volume of solutions dispensed was 20 μ L.

Stock solution vials were kept sealed to minimize evaporation up to the time of robotic transfer of solution to reaction plates, except for vials containing the quenching agents used in high-throughput quenching, which were sealed with a septum cap to prevent evaporation of the solution over the course of reaction. All solutions were dispensed into closed reaction plates to maintain accurate reaction volumes and concentrations. The deck temperature was held at 25 °C while solutions were added to the wellplates. The total volume per vial was between 200-500 μ L. After addition of all reagents, the Teflon sheet covering the wellplate was replaced with an unpierced Teflon sheet to prevent evaporation during reaction. After addition of all reagents, stirring was set to 4000 rpm. Temperatures were held constant (<1 °C) by a Julabo Presto control system. High-pressure reaction plates were sealed in reactor blocks rated to 1500 psi. Blocks were pressurized and placed in a Heated Orbital Shaker System throughout reaction. Single-time point reactions were allowed to proceed for either an arbitrarily long time to reach maximum conversion, or until a time pre-determined from time-monitored reactions, after which reactions were quenched by KTp. HT kinetic reactions were quenched over the course of 1-24 h.

2.5.3 Analysis.

Reactions were interrogated by ^1H NMR spectroscopy or by GC-FID analysis. In reactions evaluated by ^1H NMR spectroscopy, conversion values were determined by comparing the integrated ratio of substrate and product signals. For ROM/CM reactions monitored by this method, the internal standard TMB was employed to determine approximate amounts of competing ROMP formation based on missing integration from the substrate and product olefin signals (ROMP polymers were precipitated with MeOH and removed by filtration prior to analysis).^{*} Quantification by GC-FID analysis was carried out by integration of peak areas of the substrate and product relative to an internal standard tetrahydronaphthalene; and the percentage of product was corrected by use of a calibrated response factor for the product relative to the substrate. Oligomeric side-products were not observed by GC, but were quantified by difference from the molar mass of observed substrate and product relative to substrate. The identity of GC-FID product signals were confirmed by comparison to

^{*} These experiments were used to develop preliminary synthetic routes to the ROM/CM product, rather than to gain quantitative insight into reaction selectivities. For the latter, see Section 2.5.6.

authentic samples. In reactions where *E/Z* isomers or enantiomers were formed, selectivity was calculated from the percent difference in the integration for the two isomer signals.

2.5.4 Representative Procedure for the RCM of Diethyl Diallylmalonate **1**.

Stock solutions were prepared of **1** (134.4 mg, 0.560 mmol) and THN (68.8 mg, 0.520 mmol) in THF (1.120 mL, 0.5 M), and of **Ru-19b** (10.5 mg, 0.011 mmol) in THF (0.448 mL, 25 mM). To three vials (**A-C**) were added 100 μ L of the substrate solution and 300 μ L of THF. To vials **B** and **C** were added 100 μ L of the catalyst solution, such that the final concentration of **15a** was 0.1 M, and the catalyst loading was 5 mol%. Vials **B** and **C** were heated, for 15 and 60 min respectively, in an aluminum block set to 50 °C. Aliquots were removed from the t_0 vial (**A**) and the two reaction vials, and diluted to 5 mM for GC-FID analysis. Conversions: **B**, 0%; **C**, 0%.

2.5.5 Representative Procedure for Bench-top Conventional (non-HT) ROM/CM Reactions.

A stock solution of *exo*-**4** (38 mg, 0.23 mmol) and TMB (17 mg, 0.10 mmol) was prepared in THF (3.268 mL), and a portion was set aside for the t_0 analysis. The remainder (2.838 mL) was mixed with styrene (207 mg, 1.99 mmol) and **Ru-19b** (3.4 mg, 4.0 μ mol), and stirred at 60 °C for 3 h. The reaction vial was then returned to the glovebox, and an aliquot was removed under N₂. The aliquot and the t_0 sample were stripped of solvent, and the residues redissolved in CDCl₃ for ¹H NMR analysis. Conversion: 100% *exo*-**4** consumed; 62% ROM/CM product formed.

2.5.6 Representative Procedure for ROM/CM Reactions Carried Out by HTE.

A 0.5 M stock solution of *exo*-**4** (222 mg, 1.35 mmol) and internal standard THN (177 mg, 1.34 mmol) in benzene (2.302 mL) was subjected to serial dilution to afford a 0.1 M substrate stock solution. A 0.5 M stock solution of styrene was prepared similarly, by serial dilution from a 2.5 M solution (1.0056 g, 9.66 mmol styrene; 2.886 mL THF). A 10 mM stock solution of all catalysts was prepared in THF: **Ru-19b** (18.3 mg, 0.0213 mmol; 2.123

mL THF), **Ru-19c** (18.9 mg, 0.0220 mmol; 2.188 mL THF), **Ru-19a'** (17.5 mg, 0.0209 mmol; 2.086 mL THF), **Ru-21b** (19.8 mg, 0.0211 mmol; 2.104 mL THF). Serial dilution from these afforded 2.5 mM catalyst solutions. A 0.01 M solution of quenching agent **31** (19.3 mg, 0.0765 mmol) was prepared in THF (7.655 mL). Components were injected into a Teflon-sealed 96-well plate in the following order: solvent, substrate (both NBE and styrene) and catalyst. The final catalyst loading was 2.5 mol%; for other conditions, see Figure 2.1. The pierced Teflon sheet was replaced and the reaction deck was heated to 50 °C. Reactions in Columns 1-4 were quenched at 2 h, and the remainder at 6 h. After quenching the final well and cooling the plate, all solutions were diluted to 5 mM **4** and analyzed by GC-FID.

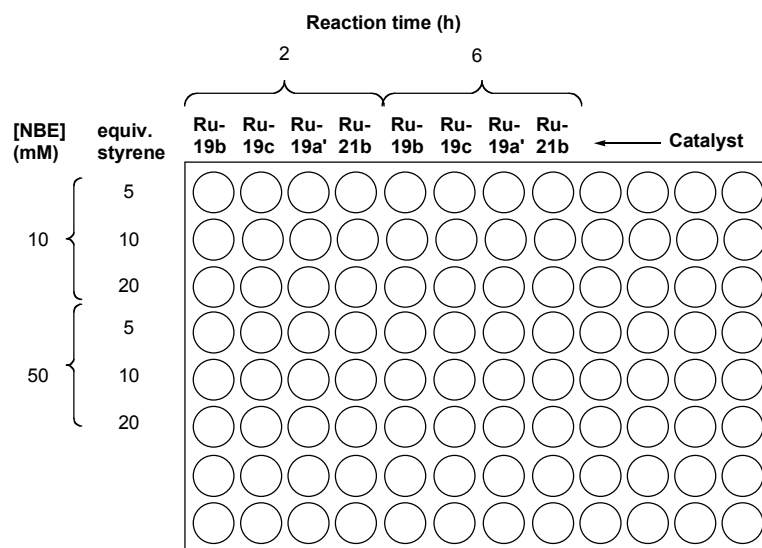


Figure 2.1. Conditions screened in optimization screen of ROM/CM with Ru(BINO)(L)(L')(=CHPh) catalysts.

2.5.7 Activation of Ru(η^3, η^1 -BINO)(IMes)(py)(=CHPh) **Ru-19b** by B(C₆F₅)₃.

Dissolving solid **Ru-19b** (17 mg, 0.020 mmol) and B(C₆F₅)₃ **24** (10 mg, 0.020 mmol) in C₆D₆ (ca. 0.7 mL) caused the green solution to lighten slightly. Immediate ¹H NMR analysis indicated low signal-to-noise ratios, and several signals between 3-5 ppm, consistent with π -coordination of an aryl ring to the ruthenium centre. Two signals are present in the alkylidene region: 19.55 (s, **Ru-19b**), 18.20 (br s; unassigned) ppm; ratio 1:4 (although the low solubility of **Ru-19b** in C₆D₆ limits the quantitative accuracy of this value). ¹¹B{¹H} NMR: -4.15 (s); agrees with the location measured for independently-prepared py•B(C₆F₅)₃.

2.5.8 Representative Procedure for High-Throughput Experimentation Single-Time Point Analysis: Screening for **Q**.

A representative procedure is given for the primary screen aimed at identifying a suitable quenching agent **Q** (**Q** : Ru = 40-100:1). A 1.00 M stock solution was prepared of substrate **1** (1.021 g, 4.050 mmol) and THN (600 mg, 4.54 mmol) in benzene (4.05 mL), as was a 5.0 mM stock solution of catalyst **Ru-1b** (14 mg, 0.0165 mmol) in benzene (3.30 mL). Stock solutions (200 mM) of the following potential quenching agents were prepared in benzene or (where solubility in benzene was insufficient) in THF. Concentrations in benzene: **25** (35 mg, 0.485 mmol); **26** (93 mg, 1.13 mmol), **28** (44 mg, 0.282 mmol); **32** (42 mg, 0.180 mmol). In THF: **31** (68 mg, 0.270 mmol); **29** (72 mg, 0.418 mmol); **30** (49 mg, 0.338 mmol). Solutions were injected into a sealed 96-well plate in the following order: solvent, substrate, **Q**, then catalyst. Final reaction conditions: 100 mM in substrate **1** and 0.5 mol% catalyst. A unique **Q** was added to each of Columns 1-8; none was added to Column 9, which serves as the control. The volume of **Q** added was increased down Rows A-D (40, 60, 80, and 100 μ L for **25**, **26**, and **28-32**, corresponding to 40, 60, 80, and 100 equiv **Q**, respectively). Identical volumes were added for neat acetonitrile **27**, corresponding to 3800, 5700, 7700 and 9600 equivalents of **27** relative to Ru. Reactions were stirred at 25 °C for 6 h, after which the wellplate was transferred to a sampling and dilution deck, where a 40 μ L aliquot was removed from each well and added to a "daughter" 96-well plate. Each aliquot was diluted to 800 μ L with CH₂Cl₂, giving a final concentration suitable for GC analysis (5.0 mM). The daughter plate was then transferred to an autosampler stage for GC-FID analysis. The results of this screen are given in Chapter 5, Figure 5.2a, and Appendix C, Table C.9. Results from other single-timepoint screens can be found in Appendix C.

2.5.9 Knockdown Efficiency of KTp **31**.

The rapidity of quenching by KTp **31** in RCM reactions promoted by both first- and second-generation catalysts **Ru-1a** and **Ru-1b** was assessed as follows, using the stock solutions described in 2.12.1. In a representative procedure, a solution of **Ru-1b** (0.5 mol%) was added to a vial containing a stirred solution of **1** in benzene, to afford a final substrate concentration of 100 mM. The reaction was allowed to proceed at 25 °C for 15 minutes, after which 10 equiv **31** were added. An aliquot was immediately removed, diluted, and analyzed by GC-

FID (total time elapsed from addition of **31** to injection ca. 2 min). The sample was reanalyzed after 1 h to assess any on-going metathesis. The sample was further analyzed after 4 h and 24 h, to simulate a wait time (e.g. queue time) for GC-FID analysis.

A control experiment was carried out without addition of **31**. In this case, the vial was sealed, removed from the glovebox, and the reaction was stirred at 25 °C for 15 minutes as before. It was then opened to air, and an aliquot was removed, diluted and immediately analyzed by GC-FID. Reanalysis was undertaken at 1 h, 4 h, and 24 h, as above. The results of both experiments are shown in Chapter 5, Figure 5.4, and Appendix C, Table C.11.

2.5.10 Representative Procedure for a High-Throughput Quenching Protocol.

A representative procedure for the RCM of allyl ether substrate **6** is provided. A 100 mM stock solution was prepared of **6** (57 mg, 0.304 mmol) in C₆H₆ (3.04 mL), with internal standard THN (41 mg, 0.310 mmol). A 10 mM stock solution of quenching agent **31** (16 mg, 0.0651 mmol) was made up in THF (6.51 mL). Stock solutions of catalysts (10 mM) were prepared as above and diluted to 1.0 mM immediately prior to robotic dispensing. Reaction components were added to a sealed 8 × 12 reaction plate at 25 °C in the following order: solvent, catalyst, then substrate. Final conditions: 10 mM **6**, 0.5 mol% catalyst, 400 μL reaction volume in C₆H₆. Vial components were kept constant within each row; catalysts differ between rows. One vial per row was left without catalyst, to serve as the *t*₀ control. After substrate addition, the temperature was increased to 30 °C. At the specified time intervals, the series of reactions down a given column were quenched by injection of **31** into each well. After complete reaction time and a cool-down period of 20 minutes, the plate was daughtered out and diluted to 5.0 mM for GC-FID analysis as above. Results for all high-throughput quenching experiments are given in Chapter 5, and Appendix C.

2.5.11 Representative Procedure for Time-Monitored Reactions in 4 mL Screw-Cap Vials.

A representative procedure for the ring-closing enyne metathesis (RCEYM) of **7** with **Ru-18b** is provided. A 1.0 M stock solution was prepared of **7** (399 mg, 2.14 mmol) and internal standard THN (284 mg, 2.15 mmol) in THF (1.448 mL). A 10 mM stock solution of catalyst

Ru-18b (34 mg, 0.0386 mmol) was prepared in THF (3.915 mL). Solutions were dispensed into 4 mL vials loaded with Teflon-coated stir-bars in a 4 × 6 reaction plate. To all 24 vials was added the substrate solution (0.050 mL), solvent (THF for half of the vials, CH₂Cl₂ for the remainder) and catalyst (0.025 mL), such that the final reaction volume was 0.5 mL, the substrate concentration was 0.1 M, and the catalyst loading was 0.5 mol%. An additional vial without catalyst served as the *t*₀ control. The reaction plate was removed from the glovebox, placed on the preheated Cavo deck (40 °C), and stirred (4000 rpm). At set reaction times (5, 10, 15, 30, 60 and 90 minutes), four vials (two THF and two CH₂Cl₂) were exposed to air, and samples were removed, diluted to 5 mM with CH₂Cl₂, and analyzed immediately by GC-FID. Results are given in Chapter 5, Figure 5.8, and Appendix C, Tables C.32-36.

2.5.12 High-Throughput Experimentation: Hydrogenation of **8'**.

A 1.00 M stock solution was prepared with substrate **8'** (172 mg, 0.721 mmol) and THN (87 mg, 0.66 mmol, 0.090 mL) in 0.631 mL CH₂Cl₂. From a 40 mM stock solution of NEt₃ (12.9 mg, 0.127 mmol) in benzene (3.187 mL), a 4 mM solution was prepared by serial dilution. An 8.0 mM stock solution for each of the hydride catalysts was prepared in benzene: **Ru-25a** (11 mg, 0.016 mmol; 1.947 mL C₆H₆), **Ru-26a** (11 mg, 0.015 mmol; 1.878 mL C₆H₆), **Ru-25b** (11 mg, 0.015 mmol; 1.900 mL C₆H₆) and **Ru-26b** (11 mg, 0.015 mmol; 1.832 mL C₆H₆). Serial dilution from these stock solutions afforded 1 mM catalyst solutions, which were injected robotically into a 96-well plate. The solvent was then removed by a centrifuge evaporator. The triethylamine solution, MeOH and benzene were injected into selected vials. The substrate solution and CH₂Cl₂ were injected by hand to eliminate inaccuracies due to robotic dispensing of volatile CH₂Cl₂ (see Chapter 5, Section 5.3.1). Final reaction conditions were as follows: 100 mM **8'**; 0.1 mol% [Ru]; 20 mol% v/v MeOH; 3 equiv NEt₃. The plate was sealed and placed in a high-pressure reaction block. The O-ring joining the two halves of the block was greased slightly to prevent leaks on pressurization. The block was sealed and the bolts were hand-tightened with an Allen wrench. The assembly was then removed from the box, and a torque wrench was used to tighten the bolts to 200 lbs/inch (tightening on alternating sides of the block to minimize differential stress). The reaction block was then connected to a gas line, the line was purged of air, and the block pressurized to 1000 psi H₂. The block was heated (55 °C) and shaken (orbital stirring) on a Heated Orbital Shaker

System for 1 h. The plate was subsequently cooled and depressurized. Solvent was removed using a centrifuge evaporator fitted with a plate holder. Residues were taken up in CDCl_3 (added via a 12-channel micropipette), and the solutions were transferred to NMR tubes held upright in a custom 8×12 NMR-tube holder. Results are given in Chapter 5 Section 5.3.6, and Appendix C.

2.6 CT-MALDI MS Analysis of Isolated Complexes and Reaction Samples.

2.6.1 A Representative Procedure for CT-MALDI MS of Isolated Complexes in Solution:

Analysis of $\text{RuCl}_2(\text{PCy}_3)_2(=\text{CH}_2)$ **Ru-2a**.

Complex **Ru-2a** (5 mg, 0.0067 mmol) was dissolved in C_6H_6 (0.5 mL), and the solution was mixed with a solution of pyrene (20 mg, 0.099 mmol) in C_6H_6 (1.0 mL) in a 5:1 ratio by volume of matrix to analyte. The resulting solution was spotted on a target plate using a micropipette tip and the solvent was allowed to evaporate. The resulting spectrum is given in Chapter 6, Figure 6.1b. Analysis conditions for all complexes studied are listed in Table 2.1 below: relevant spectra can be found in Chapter 6 or Appendix A.

2.6.2 A Representative Procedure for CT-MALDI MS of Solid Samples as a Nujol Mull:

Analysis of $\text{RuCl}_2(\text{PCy}_3)_2(=\text{CH}_2)$ **Ru-2a**.

Complex **Ru-2a** (4 mg, 0.0054 mmol) was added to a mortar with the matrix anthracene (20 mg, 0.099 mmol). Three drops of Nujol were added to the mixture, milled with the pestle, and spread on a target plate for analysis. Higher-quality spectra (in terms of S/N and spot homogeneity) were obtained for samples smeared most thinly on the target plate. Relevant spectra for **Ru-2a** found in Chapter 6, Figure 6.5.

Table 2.1. Isolated complexes analyzed by CT-MALDI mass spectrometry.

analyte	matrix	matrix solvent	analyte solvent	matrix:analyte ^[1] v/v	[matrix] ⁺⁺ Molar	Major observed	signals
Ru-1a	Pyrene	CH_2Cl_2	toluene	4:1	79:1	Y	$[\text{M}]^{++}$, $[\text{M-Cl}]^{++}$, $[\text{M-PCy}_3]^{++}$, $[\text{M-Cl-}$

							PCy ₃] ⁺⁺
Ru-2a	Anthracene	CH ₂ Cl ₂	C ₆ H ₆	5:1	37:1	Y	[M] ⁺⁺
Ru-2a	Anthracene	None, Nujol mull	None, Nujol mull		18:1	Y	[M] ⁺⁺
Ru-1b						Y	[M] ⁺⁺ , [M-Cl] ⁺⁺ , [M-PCy ₃] ⁺⁺ , [M-Cl- PCy ₃] ⁺⁺
Ru-1c	Pyrene	CH ₂ Cl ₂	tol	6:1	118:1	Y	[M] ⁺⁺ , [M-Cl] ⁺⁺ , [M-PCy ₃] ⁺⁺ , [M-Cl- PCy ₃] ⁺⁺
Ru-4c	Pyrene	CH ₂ Cl ₂	Tol	4:1	79:1	Y	[M] ⁺⁺ , [M-2Cl] ⁺⁺
Ru-26b	Pyrene	THF	THF	5:1	37:1	N	[M-CO-H ₂] ⁺⁺ , [M- HCl] ⁺⁺ , [M-HCl- H ₂] ⁺⁺ , [M-HCl- 3H] ⁺
Ru-8	Pyrene					N	[M+H] ⁺ , [M-N ₂ - HCl-H] ⁺ , [M-N ₂ - Cl] ⁺ , [M-N ₂ -HCl] ⁺⁺ , [M-N ₂ -HCl-H ₂] ⁺⁺

^[1] M = molecular ion.

2.6.3 Attempted Generation of Calibration Curves

Individual solutions of RuCl₂(PCy₃)₂(CHPh) **Ru-1a** (28 mg, 0.034 mmol) and RuCl₂(PCy₃)₂(CH₂) **Ru-2a** (25.5 mg, 0.035 mmol) were prepared in C₆H₆ (0.340 and 0.341 mL respectively), to a concentration of 0.1 M for each. Matrix solutions (0.1 M) of anthracene (20 mg, 0.11 mmol) and pyrene (20 mg, 0.035 mmol) were prepared in C₆H₆. A set of six solutions were prepared where the concentration of **Ru-2a** was held constant and that of **Ru-1a** was varied. The resulting molar ratios of **Ru-2a**:**Ru-1a** were 4, 2, 1, 0.67, 0.5 and 0.4:1. From each mixture an aliquot (0.01 mL) was removed and mixed with a constant amount of matrix (0.1 mL). The resulting solutions contained 20 mM **Ru-2a**, with

concentrations of **Ru-1a** of 5, 10, 20, 30, 40 and 50 mM. Each solution was spotted onto the target plate and analyzed by CT-MALDI MS.

2.6.4 A Representative Procedure for Analysis of RCM Reactions by CT-MALDI Mass Spectrometry: RCM of **2** with **Ru-1a** at 80 °C in Toluene.

A solution of catalyst **Ru-1a** (7.8 mg, 0.0095 mmol) in toluene (0.190 mL, 50 mM) was prepared. A 0.052 mL aliquot of this solution was added to a solution of substrate **2** (13.8 mg, 0.0518 mmol) in toluene (0.466 mL) in a 4 mL vial equipped with a stir-bar. This gave a final substrate concentration of 100 mM and a catalyst loading of 5 mol%. Two aliquots (ca. 0.020 mL each) were removed for t_0 MALDI-MS analysis with (a) pyrene and (b) anthracene matrices. The vial was then capped, removed from the glovebox and allowed to stir in an aluminum block preheated to 80 °C. After set time intervals (1, 4 and 24 h) the vial was returned to the glovebox and an aliquot was again removed. To each aliquot was added ca. 0.080 mL of matrix solution (20 mg pyrene or anthracene in 1 mL C₆H₆) to give an 80:1 molar ratio of matrix to analyte. This solution was spotted on a target plate using a micropipette tip, and the solvent was allowed to evaporate. The mass spectrum for the 1h reaction sample is given in Chapter 6, Figure 6.9. Spectra for other time intervals can be found in Appendix A. Analytical conditions for all reactions studied are listed in Table 2.2; relevant spectra can be found in Chapter 6 or Appendix A.

2.6.5 Representative Procedure for RCM Reactions Monitored by MALDI-MS and NMR Spectroscopy.

The procedure followed that detailed above (Section 2.13.3), except that each reaction was analyzed at a single time-point. After MS sample preparation, the sample was quenched with **31** (10 equiv) to arrest any further reaction; the solvent was stripped off, and the residue was taken up in CDCl₃ for ¹H NMR analysis.

Table 2.2. Reaction and MALDI analysis parameters for catalytic reactions.^[1]

analyte	Sub.	Solvent	Temp	Time	matrix	matrix:analyte
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			(°C)	(h)		v/v	Molar
Ru-1a	1	CH ₂ Cl ₂	RT	0,1,4,24	pyrene; anthracene	4/1	79:1
Ru-1c		CH ₂ Cl ₂	RT	1	pyrene	10:1	197:1
Ru-1b		C ₆ H ₆	RT	1	pyrene	4:1	79:1
Ru-1b		C ₆ H ₆	40	0,1,2,3	pyrene, anthracene	1:1	20:1
Ru-1a	2	CH ₂ Cl ₂	40	0,1,4,24	pyrene; anthracene	5:2	49:1
Ru-1a		toluene	80	0,1,4,24	pyrene; anthracene	4:1	79:1
Ru-1c		CH ₂ Cl ₂	40	0,1,4,24	pyrene; anthracene	5:2	49:1
Ru-1c		toluene	80	0,1,4,24	pyrene; anthracene	6:1	118:1
Ru-4c		CH ₂ Cl ₂	40	0,1,4,24	pyrene; anthracene	5:1	100:1
Ru-4c		toluene	80	0,1,4,24	pyrene; anthracene	4:1	79:1
Ru-1b	12	C ₆ H ₆	40, 60	1	pyrene; anthracene	4:1	79:1
Ru-1b	13	C ₆ H ₆	40, 60	1	pyrene; anthracene	4:1	79:1
Ru-1b	8 + 31	THF	40	4	pyrene		
Ru-1b	12 + K ₂ CO ₃	THF	65	4	pyrene, anthracene, naphthalene	5:2	49:1
Ru-1b	1 + K ₂ CO ₃	THF	65	4	pyrene, anthracene, naphthalene	5:2	49:1

^[1] Substrate concentration = 100 mM; catalyst loading = 5 mol%

2.6.6 A Representative Procedure for Assessment of Catalyst Decomposition in the Absence of Substrate by CT-MALDI MS: Decomposition of **Ru-1c** in Toluene at 80 °C.

From a solution of catalyst **Ru-1c** (11.4 mg, 0.013 mmol) in toluene (0.269 mL, 50 mM), a 0.055 mL aliquot was added to a 4 mL vial equipped with a stir-bar. To the vial was added 0.497 mL of toluene to give a 5 mM solution. Two aliquots (ca. 0.020 mL each) were removed for the t_0 analysis with (a) pyrene; (b) anthracene. The vial was capped, removed from the glovebox, and placed in an aluminum block preheated to 80 °C. After set time intervals (1, 4 and 24 h), the vial was returned to the glovebox and an aliquot was again removed. Prior to analysis, ca. 0.060 mL of matrix solution (20 mg pyrene or anthracene in 1 mL CH₂Cl₂) was added to each sample to give a 120:1 molar ratio of matrix to analyte, and the solution was then spotted on a target plate (see Section 2.1.8 for discussion of matrix to analyte ratios). Mass spectra for the 1 h reaction sample are provided in Chapter 6, Figure 6.11. Spectra for other time intervals and catalysts can be found in Appendix A. Analytical conditions for all solutions studied are listed in Table 2.3.

Table 2.3. MALDI analysis parameters for decomposition of catalysts without substrate.^[1]

analyte	Solvent	Temp (°C)	Time (h)	matrix	matrix:analyte	
					v/v	Molar
Ru-1a	CH ₂ Cl ₂	RT	0,1,4,24	pyrene; anthracene	4:1	79:1
Ru-1a	CH ₂ Cl ₂	40	0,1,4,24	pyrene; anthracene	4:1	79:1
Ru-1a	toluene	80	0,1,4,24	pyrene; anthracene	4:1	79:1
Ru-1c	CH ₂ Cl ₂	40	0,1,4,24	pyrene; anthracene	10:1	197:1
Ru-1c	toluene	80	0,1,4,24	pyrene; anthracene	6:1	118:1
Ru-4c	CH ₂ Cl ₂	40	0,1,4,24	anthracene	10:1	197:1

Ru-4c	toluene	80	0,1,4,24	pyrene;	4:1	79:1
				anthracene		

^[1] Catalyst concentration = 5 mM.

2.7 References.

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Chapter 3. Unprecedentedly Strong Binding of Dinitrogen at Ruthenium*

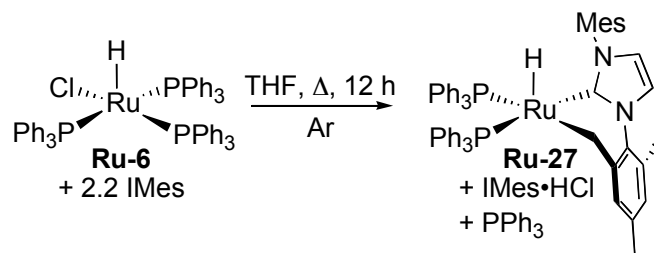
3.1 Introduction.

Metal-dinitrogen complexes are of great interest for their potential to reduce energy costs in ammonia production, and to facilitate access to nitrogen-containing organic compounds.¹⁻⁴ Since the 1965 report⁵ of $[\text{Ru}(\text{NH}_3)_5(\text{N}_2)]^{2+}$, many such complexes have been discovered, but the extent of $\text{N}\equiv\text{N}$ activation is highly variable. Maximum N_2 -bond weakening, culminating in bond cleavage, is observed with the early and mid-transition metals.^{2-4,6-9} A benchmark was set by molybdenum triamidoamine complexes reported by Yandulov and Schrock, which remain the only effective molecular catalyst for reduction of N_2 to ammonia.^{10,11} Also of note is a molybdenum-magnesium cluster complex reported by Shilov, which enables catalytic reduction of N_2 to hydrazine, accompanied by ammonia in minor amounts.¹² Iron complexes have been intensively studied in recent years, in work stimulated by the central role of iron species in catalytic reduction of dinitrogen within both industrial (Haber-Bosch) and biological (nitrogenase) contexts.^{1-3,13,14} While a series of advances has established the feasibility of various steps in the catalytic cycle for reduction, ammonia formation is sub-stoichiometric.^{1,15} As with N_2 complexes of other late transition metals, the extent of activation tends to be limited by the relatively low energy of the metal d-orbitals (which impedes back-donation into the high-energy $\text{N}\equiv\text{N}$ -antibonding orbital),^{16,17} and high N_2 lability.^{1,18-23} Fryzuk has pointed out that lability is in fact a key barrier to development of late-metal catalysts for N_2 activation.²⁴

The present work originated in studies of hydridoruthenium complexes of *N*-heterocyclic carbene (NHC) ligands, as catalysts for hydrogenation and related reactions.^{25,26} The associated synthetic chemistry led us to a report from the Morris group describing formation of the activated IMes complex **Ru-27** on thermolysis of $\text{RuHCl}(\text{PPh}_3)_3$ **Ru-6** with excess IMes under argon (Scheme 3.1).²⁷ This Chapter describes the unexpected discovery of a ruthenium dinitrogen complex, in place of **Ru-27**, on performing this reaction under N_2 . The

* Parts of this Chapter have been published: Blacquiere, J.M.; Higman, C.S.; Gorelsky, S.I.; Beach, N.J.; Dalgarno, S.J.; Fogg, D.E. *Angew. Chem., Int. Ed.* **2011**, 50, 916-919.

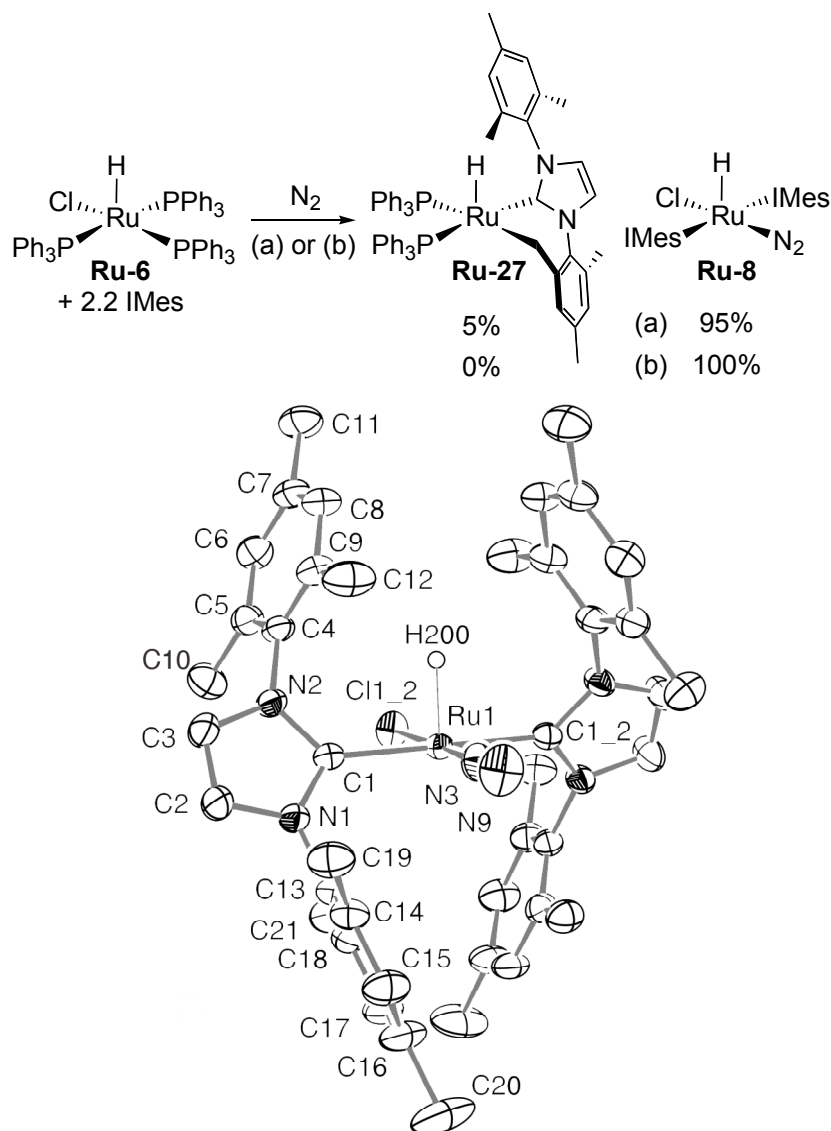
identity of the complex, and the extent of activation in the subtended N_2 ligand, was explored through spectroscopic, computational, and reactivity studies.



Scheme 3.1. Reported²⁷ formation of **Ru-27** on treatment of $\text{RuHCl}(\text{PPh}_3)_3$ with IMes (IMes = *N,N'*-bis(mesityl)imidazol-2-ylidene).

3.2 Preparation of $\text{RuHCl}(\text{N}_2)(\text{IMes})_2$.

Reaction of $\text{RuHCl}(\text{PPh}_3)_3$ with two equivalents of IMes under N_2 resulted in a color change from pink-red to orange within 12 h in refluxing THF. In situ $^{31}\text{P}\{^1\text{H}\}$ NMR analysis indicated only minor amounts of the expected product **Ru-27** (<10%; δ_p 59.35, 58.72 ppm; ABq, $^2J_{pp} = 13$ Hz), accompanied by a large signal for free PPh_3 . The implied absence of phosphine ligands in the major product **Ru-8** (see Scheme 3.2) is confirmed by the singlet multiplicity of the new hydride signal at -28.03 ppm. Reactions at ambient temperature were slower (20 hours) for complete conversion, but yielded solely **Ru-8**. The complex was isolated by filtering through Celite, concentrating the filtrate, adding hexanes to induce precipitation, and filtering cold. Isolated yields were limited to 75% by the partial solubility of **Ru-8** in hexanes. The null $^{31}\text{P}\{^1\text{H}\}$ NMR spectrum of the clean sample confirmed the absence of phosphine ligands. Single-crystal X-ray analysis indicated a mononuclear, bis-NHC structure, but persistent crystal twinning initially impeded detailed structural interpretation. On the basis of detailed NMR, IR, MALDI-TOF mass spectrometric, and combustion analysis, **Ru-8** was ultimately identified as $\text{RuHCl}(\text{IMes})_2(\text{N}_2)$.



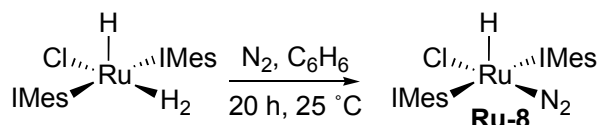
Scheme 3.2. Top: Dominant products on treating **Ru-6** with IMes in THF under N_2 a) at 66 °C, 12 h reaction; b) 24 °C, 20 h. Bottom: The ORTEP diagram of **Ru-8** is given with non-hydrogen atoms represented by Gaussian ellipsoids at the 50% probability level. The position of the hydride atom is inferred (see text).

3.3 Molecular Structure of $\text{RuHCl}(\text{N}_2)(\text{IMes})_2$.

Refinement of the X-ray data with an appropriate disorder model, once the constituents of **Ru-8** had been established by the means described below, yielded a satisfactory structural solution. Contributing to the difficulty of solving the original X-ray structure was the fact that for both complexes in the unit cell, the N_2 and Cl sites are disordered over two positions

(as found for other structures containing Cl trans to N₂);²⁸ in one, the hydride is also disordered over two positions. The excellent agreement between the model and the observed data provides unambiguous confirmation of connectivity, although the presence of the disorder limits discussion of the metrical parameters such as the N₂ bond length.

The square pyramidal geometry of **Ru-8**, and the apical position of its hydride ligand, are deduced from the upfield location of the hydride singlet (−28.03 ppm; C₆D₆) in the ¹H NMR spectrum. Integration confirms the presence of two IMes ligands per hydride. Moreover, the rotational equivalence of the IMes *ortho*-CH₃ groups (a broad singlet at 22 °C, which resolves into four singlets at 0 °C) rules out activation of a methyl C-H bond as was seen in the Morris complex **Ru-27**. Retention of the chloride ligand is confirmed by charge-transfer MALDI-TOF mass spectrometry.²⁹ The mass spectrum exhibits an excellent match between the simulated and observed isotope patterns for both [RuHCl(IMes)₂(N₂)+H]⁺ (minor signal) and [RuCl(IMes)₂−H]⁺ (major). For a more detailed discussion of gas-phase fragmentation pathways the reader is referred to Chapter 6, Section 6.2.4. The possibility that an N₂ ligand occupied the fifth coordination site was originally considered: it was discarded, however, on the basis of reactions with CO (see Section 3.4), which indicated that this ligand was not displaced, but that a monocarbonyl *adduct* was formed. This is inconsistent with the established lability of the N₂ ligand in late-metal complexes, many of which exist in dynamic equilibrium with their N₂-free derivatives even under an atmosphere of dinitrogen. The possibility was revisited, however, following an experiment involving exposure of RuHCl(H₂)(IMes)₂ to N₂ (Scheme 3.3), which resulted in the quantitative formation of **Ru-8**. A natural-abundance ¹H-¹⁵N HSQC correlation experiment was then undertaken. This provided unequivocal evidence that the hydride is coupled to a (non-IMes) ¹⁵N nucleus at −72.6 ppm, a location consistent with assignment as N_α of an N₂ ligand.^{30,31} Isotopically enriched **Ru-8**-¹⁵N₂ was obtained by synthesis of the complex under an atmosphere of 98% ¹⁵N₂. The ¹H NMR spectrum of the labelled product revealed a doublet for the hydride signal, owing to coupling to ¹⁵N_α (²J_{HN} = 4 Hz). ¹⁵N{¹H} NMR analysis enabled location of the signal for N_β, a doublet at −55.8 ppm (¹J_{NN} = 5 Hz). The inequivalence of N_α and N_β supports identification of **Ru-8** as a monoruthenium complex containing a terminally bound, η¹-N₂ ligand, in which any end-over-end N₂ tumbling in solution is slow on the NMR timescale.



Scheme 3.3. Synthesis of **Ru-8** from $\text{RuHCl}(\text{H}_2)(\text{IMes})_2$.*

The IR spectrum of **Ru-8** revealed a single strong band at 2041 cm^{-1} , in the region expected for the $\nu(\text{M-H})$ and $\nu(\text{N}\equiv\text{N})$ vibrations (Figure 3.1). Isotopic labeling resulted in the expected shift in the $\nu(\text{N}\equiv\text{N})$ band, to 1972 cm^{-1} for **Ru-8- $^{15}\text{N}_2$** : the $\nu(\text{Ru-H})$ band appears essentially unperturbed, at 2039 cm^{-1} , although attempts** to confirm the latter assignment by deuterium labeling were unsuccessful. High labeling yields are essential to have any chance of detecting the $\nu(\text{Ru-D})$ band (calculated at ca. 1440 cm^{-1}), as the C-H bending vibration for the alkyl substituents – which tend to be much stronger than $\nu(\text{M-H})$ (or M-D) bands – obscures the key IR region. Placing **Ru-8** under D_2 (C_6D_6 , RT, 5 days) resulted in only partial conversion, owing to the non-lability of the N_2 ligand; a colour change evident at this point suggested competing decomposition. Synthesis of $\text{RuDCl}(\text{PPh}_3)_3$, followed by exchange of PPh_3 with IMes under N_2 , was thwarted by extensive scrambling of the deuteride label into the IMes *o*- CH_3 groups (corroborated by ^2H NMR analysis). Finally, synthesis of $\text{RuDCl}(\text{D}_2)(\text{IMes-d}_{12})_2$ by reaction of $\text{RuHCl}(\text{H}_2)(\text{IMes})_2$ with D_2 ($55\text{ }^\circ\text{C}$, 300 psi), followed by exchange of bound D_2 by replacing the atmosphere with N_2 (C_6H_6 , RT) was also unsuccessful. Deuteration of the IMes *o*- CH_3 groups was still incomplete after 24 h, as deduced from the absence of a Ru-D bond (^2H NMR analysis), while prolonged reaction (3 days at $55\text{ }^\circ\text{C}$) resulted in decomposition. Given the experimental inaccessibility of $\text{RuDCl}(\text{N}_2)(\text{IMes})_2$, the vibrational frequencies were calculated for $\nu(\text{Ru-H})$ and $\nu(\text{N}\equiv\text{N})$ bands using DFT methods. The computed energies are very similar ($\nu(\text{Ru-H})$, 2187 ; $\nu(\text{N}\equiv\text{N})$, 2174 cm^{-1}), tending to confirm the coincident location inferred from the experimental spectrum. (It should be noted that while trends in calculated IR frequencies are significant, *absolute* values should be treated with caution, as current DFT methods are limited in their precision for vibrational analyses).³²

* Reaction of $\text{RuHCl}(\text{H}_2)(\text{IMes})_2$ with N_2 was carried out by Nicholas Beach of this laboratory.

** Synthesis of **Ru-8-D** (by Carolyn Higman of this group, and Nicholas Beach) was unsuccessful despite much effort: see text.

The location of the $\nu(\text{N}\equiv\text{N})$ band is striking in comparison to those for $[\text{RuCl}_2(\text{Cy}_2\text{P}(\text{CH}_2)_4\text{PCy}_2)]_2(\text{N}_2)$,³³ $\text{RuHCl}(\text{N}_2)(\text{PCy}_3)_2$,³⁴ and $\text{RuHCl}(\text{IMes})(\text{N}_2)(\text{PCy}_3)$ ²⁶ (2124, 2060, and 2048 cm^{-1} , respectively). As the lowest-energy location yet reported for a monometallic ruthenium complex (Table 3.1),³⁵ this suggests considerable weakening of the $\text{N}\equiv\text{N}$ triple bond.

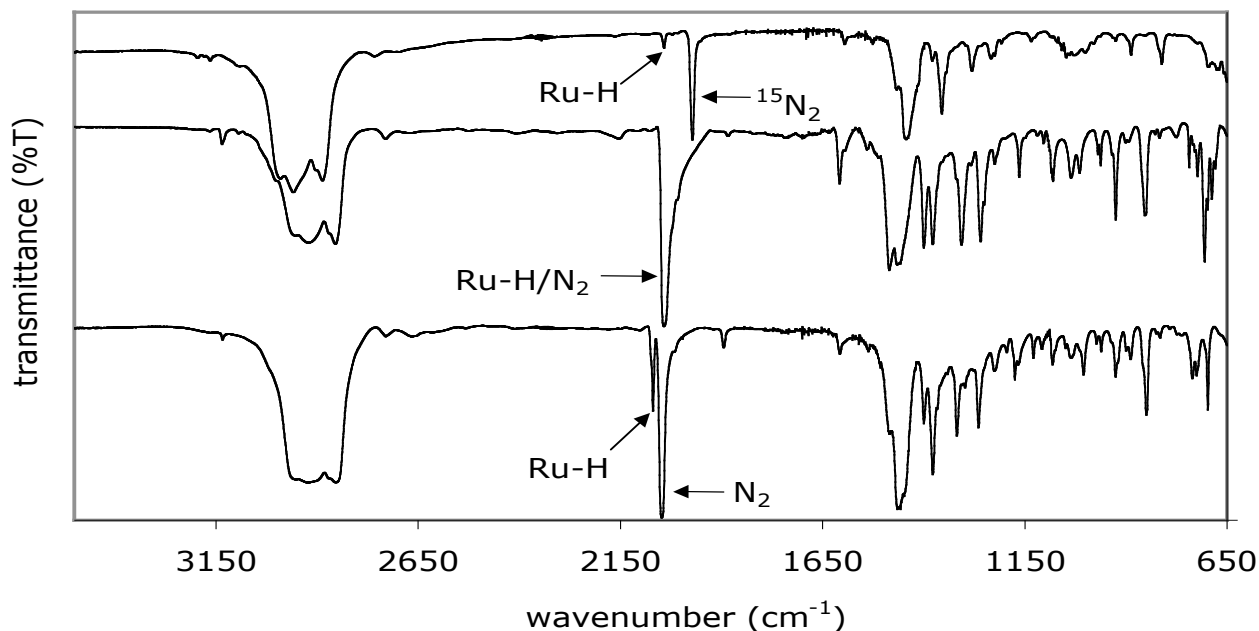
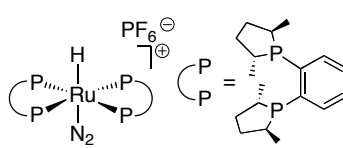
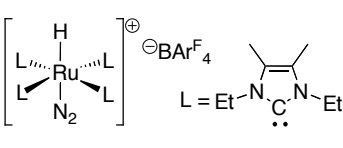
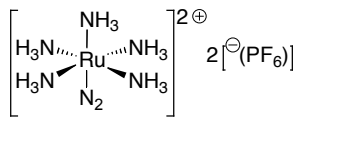
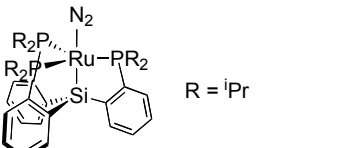
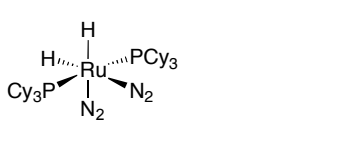
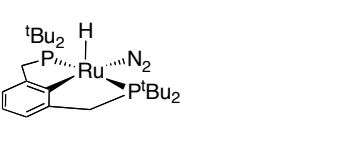
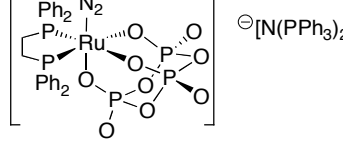
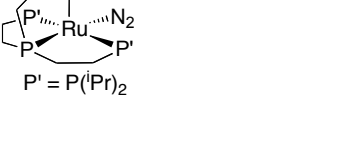
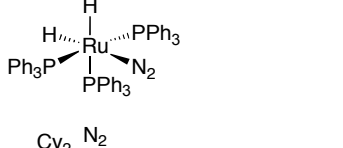
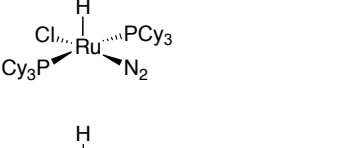
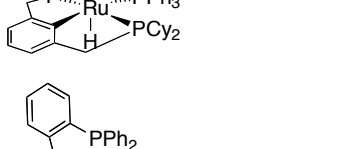
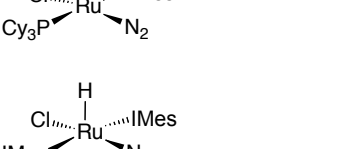
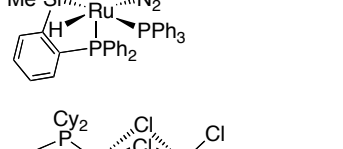
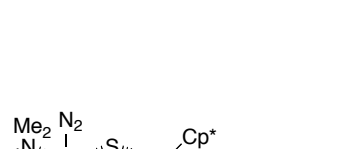
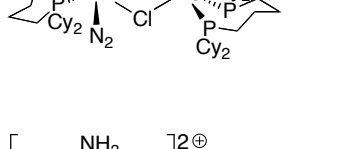
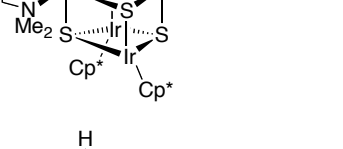
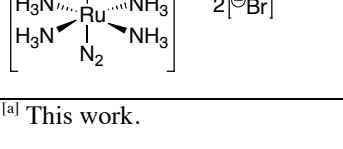
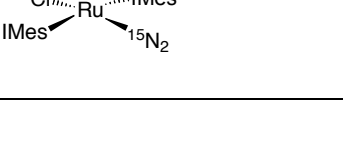


Figure 3.1. IR spectra of **Ru-8- $^{15}\text{N}_2$** (top), **Ru-8** (middle); $\text{RuHCl}(\text{N}_2)(\text{IMes})(\text{PCy}_3)$ (bottom). **Ru-8- $^{15}\text{N}_2$** : $\nu(\text{Ru-H})$ 2039 cm^{-1} , $\nu(\text{N}_2)$ 1972 cm^{-1} ; **Ru-8**: $\nu(\text{Ru-H})$, $\nu(\text{N}_2)$ 2041 cm^{-1} ; $\text{RuHCl}(\text{N}_2)(\text{IMes})(\text{PCy}_3)$: $\nu(\text{Ru-H})$ 2069 cm^{-1} , $\nu(\text{N}_2)$ 2048 cm^{-1} .

Table 3.1. IR stretches of reported Ru-N₂ complexes.

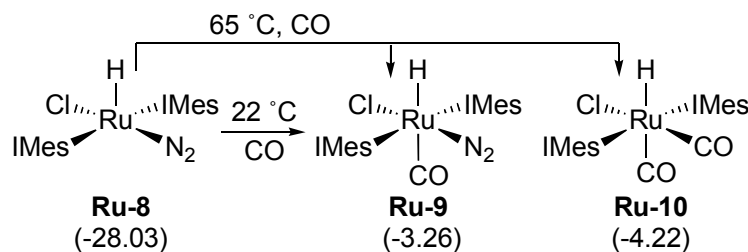
Complex	$\nu(\text{N}\equiv\text{N})$ (cm ⁻¹)	Complex	$\nu(\text{N}\equiv\text{N})$ (cm ⁻¹)
Free N ₂	2331 ²		
	2184 ²³		2100 ³⁰
	2167 ⁵		2088 ³⁶
	2163 ³⁷		2088 ³⁸
	2154 ²⁰		2083 ³⁹
	2147 ⁴⁰		2060 ³⁴
	2134 ⁴¹		2048 ²⁶
	2131 ⁴²		2041 ^[a]
	2124 ³³		2019 ⁴³
	2118 ⁵		1972 ^[a]

^[a] This work.

3.4 Reactivity of $\text{RuHCl}(\text{N}_2)(\text{IMes})_2$ with CO.

Exposure of a C_6D_6 solution of **Ru-8** to CO resulted in a time-of-mixing color change from orange to pale yellow. ^1H NMR analysis indicated a ca. 25 ppm downfield shift in the dominant hydride singlet, consistent with formation of a coordinatively saturated metal centre, but the chemical shift does not match either $\text{RuHCl}(\text{CO})(\text{IMes})_2$ – the expected kinetic product following N_2 loss – or known¹⁹ di-carbonyl complex **Ru-10** (Scheme 2). While **Ru-10** is indeed obtained under more forcing conditions (65% conversion in 1.5 h at 65 °C; C_6D_6), only traces of this species are formed at 22 °C. Instead, the major product at 22 °C, formed in ca. 90% yield, is the mono-CO *adduct* **Ru-9**. Unequivocal support for the assignment of **Ru-9** comes from the downfield location of the hydride singlet (–3.26 ppm; cf. –4.22 ppm for **Ru-10**), the observation of correlations (^1H - ^{13}C HMBC) between this signal and those due to both the carbene carbon and a new CO carbon (187.7 and 195.0 ppm, respectively), and the large $^2J_{\text{CH}}$ value for the latter signal in the ^{13}C NMR spectrum (49 Hz, consistent with coupling to a trans-disposed⁴⁴ hydride). IR bands for $\nu(\text{N}\equiv\text{N})$, $\nu(\text{Ru-H})$, and $\nu(\text{C}\equiv\text{O})$ appear at 2118, 2039, and 2005 cm^{-1} , respectively. Satisfactory microanalysis was hampered by ligand loss under vacuum, as well as the presence of trace **Ru-10**.

Five-coordinate ruthenium complexes bearing bulky donor ligands commonly react via a dissociative pathway, and the energetic accessibility of four-coordinate "sawhorse" structures is very well established.⁴⁵ The accessibility of a dissociative pathway from related bis(IMes) complexes is confirmed by the reported dynamic equilibrium between $[\text{RuH}(\text{CO})(\text{IMes})_2(\text{N}_2)] \text{BAr}^{\text{F}}$ and its N_2 -free derivative.¹⁹ Formation of **Ru-9** thus reflects a kinetic barrier to N_2 loss from **Ru-8**, which we attribute (see below) to the unusual thermodynamic stability of this N_2 adduct. The relatively strong Ru- N_2 binding impedes access to the expected four-coordinate intermediate, while the small size of the CO ligand, and the stabilization arising from push-pull σ -donor π -acceptor interactions, helps to stabilize adduct **Ru-9**.



Scheme 3.4. Products formed on reaction of **Ru-8** with CO. Values in brackets give ^1H NMR chemical shifts for the hydride singlet (C_6D_6).

The reluctance with which **Ru-8** undergoes conversion into **Ru-9** is remarkable, given the ease with which N_2 is normally displaced in late-metal complexes (including closely related hydridoruthenium-NHC derivatives).^{19,30,46,47} In comparison, treatment of $\text{RuHCl}(\text{N}_2)(\text{PCy}_3)_2$ with CO yields 50% $\text{RuHCl}(\text{CO})_2(\text{PCy}_3)_2$ within 20 min at RT.³⁴ The more forcing conditions required to convert **Ru-9** into **Ru-10** suggest that a strong Ru- N_2 interaction is retained in the former (although the presence of the π -acid CO ligand will undoubtedly attenuate N_2 binding relative to **Ru-8**). To gain deeper insight into the stability of **Ru-8**, a computational analysis was undertaken.

3.5 Computational Analysis of $\text{RuHCl}(\text{N}_2)(\text{IMes})_2$.

3.5.1 Methodology.

DFT analysis of **Ru-8** and related systems was undertaken using the Gaussian 03 package at the B3LYP⁴⁸ / DZVP⁴⁹ level of theory. The molecular orbitals were analyzed in terms of fragment orbital contributions using the AOMix program.⁵⁰ These studies were carried out on the full (i.e. non-truncated) system **Ru-8**, and compared to $\text{RuXX}'(\text{IMes})_2(\text{N}_2)$ (**Ru-8'**: $\text{X} = \text{X}' = \text{H}$; **Ru-8''**: $\text{X} = \text{X}' = \text{Cl}$), to gain insight into the influence of the σ -donor hydride and π -acceptor chloride ligands. The function of the L-donor ligand was also assessed by comparing the structures $\text{RuHCl}(\text{L})_2(\text{N}_2)$ where $\text{L} = \text{PMe}_3$, IMes and H_2IMes .

The Gibbs free energy for N_2 dissociation at 298 K (ΔG_{298}) was calculated to assess the strength of the Ru- N_2 interaction for all three complexes. Values for $\nu(\text{N}=\text{N})$ and the atomic

charges of N_α and N_β were calculated to gain insight into the effect of the ancillary ligands on the degree of N_2 activation. A more detailed understanding of ligand effects was sought through a fragment molecular orbital (FMO) analysis. In the FMO calculations, the complexes were treated as composites of their $RuXX'(IMes)_2$ (F1) and N_2 fragments. d-Orbital energies were calculated for F1, as was the proportion of ruthenium character in each orbital. The strength of N_2 binding that results from joining the fragments (i.e. turning on the F1- N_2 interaction) was probed by examining the associated change in electronic population ($\% \Delta_{pop}$) and the orbital interaction energy (E_{int}): the latter reveals the energy gain.

3.5.2 Ligand Dissociation Energies.

The calculated free energies for N_2 dissociation from $RuHCl(L_2)(N_2)$ are all within 3 kcal mol⁻¹ for the complexes in which L is PMe_3 , H_2IMes , and $IMes$ (Table 3.2). In striking contrast, the complexes in which the X-donor ligand is varied (i.e. **Ru-8**, **Ru-8'** and **Ru-8''**) exhibit widely different ΔG values, of 17.8, 5.2 and 1.9 kcal mol⁻¹, respectively (Table 3.2). That is, the L-donor ligand has little effect on N_2 lability, while the combination of hydride and chloride X-donor ligands is important in enhancing the strength of the metal-dinitrogen interaction in **Ru-8**. Unexpectedly, the magnitude of ΔG_{298} calculated for the Ru- N_2 bond is also much higher than that for the Ru- C_{NHC} bond (17.8 vs. 14.6 kcal mol⁻¹), despite the strength routinely attributed to metal-NHC bonds,⁵¹ and the weakness generally presumed for late metal- N_2 interactions.

Table 3.2. N_2 lability vs. $N \equiv N$ activation in **Ru-8** and related complexes.^[a]

Entry	Compound	ΔG_{298}	$\nu(N \equiv N)$	Atomic Charge (a.u.)	
		(kcal mol ⁻¹)	(cm ⁻¹)	N_α	N_β
1	$RuHCl(IMes)_2(N_2)$, Ru-8	18 ^[b]	2174 [2041]	-0.02	-0.10
2	$RuH_2(IMes)_2(N_2)$, Ru-8'	5	2194	-0.06	-0.09
3	$RuCl_2(IMes)_2(N_2)$, Ru-8''	2	2235	-0.01	-0.05
4	$[Ru(NH_3)_5(N_2)](PF_6)_2$	14	2319 [2167] ⁵	-0.08	+0.13

5	[FeH(depe) ₂ (N ₂)] (BPh ₄) ^{[c],16}	n.g.	— [2091]	−0.09	+0.11
6	RuHCl(H ₂ IMes) ₂ (N ₂)	17	2186	+0.04	−0.08
7	RuHCl(N ₂)(PMe ₃) ₂	20	2216 [2060] ^[d]	+0.02	−0.04
8	Mo(NN' ₃)(N ₂) ^{[e],16}	n.g.	— [1990] ^{52b]}	−0.07	−0.06

^[a] Lability gauged from ΔG for N₂ loss; activation from both $\nu(\text{N}\equiv\text{N})$ values (indicated as calculated [experimental] values), and atomic charges on N (assessed by natural population analysis). ^[b] ΔG for loss of IMes = 14.6 kcal mol^{−1}. ^[c] depe = 1,2-bis(diethylphosphino)ethane. ^[d] Experimental value refers to the PCy₃ analogue. ^[e] N' = 3,5-(2,4,6-*i*-Pr₃C₆H₂)₂C₆H₃.

3.5.3 Calculated^{*32} Stretching Frequencies and Atomic Charges for the N≡N Ligand.

In contrast with N₂ lability, N≡N *activation* is strongly influenced by both the neutral and the anionic ligands. As judged from calculated $\nu(\text{N}\equiv\text{N})$ frequencies, N₂ activation increases in RuHCl(N₂)L₂ complexes according to the trend L = IMes > H₂IMes > PMe₃ (2174, 2186 and 2216 cm^{−1} respectively; Table 3.2). Back-donation from Ru to N₂ is also maximized by the combination of strong σ -donor hydride, and π -donor chloride (H,Cl > H,H > Cl,Cl; 2174, 2194, 2235 cm^{−1}).

The atomic charges on N _{α} and N _{β} (Table 3.2), calculated by natural population analysis, reveal a negative charge at both sites for all three of complexes **Ru-8**, **Ru-8'**, and **Ru-8''**. In contrast, the Senoff complex [Ru(NH₃)₅(N₂)]²⁺, as well as [FeH(depe)₂(N₂)] [BPh₄], have a positive charge on the terminal nitrogen atom (>0.10 a.u.). Not only is the corresponding charge on N _{β} for **Ru-8** *negative*, but its magnitude indicates a more basic site than even the Schrock molybdenum system (−0.10 vs. −0.06 a.u.) Strong σ -donation from the two NHC ligands, and from hydride in the case of **Ru-8** and **Ru-8'**, appears to effectively transfer electron density to the nitrogen atoms, and particularly N _{β} .

* For caveats regarding absolute values of calculated vibrational frequencies, see above. Trends in values are more reliable, however.

3.5.4 Fragment Molecular Orbital Analysis.⁵³

The d-orbital energies for the RuXX'(IMes)₂ fragment F1 increase in the order **Ru-8"** < **Ru-8** < **Ru-8'** (Figure 3.2a), reflecting the electrostatic repulsion associated with successive replacement of chloride by the strong σ -donor hydride. The high d-orbital energy in dihydride **Ru-8'** favours F1 $\rightarrow$ N₂ π -back-donation, owing to the improved match in orbital energies, but limits σ -donation from N₂ $\rightarrow$ F1, as indicated by the lower electronic interaction energy (Figure 3.2b). Also a factor is the diluted ruthenium character of the LUFO orbital (**Ru-8'**: 43% Ru; cf. 77% and 74% for **Ru-8** and **Ru-8"**, respectively), which limits σ -donation.

On replacing both hydride ligands with chloride, as in **Ru-8"**, σ -donation is improved by the drop in LUFO energies (a consequence of the decrease in electrostatic repulsion). However, low HOFO energies, and their reduced Ru character, limit effective back-bonding. The cumulative effect is a weakened interaction manifested in the lower $-E_{\text{int}}$ and ΔG_{298} values (ca. 25 and 1.9 kcal mol⁻¹, respectively; see Figure 3.2b and Table 3.2).

Complex **Ru-8** thus occupies a "sweet spot" maximizing both σ -donation from N₂ $\rightarrow$ F1 and π back-donation from F1 into the N₂ antibonding orbital. The remarkable stability of **Ru-8** reflects the larger population changes in HOFO and LUFO, and the much higher $-E_{\text{int}}$ value (Figure 3.2). Tuzek and Lehnert¹⁷ have pointed out the importance of strong σ -donor ligands in N₂ activation: the present system illustrates the operation and limits of this effect, and the capacity of a π -donor ligand to significantly amplify it. It should be noted that the σ -donor ligand must be perpendicular to the M-N bond, so that its strong trans influence does not diminish the M-N₂ bond strength: this feature is built into five-coordinate Ru(II) complexes by the high trans influence of the hydride ligand.

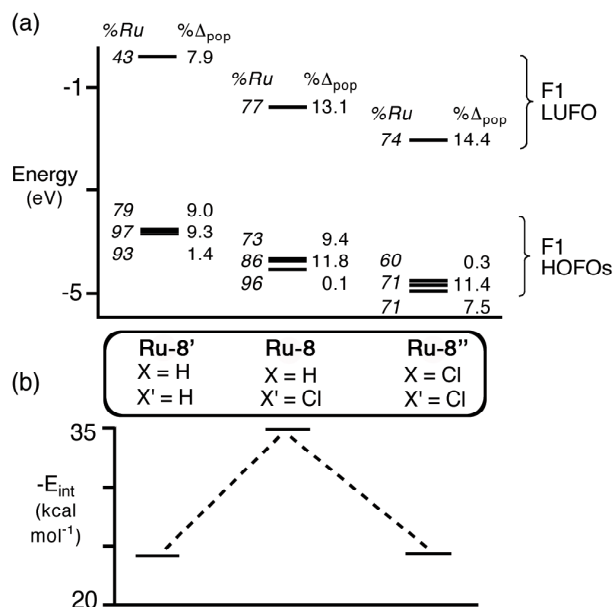


Figure 3.2. a) Energies of frontier molecular orbitals of the [RuXX'(IMes)₂] fragment (F1). %Ru = Ru character in fragment orbitals; %Δ_{pop} = change in population on turning on the F1-N₂ interaction. b) F1-N₂ Electronic interaction energy (-E_{int}).

3.6 Examining the Reactivity at the N₂ Ligand for Ru-8.

3.6.1 Methodology.

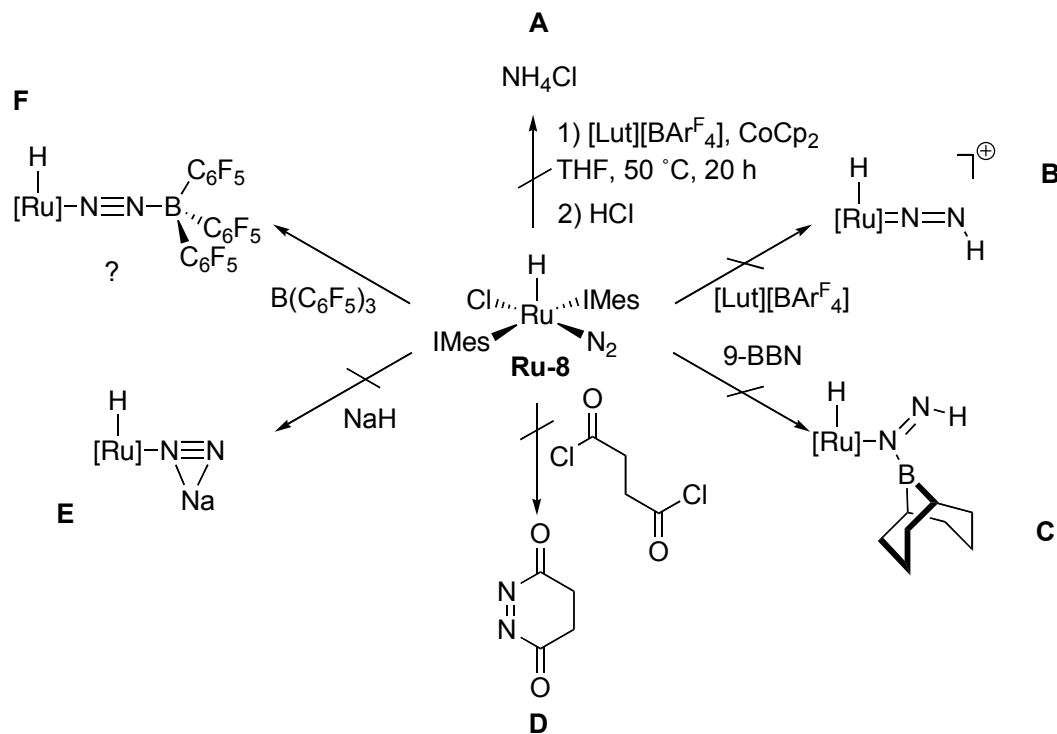
Reduction of the N₂ ligand in **Ru-8** was attempted following the Schrock protocol.^{11,54} Thus, lutidinium BAr^F₄ (2,6-dimethylpyridinium tetrakis[3,5-bis(trifluoromethyl)phenyl]borate) was used as the proton source, with CoCp₂ as the reducing agent (3.5 equiv each), in C₆H₆ or THF. To capture as NH₄Cl any NH₃ liberated, reactions were carried out with vigorous stirring at 50 °C in a Teflon-sealed vessel for up to 20 h, then vacuum-transferred (-131 °C; N₂-pentane slush bath) into a flask containing a solution of HCl in dioxane (4 M), diluted with Et₂O to 1 M. After 5 min, the Teflon valves leading to the reaction and collection flasks were sealed to trap any unreacted NH₃, and the frozen contents of the latter were allowed to warm to 0 °C by replacing the slush bath with an ice bath. The solution was stirred for at least 30 min. Concurrently, a solution of KO^tBu in benzene was added to the reaction flask to cleave any metal-bound ammonia. After 10 min, the vacuum-transfer step was repeated. The combined condensates were stirred at 0 °C for 15 minutes, after which a known amount of

1,3,5-trimethoxybenzene (TMB; internal standard for NMR analysis) was added from a stock solution in C₆H₆. The solvent was removed under vacuum, and the residue was redissolved in DMSO-*d*₆ and subjected to ¹H NMR analysis.

Functionalization of the dinitrogen moiety was attempted in a series of NMR experiments in C₆D₆ or (for the reaction with NaH) in THF.²¹ Solid TMB was added to these solutions, which were then analyzed to establish the initial integration ratio of hydride vs. TMB. The reagents of interest (see Scheme 3.5 and Table 3.3) were then added, the NMR tubes shaken to effect mixing, and the samples left to stand for 24 hours prior to reanalysis. Their ¹H NMR spectra were then examined for decreases in the integrated intensity of the hydride signal for **Ru-8**, as well as the emergence of new signals for product(s). Any change was followed up by ¹H-¹⁵N HSQC analysis, to establish whether reaction involved the N₂ functionality. Finally, the volatiles were stripped off under vacuum for IR analysis of the residues. In the case of B(C₆F₅)₃, ¹¹B{¹H} NMR spectroscopy was employed to gain insight into reaction products.

3.6.2 Attempted Reduction of N₂ to NH₃ with **Ru-8**.

Complex **Ru-8** was treated with lutidinium BAr^F₄ and CoCp₂ in a sealed flask and heated to 50 °C in THF for 20 h (Scheme 3.5). No NH₄Cl was observed on ¹H NMR analysis of the collected volatiles in three independent trials (Table 3.3, Entry 1). No evidence for ammonium chloride was observed, irrespective of whether the reduction step was carried out in benzene or THF. It may be noted that this does not preclude the possibility that protonation is successful, but reduction is not (see Scheme 3.5b). The absence of reaction was surprising given the *more negative* atomic charge on N_β relative to the Schrock molybdenum complex (see above).



Scheme 3.5. Attempts to activate the dinitrogen ligand in $\text{RuHCl(IMes)}_2\text{(N}_2\text{)}$ **Ru-8** by protonation (**A**, **B**), hydroboration (**C**), nucleophilic attack (**D**), reduction (**E**) and Lewis acid-base reaction (**F**).

3.6.3 Attempted Functionalization of the N_2 ligand of **Ru-8**.

Addition of the proton source $[\text{Lut}][\text{BAr}^{\text{F}}_4]$ to **Ru-8** in C_6D_6 at ambient temperature resulted in a perceptible shift of the hydride resonance (from -28.03 to -28.26 ppm) after 2 h; no further changes occurred over 24 h. The new signal integrates for 73% of the starting hydride (the difference implying partial decomposition and/or conversion to paramagnetic material). Surprisingly, however, ^1H - ^{15}N HSQC NMR analysis showed no change in the chemical shift of the key N_α resonance for **Ru-8**, which is expected to be highly sensitive to changes in the nitrogen environment.⁵⁵ Workup by concentration and precipitation (THF-hexanes) yielded an orange product that showed only starting **Ru-8** by ^1H NMR and IR analysis (Table 3.3, Entry 2). Protonation was therefore deemed to be unsuccessful, and the observed hydride shift was attributed to a change in solvent pH due to dissolved $[\text{Lut}][\text{BAr}^{\text{F}}_4]$. Similar attempts at hydroboration,⁵⁶ nucleophilic addition,⁵⁷ or reduction^{15d]} using 9-BBN, succinyl chloride, or NaH, respectively (Table 3.3, Entries 3-5) were unsuccessful.

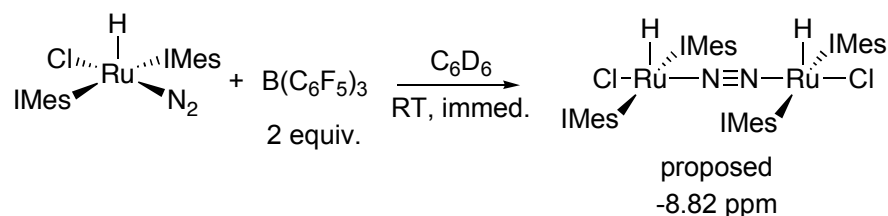
Table 3.3. Attempted transformation of the N₂ ligand with various reactants.^[a]

Entry	Reactant	Proposed reactivity at N ₂	Time (h)	Product (%)
1	[Lut][BAr ^F ₄] + CoCp ₂	Reduction to NH ₃	20	0
2	[Lut][BAr ^F ₄]	Protonation	2	0
3	9-BBN	Hydroboration	24	0
4	Succinyl chloride	Nucleophilic attack	24	0
5	NaH	Reduction	24	0
6	B(C ₆ F ₅) ₃	Lewis acid base adduct	Immed.	100

^[a] All reactions at 24 °C except Entry 1 (performed at 50 °C).

3.6.4 Reaction of **Ru-8** with the Lewis acid tris(pentafluorophenyl)borane.

Addition of two equivalents of B(C₆F₅)₃ to **Ru-8** in C₆D₆ resulted in complete and immediate conversion to a new hydride species at –8.82 ppm (Table 3.3, Entry 6; Scheme 3.6). ¹¹B{¹H} NMR analysis gave a null signal; observation of a shallow immiscible layer at the bottom of the NMR tube (i.e. beneath the probe detection zone) suggests that the boron species is not bound to ruthenium. This rules out the possibility of a Lewis acid-Lewis base adduct in which the N₂ ligand bridges between ruthenium and boron (Scheme 3.5, F).⁴⁰ Solvent was removed from both layers of the NMR sample, and the residue was combined with Nujol for IR analysis. The absence of an IR stretching band in the region expected for a terminal dinitrogen ligand (2331-2041 cm⁻¹) may indicate formation of an IR-inactive, symmetrical μ-N₂ dimer;⁵⁸⁻⁶¹ see Scheme 3.6. However, no correlation from the hydride signal to N₂ could be detected (¹H-¹⁵N HSQC). Further investigation into the new hydride species formed in benzene is warranted. Finally, addition of B(C₆F₅)₃ to **Ru-8** in CD₂Cl₂ was undertaken in an effort to maintain miscibility of all components, but decomposition prevented further insight by ¹¹B{¹H} or ¹H NMR studies.

**Scheme 3.6.** Potential formation of Ru₂(μ-N₂) dimer following addition of B(C₆F₅)₃.

3.7 Conclusion.

The foregoing describes a ruthenium NHC complex that binds N₂ with unprecedented strength. The low-energy $\nu(\text{N}\equiv\text{N})$ band, the low N₂ lability, and the negative charge calculated for N _{β} all point toward significant activation of the N₂ ligand. These findings indicate that the problem of high N₂ lability is not inherent to late transition metal complexes. This, in conjunction with the sensitivity of N₂ binding and the N-N bond strengths to superficially minor changes in the ancillary ligands, suggests potentially promising new directions for dinitrogen activation by robust late-transition metal catalysts.

The reluctance of **Ru-8** to undergo reaction is surprising given the extent of N₂ activation (including the high negative charge on N _{β}) indicated by experimental and computational analysis. This may reflect the capacity of the sterically demanding IMes ligands to block approach to the dinitrogen ligand. If this is the case, formation of a $\mu\text{-N}_2$ dimer following reaction of **Ru-8** with B(C₆F₅)₃ should also be hindered. Detailed structural elucidation of the B(C₆F₅)₃ addition product may provide insight into the steric environment around the N₂ ligand. As well, the possibility that the IMes ligands exert steric inhibition on the functionalization of the N₂ ligand should be considered. Synthesis of complexes analogous to **Ru-8**, but containing less sterically demanding NHC ligands, have promise for accessing the desired combination of N₂ stabilization and reactivity.

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Chapter 4. Chiral Metathesis Catalysts Based on the Ru-Binaphtholate Moiety: Synthesis, Coordination Modes, and Activity*

4.1 Introduction.

Asymmetric metathesis offers powerful opportunities for the synthesis of chiral molecules and tactic polymers.¹⁻³ A key series of papers by Hoveyda and Schrock showcases the fine-tuning of selectivity attainable by incorporating 1,1'-binaphthyl-2,2'-diolate (BINO) and biphenolate-derived ligands within the Schrock family of Mo catalysts,⁴⁻⁸ which set the benchmark for both activity and selectivity. In general, however, ruthenium metathesis catalysts are favored for their superior tolerance to air, water and various functional groups (the latter being real, if commonly overestimated). In the Ru systems, the usual chiral element is a desymmetrized NHC ligand (NHC = *N*-heterocyclic carbene).⁹⁻¹³ A rare¹⁴ example of an atropisomeric ligand in the Ru systems is Hoveyda's κ^2 -C,O-chelate complex.^{15,16} Despite the showcase examples in the Mo systems, which exhibit exquisite control over enantioselectivities arising from steric fine-tuning via 3,3'-functionalization of the binaphtholate rings,¹⁷ incorporation of simple BINO ligands within the Grubbs-class catalysts was unreported at the outset of this thesis work. This absence is particularly notable given the commercial availability of the Ru precursors and many relevant proligands, including chiral biphenolate, as well as BINO, derivatives.

The axial chirality of the 1,1'-binaphtholate (BINO) ligand has been widely exploited in asymmetric catalysis, in transformations ranging from Lewis acid catalysis to olefin epoxidation, oxidation and reduction, and enantioselective C-C coupling, including cycloaddition and olefin metathesis.¹⁷⁻²⁰ Most BINO catalysts are based on the early and mid-transition elements, or the lanthanides. Late-metal derivatives are limited to about a dozen examples,²¹⁻³³ although ample evidence indicates that late-metal aryloxide bonds are neither intrinsically weak nor labile³⁴⁻³⁶ (Pearson hard-soft presumptions notwithstanding).

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The first ruthenium derivatives were very recently reported by Li and coworkers (**Ru-28'**, Chart 4.1c).³⁷

Within late-metal complexes, the binaphtholate ligand often adopts the *O,O*-bound coordination mode common in the early metals.* Examples include Ir,²⁸ Fe,³¹ Pt^{21-24,26,27,30,33} and Pd^{23,25,26} complexes (Chart 4.1a). Coordination of the carbon framework has been observed, however. An $\eta^1\text{-CI}, \eta^1\text{-O'}$ coordination mode found in Pd³⁸ and Pt³² chemistry affords a five-membered chelate ring with a subtended ketone functionality (Chart 4.1b). Coordination of BINO to Ir, Rh and Ru complexes results in $\eta^3, \eta^1\text{-BINO}$ binding (Chart 4.1c).³⁷ The enolate moiety in these complexes was established based on crystallographic analysis of the Ir and Rh complexes, and the ruthenium complex was assigned on the basis of its similar ¹³C NMR BINO chemical shifts.³⁷ If this binding mode is excessively stable, and the BINO ligand irreversibly occupies the potential substrate binding sites at the metal, catalyst inhibition would be inevitable. The catalytic importance of BINAP complexes of Ru, Pd and Pt (BINAP = 2,2'-bis(diphenylphosphanyl)-1,1'-binaphthyl),³⁹ which is unimpeded by the extraordinary range of related, multi-haptic coordination modes demonstrated by Pregosin and co-workers, points toward the ease with which binding modes shift in the corresponding diphosphine chemistry. Similar features appear to be operative for BINO, as will be shown below.

* The η nomenclature is used in preference to the κ^2 designation, for ease of comparing coordination modes. Donors of higher hapticity are shown first; those of lower hapticity are designated by a prime symbol. For enolates ($\eta^3\text{-O}, \text{C2}, \text{CI}, \eta^3\text{-O'}, \text{C2'}, \text{CI'}$), full notation is cumbersome: we adopt the abbreviated notation $\eta^x, \eta^y\text{-BINO}$ for the *O*-bound isomers, but (to avoid ambiguity) not for the rarer $\eta^1\text{-CI}, \eta^1\text{-O'}$ structures. To further facilitate the distinction between coordination modes in the text the notation **Ru-#** ($\eta^1, \eta^1\text{-BINO}$), **Ru-#'** ($\eta^3, \eta^1\text{-BINO}$) and **Ru-#''** ($\eta^3, \eta^3\text{-BINO}$) is used for compound numbering.

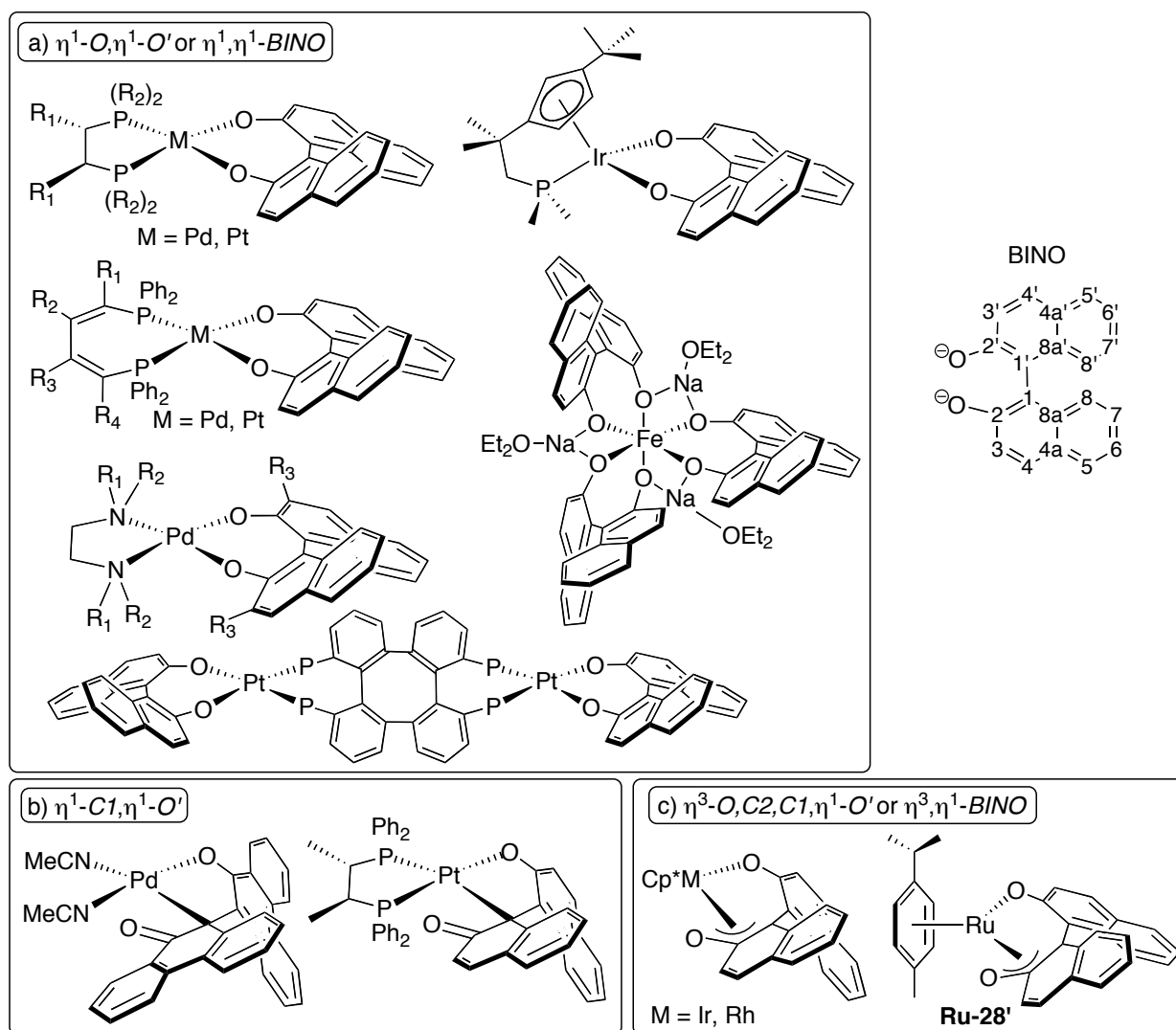
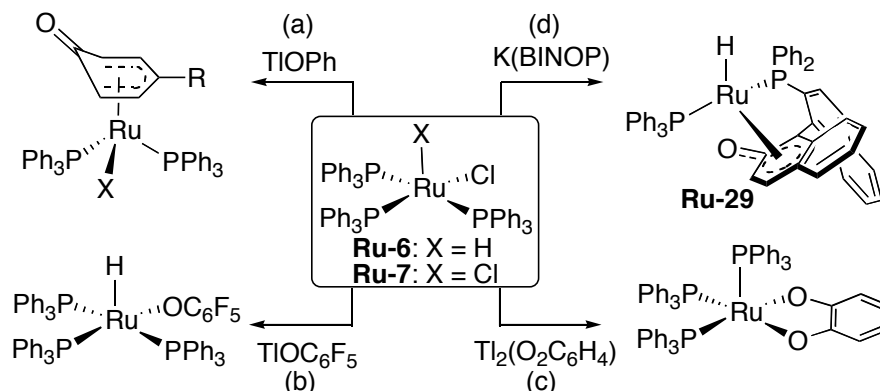


Chart 4.1. Coordination modes established for binaphtholate and related ligands in late transition metal chemistry. a) $\eta^1, \eta^1\text{-BINO}$; b) $\eta^1\text{-C1}, \eta^1\text{-O'}$; c) $\eta^3, \eta^1\text{-BINO}$.

As the foregoing suggests, few studies report on the coordination chemistry of binaphtholate with ruthenium. Insight into potential coordination modes can, however, be extracted from the established behaviour of related aryloxide ligands. Attempts to incorporate monodentate σ -phenoxide ligands into simple ruthenium complexes, such as $\text{RuClX}(\text{PPh}_3)_3$ (**Ru-6**: X = H; **Ru-7**: X = Cl), are frustrated by $\sigma \rightarrow \pi$ isomerization to form piano-stool structures (Scheme 4.1a).^{40,41} Synthesis of $\sigma\text{-OAr}$ complexes required use of electron-deficient aryloxides to deplete the donor ability of the aryl ring.⁴² Importantly, the behaviour of $\text{RuClX}(\text{PPh}_3)_3$ accurately predicted that of the Ru-benzylidene precursor $\text{RuCl}_2(\text{IMes})(\text{py})_2(=\text{CHPh})$, which

afforded σ -OC₆X₅ products (X = F, Cl, Br) on reaction with perhaloaryloxide salts (Chart 4.2a).⁴³ Likewise, chelate rings of five and six members that were shown to stabilize σ -aryloxide ligands within the RuCl₂(PPh₃)₃ platform prove suitable for incorporation into labile Ru-benzylidene complexes (Scheme 4.1d, Chart 4.2b, respectively).^{14,44-51} In contrast, reaction of RuHCl(PPh₃)₃ with the bifunctional phosphine-phenoxide ligand BINOP yields a piano-stool chelate structure **Ru-29**, with the aryloxide ring bound η^6 (Scheme 4.1d).⁴² The difference reflects the greater flexibility of the seven-membered chelate ring. On this basis, Hoveyda's report of the κ^2 -NHC-binaphtholate complex was surprising (Chart 4.2d).^{15,16,52} The stability of this seven-membered chelate against η^6 - π isomerization may reflect the very low lability of the styrenyl ether moiety, which inhibits liberation of the third coordination site required for η^{5-6} -coordination of the aryloxide ring.⁴¹



Scheme 4.1. Coordination modes observed on reaction of monodentate and bidentate aryloxide salts with RuClX(PPh₃)₃ (X = H, Cl).

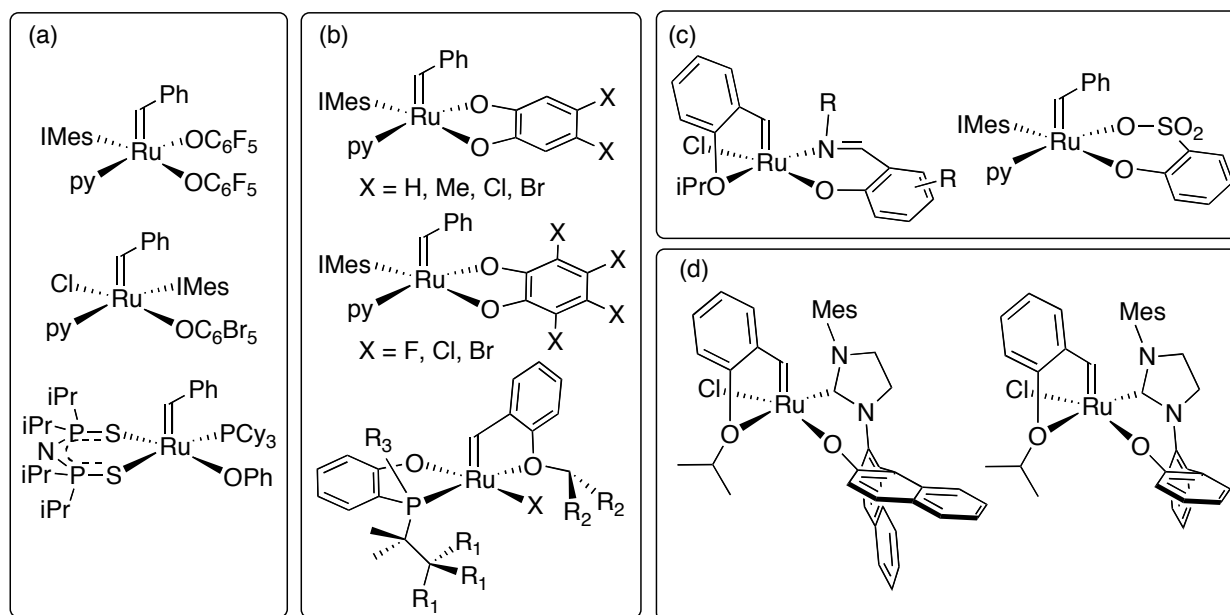


Chart 4.2. Ruthenium benzylidene complexes containing σ -bound aryloxy ligands: a) as monodentate^{53*} ligands; b) as part of a five-membered chelate ring; c) as part of a six-membered chelate ring; d) as part of a seven-membered chelate ring.

The work described in this Chapter was directed at establishing the accessibility of ruthenium-binaphtholate complexes, which at the outset of this work had been regarded as unattainable. Initial studies focused on $\text{RuCl}_2(\text{PPh}_3)_3$ **Ru-7** as a convenient model for the labile, five-coordinate benzylidene complexes that represent the ultimate targets: **Ru-7** shares the coordination number and ligand lability of the latter, without the potential for side-reactions specific to the benzylidene ligand.⁴³ Subsequent work examined the reactions of a range of Grubbs-class benzylidene complexes with BINO salts. Installation of the BINO ligand was deemed successful where (1) the benzylidene ligand is retained intact; (2) both chloride ligands are replaced; and (3) a Ru-OAr species is generated, rather than a piano-stool structure. Unexpected subtleties emerge in point (3), which will be discussed. Success

* A very recent report describes the first Ru-benzylidene complex containing a σ -phenoxide, as opposed to a perhaloaryloxy, ligand (Chart 4.2a). We speculate that its anomalously high stability against $\sigma \rightarrow \pi$ isomerization reflects either strong donation from sulfur in the disulfoimidodiphosphinate ligand $[\text{N}(\text{iPr}_2\text{P}=\text{S})_2]^-$ (which could inhibit donation from the aryloxy ring), or the low lability of the PCy_3 co-ligand (cf. Hoveyda's $\kappa^2\text{-C,O}$ chelate complex; Chart 4.2d).

was found to be highly sensitive to the nature of the ancillary ligands. The final Section of this Chapter discusses preliminary catalytic data for the Ru-BINO benzylidene complexes.

4.2 Synthetic Studies.

4.2.1 Model studies: Coordination Chemistry of $\text{Ti}_2(\text{BINO})$ with $\text{RuCl}_2(\text{PPh}_3)_3$.

4.2.1.1 Methodology.

Two types of reactions are summarized in this Section: the salt metathesis reactions of Ti_2BINO ((*R*) or (*S*), 1.2 equiv) with the model compound $\text{RuCl}_2(\text{PPh}_3)_3$ **Ru-7**, and those in which the products were treated with various neutral ligands. In either case, ligand coordination was first assessed by probe NMR reactions on ca. 10 mg scale. Optimal ratios of ligand and solvent were reaction-dependent, and are discussed individually. The absence of any diagnostic ^1H NMR handle precluded use of an internal NMR standard. However, a null region between 4.00-5.50 ppm for all products rules out an $\eta^6\text{-BINO}$ coordination mode. Conversion to new products was assessed from $^{31}\text{P}\{^1\text{H}\}$ NMR spectra, which were monitored for disappearance of starting material as well as formation of new species.

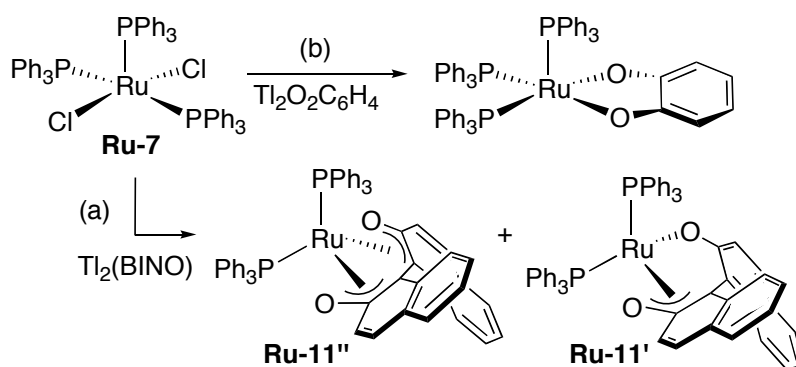
Reactions deemed of interest from these results were scaled up to ca. 100 mg of the Ru precursor, and allowed to proceed for the same period. In cases where TiCl_3 is formed as a by-product, reaction solutions were passed through Celite* to remove the salt, concentrated to a minimum volume, and treated with hexanes to precipitate the product (**Ru-12'** and **Ru-17**). Alternatively, the reaction solvent was removed completely, the residue redissolved in a minimum of THF, and the solid precipitated from chilled hexanes (**Ru-11**, **Ru-14'/Ru-15** and **Ru-16'**) at $-30\text{ }^\circ\text{C}$. The precipitates were then isolated by filtration. In some cases, reaction products were not isolable and NMR characterization was carried out on in situ-generated products (on a scale of ca. 15-20 mg of the metal precursor). In these cases, formation of the product was dependent upon the NMR solvent used ($\text{C}_6\text{D}_5\text{N}$ or 30% $_{\text{v/v}}$ CD_3CN in C_6D_6). Overlap of solvent signals with some BINO resonances hindered full signal assignment. For isolated complexes, NMR analysis was carried out in CD_2Cl_2 so that

* Filtration through Celite was not always sufficient to remove the TiCl_3 salts. Better results were generally achieved by additional filtration through a disposable pipette packed with glass-fiber filter paper cut into ca. 1 cm pieces.

the aromatic signals would not be obscured. The chemical shifts of C1/C1' and C2/C2' are most sensitive to changes in the BINO coordination mode. The locations for the latter signals are found outside of the normal aromatic region, greatly facilitating preliminary assignment. Confirmation is gained via ^1H - ^{13}C HMBC NMR experiments, in which correlations from C1/C1' and C2/C2' are observed to H3 and H4, respectively. A flow chart for assignment of the BINO ^1H and ^{13}C signals is provided in Section 4.2.3, where trends in diagnostic chemical shifts and coupling constants for the different binding modes are also discussed. The number of ancillary ligands in the BINO complexes was identified via ^{31}P and ^1H NMR experiments. Proposed structures were confirmed by single-crystal X-ray diffraction, charge-transfer MALDI-TOF mass spectrometry, and combustion analysis.

4.2.1.2 Reaction of $\text{Ti}_2(\text{BINO})$ with $\text{RuCl}_2(\text{PPh}_3)_3$.

Addition of $\text{Ti}_2[(S)\text{-BINO}]$ or $\text{Ti}_2[(R)\text{-BINO}]$ to a brown-purple suspension of **Ru-7** in THF at 25 °C caused an immediate colour change to pink, and formation of a fine precipitate of TiCl . Conversion to **Ru-11'**/**11''** (Scheme 4.2a) was quantitative within an hour, with liberation of one PPh_3 ligand. The product was isolated in 82% yield after filtering through Celite and reprecipitating from THF/hexanes. Charge-transfer MALDI-TOF MS (Figure 4.1)⁵⁴ and elemental analysis support assignment as $\text{Ru}(\text{BINO})(\text{PPh}_3)_2$. The corresponding reaction of **Ru-7** with catecholate was earlier shown to terminate in tris-phosphine complex $\text{Ru}(\eta^1, \eta^1\text{-O}_2\text{C}_6\text{H}_4)(\text{PPh}_3)_3$ (Scheme 4.2b). The difference provides an early indicator of the structural and electronic versatility that emerges as a hallmark of the more flexible BINO ligand.



Scheme 4.2. Reactions of **Ru-7** with (a) binaphtholate; (b) catecholate.

In CD_2Cl_2 at 23 °C, $\text{Ru}(\text{BINO})(\text{PPh}_3)_2$ exists as a 4:1 mixture of isomers **Ru-11''** and **Ru-11'**, giving rise to $^{31}\text{P}\{^1\text{H}\}$ NMR singlets at 56.9 and 43.5 ppm, respectively.* At 15 °C, the singlet at 43.5 ppm resolves into an AB pattern (43.7, 43.3 ppm; $^2J_{\text{PP}} = 19$ Hz), enabling assignment to the unsymmetrical η^3, η^1 -*BINO* isomer **Ru-11'**. Symmetrical **Ru-11''**, the sole species observable at 60 °C, is the first-reported example of an η^3, η^3 -*BINO* complex. Its identity is confirmed by X-ray analysis of crystals that deposited from a concentrated THF solution by vapour diffusion of hexanes (Section 4.2.4).

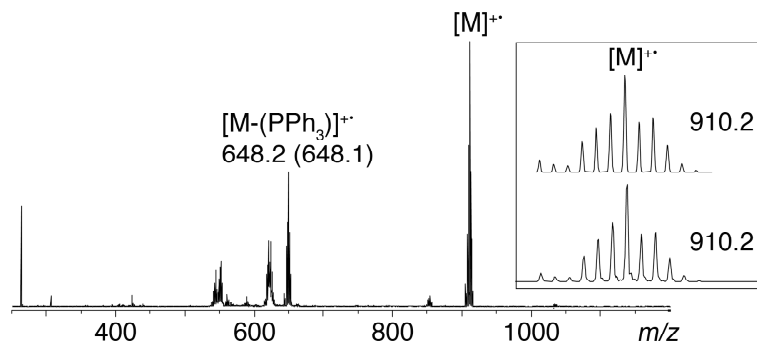


Figure 4.1. Charge-transfer MALDI mass spectrum of **Ru-11'/11''** (pyrene matrix). Inset: simulated (top) and observed (bottom) isotope patterns.

The accessibility of **Ru-11'/11''** provides a valuable opportunity to establish an NMR signature for the novel η^3, η^3 -*BINO* coordination mode. The chemical shifts were examined for the C1/C1' and C2/C2' carbons, which are most sensitive to changes in naphtholate binding, as noted above. C2 is particularly useful: not only is it shifted conveniently far downfield from the heavily populated aromatic window of 120-134 ppm, but its location is highly sensitive to the binaphtholate binding mode (Table 4.1). Assignment of the NMR signals for **Ru-11''** was possible despite the presence of 20% **Ru-11'** at 23 °C, but definitive assignment was aided by a ^1H - ^{13}C HMBC correlation experiment at 60 °C, where only **Ru-11''** is present. A single resonance is observed for C2 and C2' for this complex (as expected from the crystal symmetry): its location, at 145 ppm, is ca. 10 ppm upfield of the signal for C2 in the η^6 -naphthol unit of the Ru-BINOP complex **Ru-29**. The C1/C1' signals are

* $^{13}\text{C}\{^1\text{H}\}$ NMR analysis in CDCl_3 , while advantageous given the observation of solely **Ru-11''** in this solvent, was precluded by decomposition over the timescale of analysis.

likewise equivalent, appearing at 93 ppm, again 10 ppm downfield from the corresponding signal for **Ru-29**.

Table 4.1. Diagnostic $^{13}\text{C}\{^1\text{H}\}$ NMR signals for literature complexes, with different BINO binding modes, for comparison to **Ru-11'**/**11''** synthesized here.^[a]

Entry	Solvent	Complex	Coordination mode	Chemical shift (ppm) ^[b]			
				C1	C2	C1'	C2'
1	CDCl_3	BINOL	—	110.9	152.9	110.9	152.9
2	CD_2Cl_2	Ru-28' ³⁷	η^3, η^1	85.0	141.5	114.0	170.9
3	CDCl_3	Ru-29 ⁴²	η^6, η^1	83.0	155.6	— ^[c]	— ^[c]
4	CD_2Cl_2	Ru-11''	η^3, η^3	93.2	144.7	93.2	144.7
5	CD_2Cl_2	Ru-11'	η^3, η^1	109.1	143.1	114.2	170.4

^[a] A comprehensive table listing new Ru-BINO complexes reported in this thesis is provided in Section 4.2.3.

^[b] C1/C2 and C1'/C2' designate the rings of maximum and minimum hapticity, respectively. ^[c] See Ref. ⁴², values for PPh_2 -functionalized ring omitted.

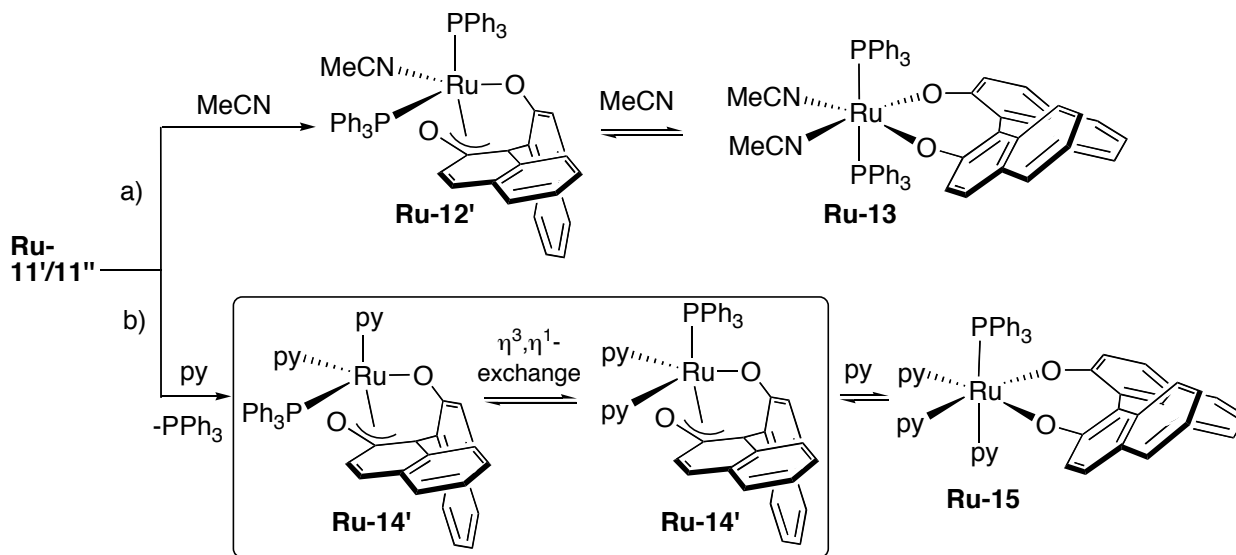
X-ray-quality crystals were not obtained for the minor isomer **Ru-11'**, but the η^3, η^1 -BINO coordination mode was elucidated by NMR spectroscopy. The diagnostic carbon signals were located from the room-temperature spectrum in CD_2Cl_2 . The low symmetry of **Ru-11'**, evident from the inequivalence of the BINO carbon signals (Table 4.1, entry 5), is consistent with the AB pattern observed in the $^{31}\text{P}\{^1\text{H}\}$ NMR spectrum. An enolate unit is present, as indicated by the 143 ppm location for C2, just 2 ppm downfield from the corresponding signal for η^3, η^1 -BINO **Ru-28'**³⁷ (Table 4.1; see Chart 4.1 for complex **Ru-28'**). The shift for C1 differs by 10 ppm from that in **Ru-28'**, but the doublet multiplicity and large coupling constant ($^2J_{\text{CP}} = 16$ Hz) indicate a direct C1-Ru interaction. The chemical shifts for C1' and C2' of the *O*-bound ring are nearly identical to those for **Ru-28'** (**Ru-11'**: C1', 114.2; C2', 170.4). On the basis of this striking similarity in chemical shifts, **Ru-11'** is identified as an η^3, η^1 -BINO derivative. The alternative possibility of an η^1 -CI, η^1 -O' binding mode, seen previously with Pt and Pd complexes (Chart 4.1),^{38,55} is readily ruled out: this results in a diagnostic downfield shift of C2 into the carbonyl region (ca. 195 ppm), and an upfield shift of C1 to ca. 80 ppm.

The **Ru-11'**/**11''** equilibrium is strongly solvent-dependent; equal proportions of the two isomers are found in THF, while only **Ru-11''** is observed in CDCl_3 . ^{31}P EXSY experiments ($\text{THF-}d_8$, CD_2Cl_2) reveal no exchange, indicating that interconversion is slow on the NMR timescale. No signal coalescence is observed by variable-temperature NMR experiments in either THF or toluene, in contrast with the behaviour of **Ru-28'**,³⁷ revealing a higher barrier to interconversion. Equilibration to **Ru-11''** is again complete at higher temperatures: 100% at 80 °C, vs. a 1:1 **Ru-11'**:**Ru-11''** ratio at –80 °C in C_7D_8 . Attempts to extract activation parameters from a van't Hoff analysis were hindered by emergence of a competing, unidentified process at high temperatures.

4.2.1.3 Reactions of $\text{Ru}(\text{BINO})(\text{PPh}_3)_2$ **Ru-11'**/**11''** with acetonitrile and pyridine: Neutral ligand coordination and exchange.

In the catecholate complex $\text{Ru}(\eta^1, \eta^1\text{-O}_2\text{C}_6\text{H}_4)(\text{PPh}_3)_3$ (Scheme 4.2b), the three PPh_3 ligands resist displacement, owing to a greater charge donation from the PPh_3 ligands to compensate for the greater electronegativity of catecholate relative to chloride.⁴⁴ In striking contrast is the lability of the phosphine ligands in **Ru-11'**/**11''** described below, behaviour central to the utility of **Ru-11'**/**11''** as a precursor to chiral Ru-BINO catalysts. This lability was first probed in experiments involving addition of MeCN to solid **Ru-11'**/**11''** (Scheme 4.3a). An orange suspension formed immediately, from which $\text{Ru}(\eta^3, \eta^1\text{-BINO})(\text{PPh}_3)_2(\text{MeCN})$ **Ru-12'** was isolated as a dark pink solid in ca. 70% yield. Single-crystal X-ray analysis revealed that the BINO ligand takes up an $\eta^2\text{-O,C2}, \eta^1\text{-O'}$ coordination mode. NMR analysis in CD_2Cl_2 confirmed the presence of one nitrile ligand (δ_{C} 120.3 ppm, δ_{H} 1.37 ppm), and two cis-disposed phosphine ligands (δ_{P} 49.1, 48.3 ppm; $^2J_{\text{PP}} = 22$ Hz). Less consistent with the X-ray data are the locations of the $^{13}\text{C}\{^1\text{H}\}$ NMR doublets for C2 and C2' (143 ppm, $J_{\text{PC}} = 2$ Hz; 172 ppm; $J_{\text{PC}} = 5$ Hz), in excellent agreement with the values found for $\eta^3, \eta^1\text{-BINO}$ complex **Ru-11'**. The chemical shifts and coupling constants for C1 and C1' (C1: 106 ppm, $J_{\text{PC}} = 15$ Hz; C1': 115 ppm, $J_{\text{PC}} = 1$ Hz) likewise support assignment as an $\eta^3, \eta^1\text{-BINO}$ structure. This is also consistent with the relative magnitudes of the P-C coupling for C1 and C2 (15 and 2 Hz, respectively). We thus conclude that the $\eta^2, \eta^1\text{-BINO}$ coordination found in the solid-state structure results from crystal packing effects.

Addition of MeCN to a solution of **Ru-12'** in benzene triggers slippage from η^3, η^1 - to η^1, η^1 -*BINO* binding, permitting coordination of a second acetonitrile ligand. $\text{Ru}(\eta^1, \eta^1\text{-BINO})(\text{PPh}_3)_2(\text{MeCN})_2$ **Ru-13** is the dominant species present in 3:1 $\text{C}_6\text{D}_6\text{-CD}_3\text{CN}$: a $^{13}\text{C}\{^1\text{H}\}$ NMR singlet for the equivalent C1 nuclei appears at ca. 128 ppm; a singlet for C2 at 169 ppm. The equivalent PPh_3 ligands (which give rise to a $^{31}\text{P}\{^1\text{H}\}$ NMR singlet at 49.0 ppm) may be mutually cis- or trans-disposed; trans-disposition is more probable on steric grounds. Attempts to precipitate **Ru-13** yielded only **Ru-12'**, indicating facile exchange between five- and six-coordinate species.



Scheme 4.3. Decreases in BINO hapticity in response to an increase in coordination number. Synthesis of a) MeCN; b) pyridine derivatives of $\text{Ru}(\text{BINO})(\text{PPh}_3)_2$ **Ru-11'/11''**.

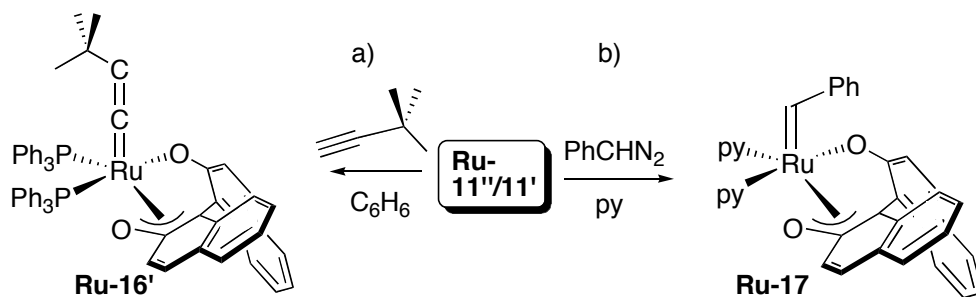
Addition of pyridine-*d*5 to **Ru-11'/11''**, in comparison, effects immediate dissolution, accompanied by a colour change from red to orange. Displacement of one phosphine ligand to afford $\text{Ru}(\eta^1, \eta^1\text{-BINO})(\text{PPh}_3)_2(\text{py})_3$ **Ru-15** (Scheme 4.3b) is confirmed by in situ $^{31}\text{P}\{^1\text{H}\}$ NMR analysis, which indicates a 1:1 ratio between the singlets for free PPh_3 and for **Ru-15** (55.6 ppm). The locations of the C2/C2' and C1/C1' signals indicate η^1, η^1 -*BINO* binding (C2, C2': 170.0, 169.7 ppm; C1, C1': 128.1, 127.8 ppm). The singlet multiplicities of C2/C2' imply that these nuclei are cis to the remaining PPh_3 ligand.

Reaction on preparative scale (100 mg) in protio-pyridine afforded an orange powder in 70% yield. X-ray quality crystals deposited by diffusion of Et₂O into a saturated THF solution. Unexpectedly, these consisted of the bis-pyridine derivative Ru(η^3, η^1 -BINO)(PPh₃)(py)₂ **Ru-14'**. NMR analysis of the isolated product in CD₂Cl₂ reveals the presence of **Ru-14'** as well as **Ru-15**, in a ratio of 5:1. The ³¹P{¹H} NMR singlet for **Ru-15** appears at 56.1 ppm, the C2 and C2' signals at 169.8 and 168.7 ppm, very close to the values observed in C₅D₅N. The proportion of **Ru-15** is highly sensitive to added pyridine: dosing the NMR solution with just 1% pyridine by volume effects rapid, complete conversion of **Ru-14'** into η^1, η^1 -BINO **Ru-15**. Complex **Ru-14'** gives rise to a broad ³¹P NMR singlet at 58.3 ppm: the breadth of the signal, as well as the absence of ¹³C NMR signals for C2/C2' at room temperature, indicate a dynamic process. Cooling the sample to –20 °C leads to considerable sharpening of the ³¹P NMR signal, and permits location of the C2/C2' and C1/C1' signals (C2, C2': 143.5, 174.4 ppm; C1, C1': 113.8, 97.6 ppm). The locations of these signals, as well as the doublet multiplicity of C1 (²J_{CP} = 19 Hz), is in accord with the η^3, η^1 -BINO coordination mode determined crystallographically. The dynamic process observed at room temperature can be attributed to η^3, η^1 -exchange (Scheme 4.3b), as observed previously with complex η^3, η^1 -BINO **Ru-28'**.³⁷ At –40 °C, a third complex is evident as a ³¹P{¹H} NMR singlet at 48.3 ppm: this is assigned to Ru(η^1, η^1 -BINO)(PPh₃)(py)₂, by analogy to the isomerization of η^3, η^3 -BINO **Ru-11''** to η^3, η^1 -BINO **Ru-11'** on cooling.

4.2.1.4 Reactions of Ru(BINO)(PPh₃)₂ **Ru-11'/11''** with *tert*-butylacetylene and phenyldiazomethane: Installation of a carbene functionality.

Reaction of **Ru-7** with terminal alkynes offers an important route to cumulenylidene derivatives.^{56,57} Treatment of **Ru-11'/11''** with *tert*-butylacetylene in C₆D₆ causes an immediate color change from red to dark purple. Quantitative conversion to vinylidene Ru(BINO)(PPh₃)₂(=C=CH^tBu) **Ru-16'** was inferred from ³¹P{¹H} NMR analysis, which revealed two new doublets (64.4, 38.3 ppm; ²J_{PP} = 27 Hz; Scheme 4.4a). The product was isolated in 40% yield by precipitation from THF-hexanes; its high solubility impairs recovery. Assignment as **Ru-16'** is supported by IR, NMR, and combustion analysis. The vinylidene ligand gives rise to a strong, diagnostic infrared C=C stretching band at 1633 cm⁻¹, and a characteristic singlet for the Ru=C=CH^tBu nucleus at 347.2 ppm, located via a ¹H-

^{13}C HMBC correlation experiment. A ^1H NMR singlet for the *tert*-butyl group appears at 0.85 ppm, which correlates by ^1H - ^1H COSY analysis to the vinylidene CH multiplet at 3.01 ppm. Integration against the aromatic signals confirms the presence of one BINO and two triphenylphosphine ligands, although only seven distinct aromatic signals are observed at ambient temperature, suggesting a dynamic process leading to signal averaging. Consistent with such a process is the null ^{13}C NMR spectrum in the 135-200 ppm window, the range established for C2/C2' in all BINO coordination modes examined in this or prior work. On cooling to -60°C , singlets for C2 and C2' at 148.0 and 162.0 ppm, respectively, and a C1' singlet at 116.0 ppm, were identified. These locations strongly suggest an η^3,η^1 -BINO coordination mode for **Ru-16'**. However, the doublet for C1 is found at 125.6 ppm ($J_{\text{CP}} = 4$ Hz), well downfield from the ca. 85-106 ppm range expected for a BINO enolate (see Section 4.2.3 for a discussion of characteristic ^{13}C ranges for C1 and C2). The reason for the discrepancy is unclear. The small C-P coupling constant suggests that the dihedral angle between the relevant centres approaches 90° (cf. $^2J_{\text{CP}} = 4$ Hz for **Ru-11''**).



Scheme 4.4. Installation of a carbene functionality into $\text{Ru}(\text{BINO})(\text{PPh}_3)_2$ **Ru-11'/11''**. Proposed products following installation of a) a vinylidene and b) a benzylidene moiety.

The successful synthesis of vinylidene complex **Ru-16'** prompted exploration of the corresponding benzylidene chemistry. Addition of phenyl diazomethane to **Ru-11'/11''** (Scheme 4.4b) in CH_2Cl_2 resulted in no reaction, but a switch in solvent to pyridine afforded $\text{Ru}(\text{BINO})(\text{py})_2(=\text{CHPh})$ in 86% yield. Complete loss of the PPh_3 ligands is indicated by the observation of solely free phosphine by ^{31}P NMR analysis of a reaction aliquot, and the benzylidene proton (20.43 ppm) is of singlet multiplicity, albeit the latter varies with the H-C-Ru-P dihedral angle, and is not always reliable.^{58,59} Detailed NMR analysis has not yet been undertaken to elucidate the coordination mode of the BINO ligand in **Ru-17**. However,

recent work by Carolyn Higman of the Fogg group suggests that **Ru-17** acts as a precursor to a catalytically active benzylidene complex (Ru(BINO)(IMes)(py)(=CHPh) **Ru-19b**, vide infra). Routes toward this and related complexes will be discussed in the following Section; catalytic activity is evaluated in Section 4.3.

4.2.2 Reaction of Ru-benzylidene complexes with TIOPh and M₂(BINO).

4.2.2.1 Methodology.

The salt metathesis reactions described in this Section were carried out by adding the aryloxide prolignand (1.2 equiv, in the case of M₂(BINO); 2.0 equiv, in the case of TIOPh) to the appropriate [Ru]=CHPh precursor (**Ru-3a-e**, **Ru-18b**, **Ru-4c**) at 25 °C. Exploratory reactions at elevated temperatures (40 °C) indicated no improvement, and were therefore abandoned. NMR-scale reactions were carried out using ca. 10 mg of the ruthenium starting material in the presence of 1,3,5-trimethoxybenzene (TMB; ca. 0.4 equiv) as an internal standard. As the BINO derivatives proved minimally soluble in benzene, reactions in C₆D₆ underestimate product yields. Probe reactions were therefore carried out in a suitable protio-solvent (typically benzene, in initial studies; subsequently pyridine), at ambient temperature.* The reaction time required for complete consumption of the benzylidene precursor was assessed in each case: typically, this was ca. 20 h. The solution was filtered to remove insoluble salts.** For reactions in benzene, this involved filtration through celite; soluble material was washed through with THF. The filtrate was stripped of solvent under vacuum, and the residue redissolved in CDCl₃ for ¹H NMR analysis.

Integration of all benzylidene signals (22-14 ppm) relative to the methoxy singlet for the internal standard at 3.77 ppm enabled quantification of the proportion of [Ru]=CHPh and non-benzylidene products (for the present purposes, the latter are termed decomposition: the

* Ambient temperatures in the glovebox ranged from ca. 23 to 25 °C, depending on the length of time the circulation was turned off. Extended stirring of solutions in 1-dram (ca. 4 mL) vials also caused perceptible heating, so these figures should be regarded as approximate.

** Filtration through Celite was not always sufficient to remove the TiCl salts. Better results were generally achieved by additional filtration through a disposable pipette packed with glass-fiber filter paper cut into small (1 cm²) pieces.

possibility that these consist of (e.g.) well-defined Ru-carbyne products was not examined). The region from 5.50-4.00 ppm was examined to detect any aromatic signals shifted upfield by π -coordination of a phenolate or naphtholate ring (Section 4.1). In no cases were such signals observed for the BINO derivatives, although they were present for the sole phenoxide reaction explored (see below). In situ yields from NMR reactions are given in Appendix B.

Reactions were scaled up to ca. 250 mg of the Ru precursor, where the probe experiments indicated >50% formation of one or two [Ru]=CHPh products. The time for reaction indicated in the NMR-scale experiments was used as a guide to reaction times required on scale-up. In all cases, complete reaction was confirmed by examining a reaction aliquot prior to workup. Products were normally isolated from reactions in pyridine by stripping off the volatiles under vacuum, redissolving the residue in THF, filtering through Celite, washing through with additional THF, then concentrating the filtrate to a minimum volume prior to precipitating the products by adding hexanes and chilling to $-30\text{ }^{\circ}\text{C}$. In some cases, washing with hexanes and pentane sufficed to purify the products. More typically, the crude products were reprecipitated from CH_2Cl_2 or THF by addition of hexanes: CH_2Cl_2 -hexanes proved generally best for the NHC derivatives, THF-hexanes for the PCy_3 derivatives. Exchange of the chloride ligands for binaphtholate was confirmed by CT-MALDI MS and elemental analysis. The BINO coordination mode was established by $^{13}\text{C}\{^1\text{H}\}$ NMR analysis, supplemented by two-dimensional ^1H - ^{13}C correlation experiments (carried out in CD_2Cl_2 to avoid overlap with solvent peaks in the aromatic region). Diagnostic NMR data for the different coordination modes are discussed in Section 4.2.3 and summarized in Table 4.3.

4.2.2.2 Reaction of $\text{RuCl}_2(\text{IMes})(\text{py})_2(=\text{CHPh})$ **Ru-3b** with TlOPh.

In prior studies,⁴¹ reactions of $\text{RuCl}_2(\text{PPh}_3)_3$ **Ru-7** with $\text{M}(\text{OAr})$ salts ($\text{M} = \text{Tl}, \text{Na}$; $\text{Ar} = \text{Ph}$, $p\text{-}^t\text{BuC}_6\text{H}_4$) at room temperature were shown to afford π -bound products, as noted in Section 4.1. Nevertheless, reaction of the "Grubbs III" benzylidene complex **Ru-3b** with TlOPh was attempted. This experiment was not so much directed at preparation of a $\text{Ru}(\text{OPh})_2(\text{IMes})(\text{py})(=\text{CHPh})$ product (no such benzylidene species having been observed in the corresponding reactions of the first- and second-generation Grubbs catalysts), but in the

hope that the reduced bulk of the pyridine ligands might reduce the multiplicity of products, enabling some insight into the fate of the alkylidene ligand.

Treatment of **Ru-3b** with TlOPh (2 equiv) at 25 °C resulted in a color change from green to red within 3 h, accompanied by complete loss of the benzylidene signal for **Ru-3b** by ¹H NMR analysis. Signal-to-noise ratios were unaffected, but no new [Ru]=CHPh signal was observed (Figure 4.2). The fate of the :CHPh fragment is unclear: α-elimination and carbyne formation is one possibility,^{43,60} but also possible is simply dissociation of the alkylidene moiety as the carbene. Several new signals were evident in the olefinic region, consistent with π-coordination of the phenoxide ligand (Figure 4.2b, inset), but the complexity of the spectrum suggests multiple products. Assuming each signal represents one proton, integration of two of these signals against TMB (**A**: 5.26 ppm, d, $J_{\text{HH}} = 5.2$ Hz; **B**: 4.95 ppm, t, $J_{\text{HH}} = 6.0$ Hz) is lower than the 1:1 ratio expected for a single π-bound product. The presence of the benzylidene group clearly complicates reactivity relative to the model studies with **Ru-7**. Given the poor selectivity and loss of the benzylidene functionality, however, this reaction was not examined in closer detail.

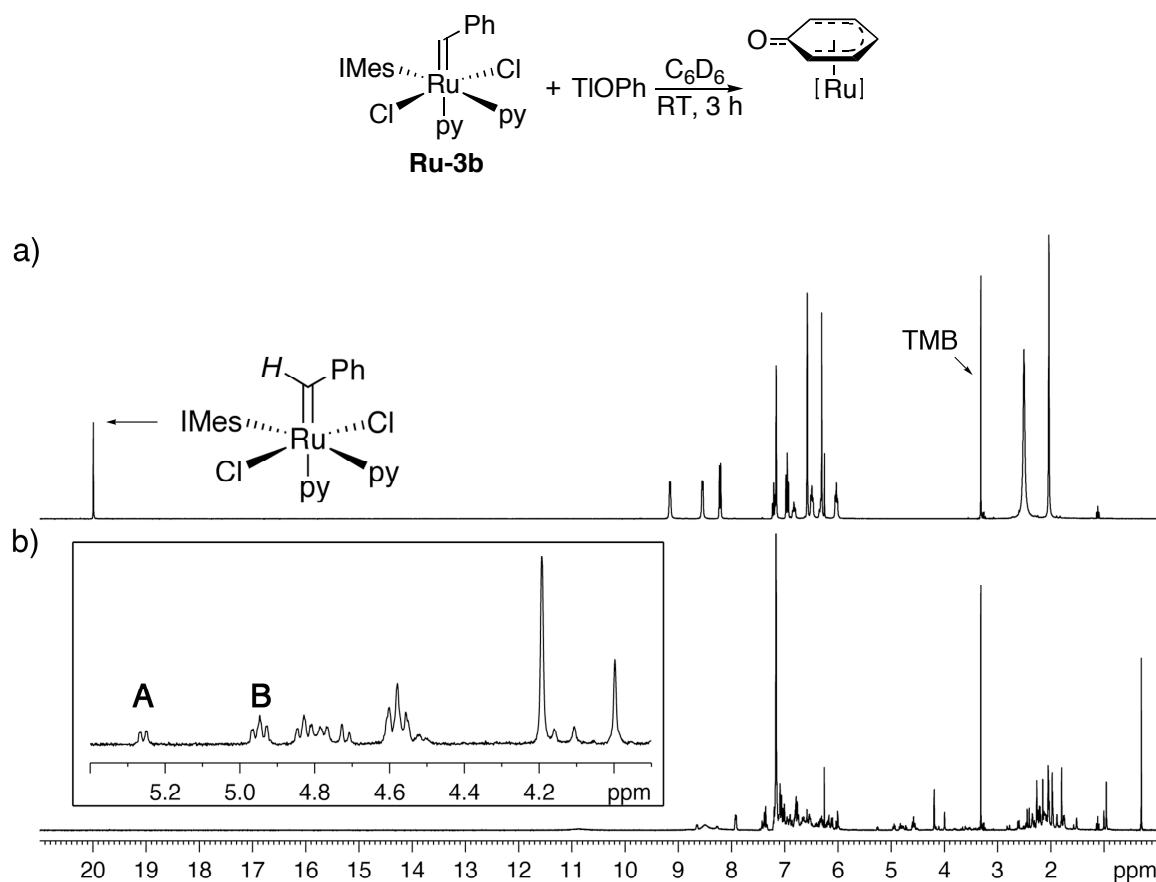


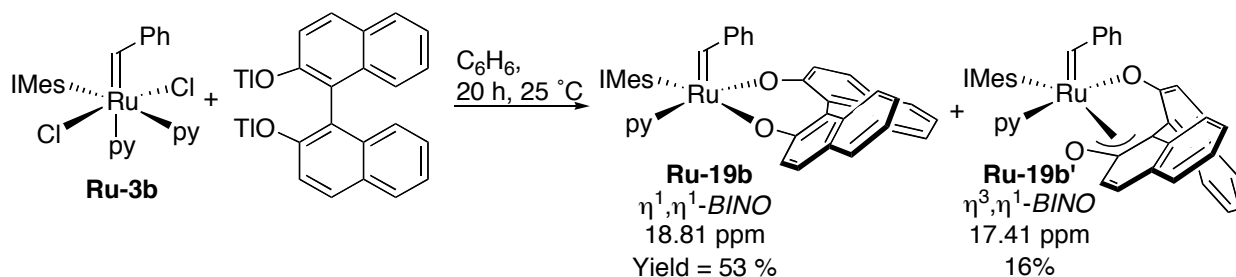
Figure 4.2. ^1H NMR spectra (300 MHz, C_6D_6) depicting a) clean **Ru-3b** with TMB as internal standard. b) The reaction of **Ru-3b** with TlOPh in benzene after 3 h at 25 °C; inset shows the olefin region.

4.2.2.3 Reaction of $\text{RuCl}_2(\text{IMes})(\text{py})_2(=\text{CHPh})$ **Ru-3b** with $\text{Ti}_2(\text{BINO})$: Synthesis of $\text{Ru}(\text{BINO})(\text{IMes})(\text{py})(=\text{CHPh})$.

Throughout this section, results from NMR-scale experiments will be discussed prior to preparative-scale experiments (where relevant). In some cases different results were found on scale-up: these will be discussed as they arise.

NMR-scale reactions of $\text{Ti}_2(\text{BINO})$ with **Ru-3b** in benzene resulted in a color change from green to brown over 20 h at room temperature (Scheme 4.5). ^1H NMR analysis at this stage indicated complete consumption of **Ru-3b**, and formation of two benzylidene species

characterized by singlets at 18.81 and 17.41 ppm (53% and 16%, respectively). Based on the criteria defined in Section 4.1, successful incorporation of the binaphtholate ligand is inferred. On scaling up to 250 mg **Ru-3b**, the green product was isolated in 72% yield by the procedure described in Section 4.2.2.1, some losses being incurred by the partial solubility of the complex in hexanes. The isolated product consisted of only the major isomer. Charge-transfer (CT) MALDI-TOF MS⁶¹ revealed a well-defined isotope pattern for [Ru(BINO)(IMes)(py)(=CHPh)-py]⁺ (**Ru-19b**-py) as the highest-mass peak (Figure 4.3). Elemental analysis likewise indicates BINO coordination, and retention of a single pyridine ligand. Assignment of the ¹³C{¹H} NMR signals for the BINO ligand by ¹H-¹³C HMBC, HMQC and ¹H-¹H COSY correlation experiments (for details, see Section 4.2.3 and Appendix E) permitted identification of the product as a η^1, η^1 -BINO species. The singlets for C1/C1' (124.2, 123.86 ppm) and C2/C2' (164.0 and 170.1 ppm) are in the regions diagnostic for this coordination mode, as discussed in Section 4.2.1 (and later in Section 4.2.3). This assignment is further supported by X-ray analysis of crystals grown by diffusion of hexanes into a THF solution (for discussion of the X-ray parameters, see Section 4.2.4). Isolation of the minor product, and consequently assignment of its key ¹³C NMR signals, was hampered by the small proportion of this species. However, the upfield chemical shift of its benzyldiene singlet (17.41 ppm) is flagged below as a potential marker for the η^3, η^1 -BINO bonding mode.



Scheme 4.5. Formation of two isomers of Ru(BINO)(IMes)(py)(=CHPh) from **Ru-3b**. In situ yields are those determined in NMR-scale reactions.

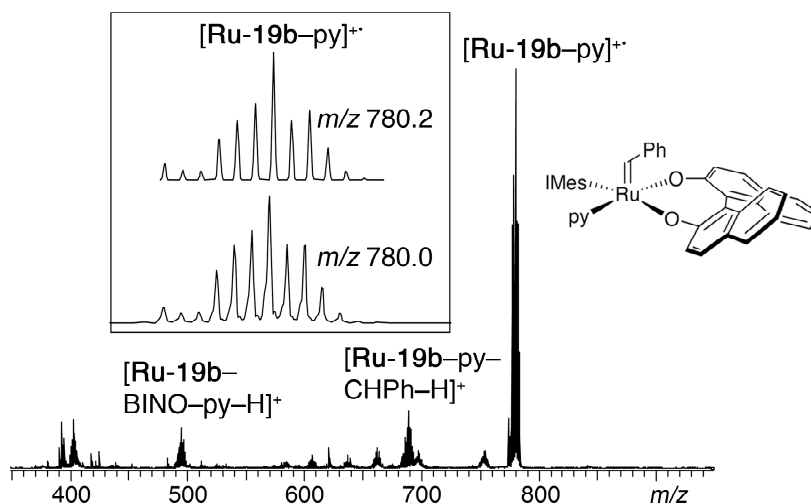


Figure 4.3. CT-MALDI mass spectrum of **Ru-19b** (pyrene matrix). Inset shows isotope patterns for the base signal (top: simulated, bottom: observed).

A range of optimization strategies was explored to increase the yield of **Ru-19b**. Reaction in CDCl_3 , CH_2Cl_2 , THF, or aromatic solvents (Table 4.2, Entries 1-4), or use of shorter reaction times at slightly elevated temperatures (Entries 5 and 6), did not increase yields. Spiking the reaction solvent with H_2O or pyridine (to increase the solubility of the BINO salt or to prevent decomposition, respectively), effected minimal improvement (Entries 7 and 8). Use of pyridine as the reaction solvent led to a breakthrough, however (cf. Entries 9 and 5). The presence of pyridine in large excess inhibits dissociation of the labile pyridine ligand, retards decomposition, and proves the key to high conversions. Thus, **Ru-19b** was formed in ca. 93% yield on reaction of **Ru-3b** with $\text{Tl}_2(\text{BINO})$ in pyridine at 25 °C for 20 h (Entry 13). Importantly, this solvent switch also permitted use of potassium binaphtholate in place of the toxic thallium salt,⁶² with essentially identical yields (91% conversion to the BINO target, with 83% formation of the η^1, η^1 -BINO isomer: compare Entries 13-14, vs. 10-12). The sodium salt was somewhat less effective (Entry 15). Addition of AgOTf did not further improve the high yields obtained using $\text{K}_2(\text{BINO})$ (Entry 16).

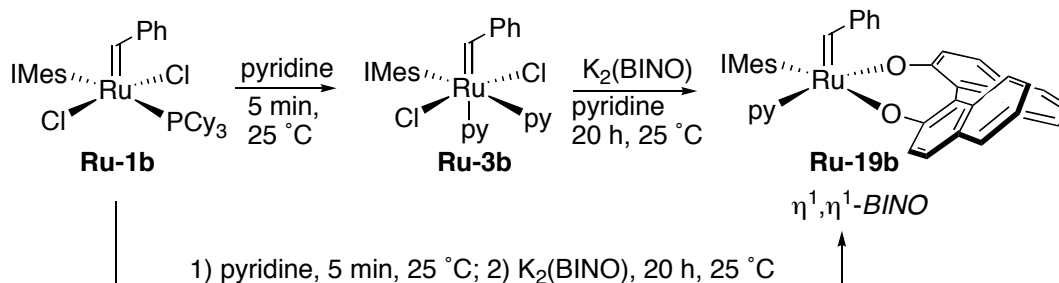
Table 4.2. Optimizing the synthesis of Ru(BINO)(IMes)(py)(=CHPh) **Ru-19b** from **Ru-3b**.^[a]

	Solvent	M	Time [h]	Temp [°C]	Conv [%]	Yield of Ru-19b [%]		Yield (other) [%]	
						η^1, η^1 - <i>BINO</i>	η^3, η^1 - <i>BINO</i>	[Ru]=CH ^[b]	Dec. ^[c]
1	CDCl ₃	Tl	5	25	91	49	11	-	30
2	CH ₂ Cl ₂	Tl	5	25	85	53	12	-	20
3	THF	Tl	5	25	70	35	7	-	28
4	C ₆ H ₆	Tl	5	25	54	30	8	-	16
5	C ₆ H ₆	Tl	3	40	77	50	13	-	14
6	toluene	Tl	3	40	77	56	5	-	16
7	3:1 THF –H ₂ O	K	2	25	>99	51	3	12	34
8	C ₆ H ₆ ^[d]	Tl	17	25	97	55	14	-	28
9	C ₅ H ₅ N	Tl	3	40	>99	73	18	-	9
10	C ₆ H ₆	Tl	20	25	>99	53	16	-	31
11	C ₆ H ₆	K	20	25	91	37	14	-	40
12	C ₆ H ₆	Na	20	25	79	20	7	12	40
13	C ₅ H ₅ N	Tl	20	25	>99	87	6	-	7
14	C ₅ H ₅ N	K	20	25	>99	83	8	-	9
15	C ₅ H ₅ N	Na	20	25	>99	68	5	-	27
16	C ₅ H ₅ N ^[e]	K	20	25	>99	56	12	11	21

^[a] Conversions, in situ yields and decomposition were assessed by ¹H NMR spectroscopy, from the integrated intensity of the benzyldiene signals relative to TMB as internal standard. ^[b] New, unassigned benzyldiene signal: Entry 7, 18.90 ppm; Entry 12, 18.88 ppm; Entry 16, 20.05 ppm. ^[c] "Dec." signifies conversion to non-benzyldiene species. ^[d] With ca. 10 equiv pyridine. ^[e] 1 equiv added AgOTf.

Reaction of K₂BINO with **Ru-3b** under these optimized conditions (i.e. in pyridine solvent for 20 h at 25 °C), followed by the standard workup, enabled isolation of η^1, η^1 -*BINO* **Ru-19b** in 72% yield. (Mass yields are limited by the partial solubility of the product in hexanes, as noted above). Comparable yields are attained with greater convenience by integrating the

synthesis of **Ru-3b** (from the second-generation Grubbs complex **Ru-1b**) with the installation of the BINO ligand, in a one-pot reaction sequence. In this protocol, **Ru-1b** is dissolved in a minimum volume of pyridine, stirred at 25 °C for 5 minutes, then treated with solid K₂BINO, and allowed to stir for 20 h prior to workup (Scheme 4.6).



Scheme 4.6. Optimized synthesis of **Ru-19b** via a consecutive, two-step or a one-pot procedure.

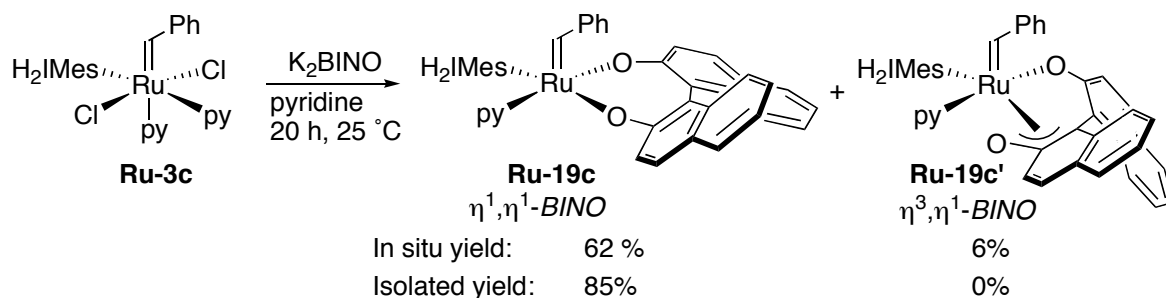
4.2.2.4 Reaction of RuCl₂(L)(py)₂(=CHPh) with K₂(BINO): L = H₂IMes, PCy₃, IPr.

This Section describes expansion of the scope of the procedures above, to include the synthesis of Ru-BINO complexes containing other *N*-heterocyclic carbene or phosphine donors.

Addition of K₂BINO to the H₂IMes precursor **Ru-3c** (Scheme 4.7) under the conditions optimized for **Ru-3b** afforded one major product, characterized by a benzylidene singlet at 18.75 ppm (62%; η^1, η^1 -BINO **Ru-19c**), accompanied by minor amounts of a second species (17.40 ppm: 6%; η^3, η^1 -BINO). The balance is composed of unidentified, non-benzylidene species. Importantly, however, some degree of reversibility is implied by the fact that the η^1, η^1 -BINO isomer was isolated as the sole product in 85% yield using the standard workup procedure described in Section 4.2.2.1. The corresponding reaction in benzene afforded η^1, η^1 -BINO **Ru-19c** as the sole observable benzylidene product, in only 16% in situ yield, even on use of Ti₂(BINO).

As with the IMes complex **Ru-19b**, CT-MALDI MS and combustion analysis indicate the presence of one BINO and one pyridine ligand in **Ru-19c**. The η^3, η^1 -BINO structure is inferred from the chemical shifts of the ¹³C{¹H} NMR signals for the key nuclei (C1: 123.94

ppm; C1': 123.87 ppm; C2: 170.3 ppm; C2': 164.0 ppm). This assignment was confirmed by X-ray analysis of crystals grown by diffusion of hexanes into a THF solution. Discussion of the crystallographic parameters is deferred until Section 4.2.4, where they are considered along with those for the PPh₃/BINO complexes. While the low proportion of the minor product again impedes location of the key ¹³C NMR signals, the upfield location of the ¹H NMR singlet for the benzyldiene proton corresponds closely to that found for **Ru-19b**, and assignment as the η^3, η^1 -BINO isomer is reasonable.

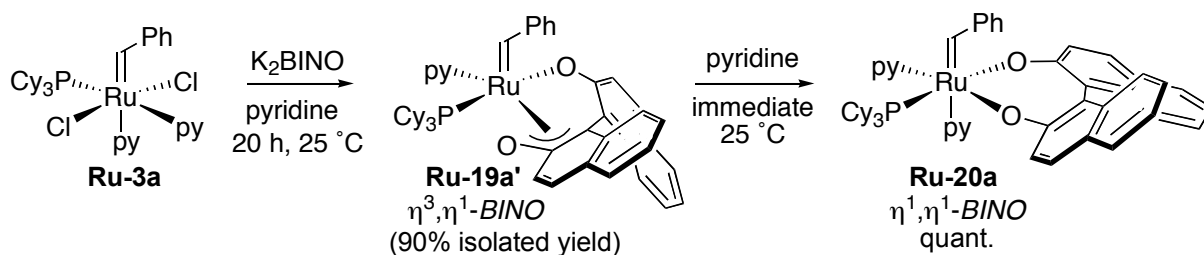


Scheme 4.7. Synthesis of η^1, η^1 - and η^3, η^1 -BINO isomers of Ru(BINO)(IMes)(py)(=CHPh) from **Ru-3c**. In situ yields of **Ru-19c** are determined from NMR-scale reactions; non-benzyldiene products account for the remainder.

The PCy₃ derivative **Ru-3a** reacts with K₂(BINO) much more rapidly than do the NHC analogues, NMR-scale reactions being near-quantitative within 2 h at room temperature (Scheme 4.8). Minor losses (10%) in the total benzyldiene integration are evident, and four new [Ru]=CHPh signals are observed on analysis in CDCl₃ (20.41 ppm, s, 6%; 20.16 ppm, d, ³J_{HP} = 11 Hz, 14%; 18.26 ppm, d, ³J_{HP} = 12 Hz, 9% assigned as Ru(η^1, η^1 -BINO)(PCy₃)(py)(=CHPh); 17.45 ppm, d, ³J_{HP} = 5 Hz, 57%). The product ratio is sensitive to the extent of pyridine remaining. For reactions on preparative (250 mg) scale, and workup according to the general procedure of Section 4.2.2.1, a brown product is isolated in 92% yield. This complex exhibits only the benzyldiene doublet at 17.45 ppm (the major product in the probe reaction). MALDI-TOF MS and combustion analysis are consistent with assignment as Ru(η^3, η^1 -BINO)(PCy₃)(py)(=CHPh) **Ru-19a'**.

The upfield location of the benzyldiene signal for this complex is striking. For the five-coordinate η^1, η^1 -BINO complexes **Ru-19b/c**, this signal appears at approximately 18.8 ppm;

for the sole well-characterized example of a six-coordinate η^1, η^1 -*BINO* complex, it is shifted further downfield, to ca. 20.2 ppm. The upfield shift in the present case accompanies coordination of the *BINO* ligand in an η^3, η^1 -*BINO* enolate form. The chemical shifts of C1' and C2' (C1': 116.8 ppm, s; C2': 174.1 ppm, d, $^3J_{CP} = 5$ Hz) are diagnostic for this coordination mode (see Section 4.2.3 for detailed discussion of trends), as is the observed coupling of C2', but not C1', to phosphorus. The 5-Hz splitting of the C2' signal is relatively large for a three-bond coupling, suggesting trans-disposition of this nucleus relative to the phosphine ligand. For C1 and C2 (95.6 and 154.1 ppm; $^2J_{CP} = 11$ and 3 Hz, respectively), the chemical shifts are consistent with those established for an η^3 -enolate moiety, as is the doublet multiplicity of *both* of these signals, which collapse to singlets in the $^{13}\text{C}\{^1\text{H}, ^{31}\text{P}\}$ spectrum. The difference in these two-bond coupling constants suggests that the η^3 -O,C2,C1 unit is skewed: the Ru-C1 interaction may be shorter, or the dihedral angle between the phosphorus centre and C2 may approach 90° , and hence a minimum on the Karplus curve for vicinal coupling. The chemical shift for the benzyldene signal at 17.5 ppm is about 1 ppm more upfield than the corresponding signals for η^1, η^1 -*BINO* **Ru-19b** and **Ru-19c**. The minor η^3, η^1 -*BINO* isomers of the IMes and H₂IMes complexes likewise are located at ca. 17.5 ppm. While this location of the benzyldene signal appears to be diagnostic for η^3, η^1 -*BINO* coordination, very similar chemical shifts were found for η^1, η^1 - and η^3, η^1 -*BINO* complexes containing an IPr ligand (see below). Where possible the *BINO* coordination mode should be confirmed by ^{13}C NMR spectroscopy and the location of the benzyldene signal should only be used as a guide.



Scheme 4.8. Synthesis of η^3, η^1 -*BINO* **Ru-19a'** and η^1, η^1 -*BINO* **Ru-20a**.

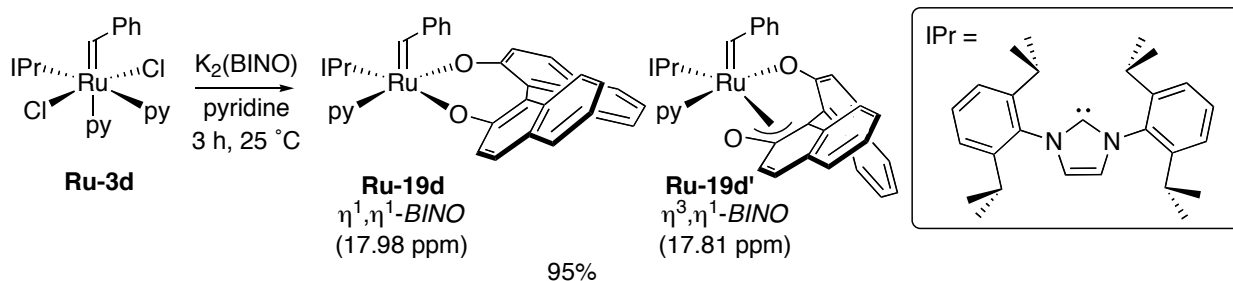
Consistent with the behaviour of the PPh_3 complex **Ru-14'** (Section 4.2.1.3), addition of even low doses of pyridine to **Ru-19a'** in CD_2Cl_2 effects partial transformation into $\text{Ru}(\eta^1, \eta^1\text{-BINO})(\text{PCy}_3)(\text{py})_2(=\text{CHPh})$ **Ru-20a** (e.g. 32% at 1% v/v pyridine), signaled by the

emergence of a benzyldiene doublet at 20.16 ppm ($^3J_{\text{HP}} = 11.4$ Hz). This reaction is quantitative in neat pyridine- d_5 (Scheme 4.8). The bis(pyridine) adduct is also observed in situ in the direct reaction of **Ru-3a** with $\text{K}_2(\text{BINO})$ in pyridine. The location of the benzyldiene resonance suggests $\eta^1, \eta^1\text{-BINO}$ coordination, and this is supported by the downfield shift of the C1/C1' and C2/C2' signals (C1: 127.3 ppm, s; C1': 127.7 ppm, s; C2: 167.9 ppm, s; C2': 169.6 ppm, d, $^3J_{\text{CP}} = 3$ Hz). The singlet multiplicity of the C1 and C1' signals again reflects the presence of four intervening bonds between these carbon centres and phosphorus. The C2' nucleus trans to phosphorus appears as a doublet, as expected: the cis-coupling is smaller, and C2 thus appears as a singlet. Attempts to isolate **Ru-20a** by precipitating from pyridine-hexanes were thwarted by loss of pyridine and isomerization, this treatment yielding predominantly $\eta^3, \eta^1\text{-BINO}$ **Ru-19a'**, with only ca. 10% **Ru-20a** present. Similar behaviour was observed for $\text{Ru}(\text{BINO})(\text{PPh}_3)_3(\text{py})_3$ **Ru-15** (Section 4.2.1.3).

NMR-scale reaction of K_2BINO with the IPr derivative **Ru-3d** (IPr = *N,N'*-bis(2,6-diisopropylphenyl)imidazol-2-ylidene) at 25 °C in pyridine was complete within 3 h. Two new benzyldiene singlets were observed in CDCl_3 (17.74 and 17.65 ppm; ratio 1.7:1), accompanied by 41% non-benzyldiene species. Use of silver salts (AgOTf or AgPF_6 ; 1 equiv) to facilitate chloride abstraction offered no improvement: the proportion of byproducts remained high, and two new, unassigned benzyldiene products formed (18.63, 18.51 ppm) in addition to those previously observed; indeed, the new signals dominate the spectrum. Scale-up was therefore carried out without silver salts. Unexpectedly, the larger-scale reaction proved considerably more tractable, affording the BINO products in excellent yields and purity (Scheme 4.9). (While the NMR-scale reactions proved a reliable guide for the reactions of the IMes, H_2IMes , and PCy_3 complexes with BINO, the present discrepancy suggests that they may under-report success: similar results were subsequently found for the 3,3'-BINO reactions, which may likewise be more promising than initially thought).

In the case of the IPr derivatives, the two products originally observed in NMR-scale reactions (at 17.74 and 17.65 ppm in CDCl_3) were isolated as a green precipitate in 95% yield by the standard workup protocol, after washing with hexanes and pentane (Scheme 4.9). The two isomers were identified as $\eta^1, \eta^1\text{-BINO}$ **Ru-19d** and $\eta^3, \eta^1\text{-BINO}$ **Ru-19d'** on

the basis of $^{13}\text{C}\{^1\text{H}\}$ NMR analysis in CD_2Cl_2 . The more downfield benzyldiene signal, at 17.74 ppm, is assigned to the η^1, η^1 -BINO isomer **Ru-19d** on the basis of its 1:1 integration relative to signals for each of H4/H4'. The latter correlated to resonances for C2 and C2' by ^1H - ^{13}C HMBC NMR analysis (167.7 and 166.4 ppm). Signals for C1/C1' are in the range of 128-121 ppm, as judged by correlations from H3 and H3', although the presence of both the η^1, η^1 - and η^3, η^1 -BINO isomers results in some signal overlap, hampering precise location of the carbon signals. η^3, η^1 -BINO derivative **Ru-19d'** gives rise to the alkylidene singlet at 17.81 ppm (17.65 ppm in CDCl_3): the BINO binding mode is assigned from the downfield shift of C2' at 166.5, and the upfield shift of C2 (152.7 ppm). The singlet for C1' (115.6 ppm) is likewise found upfield relative to the range for η^1, η^1 -BINO complexes such as **Ru-19a'**, consistent with a ruthenium interaction at the directly-adjacent C1 nucleus in **Ru-19d'** (see Section 4.2.3 for detailed discussion of diagnostic ranges). The signal for C1 could not be located even via correlation experiments, owing to the low concentration of **Ru-19d'**, and the quaternary nature of the nucleus. The benzyldiene signal for η^1, η^1 -BINO **Ru-19d** (CD_2Cl_2 : 17.98 ppm), as mentioned above, is shifted slightly upfield relative to signals for the same isomer of **Ru-19b** and **Ru-19c**.

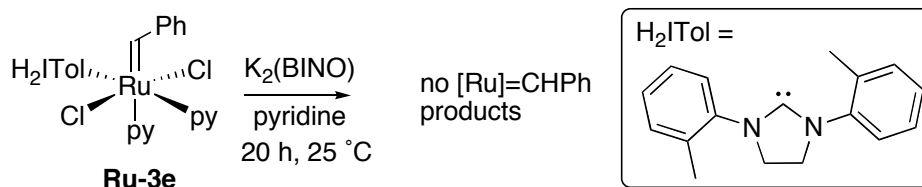


Scheme 4.9. Proposed products following reaction of **Ru-3d** with $\text{K}_2(\text{BINO})$. The combined isolated yield is shown: the ratio is solvent-dependent (CDCl_3 : 1.7:1; C_6D_6 , 1:1.5; CD_2Cl_2 : 1.5:1).

4.2.2.5 Attempted synthesis of $\text{Ru}(\text{BINO})(\text{H}_2\text{ITol})(\text{py})(=\text{CHPh})$.

Use of a small NHC ligand can dramatically enhance reactivity toward bulky reagents, as indicated by the exceptionally high reactivity of $\text{RuCl}_2(\text{H}_2\text{ITol})(=\text{CH}(\text{O}^i\text{Pr})\text{C}_6\text{H}_4)$ in RCM of tetrasubstituted olefins.⁶³⁻⁶⁵ Incorporation of the H_2ITol ligand into the Ru-BINO complexes was therefore explored. Treatment of **Ru-3e** with $\text{K}_2(\text{BINO})$ under our optimized conditions

led to complete loss of the benzyldiene signal, and emergence of broad signals in the hydride region (Scheme 4.10). As with the IMes analogue, use of slightly higher temperatures and shorter times (40 °C, 3 h) showed no improvement. This is not due to the thermal instability of **Ru-3e**, which *in the absence of added proligand* exhibits only a 4% decrease in the integrated intensity of the benzyldiene signal after 3 h at 40 °C in C₆D₆. Decomposition in both the literature report and the present case may involve C-H activation at the *ortho*-position of the tolyl ring, a site of known vulnerability,⁶⁶⁻⁶⁸ especially for electrophilic Ru centres.⁶⁷ Coordination of BINO may deplete the electron density at ruthenium, owing to the greater electronegativity of oxygen vs. chloride, and thus promote C-H activation. This behaviour may dominate during metathesis, as the methyldiene functionality is known to be less stable than the corresponding benzyldiene.^{69,70} and given related work shows that the PCy₃ analogue of **Ru-3e** decomposes within 90 min during RCM of a tetrasubstituted diene at 30 °C in CD₂Cl₂.⁶⁵



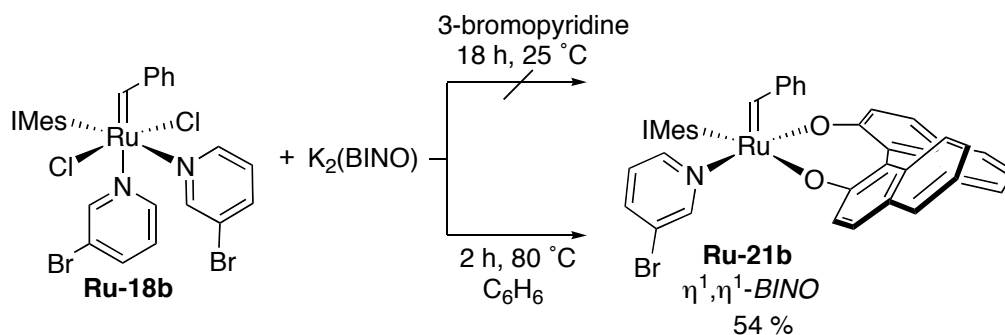
Scheme 4.10. Reaction of K₂(BINO) with **Ru-3e**.

4.2.2.6 Synthesis of Ru(η^1, η^1 -BINO)(IMes)(3-Br-C₅H₄N)(=CHPh).

Treating RuCl₂(IMes)(3-Br-C₅H₄N)₂(=CHPh) **Ru-18b** with K₂(BINO) in 3-bromopyridine at 25 °C afforded five new benzyldiene species after 18 h, but also considerable paramagnetic material (Scheme 4.11). The products include η^1, η^1 - and η^3, η^1 -BINO **Ru-21b**, as judged from the chemical shifts for the benzyldiene signals at 18.74 and 17.15 ppm (50% and 11%, respectively). Isolation and reprecipitation from THF-hexanes yielded a brown solid in 88% yield, containing η^1, η^1 -BINO complex **Ru-21b** and an additional, unassigned benzyldiene species (19.32 ppm), in a ca. 1:1 ratio.

Greater success, somewhat unexpectedly, was found on carrying out the reaction of **Ru-18b** and Ti₂(BINO) in refluxing benzene (Scheme 4.11). A colour change from green to brown was observed over 2 h. Following the standard workup procedure, the precipitate remained

brown, rather than giving way to the green colour characteristic of the η^1, η^1 -*BINO* products described above. As efforts to extract the presumed red byproduct by washing with cold Et₂O-hexanes, then pentane, had no effect, the product was reprecipitated from benzene, this affording the expected green powder in moderate yield (54%). The identity of the complex is supported by CT-MALDI MS and combustion analysis. The isotope pattern for the highest-mass signal is consistent with gas-phase loss of the labile 3-bromopyridine ligand. Only the major isomer seen previously is present: the η^1, η^1 -*BINO* coordination mode inferred from the ¹H NMR spectrum was confirmed by ¹³C{¹H} NMR analysis (C1: 123.8 ppm; C1': 124.2 ppm; C2: 163.8 ppm; C2': 170.0 ppm).

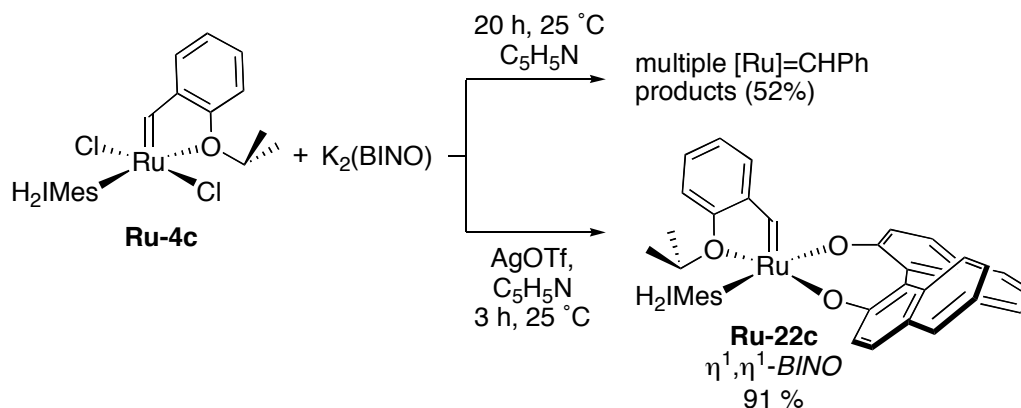


Scheme 4.11. Synthesis of η^1, η^1 -*BINO* **Ru-21b**. Isolated yield is shown.

4.2.2.7 Attempted synthesis of Ru(BINO)(H₂IMes)(=CH(3-OⁱPr-C₆H₄)).

Treatment of **Ru-4c** with K₂(BINO) in pyridine at 25 °C resulted in nearly 50% loss of the benzylidene ligand after 20 h, accompanied by formation of multiple benzylidene complexes (six [Ru]=CHPh signals; total 52%). Reaction is faster and cleaner in the presence of AgOTf, a single new benzylidene singlet at 18.85 ppm being observed after 3 h, with only 9% decomposition (Scheme 4.12). We rule out the possibility that this product is formed by exchange of chloride for triflate, as a control reaction between AgOTf and **Ru-4c** in the absence of K₂(BINO) resulted in two broad benzylidene signals (19.41 and 19.00 ppm) assigned to mono- and bis-triflate products. Instead, the product is provisionally assigned as Ru(η^1, η^1 -*BINO*)(H₂IMes)[=CH(3-OⁱPr-C₆H₄)] **Ru-22c**. Identification of this complex as a η^1, η^1 -*BINO* species on the basis of its downfield benzylidene signal presumes that the trends in chemical shift established for the pyridine derivatives **Ru-19a-c** are applicable to their styrenyl ether analogues. Attempts to isolate this complex for full characterization by the

usual method afforded a green crystalline solid in 72% yield, but ^1H NMR analysis showed seven different benzyldene signals, indicating decomposition on workup. A suitable synthetic method has not yet been identified.



Scheme 4.12. Reactions of **Ru-4c** with K_2BINO . In situ yields are shown: non-benzyldene products account for the remainder.

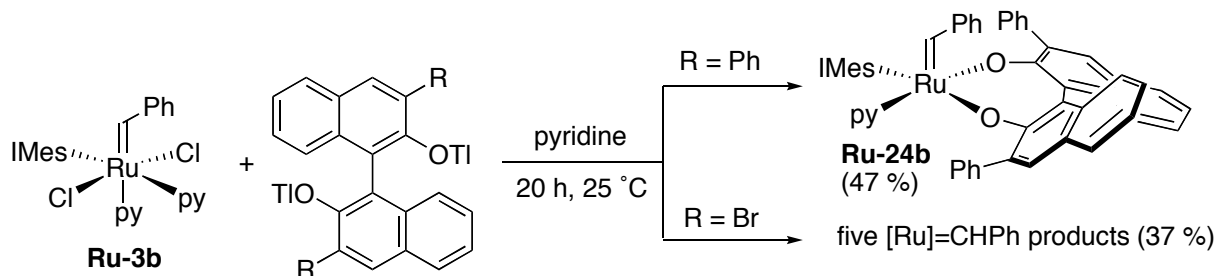
4.2.2.8 Attempted synthesis of $\text{Ru}(3,3'\text{-R}_2\text{BINO})(\text{IMes})(\text{CHPh})(\text{py})$ ($\text{R} = \text{Ph}, \text{Br}$).

This Section describes a preliminary study of routes to 3,3'-functionalized BINO derivatives of **Ru-3b**, as depicted in Scheme 4.13. Thallium binolates were employed in these reactions because the salts of these costly proligands had been prepared prior to the discovery that the potassium binolates could be successfully used in pyridine solvent.

Reaction of $\text{Tl}_2(3,3'\text{-Ph}_2\text{BINO})$ with **Ru-3b** in pyridine at 25°C afforded a single product after 20 h (Scheme 4.13), for which a benzyldene singlet is observed at 19.11 ppm in the ^1H NMR spectrum. From the values established for the well-characterized PCy_3 system, this chemical shift is consistent with a η^1, η^1 - BINO product, although the ca. 18 ppm location found with the IPr derivative serves as a reminder that these trends depend on the nature of the neutral L-donor ligands present. CT-MALDI MS analysis of a reaction aliquot confirms the presence of the BINO ligand, the highest-mass signal exhibiting an excellent isotope match for $[\text{M-py}]^{+}$, but the coordination number remains ambiguous owing to gas-phase loss of pyridine. A mono-py structure is more likely, given the increase in steric crowding relative to the corresponding BINO complex. However, attempts to confirm this by microanalysis

were frustrated by product decomposition during workup by the usual method (albeit involving use of CH_2Cl_2 in place of THF). The resulting red precipitate contained, in addition to η^1, η^1 -BINO complex **Ru-24b**, nearly 40% of additional benzyldiene species (characterized by ^1H NMR singlets at 18.31 ppm (14%), 16.86 ppm (19%), and 16.03 ppm (6%)), as well as non-benzyldiene coproducts. New signals in the 1-3 ppm region may indicate activation of IMes methyl groups, or activation of the benzyldiene functionality itself. The steric bulk of the BINO ligand thus appears to enable undesired reaction pathways at the isolation stage, which warrant exploration of alternative workup methods.

The corresponding reaction of $\text{Ti}_2(3,3'\text{-Br}_2\text{BINO})$ effected 96% consumption of the Ru precursor after 20 h, but a 59% loss of the total benzyldiene integration was evident, accompanied by formation of multiple minor benzyldiene species. A larger-scale reaction in benzene, however, afforded three new benzyldiene species in the range of 17.02-17.37 ppm. Again, this behaviour merits more detailed investigation.

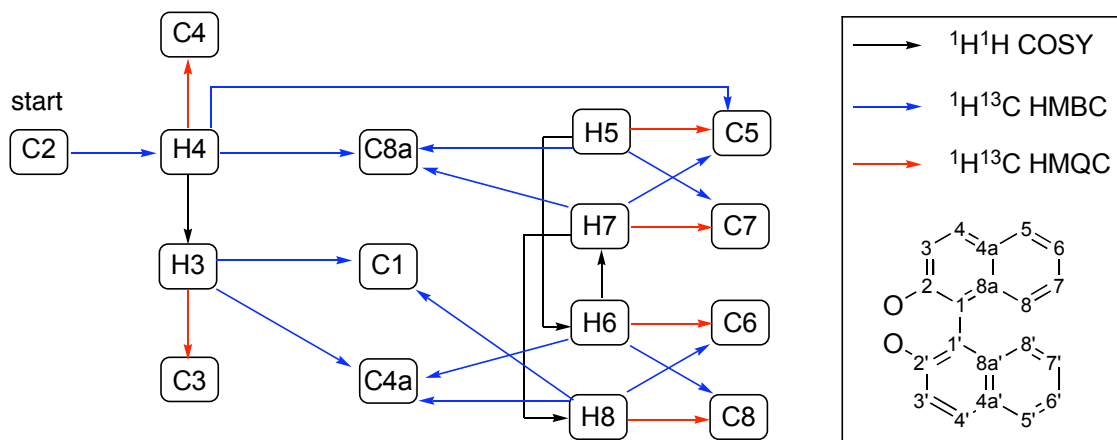


Scheme 4.13. Attempted synthesis of 3,3'-functionalized BINO derivatives of **Ru-3b**. In situ yields are shown: non-benzyldiene products account for the remainder.

4.2.3 Diagnostic NMR signals for BINO coordination modes.

The diagnostic value of the ^{13}C NMR chemical shifts in deducing the BINO coordination mode will be eminently clear from the discussion above. Signal assignment, however, can be non-trivial. A schematic of the expected 2D NMR correlations is provided here as a guide to assignment (Scheme 4.14). It should be noted that in aromatic rings, $^2J_{\text{HC}}$ coupling constants are generally much smaller than $^3J_{\text{HC}}$ couplings;⁷¹ a correlation between H4 and C2 is thus expected, but not between H3 and C2. The signals for C2/C2', found in the region 140-200

ppm, are shifted out of the typical aromatic window (120-135 ppm), and are the best starting point for assignment of the BINO signals.



Scheme 4.14. NMR correlations observed for the BINO ligand.

C1/C1' and C2/C2' shifts for the BINO complexes described in the previous Sections are compiled by coordination mode in Table 4.3. Trends in chemical shift ranges and C-P coupling are outlined here. Characteristic of the η^1, η^1 -BINO binding mode are C2 and C2' signals in the 163-170 ppm region. Signals for C1 and C1' (121-128 ppm) are less discernible, as they fall within the typical aromatic window. In compounds containing ancillary phosphine ligands, the three-bond $^3J_{\text{CP}}$ coupling is observed for C2 or C2' nuclei located trans to phosphine only; the four-bond coupling to C1/C1' is not observed.

Formation of a η^1 -C1, η^1 -O'-BINO complex is signaled by a drastic downfield shift in C2 (to 195-200 ppm), associated with the much increased carbonyl character at C2. The direct metal-C1 interaction effects an upfield shift of the carbon resonance, to 82-88 ppm. Few examples of this type have been observed to date. Still rarer is the η^3, η^3 -BINO coordination: **Ru-11''** is the only known complex of this type reported to date (Section 4.2.1.2), and the range of potential shifts is therefore uncertain. In **Ru-11''** itself, C2 and C1 are found at 144.7 and 93.2 ppm, respectively, both >20 ppm upfield of η^1, η^1 -BINO resonances. As a cautionary note, the similarity between these shifts and values observed for the η^6 -aryl coordination in the Ru-BINOP complex **Ru-29** should be recognized.⁴² In contrast to **Ru-29**,

C3, C4, C4a or C8a exhibit no upfield shift, arguing against metal interaction with these centres.

The η^3, η^1 -*BINO* complexes exhibit characteristics of both the η^1, η^1 - and η^3, η^3 -*BINO* forms. As for η^3, η^3 -*BINO*, the enolate moiety exhibits a ca. 20 ppm upfield shift for C2 (range: 141-153 ppm), relative to η^1, η^1 -*BINO* derivatives. The signal for C1 is likewise shifted upfield, but the literature examples and complexes reported here suggest a rather broad range, with values between 85 to 109 ppm.* Important evidence for the direct Ru-C1 interaction, for phosphine derivatives, is the large (ca. 15 Hz) coupling between C1 and ^{31}P . In all complexes observed to date, the enolate moiety has been skewed, resulting in a relatively small $^2J_{\text{CP}}$ for C2 of only 2-3 Hz. For the *O*-bound ring, C2' appears in the range of 166-174 ppm, as expected, but C1' is shifted ca. 10 ppm upfield from its location in η^1, η^1 -*BINO* complexes, to ca. 115 ppm. Indeed, the location for C1' in these complexes is nearly identical for all six η^3, η^1 -*BINO* compounds reported here, suggesting that the location of this signal has more reliable diagnostic value than does C1. Coupling to C1' is discernible for phosphine derivatives. While the small size of the $^3J_{\text{CP}}$ coupling constants (1-2 Hz) means that they may not be detected, their observation provides valuable evidence for the coordination mode, as the corresponding four-bond coupling is not observed for η^1, η^1 -*BINO* complexes. Both the chemical shift and coupling of C1' reflect the sensitivity of this nucleus to the environment of the directly-attached C1 atom.

Table 4.3. Summary of diagnostic $^{13}\text{C}\{^1\text{H}\}$ NMR data enabling assignment of the *BINO* coordination mode for new *BINO* complexes described in this work.^[a]

Coord. Mode	Complex	Solvent	$^{13}\text{C}\{^1\text{H}\}$ NMR δ and $J_{\text{CP}}^{\text{[b]}}$ assignments (ppm; Hz)			
			C1	C2	C1'	C2'
η^1, η^1 - <i>BINO</i>	BINOL	CDCl_3	110.9	152.9	110.9	152.9
	Ru-13	30%v/v CD_3CN in C_6D_6	127.4	168.9	127.4	168.9

* The relatively downfield location for C1 in vinylidene complex **Ru-16'** does not follow the trend established for all other η^3, η^1 -*BINO* complexes, but the values for C1', C2 and C2' are all consistent with this coordination mode.

	Ru-15	C ₅ D ₅ N	128.1	171.0	127.8	169.7
	Ru-19b	CD ₂ Cl ₂	124.2	164.0	123.9	170.1
	Ru-19c	CD ₂ Cl ₂	123.9	170.3	123.9	164.0
	Ru-19d	CD ₂ Cl ₂	128-121	167.7	128-121	166.4
	Ru-20a	CD ₂ Cl ₂	127.3	167.9	127.7	169.6
						(³ J _{CP} = 3 Hz)
	Ru-21b	CD ₂ Cl ₂	123.8	163.8	124.2	170.0
η ¹ -Cl, η ¹ -O'	Pt-1 ³²		82.4	195.5	n.r.	n.r.
	Ru-30b *		88.2	200.5	n.r.	169.7
η ³ , η ³ -BINO						
	Ru-11''	CD ₂ Cl ₂	93.2	144.7	93.2	144.7
			(² J _{CP} = 4Hz) ^[c]		(² J _{CP} = 4Hz) ^[c]	
η ³ , η ¹ -BINO						
	Ru-28 ¹³⁷	CD ₂ Cl ₂	85.0	141.5	114.0	170.9
	Ru-11'	CD ₂ Cl ₂	109.1	143.1	114.2	170.4
			(² J _{CP} = 16 Hz)		(³ J _{CP} = 2 Hz)	(³ J _{CP} = 5 Hz)
	Ru-12'	CD ₂ Cl ₂	106.4	143.3	115.2	172.1
			(² J _{CP} = 15 Hz)	(² J _{CP} = 2 Hz)	(³ J _{CP} = 1 Hz)	(³ J _{CP} = 5 Hz)
	Ru-14' ^[d]	CD ₂ Cl ₂	97.6	143.5	113.8	174.4
			(² J _{CP} = 19 Hz)			
	Ru-19a'	CD ₂ Cl ₂	95.6	154.1	116.8	174.1
			(² J _{CP} = 11 Hz)	(² J _{CP} = 3 Hz)		(³ J _{CP} = 5 Hz)
	Ru-19d'	CD ₂ Cl ₂	N/A	152.7	115.6	166.5
	Ru-16' ^[d]	CD ₂ Cl ₂	125.6	148.0	116.0	162.0
			(² J _{CP} = 4 Hz)	(² J _{CP} = 3 Hz)		

^[a]Literature complexes **Pt-1** and **Ru-28'** are included to help designate the chemical shift ranges; an abbreviated list of ¹³C signals for reported coordination modes is found in Section 4.2.1.2. ^[b]All coupled signals are doublets, unless otherwise indicated. ^[c]Triplet multiplicity. ^[d]NMR characterization carried out at -20 °C for **Ru-14'** and -60 °C for **Ru-16'**.

4.2.4 X-ray analysis of Ru-BINO complexes.

X-ray quality crystals of η¹, η¹-BINO benzylidene complexes **Ru-19b** and **Ru-19c** (CCDC structures 755131 and 755132, see Appendix D for acquisition parameters) were obtained by diffusion of hexanes into THF solutions, and were analyzed by single-crystal X-ray diffraction. The complexes crystallize in the same space group and exhibit very similar unit cell dimensions. Their ORTEP diagrams (Figure 4.4) confirm the η¹, η¹-BINO binding mode. The structures differ chiefly in the C-C and N-C distances within the heterocyclic ring (Table

* Ru(BIANTH)(IMes)(py)(=CHPh) **Ru-30b** was synthesized by Dr. Adrien Normand of this research group.

4.4). In both cases, the strong σ -donor NHC ligand) results in elongation of the trans Ru–O bond (2.0841(13) Å and 2.0783(11) Å for the IMes and H₂IMes complexes, respectively, vs. 2.0504(13) Å and 2.0577(10) for the Ru–O bond trans to pyridine). The O(1)–Ru–O(2) bond angles are 89.57(5)° for **Ru-19b**, and 89.37(4)° for **Ru-19c**. Similar values for M–O bond distances and O–M–O angles (Pt: 2.0706(17) and 2.0353(17) Å and 87.67(7)°; Pd: 2.034(4) and 2.028(4) Å and 94.97(14)°) were reported for Pt(η^1, η^1 -*BINO*)(BIPHEP) and Pd(η^1, η^1 -*Me₂BINO*)(EN₂) (BIPHEP: 2,2'-bis(diphenylphosphino)-1,1'-biphenyl; *Me₂BINO*: 3,3'-dimethyl-1,1'-binaphth-2,2'-olate; EN: *N,N'*-dibenzylethylenediamine) complexes.^{25,30}

The dihedral angle between the naphtholate rings (**Ru-19b**, 62.57°; **Ru-19c**, 62.41°) is very similar to the value of 65° found for an η^1, η^1 -*BINO* molybdenum alkylidene complex,⁵ and much smaller than the 110.18° value found for η^3, η^3 -*BINO* **Ru-11''**. Larger values are also reported for a BIPHEN analogue (88.6(15)°) and a [Mo]-H₈BINO complex (102.2(8)°).^{72,73} The higher activity and enantioselectivity of the latter catalyst was proposed to be due to its larger dihedral angle.¹⁸ In the Ru-BINO complexes, the significance of this parameter is not clear-cut. While η^3 -enolate coordination undoubtedly creates a smaller, more well-defined chiral pocket, which could promote greater selectivity, isomerization in response to the steric congestion at Ru may limit its relevance during catalysis. As well, the PPh₃ complexes below indicate that torsion angles for the η^3, η^1 -*BINO* are more similar to those found for η^1, η^1 -*BINO* than η^3, η^3 -*BINO* coordination modes.

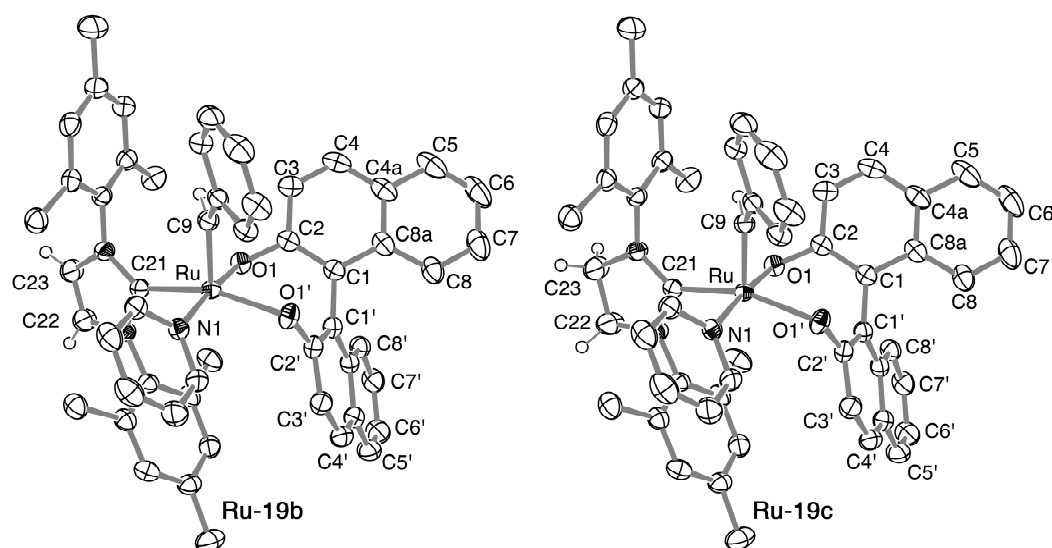


Figure 4.4. ORTEP diagrams of **Ru-19b** and **Ru-19c**. Non-hydrogen atoms are represented by Gaussian ellipsoids at the 50% probability level. Hydrogen atoms on C(22), C(23), and C(9) are shown with arbitrarily small thermal parameters; other hydrogen atoms are not shown.

Table 4.4. Selected bond lengths and angles for **Ru-19b** and **Ru-19c**.^[a]

Bond Length (Å)	Ru-19b	Ru-19c	Bond Angle (°)	Ru-19b	Ru-19c
Ru-O(1)	2.0504(13)	2.0577(10)	O(1)-Ru-O(1)'	89.57(5)	89.37(4)
Ru-O(1)'	2.0841(13)	2.0783(11)	O(1)-C(2)-C(1)	122.26(16)	122.42(13)
O(1)-C(2)	1.337(2)	1.3309(17)	O(1)'-C(2)'-C(1)'	123.85(17)	123.91(14)
O(1)'-C(2)'	1.335(2)	1.3328(18)	C(2)-C(1)-C(1)'	120.07(16)	120.10(12)
Ru-C(9)	1.8302(18)	1.8274(14)	C(2)'-C(1)'-C(1)	119.91(16)	119.85(13)
Ru-C(21)	2.0309(17)	2.0142(14)	N(2)-C(21)-N(3)	103.36(14)	106.91(12)
Ru-N(1)	2.0860(15)	2.0905(12)	C(21)-N(2)-C(22)	111.92(15)	113.96(12)
C(21)-N(2)	1.367(2)	1.3504(18)	C(23)-C(22)-N(2)	106.25(17)	102.58(13)
C(21)-N(3)	1.367(2)	1.3466(18)	C(22)-C(23)-N(3)	107.39(17)	103.27(13)
N(2)-C(22)	1.388(2)	1.469(2)	C(21)-N(3)-C(23)	111.02(15)	113.26(12)
N(3)-C(23)	1.392(2)	1.475(2)			
C(22)-C(23)	1.341(3)	1.508(2)	C(2)-C(1)-C(1)'-C(2) ^[b]	62.57°	62.41

^[a] Acquisition parameters and full tables of bond lengths and angles are provided in Appendix D. ^[b] Dihedral angle.

Diffusion of hexanes into a saturated solution of η^3, η^3 -*BINO* complex **Ru-11''** in THF afforded red prismatic crystals. The ORTEP diagram indicates a C_2 -symmetric structure, in which each of the two Ru-P and Ru-naphtholate interactions are similar (Figure 4.5). The Ru-O1/O1' distances are nearly 0.1 Å longer than those in η^1, η^1 -*BINO* complex **Ru-19b** (**Ru-11''**: 2.1348(17), 2.1696(16) Å, vs. **Ru-19b**: 2.0804(13), 2.0841(13) Å; Tables 4.5 and 4.4). The Ru-C1/C1' distances for **Ru-11''** (2.257(2), 2.266(2) Å) are slightly shorter than Ru-C2/C2' (2.273(2), 2.310(2) Å), indicating a slightly skewed Ru-enolate interaction, as expected from the $^2J_{CP}$ values extracted from the ^{13}C NMR data. This interaction results in a slight lengthening in the C1-C2 and C1'-C2' bond distances relative to those in **Ru-19b** (**Ru-11''**: 1.428(3), 1.430(3) Å; **Ru-19b**: 1.390(3), 1.397(3) Å).

Crystals of the acetonitrile **Ru-12'** and pyridine **Ru-14'** complexes deposited from concentrated solutions in THF by vapour diffusion of Et₂O (Figure 4.5). The Ru-O1' distances (**Ru-12'**: 2.043(4) Å; **Ru-14'**: 2.0550(18) Å) are ca. 0.12 Å shorter than that in **Ru-11''**, consistent with an η^1 -O bond, as in **Ru-19b/c** (Table 4.5). Partial π -coordination of the second naphtholate ring is evident from the Ru-O1 and Ru-C2 bond lengths in **Ru-12'** and **Ru-14'**. The long, non-bonding, interaction between Ru and C1 in **Ru-12'** (2.592(4) Å) indicates an η^2, η^1 -BINO structure. This may be an effect of crystal packing, as the NMR data support assignment as a η^3, η^1 -BINO complex, and the compressed C1'-C1-C2 angle suggests minor pyramidalization of C1 occurs (Table 4.5). The shorter Ru-C1 distance in pyridine complex **Ru-14'** is consistent with enolate bonding, as in **Ru-11''**. The torsion angles for η^2, η^1 -BINO **Ru-12'** and η^3, η^1 -BINO **Ru-14'** (75.3°, 75.1°) are considerably smaller than for η^3, η^3 -BINO **Ru-11''** (110.2°), but similar to those for η^1, η^1 -BINO **Ru-19b/c** (62.57°, 62.41°).

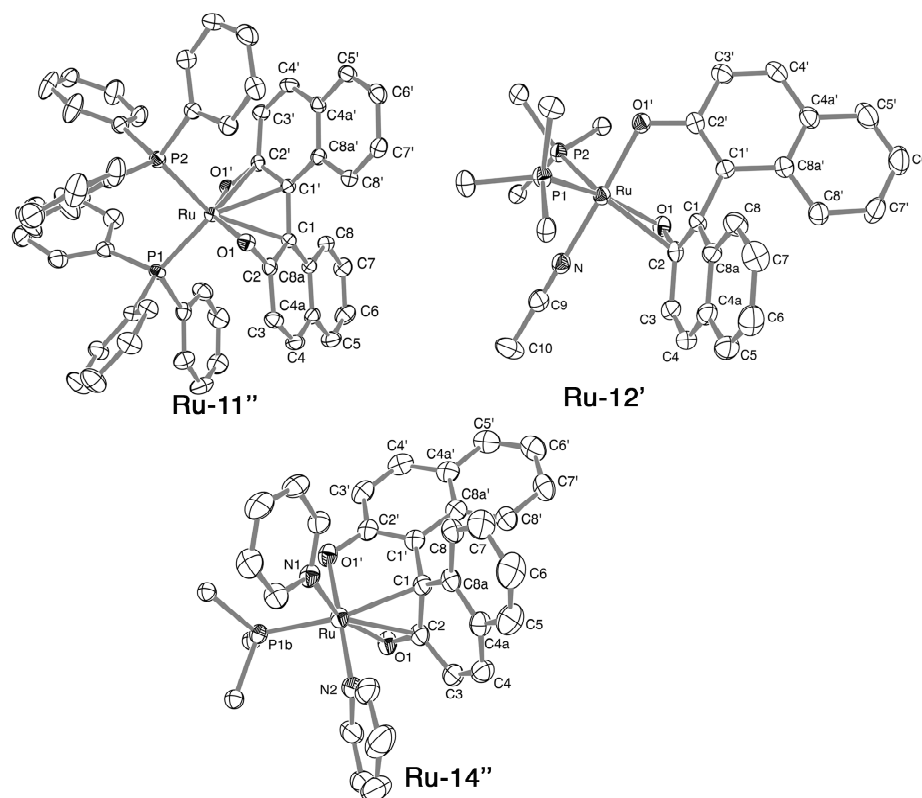


Figure 4.5. ORTEP diagrams of **Ru-11''**, **Ru-12'** and **Ru-14'**. Non-hydrogen atoms are represented by Gaussian ellipsoids at the 50% probability level. Phosphine phenyl carbons (except C_{ipso}) in **Ru-12'** and **Ru-14'** are omitted for simplicity. Hydrogen atoms are not shown.

Table 4.5. Selected bond lengths and angles for **Ru-11''**, **Ru-12'** and **Ru-14'**.^[a]

	Ru-11''	Ru-12'	Ru-14'
Bond lengths (Å)			
Ru-O1	2.1348(17)	2.159(3)	2.1728(16)
Ru-O1'	2.1696(16)	2.043(2)	2.0550(18)
Ru-C2	2.273(2)	2.315(4)	2.256(2)
Ru-C2'	2.310(2)		
Ru-C1	2.257(2)	2.592(4)	2.323(2)
Ru-C1'	2.266(2)		
Ru-P1	2.2613(7)	2.2968(11)	2.296(5)
Ru-P2	2.2836(7)	2.2793(11)	2.0853(19)
Ru-N1		2.017(3) ^[a]	2.0853(19) ^[b]
Ru-N2			2.084(2) ^[b]
C1-C2	1.428(3)	1.422(5)	1.444(3)
C1'-C2'	1.430(3)	1.384(5)	1.391(4)
Angles (°)			
C1'-C1-C2	119.3(2)	118.9(3)	119.1(2)
C2'-C1'-C1-C2 ^[b]	110.18	75.3(5)	71.1(3)

^[a] Acquisition parameters and full tables of bond lengths and angles are provided in Appendix D. ^[b] Dihedral angle

4.2.5 Circular dichroism analysis of (*R*)-**Ru-11'/11''**, η^1, η^1 -*BINO* (*R*)-**Ru-19b**, (*R*)-**Ru-19c** and η^3, η^1 -*BINO* (*R*)-**Ru-19a'**.

Incorporation of enantiomerically pure BINO ligands into **Ru-11'/11''** and **Ru-19a-c** affords optically active complexes (Figure 4.6a). Bringmann and Breuning have summarized cases in which racemization of free BINOL occurs. Protonation at C1 to give an sp³ center can effect racemization, owing to expansion of the angle between the naphthyl rings, which relieves the restricted rotation on which the atropisomeric chirality of the proligand rests.⁷⁴ We therefore considered the possibility that racemization could result from the enhanced sp³ character at C1 resulting from the η^3, η^1 -*BINO* coordination mode. Near-identical circular

dichroism spectra were observed for solutions of **Ru-19a'** allowed to stand for varying periods in solution prior to analysis (Figure 4.6b), suggesting that rotation of the naphthyl rings is restricted by the bidentate coordination of the ligand. A more rigorous probe, involving time-dependent measurements, would give added weight to this inference.

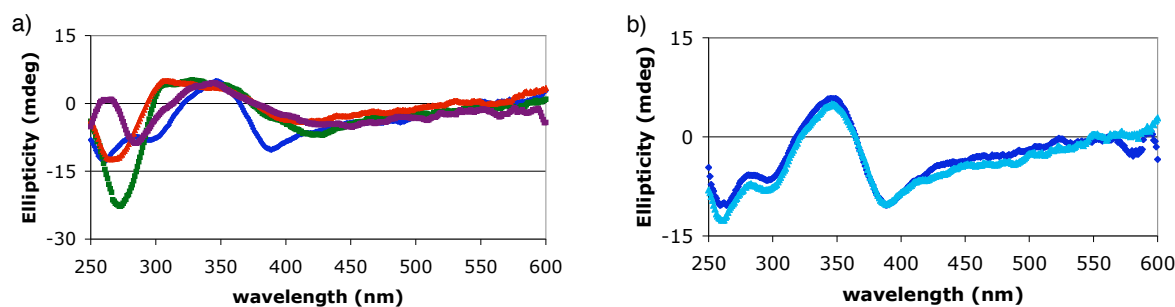


Figure 4.6. CD spectra of Ru-BINO complexes, a) (*R*)-**Ru-11'/11''** (purple), η^1,η^1 -BINO (*R*)-**Ru-19b** (green), η^1,η^1 -BINO (*R*)-**Ru-19c** (red) and η^3,η^1 -BINO (*R*)-**Ru-19a'** (blue) and b) two independently prepared samples of **Ru-19a'**. All samples were analyzed in CH₂Cl₂ (10⁻⁵ M).

A short discussion is included here that pertains to the technical challenges involved in CD analysis of the Ru-BINO complexes. All of the complexes are air-sensitive, particularly in the solution state, requiring use of sealed cuvettes (Figure 4.7). A septum-sealed cell (Figure 4.7a) is sufficient for most complexes, but the high sensitivity of **Ru-11'/11''** required analysis in a screw-cap cuvette (Figure 4.7b). A more desirable cuvette configuration, shown in Figure 4.7c, would involve a glass connection between the cuvette and a flask with a side-arm equipped with a PTFE stopcock (Figure 4.7c). This configuration is ideal for stirring reactions or for reagent addition between analyses. However, as noted by Shriver and Drezdon,⁷⁵ modification of the spectrometer cover is required to accommodate the additional height of such cells; sufficient space must also be available for the reaction cell in the sample chamber.

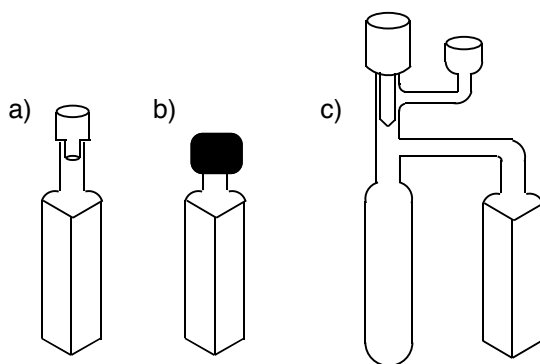


Figure 4.7. Cuvettes for air-sensitive samples. Cells are sealed with: a) a septum plug; b) a screw cap; and c) a PTFE stopcock with side-arm for reagent addition.

4.3 Catalytic studies.

4.3.1 Methodology.

The activity of $\text{Ru}(\eta^1, \eta^1\text{-BINO})(\text{IMes})(\text{py})(=\text{CHPh})$ **Ru-19b** and $\text{Ru}(\eta^1, \eta^1\text{-BINO})(\text{IMes})(3\text{-bromopyridine})(=\text{CHPh})$ **Ru-21b** was initially benchmarked against that of the highly reactive third-generation IMes and H_2IMes Grubbs catalysts (**Ru-3b** and **Ru-18b**, respectively), in the RCM of diethyl diallylmalonate **1** and *N*-tosyl-*N,N*-diallylamine **3**. These dienes were selected for their strong bias toward cyclization, which renders them essentially immune to the competing oligomerization (or oligomerization-backbiting) pathways established for larger rings,⁷⁶ even at relatively high concentrations (100 mM). Given the low activity that emerged from these studies, more extensive screening of these and subsequently-developed BINO catalysts was undertaken in ROM/CM reactions of *cis*-5-norbornene-*exo*-2,3-dicarboxylic anhydride **4** with styrene, in which the ring strain of the norbornene ring facilitates the initial, ring-opening metathesis step. Attenuated catalyst activity is often essential in such reactions, as it tends to inhibit competing ROMP.

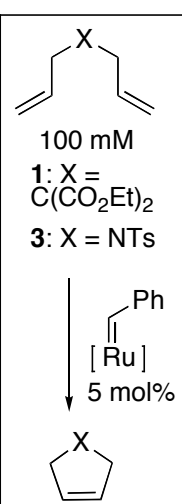
RCM activity was assessed from consumption of diene and formation of the RCM product (each being quantified by ^1H NMR or GC-FID analysis, as discussed in Chapter 2, Section 2.10.3). ROM/CM activity was determined from consumption of norbornene (measured by calibrated GC-FID). Catalyst selectivity for ROM/CM vs. ROMP was determined by

subtraction of the GC yield of the ROM/CM product from the conversion of the starting norbornene monomer. Thus, yields of involatile polymers were inferred from the loss in total GC-FID integration. Regio- and enantioselectivities (enantiomeric excesses, % e.e.) were determined by the percent difference of GC-FID signals for the *E/Z* isomers and enantiomers, respectively.

4.3.2 RCM of **1** and **3** by Ru(η^1, η^1 -*BINO*)(IMes)(py)(=CHPh) **Ru-19b** and Ru(η^1, η^1 -*BINO*)(IMes)(py') (=CHPh) **Ru-21b**.

Catalysts **Ru-19b** and **Ru-21b** exhibited unexpectedly low RCM reactivity, with no consumption of DDM at 50 °C in THF after 1 hour, even at 100 mM concentrations of the diene and catalyst loadings of 5 mol% (Table 4.6, Entries 1-4). Under the same conditions, dichloride catalyst **Ru-3b** effects quantitative RCM within 15 min (Entry 5). Similarly, RCM of **3** at 40 °C in CH₂Cl₂ revealed minimal activity for **Ru-21b** (7% conversion), as compared to 100% for the analogous dichloride 3-bromopyridine catalyst **Ru-18b** (Entries 6, 7). These low conversions are unsurprising, given that cis-anionic geometries appear to generally correlate with reduced metathesis activity in ruthenium metathesis catalysts.⁷⁷⁻⁸¹ Within the catecholate family of catalysts, however, a systematic study indicated that metathesis activity increases as the p*K*_a of the anionic ligand increases.⁴⁵ On this basis, we had anticipated that the Ru-BINO catalysts should be more active than (e.g.) the bis-(OC₆F₅) catalyst, or the tetrahalo-catecholate catalysts (Chart 4.2 a and b). Instead, the activity of **Ru-19b** is lowest of all aryloxy catalysts that we have yet studied.^{45,46,82} To determine whether this is due simply to poor initiation (as is the case for cis-dichloride catalysts,^{77,83} as well as the catecholate catalysts⁸⁴), reactions were carried out as above, but in the presence of Lewis acids designed to scavenge the pyridine ligand.

Table 4.6. Assessing the metathesis activity of Ru-BINO in RCM of benchmark dienes.

	Entry	Substrate (0.1M)	[Ru] (5 mol%)	Solvent	Temp. (°C)	Time (min)	Conv. (%) ^[a]
100 mM 1: X = C(CO ₂ Et) ₂ 3: X = NTs	1	1	Ru-19b	THF	50	15	0
	2					60	0
	3					15	0
	4					60	0
	5					15	100
	6	3	Ru-21b	CH ₂ Cl ₂	40	15	7 ^[b]
7	Ru-18b					15	100 ^[b]

^[a] Reactions analyzed by GC-FID unless otherwise specified. ^[b] Determined by ¹H NMR analysis.

In the presence of 10 equiv of chlorocatecholborane **14** or triphenylborane **15**, RCM yields reached 38% and 13%, respectively, at 1 h (Figure 4.7). Control reactions with the Lewis acids themselves, i.e. in the absence of **Ru-19b**, showed no RCM activity, as expected. Despite this improvement in activity, the Ru-BINO catalysts remain far inferior not only to the parent Grubbs systems **Ru-3b** and **Ru-18b**, but the majority of chiral molybdenum and ruthenium metathesis catalysts, for which ARCM of trienes is a standard probe reaction.^{9,10,12,83,85,86} Similarly low reactivity was reported for Hoveyda's κ^2 -C,O NHC-BINO catalyst (Chart 4.2d).⁸⁷ We thus turned to ROM/CM reactions, which are of considerable interest as a target for efficient, robust enantioselective transformations.

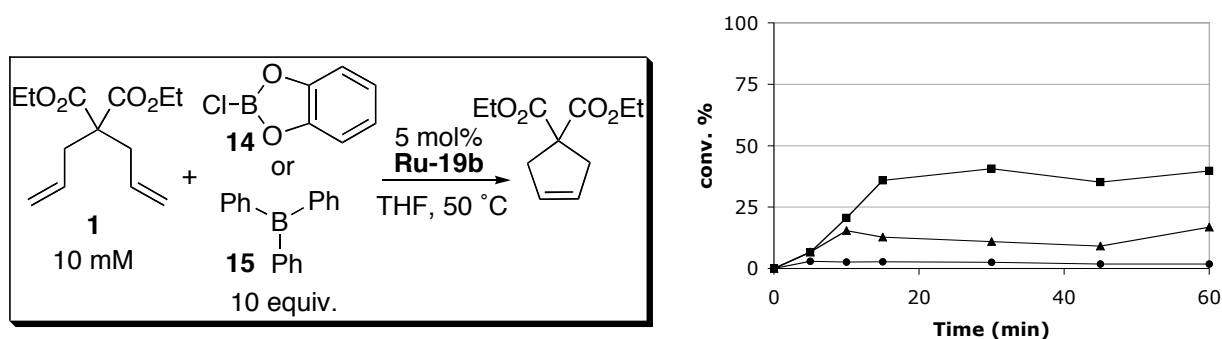
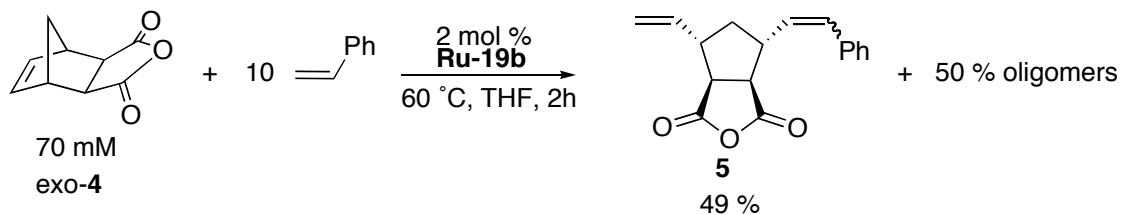


Figure 4.8. Effect of additives on the activity of **Ru-19b** in RCM of **1**. Legend: no additive (●); with **14** (■); with **15** (▲).

4.3.3 ROM/CM of *exo*-**4** with Ru-binaphtholate catalysts.

In a probe ROM/CM experiment, *exo*-**4** (70 mM in THF) was treated with a tenfold excess of styrene and 2 mol% of **Ru-19b**, and heated to 60 °C for 2 h (Scheme 4.15). GC-FID analysis indicated complete consumption of the norbornene monomer, but only 49% yield of the ROM/CM product, the balance being due to competing ROMP. Slightly higher ROM/CM yields (63%) were reported for Hoveyda's κ^2 -C,*O* NHC-BINO catalyst (Chart 4.2d), albeit at higher **4** concentrations (100 mM) and only two equiv of styrene.⁸⁷ A greater avidity for ROMP in preference to ring-opening cross-metathesis commonly accompanies higher reactivity, as noted above.^{88,89} Key parameters used to limit ROMP activity are reduced norbornene concentrations and higher proportions of the cross-metathesis partner.



Scheme 4.15. Preliminary reactivity of Ru-BINO **Ru-19b** in the ROM/CM of **4** and styrene.

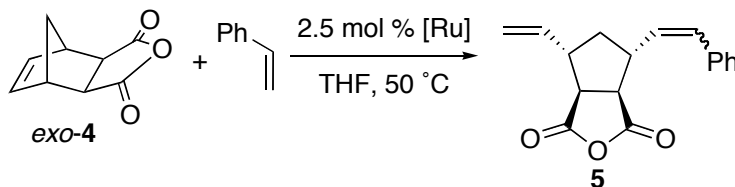
4.3.4 HT Optimization: ROM/CM of **4** via Ru-binaphtholate catalysts, **Ru-19b-c**, **Ru-21b**.

High-throughput screening experiments were carried out at a series of NBE concentrations, lower than those employed in the study above, and with higher proportions of styrene. These

modifications were expected to increase selectivity for ROM/CM product **4** over the polymerized products observed above. Thus, **4** concentrations of 10 and 50 mM and 5, 10 and 20 equiv of styrene were investigated (Figure 4.8). All reactions were carried out in THF at 50 °C with 2.5 mol% **Ru-19b-c**, **Ru-21b**. Conversions were assessed at 2 and 6 h by GC-FID analysis.

The data of Figure 4.8 show the following order of catalyst activity: **Ru-19c** > **Ru-19b** > **Ru-21b** > **Ru-19a'**. Of these, only **Ru-19c** effects complete consumption of **4** within 2 h (Figure 4.8b): the next most active catalyst, IMes analogue **Ru-19b**, requires 6 h reaction to approach the same conversions. This trend accords with that reported for the second-generation Grubbs catalysts **Ru-1b** and **Ru-1c** in RCM studies employing **1** as substrate.^{90,91} The 3-bromopyridine complex **Ru-21b** shows lower activity, despite the higher lability of this catalyst. As with its py analogue, this catalyst yields minimal increases in conversion on increasing the reaction time threefold. Both features point toward catalyst deactivation. The correlation between higher lability and enhanced deactivation has been noted previously.⁹² Given its poor performance, this catalyst was excluded from further screening. The η^3, η^1 -*BINO* catalyst is relatively unaffected by these conditions, consuming ca. 36% **4** in all cases, although at least 10 equiv styrene are required to maximize yields of the target diene.

a)



Condition No.	[4] (mM)	Styrene: 4
1	10	20
2	10	10
3	10	5
4	50	20
5	50	10
6	50	5

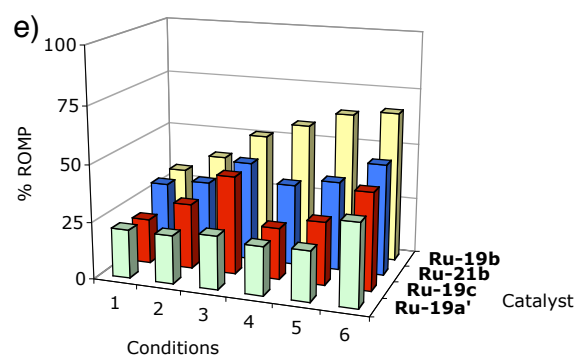
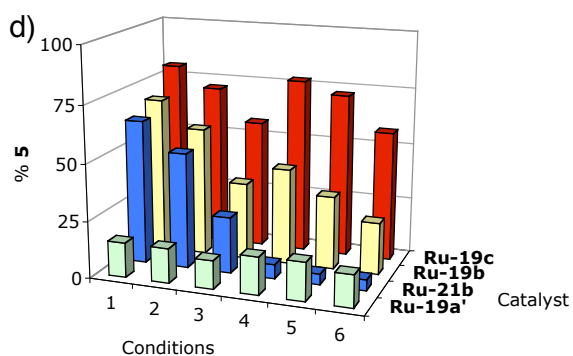
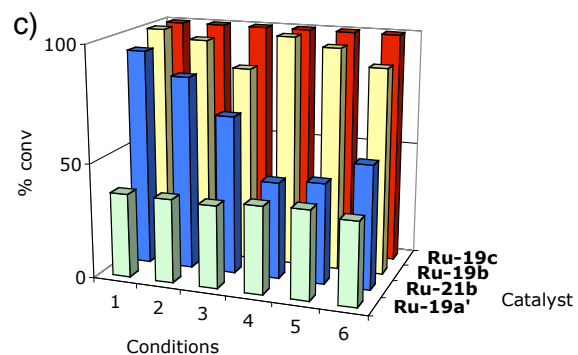
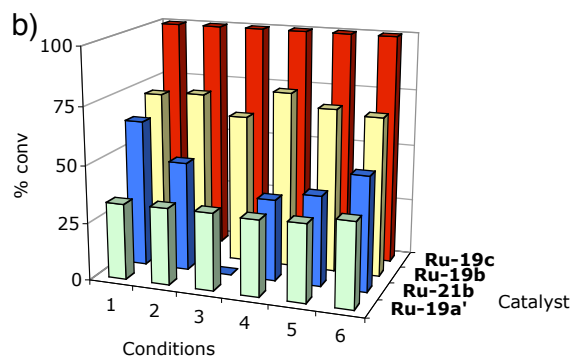
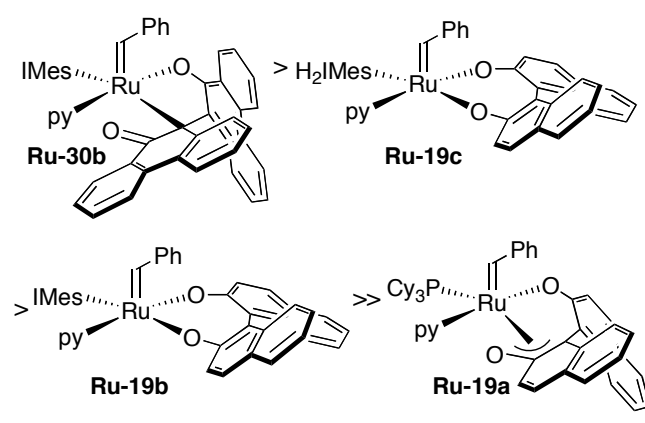


Figure 4.9. Evaluation of the optimum norbornene concentration and styrene ratio in ROM/CM experiments. a) Conditions employed; b) **4** consumed at 2 h; c) **4** consumed at 6 h; d) Yield of ROM/CM product **5** at 6 h; e) Yield of polymer at 6 h. Red: **Ru-19c**; yellow: **Ru-19b**, blue: **Ru-21b**, green: **Ru-19a'**.

Highest conversions to **5** are achieved with a low concentration of **4** (10 mM) and a 20-fold excess of styrene (Figure 4.8c,d). Significant ROMP is still observed under these conditions:

21% for **Ru-19c**, 31% for **Ru-19b**, 30% for **Ru-21b**, and 21% for **Ru-19a'**. These values increase to 36%, 43%, 49% and 66%, respectively, on increasing **4** to 50 mM and restricting the proportion of styrene to 5 equiv (Figure 4.8d). Interestingly, the most active catalyst **Ru-19c** affords 43% ROMP at 5 equiv styrene, irrespective of whether the reaction is 10 or 50 mM in norbornene. The corresponding figures for the IMes analogue are 51% ROMP at 10 mM, and 66% ROMP at 50 mM **4**. For **Ru-19a'**, the proportion of ROM/CM product likewise decreases with increasing norbornene concentration, but the effect is attenuated by its low inherent activity.

The *E/Z* ratios and enantiomeric purity of the products were determined by GC-FID and chiral GC-FID, respectively (Chapter 2, Section 2.1.6; Table 4.5). The NHC catalysts showed minimal *E/Z* selectivity: 1.3:1 for **Ru-19b** and 1:1 for **Ru-19c**, vs. 3.4:1 for the PCy₃ catalyst **Ru-19a'** (Figure 4.9). Enantioselectivities were consistently low, but **Ru-19a'** again showed most promise, at 9% e.e. (vs. 5% for **Ru-19b** and 2% for **Ru-19c**). Both parameters suggest the presence of a more well-defined chiral pocket in the phosphine catalyst, probably reflecting the greater three-dimensional bulk of the PCy₃ ligand. Whether the η^3, η^1 -*BINO* coordination mode (which increases the dihedral angle between the naphthyl rings by ca. 10°; Section 4.2.2.3) also plays a role is unclear: the sensitivity of the *BINO* binding mode to steric pressure may favour η^1, η^1 -*BINO* coordination under conditions of catalysis, as noted above. More generally, however, these results suggest that 3,3'-functionalization of the *BINO* ligand may be essential to maximizing catalyst selectivity.



[Ru] (mol%)	Tim e (h)	% Conv.	% 11	% e.e. (<i>E:Z</i>)
Ru-19c (2.5)	2	100	78	2 (1:1)
Ru-19b (2.5)	2	72	38	5 (1.3:1)
Ru-19a' (2.5)	2	33	9	9 (3.4:1)
Ru-30b (1)	6	100	100	(1.2:1)
Ru-19c (1)	6	100	92	(1.3:1)
Ru-19b (1)	6	88	86	(1.3:1)
Ru-19a' (1)	6	5	0	N/A

Figure 4.10. ROM/CM conversions and selectivity for catalysts **Ru-19a-c** and **Ru-30b** under optimized conditions (10 mM **4**, 20 equiv styrene at 50 °C in THF).

Quantitative conversions of **4** are maintained for **Ru-19c** (and $\eta^1\text{-Cl}, \eta^1\text{-O'}$ complex **Ru-30b**⁹³) on decreasing the catalyst loading to 1 mol % Ru, but extending reaction times to 6 h (Figure 4.9). In comparison, 88% conversion was observed for **Ru-19b**, and just 6% for **Ru-19a'**. The high activity of **Ru-30b** is noteworthy given its $\eta^1\text{-Cl}, \eta^1\text{-O'}$ coordination mode and the bulk at the 3,3'-positions. This tends to suggest that the low activity of **Ru-19a'** is due to the presence of the PCy₃ ligand, rather than the $\eta^3, \eta^1\text{-BINO}$ coordination mode.

4.3.5 Use of additives to increase catalyst activity.

Section 4.3.2 described the capacity of Lewis acids to increase the metathesis activity of **Ru-19b**. Certain phenols (particularly butylated hydroxytoluene **17**) has been shown to improve the RCM activity of aryloxide metathesis catalysts,⁹⁴ as well as the first-generation Grubbs catalysts,⁹⁵ perhaps via hydrogen-bonding, although the precise mode of action is unclear. Hoveyda has proposed that intramolecular coordination of a hydroxy group situated at the β -

position of the vinylic CM partner can improve enantioselectivities.⁹⁶ Both Lewis acids and H-bond donors were examined for their capacity to increase activity in ROM/CM of **10** with styrene in reactions promoted by **Ru-19b** and **Ru-19a'**. Additives screened included monodentate and bidentate phenols or alcohols, primary and secondary amines, and boron Lewis acids (Chart 4.3), each used in 20-fold excess relative to ruthenium. Figure 4.10 depicts the results of this study, which employed the conditions optimized in Section 4.3.4, albeit at lower catalyst loadings and longer reaction time (1 mol% Ru; 6h). Under these conditions, baseline conversions for **Ru-19b** and **Ru-19a'** are 88% and 6%, as noted above.

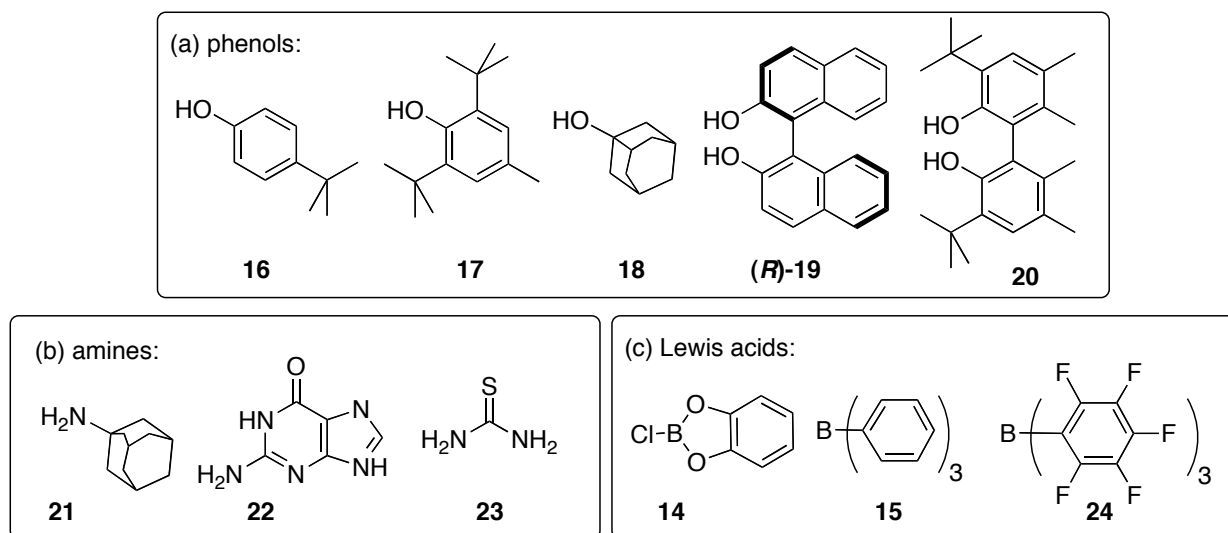


Chart 4.3. Additives examined in ROM/CM reactions.

In reactions using **Ru-19b** as catalyst, addition of primary and secondary amines **21-23** impaired conversions (to 58, 68 and 3%, respectively); similar poisoning effects were earlier reported for the Grubbs systems.⁹⁷⁻⁹⁹ Consistent with previous metathesis studies with various H-bond donors,^{94,95,100} phenol additives **16**, **17**, **19**, and **20** increased conversion to 100%; for adamantyl alcohol **18**, 95% conversion was observed. For catalyst **Ru-19a'**, these additives offered no improvement in activity, but the Lewis acids **14**, **15** and **24** effected a dramatic increase, to 100, 53 and 100% **5**, respectively.

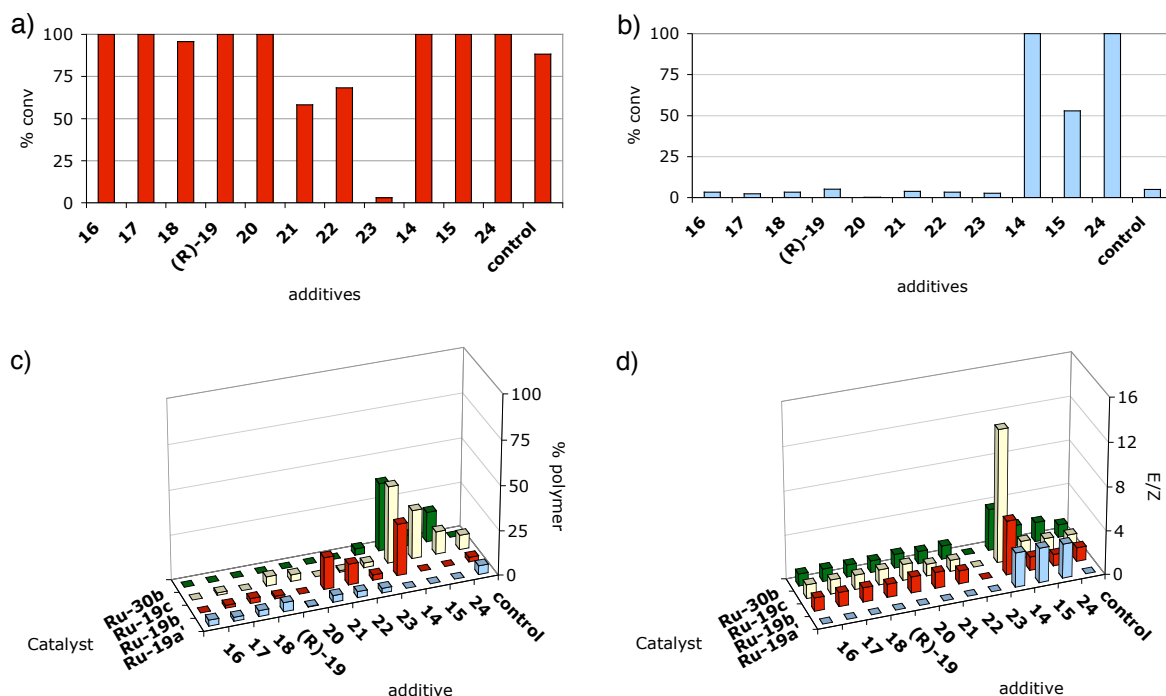


Figure 4.11. Effect of additives on ROM/CM of **4** to form **5**. a) with **Ru-19b**; b) **Ru-19a'**; c) % polymer formed with **Ru-19a-c** and **Ru-30b**; d) *E/Z* selectivity with **Ru-19a-c** and **Ru-30b**.

For the more active NHC catalysts, the Lewis acid additives have the undesirable effect of promoting ROMP, in preference to ROM/CM (Figure 4.10c). Use of chlorocatecholborane **14** increases ROMP yields from 3%, 8% and 0% for **Ru-19b**, **Ru-19c** and **Ru-30b** to 29%, 43% and 38%, respectively. This effect is less dramatic with the bulky Lewis acid trispentafluorophenylborane **24** (corresponding ROMP yields: 0%, 13%, 17%). As an additional, unexpected but potentially important effect, however, use of chlorocatecholborane **14** increased the *E/Z* selectivity of **Ru-19c** by an order of magnitude (from 1.3:1 to a remarkable 12:1 ratio). This is notable given the fact that the majority of ruthenium metathesis catalysts give very poor control over *E/Z* selectivity (typically ca. 1:1);⁸⁶ indeed, Schrock has suggested that this may be a feature inherent to the architecture of the Ru catalysts. Recently however, a Ru catalyst with a C_1 -symmetric NHC gave unexpectedly high regioselectivity, favouring the *E* isomer by 30:1.¹³ Limitations in *E/Z* selectivity may thus be a function of the C_2 -symmetric NHC ligands most commonly

employed in the ruthenium catalysts. The improved selectivity observed for **Ru-19c** in the presence of borane **14** is apparently specific to this catalyst-additive combination: increases with **Ru-19b** and **Ru-30b** are less significant, **Ru-19a'** shows no effect, and the other Lewis acids **15** and **24** showed no improvement over control reactions.

The hydrogen-bond donors showed essentially no effect on ROM/CM or *E/Z* selectivity. The effect of chlorocatecholborane **14** on *E/Z* selectivity may reflect in situ conversion to a dichloride Grubbs catalyst, but this does not satisfactorily account for the remarkable selectivity observed (addition of **Ru-1b** to endo-**4**, a 1:1 mixture of *E:Z* is formed).⁸⁶ Incomplete chloride exchange may afford a monodentate BINO ligand, a motif that has recently proved highly successful in Schrock-type molybdenum catalysts.^{8,18} Further investigation into this behaviour is warranted. For the mechanistic study below, only additive tris(pentafluorophenyl)borane **24** was examined, given its more general behaviour and a greater selectivity for ROM/CM product **5** over oligomeric species.

4.3.6 Mode of action of tris(pentafluorophenyl)borane.

The role of the Lewis acid additive **24** was examined by adding it to a solution of **Ru-19b** in C₆D₆, and subjecting the mixture to immediate ¹¹B{¹H} NMR analysis (Figure 4.11). A single broad resonance was observed at -4.2 ppm, considerably upfield from that for **24** (cf. 59.4 ppm)¹⁰¹ and within the range expected for tetrahedral boron.¹⁰² The signal is assigned to the borane-pyridine adduct based on comparison to literature values¹⁰³ and a control experiment in which pyridine was added to **24**.

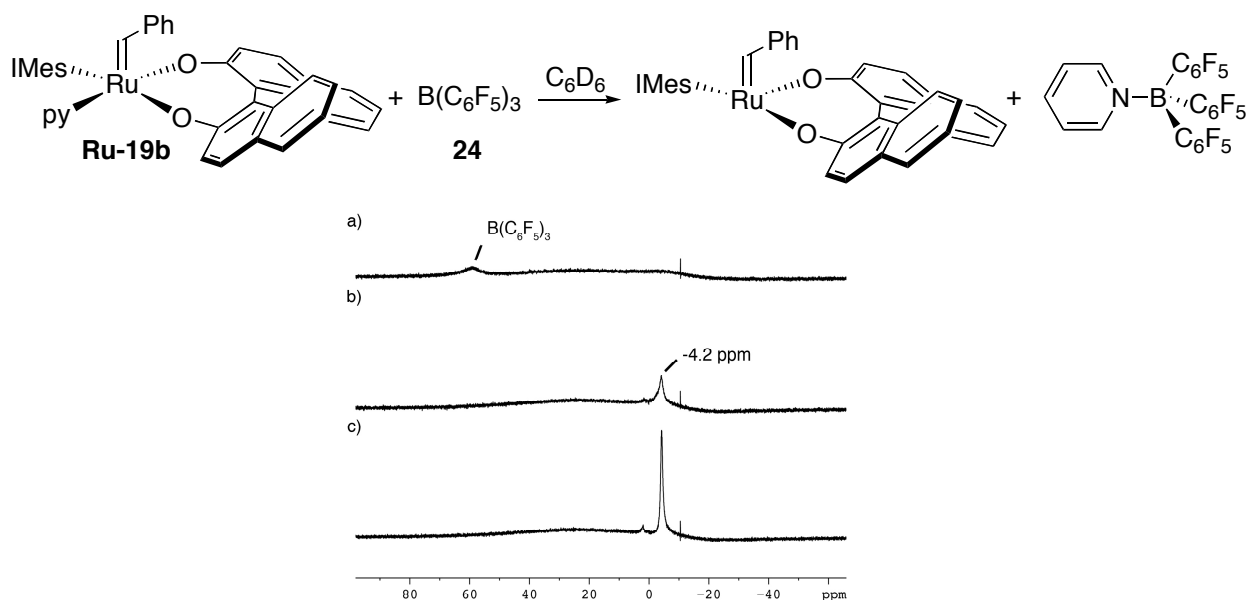


Figure 4.12. Sequestering the labile pyridine ligand from **Ru-19b** with borane **24**. Analysis by $^{11}\text{B}\{^1\text{H}\}$ NMR of a) isolated **24**; b) a mixture of **Ru-19b** and **24**, and c) a mixture of **24** and excess pyridine.

While Lewis acid additives are commonly used to inhibit catalyst poisoning by coordination of substrate carbonyl groups (Figure 4.12),¹⁰⁴ the experiment above suggests that the major role of these additives is efficient sequestration of the pyridine ligand liberated during catalyst initiation (required to generate the catalytically active, 14-electron intermediate). Addition of CuCl to second-generation phosphine catalysts has been used to increase catalyst activity in an analogous manner.^{105,106} Consistent with this is the observed increase in activity, but minimal effect on *E/Z* selectivity, on addition of **24** to ROM/CM reactions (Section 4.3.5). Removal of pyridine is thus a two-edged sword. While this accelerates catalyst initiation, it also promotes deactivation, limiting catalyst productivity.

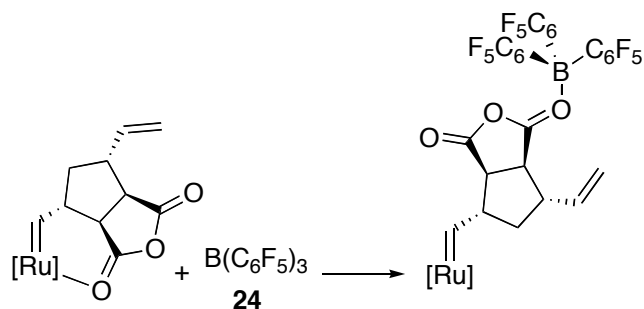


Figure 4.13. Possible mode of action for **24** during ROM/CM of **4**.

4.4 Conclusion.

This Chapter describes the first entry point into a new family of asymmetric olefin metathesis catalysts, which bridges the gap between the Schrock molybdenum systems and the Grubbs-class ruthenium catalysts by incorporating the tunable binaphtholate ligand into the ruthenium context. Use of pyridine as a stabilizing donor solvent enabled a breakthrough in the high-yield synthesis of $\text{Ru}(\eta^1, \eta^1\text{-BINO})(\text{IMes})(\text{py})(=\text{CHPh})$ **Ru-19b** and related complexes. (Less satisfactory results are obtained with 3-bromopyridine as the solvent, this resulting in decomposition on attempts to isolate the benzyldiene product). The successful synthesis of **Ru-19b** was unexpected, given ample precedents for preferential π -coordination of monodentate aryloxides, and the closely related BINOP ligand, to Ru centres bearing labile ligands. However, examination of the reaction between BINO and the model complex $\text{RuCl}_2(\text{PPh}_3)_3$ revealed that the BINO ligand occupies an intriguing midway point between the $\eta^{5/6}$ -aryl binding earlier observed, and σ -OAr coordination. The $\text{Ru}(\eta^3, \eta^3\text{-BINO})(\text{PPh}_3)_2$ product **Ru-11''** is stabilized by an $\eta^3, \eta^3\text{-BINO}$ structure, which undergoes facile conversion to η^3, η^1 - or $\eta^1, \eta^1\text{-BINO}$ derivatives as coordination numbers increase. The triphenylphosphine complex **Ru-11'/11''** is of interest in its own right as a potentially versatile entry point into Ru-BINO catalysts, in addition to the benzyldiene and vinylidene derivatives explored.

The dynamic coordination of the BINO ligand likewise proved key to expanding the family of Ru-BINO metathesis catalysts to include other NHC and phosphine ligands. The bulkier ancillary ligands PCy_3 and IPr yield $\eta^3, \eta^1\text{-BINO}$ complexes, perhaps because isomerization to the enolate binding mode relieves the steric pressure otherwise present in the basal plane.

In contrast, complexes of the smaller H₂ITol ligand could not be prepared: rapid and complete loss of the benzyldiene functionality resulted, possibly owing to C-H activation of the tolyl ring. Incorporation of a sterically undemanding styrenyl ether ligand also proved unsuccessful. Preliminary experiments indicated that installation of 3,3'-functionalized BINO ligands is successful in some cases, but more work will be required to circumvent decomposition on workup, which inhibited isolation.

The low activity of the Ru-BINO catalysts in RCM metathesis reactions limits them to ROM/CM reactions. Catalyst initiation can be accelerated through addition of Lewis acid additives, and one such additive results in dramatic increases in E/Z selectivity. Their low enantioselectivity presents a greater challenge: this finding underscores the potential importance of the derivatives containing 3,3'-functionalized BINO ligands, and represents an important vector for future work.

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Chapter 5. High-Throughput Screening of Ruthenium-Catalyzed Olefin Metathesis, Hydrogenation and Isomerization: Methodologies and Case Studies*

5.1 Introduction.

Over the past ten years, high-throughput experimentation (HTE) has expanded beyond its base in biotechnology into prominence in new areas, including the discovery and optimization of homogeneous catalysts.¹⁻⁶ Showcase advances have been achieved in polyolefins research and development, in particular, where HTE has greatly expanded the volume, scope, and quality of data available, while minimizing materials consumption relative to conventional bench-top techniques.^{7,8} More generally, these methodologies have been the focus of much interest in the industrial context, where the typically high capital costs of the equipment can be sustained, and there is an urgent financial imperative to reduce lead times from discovery to market for new catalytic technologies. A seminal review by DSM researchers de Vries and de Vries highlights practical considerations and applications of HTE in the fine chemicals industry.⁴ The same group recently described the astonishingly compressed discovery and implementation of a new asymmetric hydrogenation process (25 days from screening to scale-up),⁹ a process that may have taken months, if not years, by conventional iterative screening, presuming that the key "hit" was in fact observed under the necessarily more circumscribed set of experiments.

Reaction optimization is the dominant focus of HTE in homogeneous catalysis. The standard approach involves screening a library of catalysts, often generated in situ from different metal-ligand combinations, under a range of conditions.^{2,6,10-13} Areas of major advance include olefin polymerization^{7,8} and asymmetric hydrogenation,^{4,9,14} as noted above. A more recent approach, described as 'accelerated serendipity'^{**15} by MacMillan, focuses on the

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** Many major scientific advances have emerged from chance discoveries. Well-known, transformative examples include X-ray radiation, cisplatin, the penicillin antibiotics, and new materials ranging from urea to Teflon and low-density polyethylene. HTE offers a way to accelerate chance discoveries, and hence to create

discovery of *unexpected* reactions or products.⁴ This has led to the discovery of new multicomponent reactions,¹⁶ as well as unexpected reactivity of alkynyl aldehydes¹⁷ and polycyclic iminium ethers.¹⁸

In either case – that is, reaction optimization and reaction discovery – a 'hit or miss' tactic is adopted, in which misses are discarded, and only hits are followed up. A large volume of the generated data is thus cast aside. As a third approach, complementary in its aims, we sought to harness HTE for efficient compilation of mechanistic data in catalysis. This strategy goes beyond hit and miss, capturing all of the data generated from the wellplate, and using it to formulate the deeper understanding essential to optimize the reaction in hand, and to expand the fundamental knowledge on which deeper insight rests. The goal is not to cut down on the total number of experiments that would be carried out in serial experimentation (on the contrary, this number may well increase), but by carrying them out much faster, to compress the time penalty otherwise associated with large numbers of unsuccessful experiments.

The ideal, in HTE kinetics, involves monitoring reactions over time to acquire kinetic data. This could enable not only mechanistic, but practical insight (enabling identification, for example, of fast-initiating but readily deactivated systems, vs. slow but robust catalysts). The technical requirements for on-line analysis of the entire reaction plate in real time over the course of the experiment are daunting, however.^{*19} A major obstacle lies in the capacity of current analytical instrumentation to sample 96 parallel reactions in near-simultaneity, in microscale, and at standard dilutions. To date, simultaneous, parallel analysis of reaction wells is only feasible in specialized cases. Quantitative monitoring of ethylene polymerization was achieved by gas uptake of up to 48 parallel reaction wells (albeit for reactions carried out on relatively large scale for HTE: 100-200 mg of polymer per well).⁷ The large exotherm characteristic of the reaction has also been exploited for *qualitative* insight from infrared thermography.²

new knowledge and new technologies that (in the spirit of the Kornberg dictum "Invention is the mother of necessity") can rapidly become essential to modernity.

* A non-high-throughput but highly parallelized means of compiling large volumes of mechanistic data (including activation parameters) was also reported by Plenio, Rothenberg and co-workers, by screening multiple substrates in a single reaction vessel. Separate screening reactions must be conducted for each catalyst system, and cross-reactions are a potential hazard.

Such techniques are less well adapted to monitoring HT homogenous catalysis in organic solvents, in which substrate concentrations are typically much lower (normally 1-100 mM), and the solvent functions as a heat sink. In a clever inversion of the usual approach, Reetz and co-workers assessed the relative activity of RCM catalysts from 'cold spots' generated in this endothermic reaction.²⁰ High concentrations of diene are required, a condition feasible for the substrate employed (diethyl diallyl malonate; 4 M), but one that prevents use of this method to monitor the progress of reactions that proceed only at high dilutions (e.g. RCM synthesis of medium or large rings). An ingenious, if also non-general, alternative solution described parallel analysis of 96-well plates using a spatially addressable fluorescence assay, in which an amine "molecular sensor" (present in the reaction medium) reacted with an acidic coproduct to generate the fluorophore.²¹ Similarly, tagged substrates for aldol,²² Heck or Suzuki²³ reactions have been prepared that give access to fluorimetric rate data.

Pending development of appropriately sensitive on-line monitoring methods that can independently address all 96 wells, off-line analysis remains essential for screening across broad substrate and reaction classes. Parallel thin-layer chromatography using a multi-tipped needle assembly is attractive for its simplicity, throughput, and the ease with which insight can be gained into selectivity and the evolution of reactions (including induction periods).^{24,25} It is limited, however, by the fact that the data are merely qualitative. More specialized, but of interest for both sensitivity and quantitative insight, are the gas-phase, electrospray mass spectrometry screening methods pioneered by Chen.²⁶⁻²⁸ Typically, however, quantitative analysis relies on use of conventional gas chromatography (GC) or high-performance liquid chromatography (HPLC) to evaluate reaction progress and product speciation.^{1,4,6}

In a discussion of some of the technical challenges in fast sequential analysis, Rothenberg notes that rapidly evolving reactions should be sampled more frequently than slower ones, but that this is a "chicken or the egg" problem, requiring prior knowledge of catalyst behaviour.²⁹ More generally, it should be recognized that acquisition of real-time kinetic profiles using serial instruments is suitable only for relatively slow reactions, because the intervals at which each well can be interrogated must accommodate the time for analysis. As

a case in point, Schubert and co-workers described rapid sampling of 13 parallel polymerization reactions (<5 minutes per well), but the cumulative time, as well as that required for analysis of all 13 samples, meant that only one data-point per hour could be obtained for any individual reaction.³⁰ Much current effort is directed at solving these problems. In one interesting approach, Trapp and coworkers reported extraction of reaction rate constants and activation parameters by using the polymeric stationary phase of a chromatographic capillary tube to both immobilize catalysts and separate the products. Specialized columns were prepared for Pd nanoparticle-catalyzed hydrogenation and Ru-catalyzed RCM: in the former, a throughput of nearly 170 samples per hour was obtained.³¹ Against this, however, it should be noted that immobilization of highly successful homogeneous catalysts is itself an area with many challenges.

Multi-channel methods are of interest for their potential to eliminate the bottleneck of serial analysis, but sampling time remains an issue. Emerging methods for multiplexed GC can handle up to 450 samples per hour.³² and comparably impressive throughput has been described in flow NMR³³⁻³⁵ and capillary electrophoresis (CE).^{36,37} Some disadvantages remain present in each case, however. For GC or CE, response factors must be measured, although CE has been used chiefly for the less demanding problem of determining enantioselectivities (where response factors are immaterial), rather than conversions. For flow NMR, sensitivity generally suffers, given the low number of scans employed, but recent advances³⁵ with microflow (ca. 0.2 μ L probe volume) hardware show improved reproducibility, the output comparing well with data from conventional NMR analysis. Further development of these techniques may offer great promise for rapid serial throughput, particularly as they become widely available.

At present, the capacity for mechanistic studies in HTE is thus restricted by the inaccessibility of analytical instruments capable of real-time quantitative analysis, whether in parallel or via rapid serial throughput. As well, the method must accommodate analysis across broad substrate classes and reaction types at concentrations relevant to the majority of homogeneously-catalyzed organic reactions.³⁸ This Chapter describes the first methodology

that enables kinetic analysis in HT homogeneous catalysis.* This approach circumvents the need for online, parallel data acquisition, and enables evaluation of product distributions at time intervals as short as 30 seconds. These methods are developed for the specific case of olefin metathesis, and extended to other contexts from there.

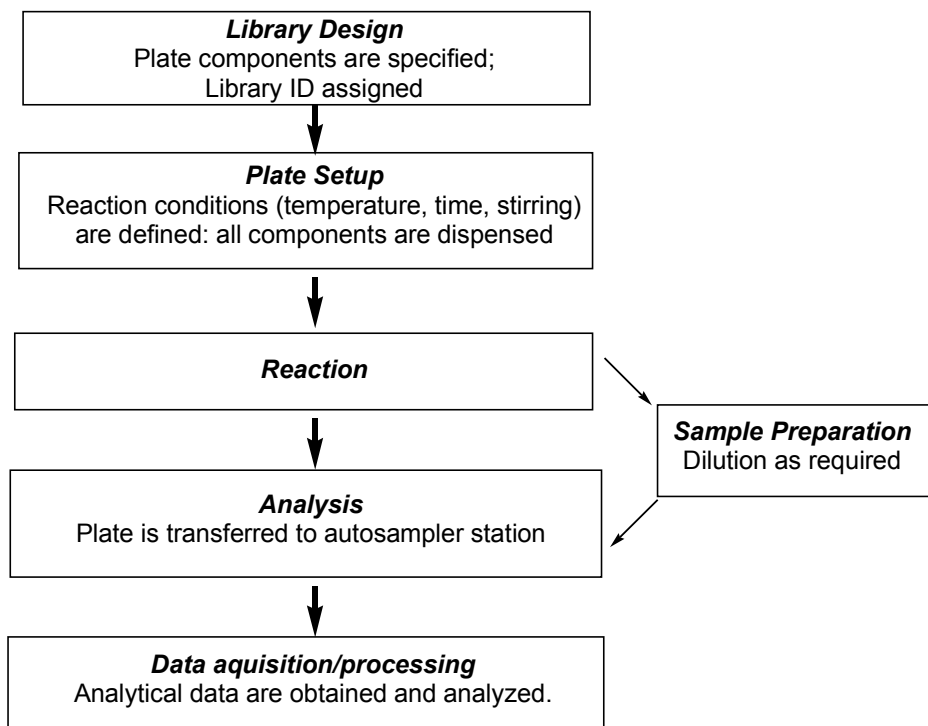
Olefin metathesis catalysis was chosen as a focus area because progress in this area is hampered by a proliferation of catalysts without clear trends in activity, selectivity, or optimal conditions,³⁹ and HTE is thus of keen interest. Furthermore, it is essential to monitor the arrayed reactions, rather than relying on the "single time-point" experiments that dominate HTE, because initiation and deactivation rates are highly sensitive to the combination of catalyst and substrate, and to the reaction conditions. While this is broadly true in homogeneous catalysis,^{19,29,40,41} a number of problems specific to olefin metathesis make it an appropriately challenging test ground (e.g., the dilutions required for ring-closing metathesis to form medium-sized or macrocyclic rings; intolerance to catalyst anchoring; sensitivity to the ethylene byproduct). Case studies describe the application of these methods to the rapid interrogation of ruthenium-catalyzed metathesis, hydrogenation, and isomerization reactions. A final section presents a user guide to the technical challenges involved in HTE as applied to homogeneous catalysis.

5.2 HT Quenching.

5.2.1 Methodology.

High-throughput experiments were carried out using commercial software and hardware from Symyx Technologies®. In the first step, the composition of the reaction plate (that is, the reagents, solvents, and additives used in each well) is specified via the Library Studio® software.² An identification number is assigned to each plate, which links the plate composition data to the reaction conditions and analytical data, each of which is specified or obtained in subsequent steps (Scheme 5.1).

* An alternative approach was subsequently reported, but overlooks a number of the key issues delineated in the following discussion. See Section 5.2.6.



Scheme 5.1 High-throughput screening stages.

In the *Plate Setup* stage, a Cavro robot housed in an N₂-filled glovebox was used to dispense reagents and solvents to reaction vials fitted into a 96-well aluminum block. The vials were covered with a common Teflon sheet, rubber gasket, and plate cover, held in place with seven screws (Figure 5.1). Holes in the cover permit needle access to the sealed reaction wells. Stock solutions of substrate, catalyst and potential quenching agents (all normally an order of magnitude more concentrated than the wellplate solutions) were prepared manually, and then robotically dispensed. Solutions were capped up to the time of use, to minimize evaporation. Robotic transfer of solutions was controlled by the Epoch[®] program, in volumes defined in the *Library Design* stage. Solutions were dispensed into a closed reaction plate to minimize solvent evaporation, following which the Teflon sheet was replaced with a new, unpierced, sheet. To maintain volumetric accuracy in transfers made using the standard 500 µL syringe, the minimum volume of solutions dispensed was specified as 20 µL. Use of small volumes reduces the time required to dispense reagents, and limits the need to refill the syringe, thus enabling rapid addition of additives, catalysts and substrates. The time lag between additions to the first and last wells (A1 and H12) can therefore be minimized, although the t_0 values for each row are offset by ca. 1 min each. To ensure precise

temperature control, "room temperature" reactions were maintained at 25 °C rather than the actual ambient temperature of 27-28 °C.

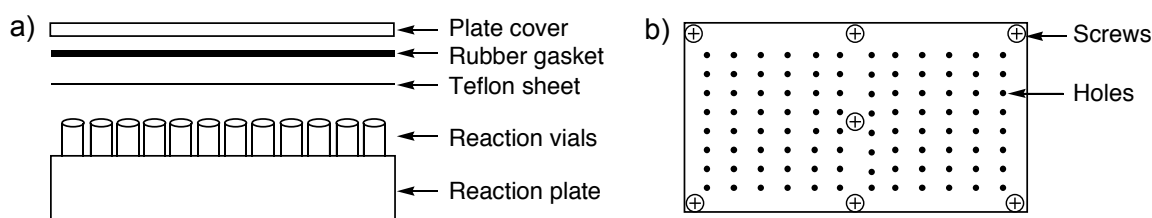


Figure 5.1. Schematic of a 96-well plate assembly. a) Side view; b) Top view.

This study commenced with the intention of developing a protocol that could permit monitoring of HT reactions without online analysis (Section 5.2.2). Ru-catalyzed olefin metathesis was explored as an illustrative, demanding problem, which could be used to develop a broad-spectrum, general approach. Several reagents were identified as potential quenching agents (**Q**) for the ruthenium metathesis catalysts of dominant interest. These candidates were evaluated for their efficacy in terminating RCM of the benchmark⁴² substrate diethyl diallyl malonate **1** via **Ru-1b**, the so-called second-generation Grubbs catalyst. The strong driving force for cyclization of **1**⁴³ (a function of the gem-dialkyl effect and small ring size), in conjunction with the voracity and robustness of **Ru-1b**, set a suitably high bar for quenching efficacy.

Reactions were carried out in benzene at 25 °C, at a diene concentration of 100 mM, and at a catalyst concentration of 0.5 mol% Ru. To maximize product formation, reactions were allowed to proceed over long periods (>6 h). A different RCM substrate, six-membered ether **6**, was employed in a subsequent "proof-of-principle" experiment aimed at testing the efficacy of this HT quenching approach, using a modified experimental design (Section 5.2.2). In either case, residual catalyst activity was assessed by analyzing the organic constituents in each well, via dilution (to 5 mM, using a 12-channel micropipette), and GC-FID analysis. Rate plots were assembled showing the loss of diene and formation of the RCM product, as discussed in Chapter 2, Section 2.9.3. These are depicted graphically below: numerical values are given in Appendix C.

5.2.2 Design of High-Throughput Quenching Experiments.

This Section outlines the conceptual and experimental details underlying the development of a high-throughput quenching methodology. The 96-well plates are set up such that the constituents are identical within any one of Rows A-H, but differ down each of Columns 1-12 (Figure 5.2a). Thus, a variety of conditions can be screened along the rows and time is the variable across the columns. Reaction can be arrested at any desired time interval x within each row, by instructing the robots to add a quenching agent down one of the 12 columns. In the resulting rate plots, the time intervals are thus simply the quenching intervals x , which can be as short as 30 seconds. Acquisition of 12 such time-points permits HTE on eight different reactions simultaneously (Figure 5.2b). Following the final quenching stage, the entire plate is transferred to an autosampling deck for analysis by robotic sampling, with an intervening dilution stage if required, as noted for the RCM reactions above.

Implementation of this methodology required only minor modification of the conventional HT process (Scheme 5.1).^{*} Thus, the time intervals x are user-defined during the *Plate Setup* stage. During the *Reaction* stage, the software retrieves these values and the robot dispenses **Q** to the reaction plate. Actual dispensing times for each well are stored and can be retrieved by the user during *Data Acquisition/Processing*.

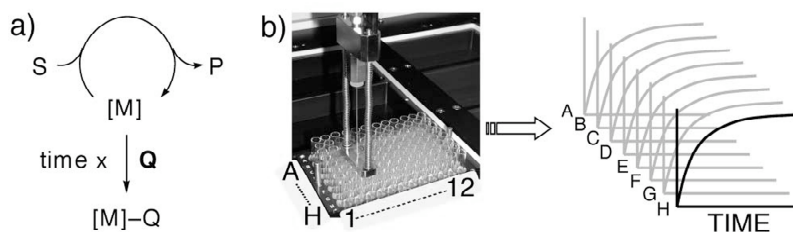


Figure 5.2. Simultaneous compilation of eight kinetic profiles in an HT array experiment. a) Quenching agent **Q** deactivates catalyst ([M]), leaving organic constituents unperturbed (S: substrate; P: product); b) Automated addition of **Q** down a column at time intervals x . Analysis gives kinetic profiles; curves represent potential output from a single plate.

^{*} Programming of the HT quenching protocol was carried out with the Symyx Epoch[®] software by Roxanne Clément.

Advantages of this protocol are its flexibility, versatility, and density of information. First, because quenching arrests further changes in product distribution, the entire plate can be analyzed at any convenient time. Secondly, because this approach decouples sampling from analysis (by converting conventional "sampling" intervals into quenching intervals), the minimum time interval x at which reactions are probed is no longer dependent on the cumulative time for analysis of all eight samples. It is instead determined only by the 30-60-seconds required to add the quenching agent down one column, replenish, and return to the next. Moreover, x need not be constant: thus reactions can be interrogated more frequently in the fast-evolving stages, and less as rates decline. (Of interest in this context is Rothenberg's "information gain ratio" parameter χ_r , which quantifies the useful information accessible through interrogation at any given time, and can thus aid in deciding on quenching strategies and intervals).^{29,44} Thirdly, the scope of the method is very broad: any analytical method can be used, whether serial or multiplexed, as well as techniques utilizing special tags, chromophores, etc. Finally, multiple analyses of different types (e.g. GC-FID, GC-MS, LC, NMR, SFC; SFC = supercritical fluid chromatography) are readily applied to the entire plate or selected wells. Volpe and co-workers have pointed out the critical importance of being able to utilize a variety of screening tools to assess product streams.²

5.2.3 Identification of **Q**.

This methodology rests on identification of a quenching agent, **Q**, suitable for the catalytic reaction under study. We propose a five-stage general search process. This consists of candidate selection; primary screening at high **Q** levels using a robust, highly active example of the catalyst family under consideration; secondary screening at lower **Q** ratios; confirmation of rapid annihilation of activity, and validation of the optimal quenching agent by assaying across a broad family of relevant catalysts.

For the first stage, identification of an optimal quenching agent, the following criteria are identified: (1) **Q** must quench all catalyst reactivity; (2) **Q** must be stable against decomposition to species that can promote formation of further organic byproducts over the time and conditions (particularly temperature) required to complete and analyze the plate; (3) **Q** must be a solid or liquid soluble in common organic solvents, to facilitate robotic

dispensing (injection of gases in the standard 96-well format is not currently supported: see, *inter alia*, puncturing issues discussed in Section 5.2.6); (4) **Q** must be involatile over the reaction temperature range of interest, plus 20 °C (this window allowing a safety margin to ensure consistent proportions of **Q**); (5) **Q** must be fast-acting and irreversible, such that injection times correspond to "knockdown" times; (6) **Q** should be effective at low loadings, to minimize interference with analysis; (7) **Q** should be affordable and, ideally, commercially available.

Within the context of olefin metathesis, the robustness of many of the ruthenium catalysts (Chart 5.1) limits the pool of potential quenching agents. Nevertheless, several effective poisons have been reported. Included in this study were ethyl vinyl ether **25**,^{45,46} methylimidazol **26**,^{47,48} acetonitrile **27**,⁴⁹⁻⁵¹ and selected bidentate or tridentate prolignands (**28-32**) with potential to deactivate the catalysts by coordination and oxidation or protonolysis (Chart 5.2). We include ethyl vinyl ether **25** for the sake of its widespread use, despite its high volatility (which violates Criterion 4) and its potential to violate Criterion 2 by promoting thermal decomposition of the catalysts to isomerization-active Ru hydrides.^{46,52,53} It may also violate Criterion 1, as judged from the reported metathesis activity of the complex formed on reaction of **Ru-1b** with **25**:⁴⁶ the isolated Fischer carbene complex was found to promote RCM of diethyl diallyl malonate **1** and ROMP of cyclooctadiene. Certain quenching agents were excluded despite their suitability in other contexts, on the basis of restrictions specific to quenching HT reactions, as outlined above. Thus, quenching with CO (successful in non-HT metathesis via **Ru-1c**)⁵⁴ is precluded by Criteria 3 and 4, while thiol poisons such as 2-mercaptosuccinic acid (successful with **Ru-4b**)⁵⁵ are potentially persistent in the robotic feed lines. Di(ethyleneglycol)vinyl ether⁵⁶ violates Criterion 5, requiring 30 minutes to deactivate catalysts **Ru-1a** or **Ru-1b** at room temperature. Isocyanide poisons reported by Diver and co-workers⁵⁷ are attractive on the basis of Criteria 1-6, but were not commercially available at the time of this study, and were eliminated on this basis. It should be noted, however, that the point of this study was not so much to identify the best of all possible quenching agents for this specific problem, but to develop a general protocol by which suitable quenching agents could be rapidly identified for any catalytic reaction, and to develop a robust protocol for HT kinetics.

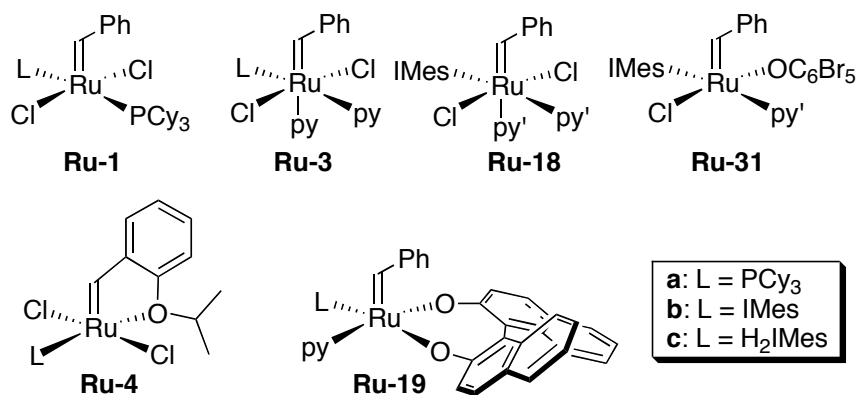


Chart 5.1. Ruthenium metathesis catalysts explored. IMes = *N,N'*-bis(mesityl)imidazol-2-ylidene, py = pyridine, py' = 3-bromopyridine.

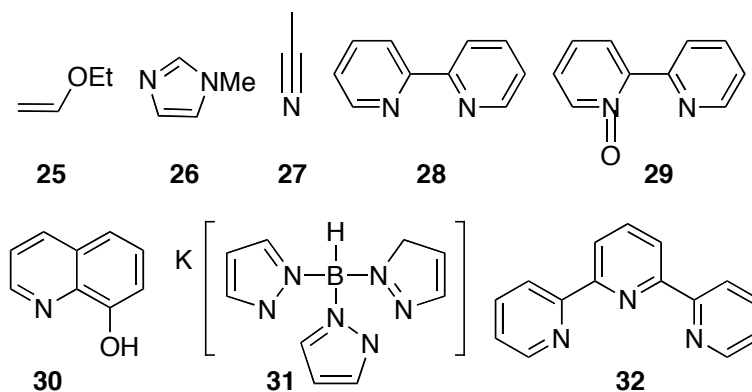


Chart 5.2. Potential quenching agents explored.

Primary screening experiments were designed to maximize sensitivity to any RCM activity, by adding the quenching agent prior to catalyst, and allowing reactions to continue for extended periods of 6 h at ambient temperature. Because **Q** is present from the outset, any evidence of RCM (above the $\pm 3\%$ reproducibility limit) suffices to disqualify it from further consideration. Reactions were carried out using 100 mM solution of **1** and 0.5 mol% **Ru-1b**: the avidity of the catalyst and substrate means that RCM remains facile, despite the use of low catalyst loadings⁴² to reduce plate costs. Prior to catalyst addition, as noted above, each potential quenching agent was added to the plate, at 40, 60, 80 and 100 equivalents relative to Ru.* This created 36 experiments, including four unquenched controls. Reactions were

* Titel Jurca is acknowledge for his assistance in selecting potential quenching agents and carrying out the primary screen depicted in Figure 5.3a.

allowed to proceed for 6 h at 25 °C, then analyzed by GC-FID (Figure 5.3a). Residual RCM activity was observed in the presence of terpyridine **32**, acetonitrile **27**, and ethyl vinyl ether **25**, each of which was therefore discarded from further consideration.

In a more aggressive secondary screen, **Q** loadings were reduced to as little as 5 equivalents, and the reaction time was extended to 18 h (Figure 5.3b). Potassium hydrotris(pyrazolyl)borate (KTp) (**31**) and MIM (**26**) exhibited maximum knockdown efficiency, with conversions being limited to 5% and 2%, respectively, at 5 equivalents **Q**. The null reactivity reported for an *isolated* Ru-Tp adduct at 70 °C⁵⁸ suggests that **31** retains its quenching ability over a wide thermal range. In contrast, irreproducible results were reported⁵⁹ for flow reactions quenched by **26** at 40 °C and above; this points toward the potential lability of **26** at high temperature. All subsequent HT quenching reactions therefore focused on **31**.

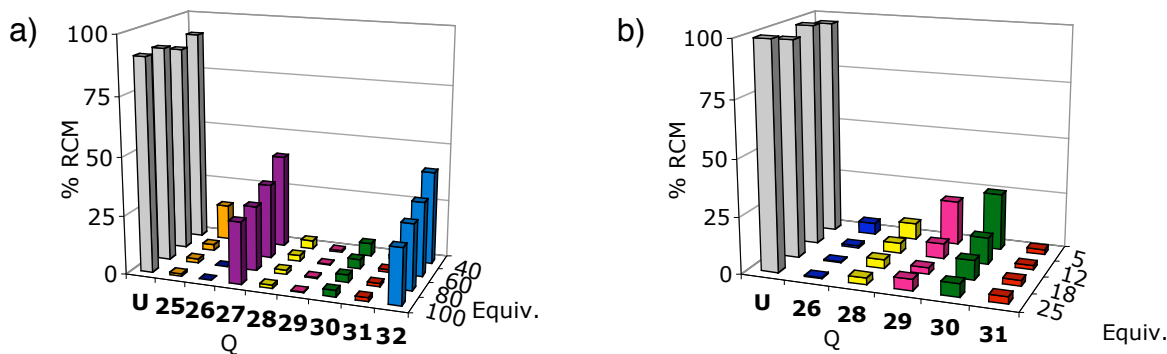
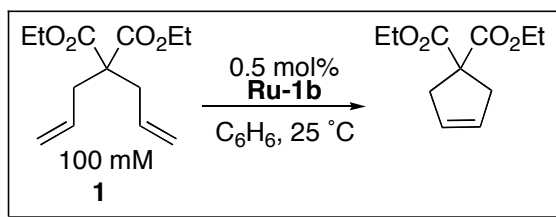


Figure 5.3. Efficacy of quenching agents **Q** in RCM of **1** (100 mM, 25 °C, 0.5 mol% Ru; **Q** added at outset; control U = unquenched). a) 1° screen: 40-100 equiv **Q**, analyzed at 6 h; b) secondary screen: 5-25 equiv **Q**; 18 h. Experiments in duplicate, $\pm 3\%$. For numerical values, see Appendix C, Table C.9 and C.10.

5.2.4 Quenching Efficiency **31**.

A tertiary screen was designed to probe whether **31** meets Criteria 1 and 5: that is, complete and rapid quenching of all catalyst reactivity. For ring-closing or cross-metathesis reactions, effective, general quenching requires knockdown of the catalyst in its resting state, not merely the (more reactive) benzylidene precatalyst. Evaluation of Criterion 1 thus necessitates examination of the performance of **31** with the corresponding $[\text{Ru}]=\text{CH}_2$ species. To this end, the first- and second-generation benzylidene complexes **Ru-1a** and **Ru-1b** (0.5 mol%) were stirred with diene **1** (100 mM) at 25 °C for 15 minutes to preform the methylidene resting state **Ru-2a/Ru-2b**, without allowing sufficient time for complete consumption of diene (Figure 5.4). Samples were then removed and quenched with 10 equiv **31** (Figure 5.4). Analysis was carried out immediately (ca. 2 minutes from quenching to GC injection) and again after delay times of 1, 4 and 24 h.* Immediate analysis indicated conversions of 8% and 44% for **Ru-1b** and **Ru-1a** respectively, consistent with the slower initiation of **Ru-1b** at room temperature.⁴⁵ These values showed no change over 24 h, establishing that **31** effects complete quenching of both the benzylidene and methylidene catalysts, and that quenching is complete within the two-minute period that precedes the first analysis.

In comparison, samples that were removed and simply exposed to air exhibited RCM conversions ca. 10% higher than the **31**-quenched samples. Further increases were observed over 24 h, to 67% and 98% for **Ru-1b** and **Ru-1a** respectively. Clearly, air-quenching with these catalysts is too slow and inefficient to enable reliable quantitation.

* Joseph Weiss is acknowledged for carrying out reactions quenched by air (Figure 5.4, grey bars).

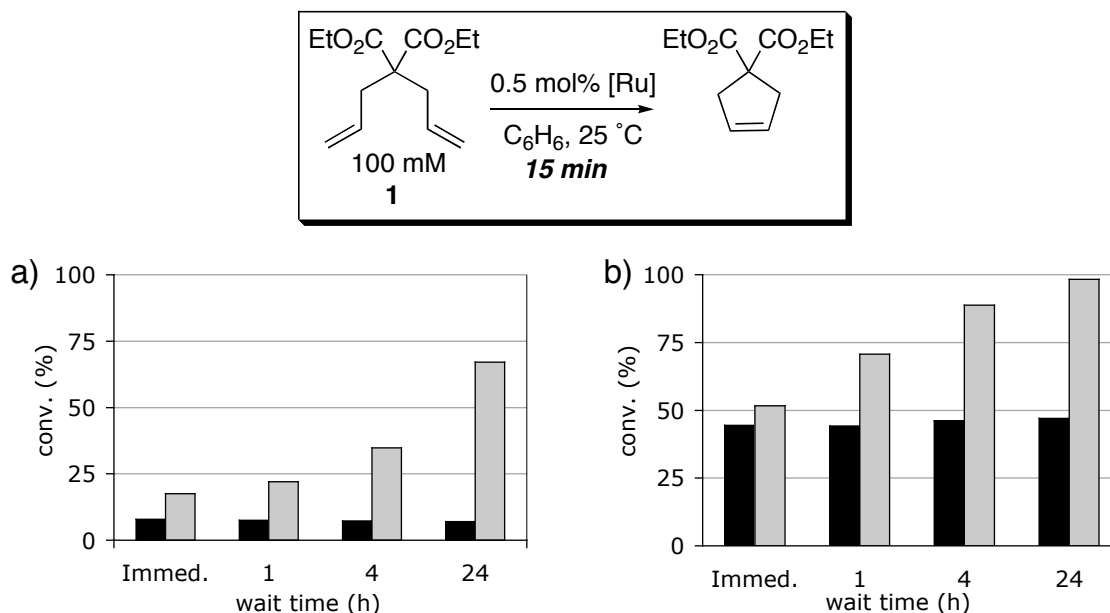


Figure 5.4. Knockdown speed of quenching agent **31** and effect of analysis delay times. When the RCM of **1** (100 mM) was tested in benzene at 25 °C, reactions were allowed to proceed for 15 minutes prior to quenching. Black: **31**-quenched; grey: air-quenched. "Delay time" signifies time elapsed between quenching and analysis. a) Catalyst **Ru-1b**; b) catalyst **Ru-1a**; both 0.5 mol%.

5.2.5 Scope: Capacity of **31** to Quench a Range of Metathesis Catalysts.

The quenching ability of **31** was assessed against a range of metathesis catalysts (Chart 5.1), again by adding **31** to malonate **1** (Q:Ru = 0, 1, 5, 10:1) prior to adding the catalyst (**Ru-3b,c**; **Ru-19b,c**; **Ru-1a-c**; **Ru-18b**; **Ru-4c**; **Ru-31**) (Figure 5.5). Reactions were stirred for 18 h at 25 °C, then analyzed. For most of these catalysts, catalytic activity is annihilated by 5 equiv **31**, although larger proportions (up to 10 equiv) were required for **Ru-3c** and **Ru-4c**. The quenching ability of **31** is thus sustained across all twelve metathesis catalysts. The higher proportion of **Q** required for **Ru-3c** and **Ru-4c** is attributed to, respectively, the high metathesis activity of **Ru-3c**,^{60,61} (which increases the demand for rapidity in quenching), and the stability of the styrenyl ether chelate in **Ru-4c**,^{62,63} which retards uptake of Tp. Of note, quenching of the ruthenium binaphtholate catalysts **Ru-19b** and **Ru-19c** was achieved using just one equivalent of **31**, despite the steric bulk of these bidentate anionic ligands, which might be expected to impede access of Tp to the metal center.

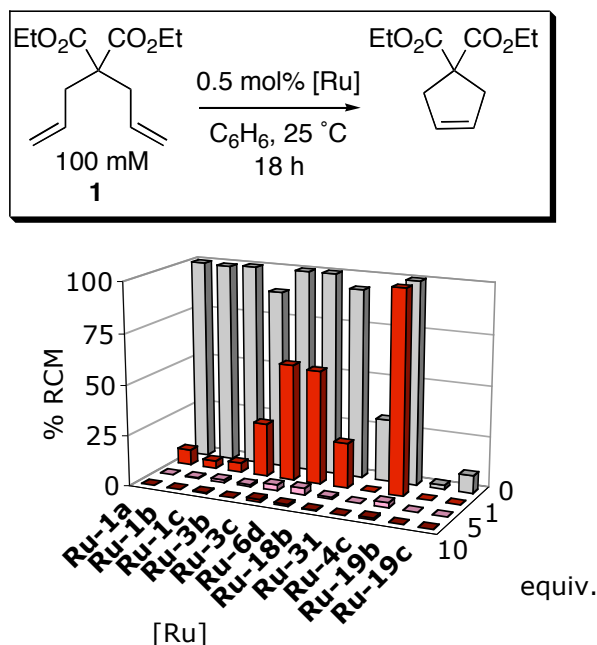


Figure 5.5. Scope of the quenching agent **31** over a range of catalysts. Conditions: 100 mM **1** with 0, 1, 5, 10 equiv **31**; 0.5 mol% of catalysts **Ru-3b,c**, **Ru-19b,c**, **Ru-1a-c**, **Ru-18b**, **Ru-4c**, **Ru-31**; 25 °C; 18 h.⁶⁴

5.2.6 Monitoring High-Throughput RCM of **6**.

With a suitable quenching agent and methodology in hand, the high-throughput quenching methodology was used to construct reaction profiles in metathesis reactions. For illustrative purposes, RCM of **6** to yield a pyran derivative was investigated. At least two variables for substrate concentration, solvent, catalyst loading and catalyst type were explored, to test the robustness of the technique. Solutions of **6**, at concentrations of 10 or 180 mM, were treated with 0.5 or 1 mol% catalyst (**Ru-3b**, **Ru-1b**, **Ru-1a**, **Ru-18b** and **Ru-4c**) in THF or benzene (Figure 5.6). The well-block was heated to 30 °C, following which robotic addition of quenching agent **31** to each of the 12 columns was undertaken at predefined time intervals. Following the final addition, reactions were diluted and analyzed as discussed above.

Eight conversion curves were thus obtained, the information content of which is relevant to both reaction optimization and catalyst redesign strategies (Figure 5.6). From the perspective of target-focused organic synthesis, the optimal reaction conditions are of key importance. Using **Ru-3b**, **Ru-4c** or **Ru-18b** (orange, purple and blue lines respectively), maximum

conversions were reached within 20 minutes; for the latter catalyst, loadings must be increased from 0.5 to 1 mol% (blue circle vs. blue square). Higher solvent concentrations can be tolerated (180 mM, green dashed versus 10 mM green solid). Most relevant from the perspective of catalyst (re)design are the structure-activity relationships that can be extracted; e.g. the effect of ligands on activity and lifetime. For example, the rapid initiation and short lifetime of third-generation **Ru-18b**^{61,65} (blue; 0.5 mol%) enables it to reach its maximum conversion after just six minutes, but only 56% RCM is achieved. At the same loading first-generation **Ru-1a** (red) is much slower, taking 24 h to reach its maximum output, but 98% conversion of **6** to product is attained. A wide range of other potential parameters could be screened, depending on the substrates involved. Important examples may include the influence of ligands or additives on catalyst performance, or of the effect of concentration on RCM selectivity.^{66,67} Examples of each will be discussed in the following Section.

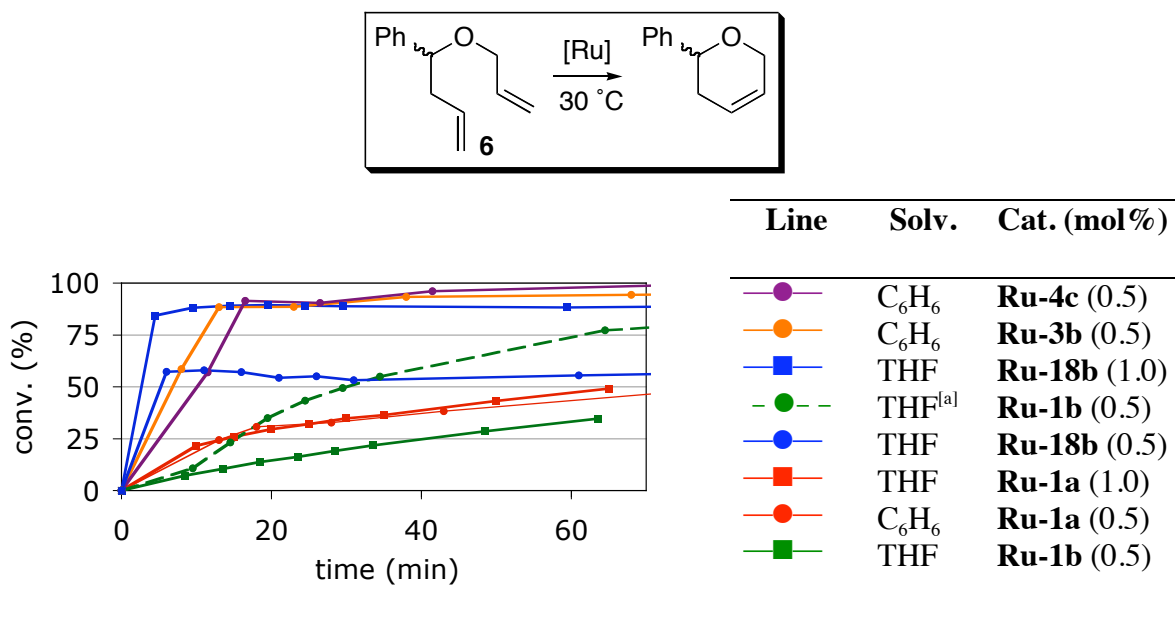


Figure 5.6. Reaction profiles compiled by HT quenching for RCM of **6**. Conditions: 10 mM **6**; 30 °C. ^[a]Concentration of **6**: 180 mM.

Following disclosure^{68,69} of the methodology above, the Grubbs group reported a somewhat related quenching protocol^{70,71} closely similar to a methodology earlier described by the Merck group.⁷² Rather than adding a quenching agent, this method relies on repeated sampling. Reaction aliquots are removed from individual wells at multiple time intervals, and dispensed into a wellplate loaded with solutions of the quenching agent (5%_{v/v} ethyl vinyl

ether) at $-20\text{ }^{\circ}\text{C}$. This eliminates the need for sets of identical reactions, and thus expands the number of parallel reactions that can be monitored per plate. The minimum 'query interval' necessarily increases with the number of reactions: this period approaches an hour for a 96-well plate (cf. a 30-second interval for eight parallel reactions in the protocol developed above), once a rinsing step is incorporated. More seriously, repeated piercings of the same gasket will degrade the Teflon and rubber seal; in our hands even a single piercing results in solvent loss and changes in reaction concentration for reactions carried out at reflux. Regardless of the specific quenching protocol employed, however, it is essential to confirm that quenching is complete and immediate, otherwise the proportions of product and substrate will continue to evolve prior to analysis.

5.3 Case Studies: Applications of HTE in Homogeneous Catalysis.

The case studies presented below explore the capacity of HTE to answer mechanistic questions in olefin metathesis, within the specific contexts of enyne metathesis, RCM macrocyclization, and optimization of activity in challenging RCM reactions. Each of these reaction types uncovers different challenges to HTE, allowance for which must be made in developing methods or, at worst, in interpreting the data. Also discussed are more straightforward experiments that explore catalyst activity in hydrogenation and isomerization reactions. Some studies antedate development of the HT quenching protocol described above, and utilize single time-point analysis: others adopt this or HT quenching methods, as appropriate.

5.3.1 Methodology.

General experimental procedures follow those described in Section 5.2.1. Monitoring of ring-closing enyne metathesis reactions (RCEYM, Section 5.3.2), however, was undertaken using a less sophisticated HT protocol than that of Section 5.2. Thus, solutions were dispensed robotically into 4 mL screw-cap vials in a 4×6 aluminum block: this was heated and stirred on the Cavo deck outside the glovebox so that individual vials could be opened and diluted for analysis over the course of reaction, followed by immediate analysis to preclude run-on metathesis. Hydrogenation reactions (Section 5.3.6) were carried out in reaction plates designed for insertion into a high-pressure casing (Figure 5.7). Stirring was achieved through

orbital shaking instead of magnetic stirring; borosilicate beads facilitated mixing. These reactions were effectively quenched by venting of the H₂ atmosphere.

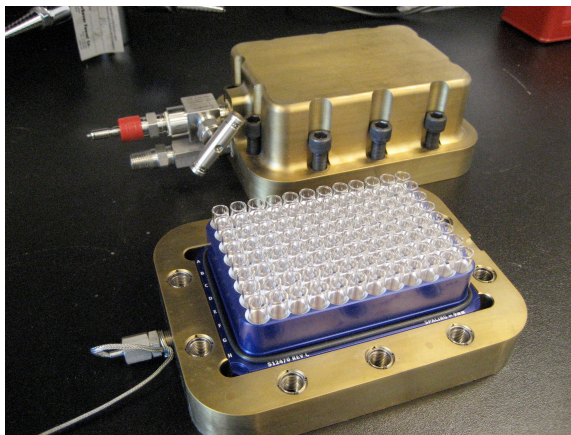


Figure 5.7. 96-Well plate and block for high-pressure reactions.

A powerful feature of the Symyx equipment is its capacity for microscale operation. In conjunction with this come hazards of lesser import in larger-scale reactions. Among these is the volatility of the solvents used. Dichloromethane, for example – a favoured solvent in ruthenium chemistry – must be used with caution in HT experiments, as its high volatility (b.p. 39.6 °C) can limit accuracy in stock solution concentrations. Its high density (ρ 1.33 g/mL) is also potentially problematic: under-aspiration of specified volumes of solutions may occur when using a standard robotic syringe, while back-pressure generated during solvent aspiration can cause dripping from the transfer needle. These problems are not invariable: in two cases described below, methylene chloride was used as solvent without any adverse effects on reproducibility. The first involved RCEYM reactions in small arrays (16 $\times$ 4-mL vials; each 500 μ L in solvent), for which each vial was individually capped immediately following solvent addition. The second involved hydrogenation reactions undertaken for comparison to parallel experiments in conventional high-pressure autoclaves. In this case, the solvent was hand-dispensed, and solutions were again sealed immediately. More generally, however, 1,2-dichloroethane (DCE) was used as a lower-volatility surrogate for methylene chloride, although problems with the former (specifically, decomposition of **Ru-3** and **Ru-18** resulting in reduced conversions; see Section 5.4.1) were reported by Dr. Jay Conrad of this research group.

For kinetics experiments involving RCM of lactone **8** and diethyl diallyl malonate **1**, reactions were quenched over 1-24 h using the HT quenching protocol. Other plates were worked up at a time chosen from prior kinetics studies, or (more conventionally) after an arbitrarily long time interval, which were presumed to permit maximum conversions. Well-plates were allowed to cool if required, prior to diluting for GC analysis as above. Yields of involatile oligomers were inferred from decreases in calibrated GC-FID integration. Results are presented as rate curves or bar graphs, with numerical values tabulated in Appendix C.

5.3.2 Alternative Reaction Pathways in Enyne Metathesis: RCEYM of **7** by $\text{RuCl}_2(\text{L})(\text{L}')(\text{=CHPh})$.

RCEYM⁷³⁻⁷⁵ reactions were conducted by dispensing allyl ether **7**, catalyst solutions and THF or CH_2Cl_2 solvent (b.p. 66 °C or 39.6 °C; see comments regarding the latter above) into 4 mL screw-cap vials. All reactions were carried out using 100 mM of enyne **7**, at a catalyst loading of 0.5 mol% (Figure 5.8). Reactions were stirred on a pre-heated (40 °C) reaction deck. Timed addition of **31** was not carried out, as this study was undertaken prior to development of the HT kinetics protocol: indeed, development of the latter was driven in part by the needs revealed by these experiments. At intervals over a total of 90 minutes, individual vials were manually removed, cooled, opened to air, diluted using non-dried solvents, and analyzed immediately, to eliminate potential "run-on" metathesis arising from incomplete quenching by O_2 . Catalysts **Ru-1a**, **Ru-3b** or **Ru-18b** all effected complete or near-complete RCEYM, and reaction profiles in THF and CH_2Cl_2 were very similar. Replicate runs were in excellent agreement (within $\pm 3\%$: Appendix C, Tables C.32-36), indicating that the reproducibility of robotic dispensing is unimpeded by the volatility of these solvents.

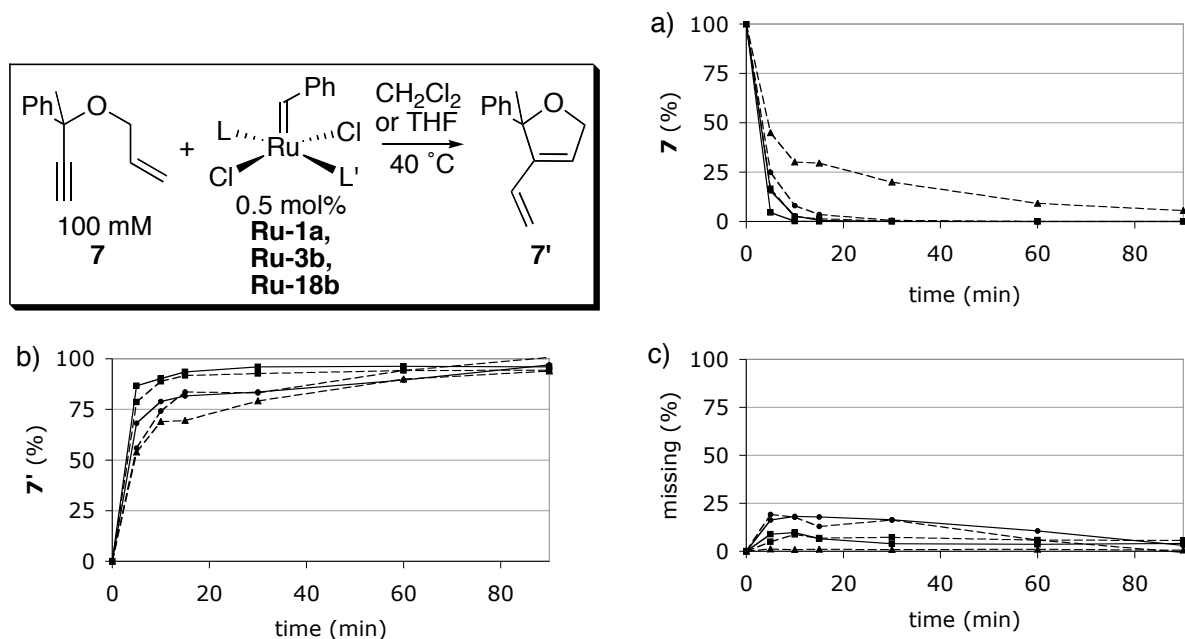
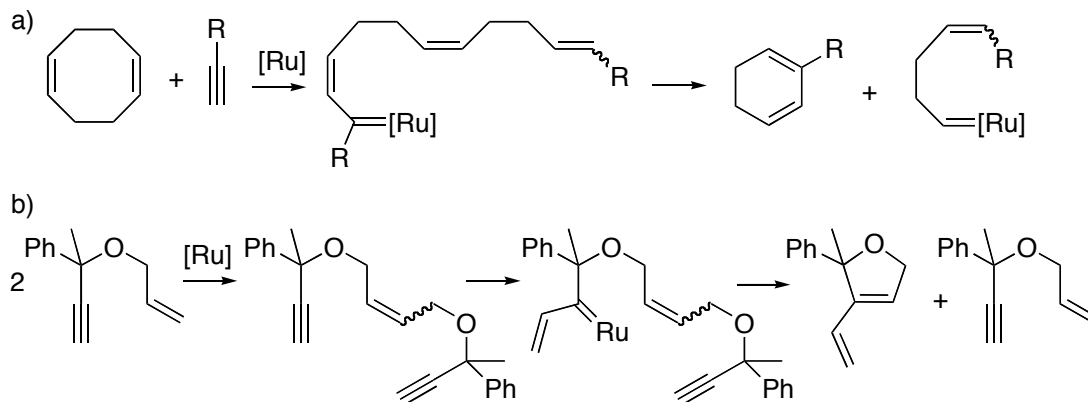


Figure 5.8. RCEYM of **7** (100 mM) at 40 °C with 0.5 mol% **Ru-1a** (▲), **Ru-3b** (●) and **Ru-18b** (■) in THF (solid) or CH₂Cl₂ (dashed). Values for a) % enyne **7** consumed; b) % RCEYM product **7'** formed; c) % of missing material.

Conversion of **7** to **7'** by first-generation catalyst **Ru-1a** was slow, and no side-products were detected. The more active third-generation complexes consumed **7** within 10 min. The major product was **7'**, but minor amounts of oligomers were also formed, which declined over the course of reaction (**Ru-3b**: from 10% to 4%; **Ru-18b**: from 20% to 4%). Diver has reported⁷⁶ an example of competing alkyne oligomerization^{77,78} in intermolecular enyne cross metathesis (EYCM). No such problem in intramolecular RCEYM has been put forward in the literature, but Dr. Anne Grotevendt of this research group has evidence to support oligomerization as the cause for low yields^{75,79,80} in RCEYM reactions carried out in the absence of ethylene. The slow disappearance of the oligomers implies a backbiting pathway, though the intimate mechanism presumably differs from that operative during RCM macrocyclization (Section 5.3.2).^{43,66} Backbiting has been proposed to account for the formation of 1,3-cyclohexadienes during EYCM of COD and alkynes (Scheme 5.2a),⁸¹⁻⁸³ and a similar mechanism could be operative here: Scheme 5.2b. Further investigations are needed to determine if backbiting is promoted by the catalyst, by the conformational bias associated

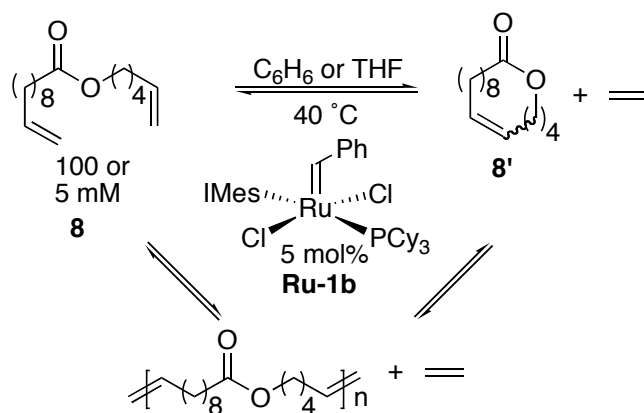
with propargylic substitution of the substrate,⁸⁴⁻⁸⁶ as Grotevendt proposes, or by the presence of trapped ethylene in the sealed reaction vessel.



Scheme 5.2. Backbiting mechanism in enyne metathesis. a) Formation of 1,3-cyclohexadienes from alkynes and COD;⁸¹⁻⁸³ b) Possible pathway for the generation and consumption of dimers during RCEYM of **7**.

5.3.3 Examining the Suitability of HTE for RCM of Macrocycles: Macrocyclization of **8** by RuCl₂(IMes)(PCy₃)(=CHPh).

HTE methodologies are of enormous interest for their potential to reduce the time-consuming process of optimizing RCM macrocyclizations relevant to pharmaceutical^{55,67,87,88} and natural products synthesis.⁸⁹⁻⁹¹ RCM of **8** via **Ru-1b** (5 mol %) was carried out in THF and C₆H₆ at 40 °C, using diene concentrations of 5 and 100 mM (Scheme 5.3). Using the HT quenching protocol established in Section 5.2, metathesis was arrested at time intervals up to 4 h. Reactions in THF were slower than those in benzene, in keeping with literature precedents,⁵⁵ but were deemed of interest for their potential to affect the ring-chain equilibrium. Work from our group has described the concentration-dependent oligomerization-backbiting pathway in this and related RCM reactions.^{43,66} We reported that in the specific reaction of Scheme 5.3, carried out at 5 mM diene, substrate **8** was completely consumed within 30 min, the products being distributed between **8'** and ca. 40% oligomeric species. The latter are converted via backbiting into **8'** over a further 3 h.^{59,66} The difference relative to malonate **1** arises from the lower driving force for formation of the 16-membered ring **8'**, owing to the presence of some ring strain, and the absence of a conformational bias toward cyclization exerted by the Thorpe-Ingold effect.⁴³



Scheme 5.3. RCM of **8** with **Ru-1b** to produce the macrocycle **8'** or oligomeric products.

HT RCM of **8** was explored at high and low diene concentrations (100 mM and 5 mM). In contrast to the standard Schlenk RCM reactions, consumption of **8** was incomplete in either case even after 3 h, (2-11% **8** remaining). We attribute the difference to retention of ethylene within the sealed HTE vials, in contrast to the standard bench-top procedures carried out in vessels open to argon or N_2 . Ethylene trapping has been shown to limit catalyst productivity by increasing degenerate metathesis,⁹²⁻⁹⁴ as well as decomposition mediated by the less stable methyldiene complex.^{43,45,93,95} A more subtle contributor to the apparently slower rate of consumption of **8** may be reformation of the diene via cross-metathesis of RCM or oligomeric products with the trapped ethylene. While the dominant products in the 100 mM HT reactions are indeed the involatile oligomers expected from the Schlenk reactions (Figure 5.9b,d), use of high dilutions results in profound differences in speciation. Under Schlenk conditions, oligomers are preferentially formed at short reaction times, and diminish as metathesis is allowed to continue. Under the HTE conditions, diene consumption is slower, but the proportion of oligomerization to RCM yields is low (particularly at short reaction times: the yield of oligomers increases over time, however, reaching 17% in THF after 4 h). This dramatic difference in speciation is highly troubling: in short, it means that HTE screening conceals one of the major issues at play in RCM macrocyclization of dienes, and misrepresents the bench-top behaviour.

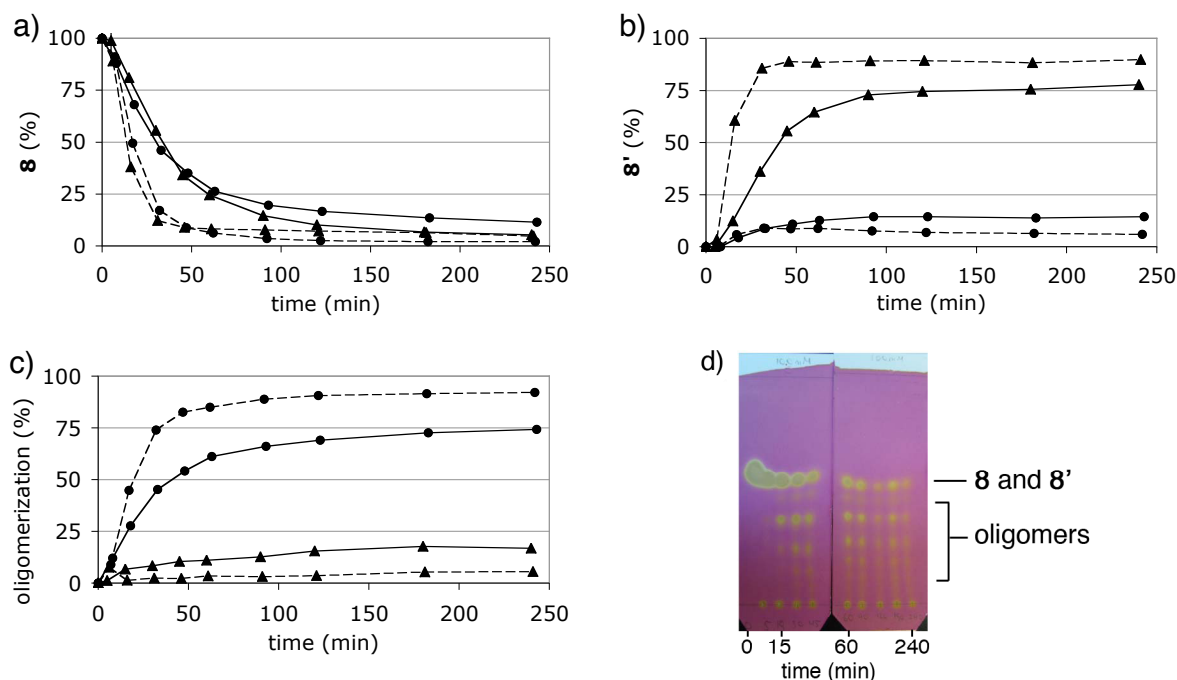


Figure 5.9. RCM of **8** with **Ru-1b** (5 mol%): a) Substrate consumption; b) RCM product formation; c) oligomerization; d) TLC analysis of reaction at 100 mM in THF (eluant 10% CH_2Cl_2 , 5% EtOAc, 85% hexanes). Conditions: ▲, 5 mM; ●, 100 mM; dashed lines, C_6H_6 ; solid, THF. For numerical data, see Tables C.21-24.

The study above suggests that HTE screening is at present of little value for optimizing the RCM of macrocycles or – more challenging yet – medium-sized rings. The fundamental problem is simply that reactions in sealed vials do not accurately reflect behaviour under standard conditions. In one of the major applications of interest, screening of different catalysts for their efficiency and selectivity in RCM macrocyclization, the validity of these comparisons are likely to be further undermined by differences in lifetime for the different methyldiene species formed, and in their selectivity for reaction with ethylene vs. diene. It remains unclear whether context-specific catalyst decomposition will have a similarly misleading effect on reaction outcomes in HTE studies of CM, ROM/CM, or indeed RCM of common (5-7-membered) rings, all of which generate ethylene as a byproduct. These concerns could potentially be addressed by adapting the HT equipment to enable the escape of ethylene (but not solvent) using 12-reactor arrays fitted with reflux condensers. Such assemblies are available through Radleys or Chemspeed, though it is unclear whether they

can be readily adapted to support reaction sampling or addition of quenching agents. Such kinetics methods are essential to monitor the progress of oligomerization-backbiting reactions, and the approach to equilibrium.

5.3.4 Effect of the NHC Ligand on Activity of Third-Generation Catalysts: RCM of **1** and **3** by $\text{RuCl}_2(\text{NHC})(\text{py})_2(=\text{CHPh})$.

This Section examines the effect of the NHC ligand on the RCM activity of third-generation metathesis catalysts, $\text{RuCl}_2(\text{NHC})(\text{L})_2(=\text{CHPh})$ **Ru-3** and **Ru-18** (Chart 5.3). To date, the role of the NHC ligand has only been compared in second-generation phosphine catalysts. Diethyl diallyl malonate **1** was employed as the substrate, to circumvent the problems of oligomerization described above.

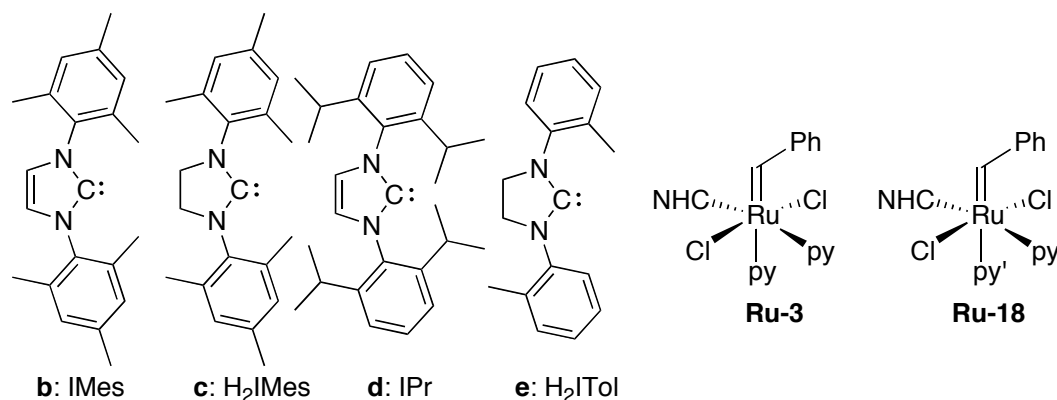


Chart 5.3. NHC-containing ruthenium olefin metathesis catalysts. IMes = 1,3-bis-(2,4,6-trimethylphenyl)imidazol-2-ylidene; H_2IMes , IPr = 1,3-bis-(2,6-diisopropylphenyl)imidazol-2-ylidene; H_2ITol = 1,3-bis-(2-methylphenyl)imidazol-2-ylidene; py' = 3-bromopyridine.

Initial studies focused on RCM of **1** using the highly reactive bromopyridine catalyst **Ru-18b**, to identify optimal conditions for comparison of a series of catalysts (viz. **Ru-3b-e** and **Ru-18b-e**). Reaction profiles were compiled using the HT quenching methodology, using 10 mM **1**, and exploring the effect of solvent (THF, benzene, 1,2-dichloroethane), at catalyst loadings of 0.05 and 0.1 mol% **Ru-18b** (Figure 5.10). Reactions were monitored over ca. 70 minutes. In all cases, maximum conversion was reached within 10 minutes, characteristic behaviour of these pyridine-functionalized catalysts.^{42,61,96} The plateau in conversion indicates that, for the purpose of comparing catalysts **Ru-3** and **Ru-18**, single time-point analysis at 30

minutes should suffice for a secondary screen. Near-zero conversions were observed in THF at both catalyst loadings, eliminating this solvent from subsequent screening. At 0.5 mol% Ru, reactions plateaued at ca. 12% in both C₆H₆ and 1,2-dichloroethane (DCE). At 0.1 mol% **Ru-18b**, conversion in C₆H₆ is 11% higher than in DCE (32 and 21%, respectively). Despite this, DCE was included in the subsequent secondary screen, as a stand-in for the common metathesis solvent methylene chloride.⁴² Given the low conversions, catalyst loadings were increased to 0.2 mol% for the secondary screen.

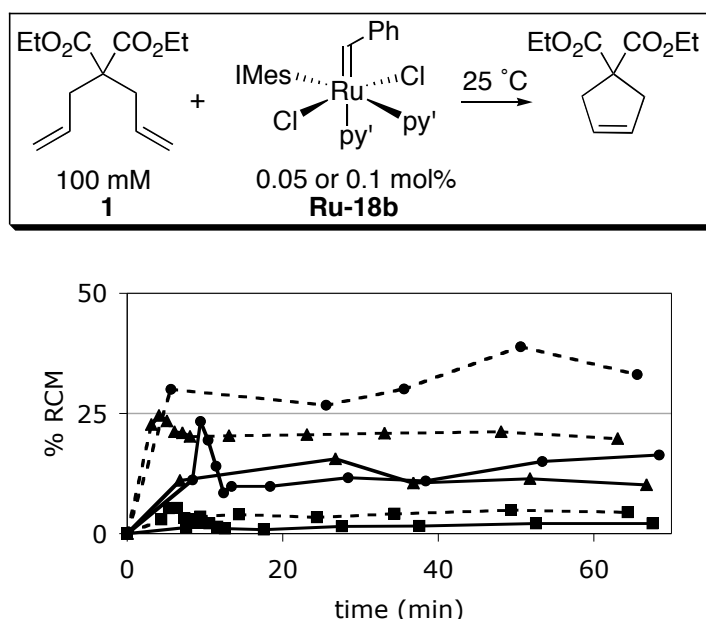


Figure 5.10. RCM of **1** with **Ru-18b**. Screened reaction conditions: 0.05 mol% **Ru-18b** (Solid) and 0.1 mol% **Ru-18b** (dashed); C₆H₆ (●), THF (■) and DCE (▲).

Secondary screening was conducted using both **1** and tosyl-amine **3**, another benchmark RCM substrate, at a diene concentration of 10 mM (0.2 mol% Ru, 25 °C; Figure 5.11). After 30 minutes all reactions were quenched with 10 equivalents of KTp **31**. Despite the low catalyst loading, conversion of both substrates was near-quantitative in C₆H₆ for all catalysts except **Ru-3e**. In DCE, the trend in NHC activity is IPr > H₂IMes ≈ IMes > H₂ITol: representative conversion of **1** for the 3-bromopyridine catalysts **Ru-18b-e** were 76, 49, 50 and 27%, respectively (Figure 5.11). The superior activity of **Ru-18d** is in keeping with the ca. 10% higher activity of RuCl₂(IPr)(PCy₃)(=CHPh) **Ru-1d** relative to its IMes analogue **Ru-1b** in RCM of **1**.⁹⁷ A similar trend was observed in the RCM of **1** and cross-metathesis of

1-octene with the corresponding catalysts containing the saturated NHC ligands H₂IPr and H₂IMes.^{98,99}

The IMes and H₂IMes complexes **Ru-18b** and **Ru-18c** exhibited essentially identical activity in RCM of **1** and **3** (ca. 50 and 70% conversion, respectively). Within the pyridine catalysts **Ru-3b**/**Ru-3c**, the latter, H₂IMes derivative was superior, if only slightly in some cases (for **1**: 42% vs. 48%, **3**: 62% vs. 75% conversion). Some literature reports propose that the saturated NHC offers generally higher productivity within the second-generation systems,¹⁰⁰ but, in other examples, the IMes catalyst **Ru-1b** gives similar or indeed improved results relative to **Ru-1c**.^{42,101-103} At moderate temperatures (RT to 35 °C), initiation appears to be slower for IMes catalyst **Ru-1b** versus H₂IMes **Ru-1c**, but final yields were typically within 20%.^{42,101} Faster phosphine exchange rates for **Ru-1c** have also been documented.⁴⁵ In the third-generation systems, rapid dissociation of 3-bromopyridine⁶¹ suggests that initiation rates with this labile ligand will be similar for the IMes and H₂IMes complexes. Indeed, conversions for both substrates are essentially the same for catalysts **Ru-18b** and **Ru-18c** (difference **1**: 1%; **3**: 2%). In contrast, the distinction between the IMes and H₂IMes catalysts observed in the second-generation catalysts **Ru-1b** and **Ru-1c** must reflect the slower rate of phosphine loss from the former.

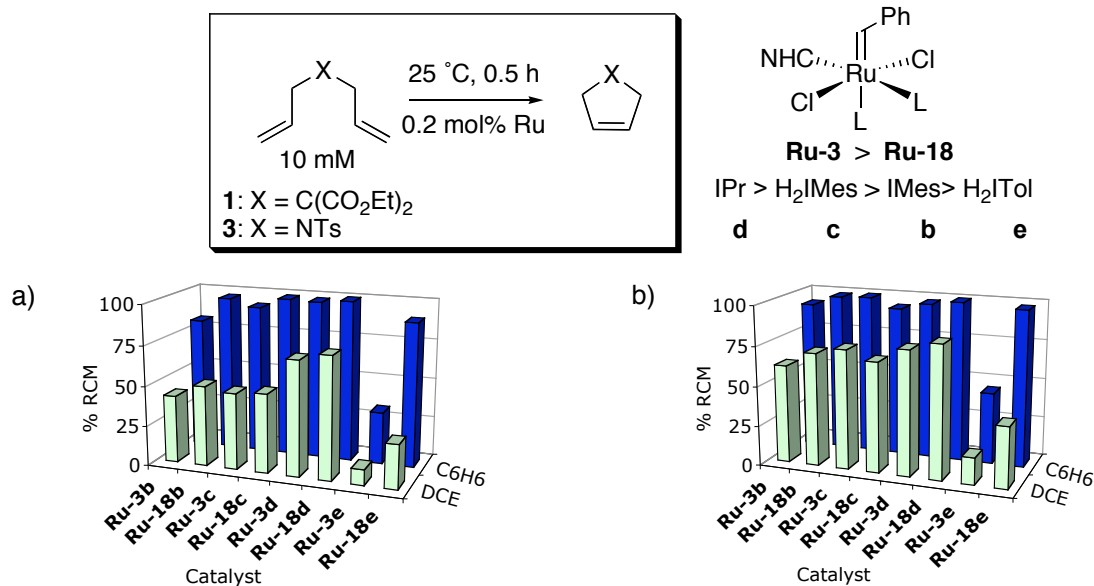


Figure 5.11. Activity trends in RCM of a) **1**; b) **3** with third-generation catalysts **Ru-3** and **Ru-18**. Conditions: 0.2 mol% [Ru] in C₆H₆ or DCE, 25 °C, 30 min.

The H₂ITol catalysts **Ru-3e** and **Ru-18e** show the lowest activity of the series, effecting only 21% and 53% conversion (respectively) of **3** in DCE. This contrasts with the high activity of their second-generation and styrenyl ether derivatives, **Ru-1e** and **Ru-4e**, in RCM of tetrasubstituted olefins.¹⁰⁴⁻¹⁰⁶ The low conversions seen here may reflect low catalyst stability. The ortho-position of the tolyl ring is known to be susceptible to C-H activation,^{107,108} and the second-generation catalyst **Ru-1e** is reported to suffer from facile decomposition.¹⁰⁶ The greater stability of styrenyl ether precatalyst **Ru-4e** is cited as a performance advantage.¹⁰⁶ It seems likely, however, that its higher productivity is due simply to slower (and hence more sustained) catalyst turn-on, rather than a greater invulnerability to C-H activation, as both catalysts will converge on a common intermediate, and must therefore be subject to identical decomposition pathways (barring the much-discussed and still contentious possibility of recapture of the styrenyl ether). Conversely, high activity for the H₂ITol systems **Ru-3e** and **Ru-18e** in the present work may be masked by fast, homogeneous turn-on and decomposition. While the higher lability of the 3-bromopyridine ligand, vs. pyridine,⁶¹ resulted in only marginally higher activity for most members of catalyst series **Ru-18** and **Ru-3**, this was not the case for the H₂ITol catalysts, where the 3-bromopyridine derivative **Ru-18e** out carried pyridine catalyst **Ru-3e** by at least 17% under all conditions. This suggests a disproportionate increase in the rate of metathesis vs. decomposition.

A tertiary kinetics screen of the eight catalysts is warranted: given that activity trends were independent of solvent and substrate, one set of conditions could suffice to assess whether indeed rapid initiation in the 3-bromopyridine catalysts eliminates any discernible differences between IMes and H₂IMes. The susceptibility of the H₂ITol catalysts to decomposition or slow initiation would likewise be elucidated.

5.3.5 HT Screen of RCEYM of **9** with H-Bond Donor Additives.

Previous work by Dr. Jay Conrad of this research group¹⁰⁹ described a HT screen of phenolic additives in the RCEYM of **9** by aryloxide catalyst **Ru-31**. From this study, butylhydroxytoluene (BHT, **17**) was identified as beneficial, serving to increase overall

yields from ca. 87% to quantitative levels. This Section examines the performance of the dichloride catalyst **Ru-18b** with the same set of additives (Chart 5.4).

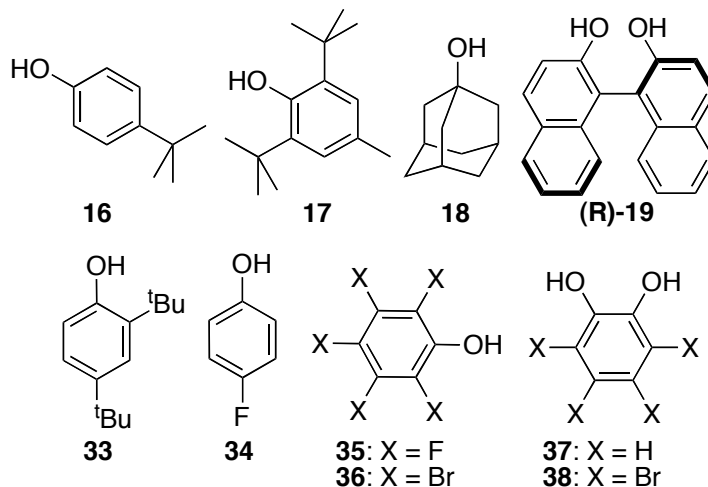


Chart 5.4. HBDs employed as additives in the RCEYM of **9** with **Ru-18b**.

A HT plate was prepared with 10 mM **9**, 1 mol% **Ru-18b** and additives **16-19** and **33-38**, used in 10, 20, 70 and 100 equiv relative to the catalyst (Figure 5.12). Reactions were carried out at 55 °C in DCE, and were left for 16 h to maximize conversions. In the absence of any additive, only 12% **9'** was observed, emphasizing the challenging nature of this substrate.^{39,85,110-112} Almost all of the additives diminished yields slightly, the sole exception being **34**, which at 20 mol% effected a negligible increase of 2% (Figure 5.12b). Of particular note, addition of BHT **17** resulted in slight decreases in conversion at all proportions: yields of **9'** reached only 9% with 70 or 100 equiv **17**. This contrasts sharply with the positive impact of this additive on the activity of **Ru-31**, alluded to above, in which a considerable increase in conversion was found on addition of 80 mol% **17**.¹⁰⁹

Phenols have previously been shown to exert a positive effect on productivity in metathesis via the first-generation Grubbs catalyst. This influence is proposed to arise from hydrogen-bonding to the chloride ligand.^{109,113} We had anticipated that the resulting decrease in electron density at the metal center **Ru-18b**, for which the rate-determining step is presumed to be olefin (alkyne) binding, would facilitate reaction. The negative effects of added phenols in the RCEYM via **Ru-18b** was thus unexpected. We note that H-bonding to aryloxide seems

improbable as an origin of the favourable effect of BHT on **Ru-31**: while aryloxides participate readily and strongly in H-bonding (including in related systems),¹¹⁴ further increases to the already more electrophilic nature of **Ru-31**¹¹⁵ would be expected to impede initiation further, while the steric bulk of BHT is also difficult to reconcile with such a mechanism. The study above demonstrates that the beneficial effects of **17** are unique to aryloxide catalyst **Ru-31**, and suggest that its role in this system extends beyond simple interaction with the anionic ligands. We speculate that it may instead reflect rapid sequestration of the dissociated pyridine ligand, in conjunction with a level of steric bulk that impedes the ability of this phenol to approach and block access to the metal center.

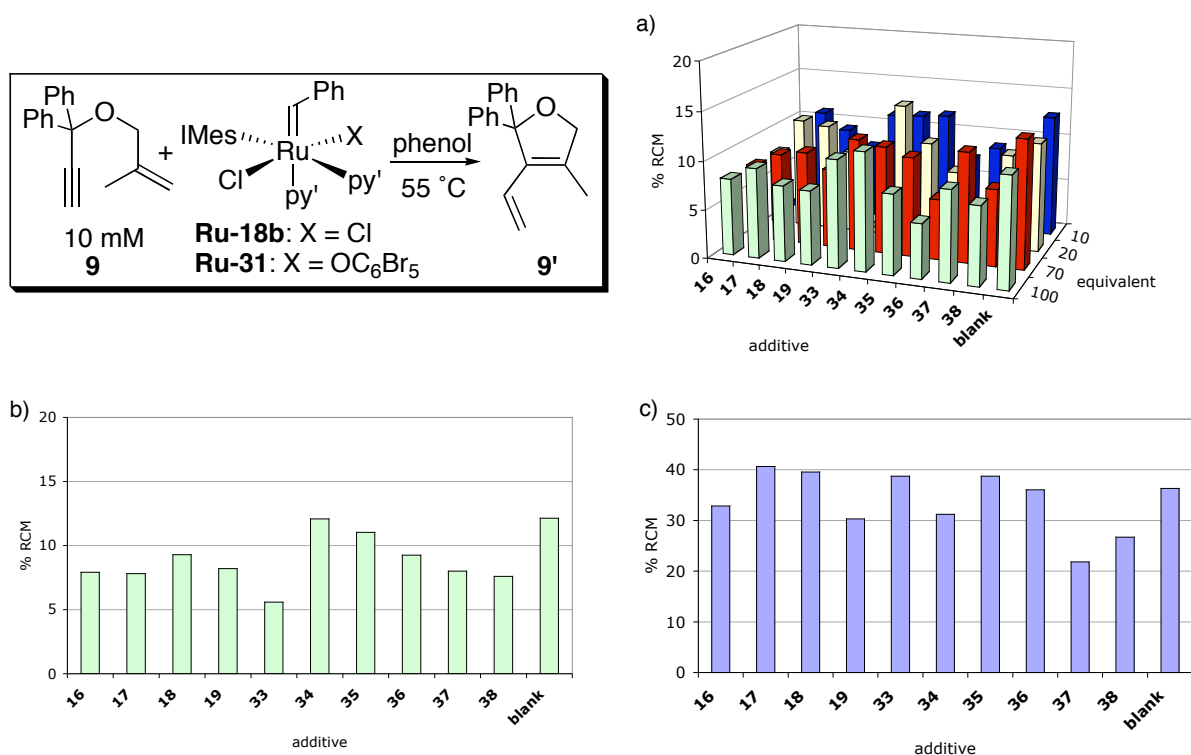


Figure 5.12. Phenol screen for the RCEYM of **9**. Reaction conditions: a) 1 mol% **Ru-18b** with 10, 20, 70 and 100 mol% additive, in DCE, at 55 °C for 16 h; b) 1 mol% **Ru-18b** with 100 mol% additive, in DCE, at 55 °C for 16 h; c) 5 mol% **Ru-31** with 1 mol% additives, CH₂Cl₂ for 6 h at 55 °C.

5.3.6 HT Studies of Hydrogenation and Isomerization Promoted by $\text{RuHCl}(\text{L})(\text{L}')(\text{PCy}_3)$ ($\text{L} = \text{H}_2, \text{CO}$; $\text{L}' = \text{IMes}, \text{PCy}_3$).

Work in our research group has contributed significantly to the development of "back-door" routes to specialty polymers via tandem ROMP-hydrogenation. These methodologies are most efficiently realized through post-metathesis transformation of ruthenium alkylidene species into the hydrogenation catalysts $\text{RuHCl}(\text{L})(\text{L}')(\text{PCy}_3)$ (Figure 5.13).¹¹⁶⁻¹¹⁸ In situ transformation of $[\text{Ru}]=\text{CH}_2$ to $[\text{Ru}]-\text{H}$ is correspondingly attractive for applications in RCM-hydrogenation or RCM-isomerization. Of particular interest in the former context is the formation of macrolactone **8''**, a commercial musk perfume.¹¹⁹ Hydrogenation of internal olefin **8'** by closely related catalysts containing a dihydrogen or carbonyl ligand (**Ru-25a/b** and **Ru-26a/b**, respectively) was undertaken, as a collaboration with Nicholas Beach of this research group, to evaluate their respective influence on hydrogenation yields, and hence the optimum protocol for these tandem catalysis experiments.

For this study, the reaction plate was loaded with the macrocyclic lactone **8'** (100 mM) in C_6H_6 or CH_2Cl_2 . For the reactions in CH_2Cl_2 , base, or base and methanol, were added to selected wells. The chlorinated solvent was added manually to avoid potential dispensing problems (Section 5.3.1). Catalysts **Ru-25a/b** and **Ru-26a/b** (0.1 mol%) were added from stock solutions, following which the block was sealed, the gas-line purged with inert gas, and the reactor pressurized to 1000 psi with H_2 . The block was heated to 55 °C on a Watlow heating mount, subjected to orbital shaking for 1 h, then cooled and depressurized. The solvent was removed using a centrifuge evaporator fitted with a plate holder. Residues were then taken up in CDCl_3 (added via a 12-channel micropipette), and the solutions were transferred to NMR tubes held upright in a custom 8 × 12 NMR-tube holder. Catalyst activity was assayed from the formation of **8''**, quantified by ^1H NMR analysis using a 400 MHz carousel instrument.

Consistently higher conversions were found for reduction in methylene chloride, relative to benzene (Figure 5.13). In either solvent, the CO complexes **Ru-26** outperform their H_2 analogues **Ru-25**. Studies probing the stability of **Ru-25** and **Ru-26** suggest that the difference reflects the higher thermal stability of the latter catalyst.¹²⁰ Examination of this

point more directly from rate curves is desirable, but would require sampling capabilities beyond those currently accessible. The improved performance of the bis-phosphine complexes **Ru-25a** and **Ru-26a** over their NHC-containing analogues **Ru-25b** and **Ru-26b** is attributed to the low lability of PCy₃ trans to NHC in the latter, a feature also evident in the benzylidene catalysts.^{45,121} Addition of base improves activity slightly, particularly for the IMes derivatives, suggesting that this remedies competing chlorination of these hydride catalysts by the chlorocarbon solvent.¹²² Finally, the difference in activity between the H₂ and CO series of catalysts is minimized in the presence of MeOH, presumably because the dihydrogen catalysts undergo carbonylation in this solvent.¹²³⁻¹²⁶

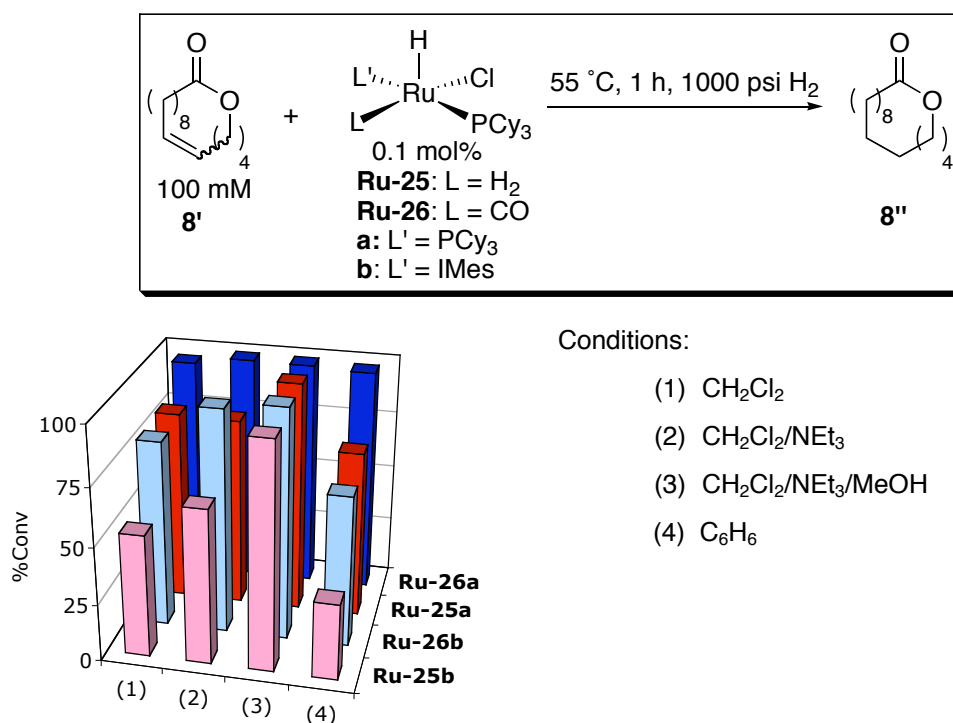
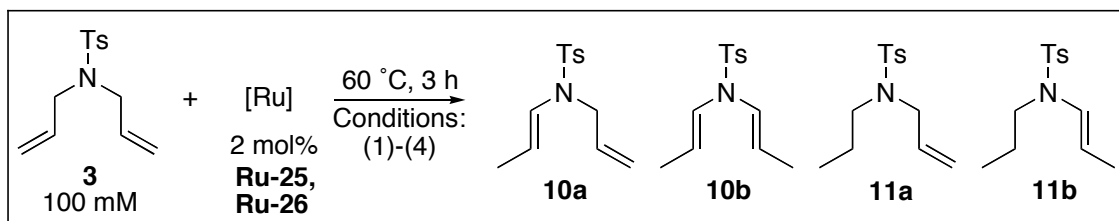


Figure 5.13. Effect of solvent and additives on the hydrogenation of **8'** by catalysts **Ru-25** and **Ru-26**. Additive amounts: NEt₃, 3 equivalents to [Ru]; MeOH, 20%_{v/v}.

A further study examined olefin isomerization via these Ru-H complexes. Tandem RCM-isomerization protocols present an attractive alternative route to cyclic vinyl ethers and vinyl amines, which are challenging targets for direct RCM.^{127,128}

Isomerization of five-membered tosyl-amine **3** via **Ru-25a/b** and **Ru-26a/b** (2 mol%) was carried out in CH₂Cl₂ and C₆H₆, both with and without 20%_{v/v} MeOH co-solvent (Figure 5.14). The well-plate was heated at 60 °C for 3 h, after which conversions were quantified by GC-FID, and product identity was confirmed by GC-MS and ¹H NMR analysis. Predominant products of all reactions are **10a** and **10b**, formed via isomerization of one or both allyl units in **3** (Figure 5.14a). As for the hydrogenation of **8'**, the CO catalysts **Ru-26** outperform their H₂ analogues **Ru-25** under all conditions. No consistent trend is found between the diphosphine or NHC complexes, however. Addition of protic co-solvent increased conversion in all cases: this is not due simply to carbonylation¹²⁶ (i.e. conversion of **Ru-25** to **Ru-26**), as the activity of CO catalysts **Ru-26a/b** also improves. The increased dielectric constant of the medium may aid in isomerization.

While the difference in conversions may again reflect the greater stability of the CO complexes, the lower selectivity of the H₂ catalysts **Ru-25** is of interest. Competing hydrogenation yields minor amounts of **11a,b** (<15%). Isomerization and hydrogenation mechanisms have a common Ru-alkyl intermediate (Scheme 5.4): the successive transfer of the dihydrogen ligand to olefin suggests that hydrogenation is kinetically favoured. Transfer of H₂ to the olefin may also be a factor in limiting catalyst lifetime, as the absence of additional H₂ to regenerate the resting state is likely to promote decomposition. For reasons of both productivity and selectivity, therefore, the CO complexes appear preferable in these isomerization reactions.



Conditions:

- (1) CH₂Cl₂
- (2) CH₂Cl₂/MeOH
- (3) C₆H₆
- (4) C₆H₆/MeOH

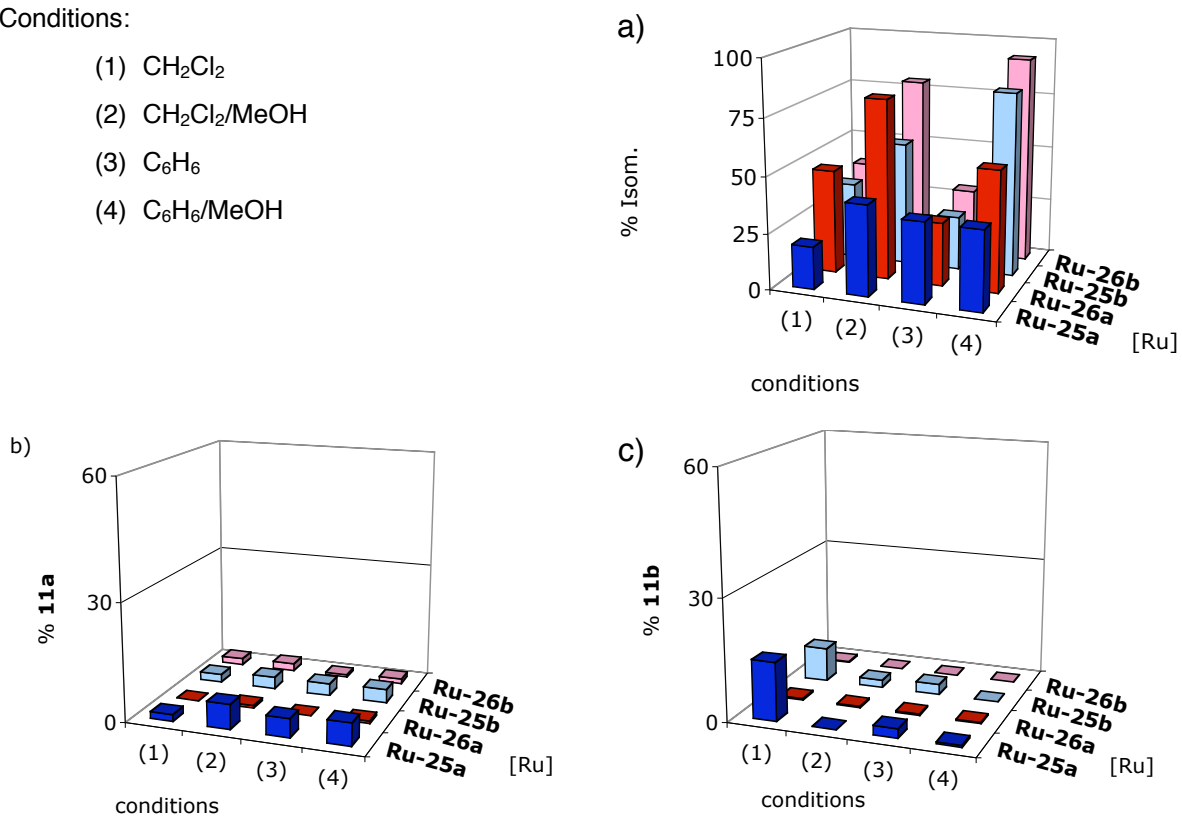
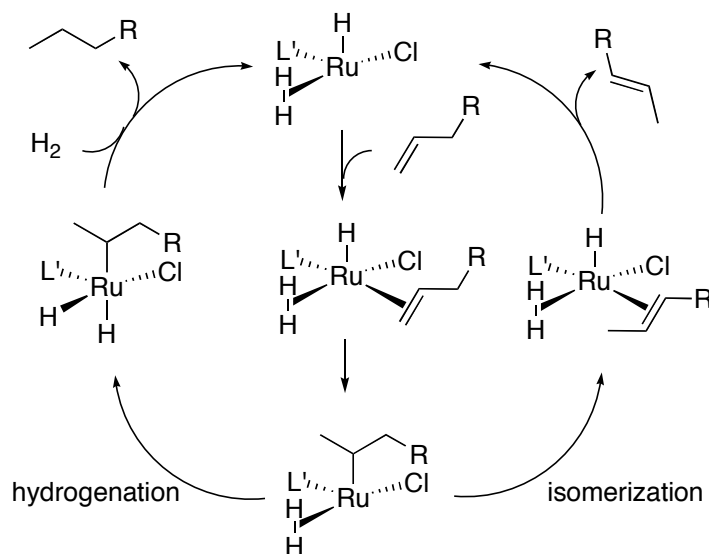


Figure 5.14. Comparison of catalysts **Ru-25** and **Ru-26** in the isomerization of **3**. a) Olefin units isomerized to form **10a** and **10b**; b) % **11a**; c) % **11b**.



Scheme 5.4. Mechanism for hydrogenation and isomerization by a Ru-hydride catalyst.

5.4 How to Use HT Methods within Homogeneous Catalysis Research Programs.

The power of HTE to accelerate chemical research^{3,4} is reinforced by the studies presented here, and amplified through incorporation of kinetics capabilities via our quenching protocol. The HT facilities within the uOttawa Centre for Catalysis Research and Innovation represent exceptionally powerful tools for research and training. The latter are particularly important with the increasing demand for skilled and knowledgeable HT practitioners in the materials and pharmaceutical industries.¹²⁹ In the hope of facilitating uptake of HT methodologies among local and visiting researchers, the following is provided as a practical overview, with recommended approaches and illustrative solutions to commonly-encountered problems.

5.4.1 Practical Considerations.

In HT experiments, the scale of reactions decreases while the number of reactions expands relative to bench-top methods. While the cost per "screening experiment" is generally significantly lower than that usual in conventional catalyst screening, the cost per plate can remain substantial, particularly if precious substrates or catalysts are employed. Minimizing substrate concentrations is often important in limiting plate costs. As a rule of thumb, concentrations are reduced by an order of magnitude relative to conventional reactions (10

mM was commonly used here). While reactivity trends are generally unaffected, this will limit the capacity to infer rates for bench-top experiments. In certain cases, changes in concentration may have more dramatic effects that must be considered, as was shown above for the concentration-dependent ring-chain equilibrium in RCM macrocyclization.

As with catalytic reactions in NMR tubes,⁴² the closed vials customarily employed in HT reactions can result in a pressure buildup if gases are evolved during reaction. In some cases, the evolved gas participates in and influences the reaction. In the olefin metathesis chemistry described above, for example, the presence of ethylene affects speciation and catalyst lifetimes. (Section 5.3.2). The extent of the implications of this behaviour for RCM reactions that have a high bias toward cyclization is as yet uncertain. Screening reactions can in principle be carried out in an open plate,^{71,130} given a suitable non-volatile solvent, but caution is required to prevent solvent evaporation or contamination by constituents of the glovebox atmosphere.

As a related issue, stock solutions that are dispensed over extended periods must be septum-sealed to inhibit evaporation, rather than leaving them uncapped, as is usual where short dispensing intervals are involved. The kinetics/quenching protocol developed herein is a case in point. Pre-piercing of the septum was found to be essential to prevent coring and lodging of small pieces of the rubber septum in the needle, which impede solution flow and cause inaccuracies in the volume of quenching agent dispensed. For this purpose, an additional loop was added to the HT quenching protocol prior to the first quenching stage. In this loop, the robot is directed to pre-pierce the cap, following which unimpeded flow is ensured by aspirating and redispensing the solution into the stock vial.

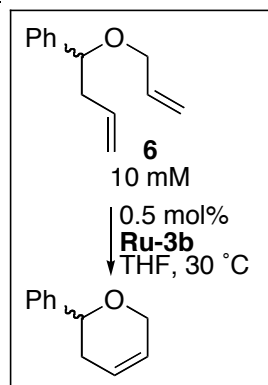
Dense solvents such as dichloromethane tend to introduce air bubbles on aspiration, and to drip from the needle while it is moving. Aspiration and needle movement speeds can be optimized to reduce solvent loss or inaccuracies in the volumes dispensed. Reproducible data can be obtained by these methods, or by hand-dispensing, but in general, use of dichloromethane is not recommended. The standard surrogate, 1,2-dichloroethane (DCE), we found unreliable: it resulted in reduced yields for dichloride and aryloxide metathesis

catalysts, relative to parallel experiments in dichloromethane,¹⁰⁹ and caused rapid colour changes (e.g. from green to reddish-brown within minutes for third-generation catalysts **Ru-3** and **Ru-18**. Successful RCM with these catalysts described in Section 5.3.4 indicates that complete decomposition does not occur within a 30 min time frame however). This behaviour was observed despite use of 99.8% solvent, distilled from CaH₂ under N₂ and passed through neutral alumina, as for other chlorinated solvents, prior to use. It may be noted that others have found no such problems. The Mol group, for example, reported similar reactivity for RuCl₂(PCy₃)₂(=CHPh) in these two solvents; Grela and co-workers note no issues,³⁹ and the Keissling group routinely uses dichloroethane for highly sensitive ROMP oligomerization studies with the first-generation catalyst **Ru-1a**.¹³¹ More recent studies by the latter group, however, which use **Ru-18c** as initiator, employ CH₂Cl₂ for the metathesis step.^{132,133} Given the experience above, we recommend use of benzene/toluene or THF as solvents for HT olefin metathesis.

Reproducibility in single-point and monitored HT experiments is generally very good, with errors often below $\pm 2\%$. However, larger errors are found for fast-initiating catalysts during early stages of reaction (Table 5.1, Entry 3).

Table 5.1. Low error for HTQ reaction profiles.^[a]

Entry	Time (min)	RCM (%) ^[b]	error (+/-)
1	0	0	0.0
2	8	59	1.6
3	13	88	7.9
4	23	89	2.1
5	38	93	1.9
6	68	94	0.5
7	128	96	1.2
8	248	96	1.2
9	368	97	1.9
10	548	96	1.2
11	728	96	1.7
12	1448	95	1.1



^[a] RCM of **6** (10 mM) with 0.5 mol% **Ru-3b** in C₆H₆ at 30 °C. ^[b] Average of two runs.

5.5 Conclusions.

High-throughput experimentation has proven a powerful tool for catalyst discovery and optimization in many areas of catalysis. The high-throughput quenching methodology outlined in this Chapter, including guidelines for selection of appropriate quenching agents for any catalytic reaction, and a robust protocol for monitoring HT reactions, offers the most powerful and rigorous means currently attainable for extracting HTE kinetics data in parallel, in real time, and under real conditions. Also presented is a practical guide to designing and conducting HT experiments. It is hoped that these contributions, along with continuing advances in analytical instrumentation and software put forth by the broader chemistry community, will aid in the uptake of HTE as an integral tool for accelerated mechanistic analysis and catalyst redesign.

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Chapter 6. Development of MALDI Mass Spectrometry as a Tool for Establishing the Identity and Behaviour of Reactive Organometallic Species^{*}

6.1 Introduction.

Alluded to in previous chapters is the transformative impact of discoveries in homogeneous catalysis on organic chemistry and materials science. These have enabled major advances in sectors ranging from pharmaceutical to polymer synthesis, and will be central to the exploitation of sustainable feedstocks.¹ Underlying these discoveries, however, is an enormous body of work directed at synthesizing transition-metal catalysts, developing mechanistic understanding into their behaviour, and using this insight, accompanied by kinetic activity/selectivity performance data, for iterative redesign. While HT methods have much to offer in accelerating progress (see Chapter 5), a rate-limiting obstacle in advancing understanding remains the simple problem of elucidating the structures of transition-metal complexes. Despite a steady expansion in our knowledge about the rich chemistry of the transition metals, reduction of planned syntheses to practice is still non-trivial, and novel pathways and unexpected products are commonplace. A key bottleneck is the identification of actual, as opposed to intended, products of organometallic syntheses: this typically takes considerably longer than the reactions themselves, while elucidation of catalytic mechanisms occurs on a timescale of years.

Structural identification in organic chemistry is greatly simplified by the capacity of mass spectrometry (MS) to report on molecular composition, via measurements of mass-to-charge (m/z) ratios and isotope patterns. However, the standard high-energy MS ionization methods suitable for analysis of organic compounds – most typically, electron-impact MS – induce decomposition of all but the most unreactive organometallic molecules.² "Soft" ionization techniques such as electrospray ionization (ESI)³ and matrix-assisted laser desorption/ionization (MALDI),⁴ which ionize fragile complexes with minimal fragmentation, have tremendous potential to simplify and expedite analysis. This Chapter

^{*} Parts of this Chapter have been published: Eelman, M.D.; Blacquiere, J.M.; Moriarty, M.M.; Fogg, D.E. *Angew. Chem., Int. Ed.* **2008**, 47, 303-306.

begins with a review of the strengths and limitations of ESI-MS relative to the MALDI-MS methods current at the outset of this work, and proceeds to describe advances that have enabled a breakthrough in the application of MALDI-TOF MS (TOF = time-of-flight) to analysis of reactive organometallic molecules. Exemplary studies are presented that showcase the power of these new methodologies for insight into both the identity and the reaction chemistry of organometallic complexes and catalysts.

6.2 A Comparison of ESI-MS and MALDI-MS Methods for Analysis of Organometallic and Inorganic Molecules.

In ESI-MS experiments, a dilute solution of the analyte (usually a cationic or anionic molecule) is introduced via a metal capillary in the presence of a strong electrical field: in solution, the charged species move in the field direction and form a "Taylor cone" from which small charged droplets are ultimately emitted. Fragmentation can be limited by minimizing the cone voltage, and tandem MS techniques can be used to aid in signal assignment, as well as to probe reactivity. ESI-MS methods have been used for structural elucidation and mechanistic analysis in organometallic chemistry and catalysis, and to gain insight into fundamental properties such as metal-ligand bond strengths.⁵⁻⁹ Despite its power, however, ESI-MS suffers from limitations that have impeded uptake by non-expert groups. Most challenging, for analysis of reactive organometallic species on instruments used for general departmental purposes, is the need to rigorously exclude air and water, as well as contaminants that can give rise to misleading, in situ coordination chemistry. As a flow method, ESI-MS is vulnerable to contamination, and the presence of persistent analyte and additive residues in the instrument tubing is thus a further hazard for analysis of reactive complexes, particularly at the high dilutions required. For this reason, best results have been seen for analysis of more robust species, or from groups that have inorganic-dedicated MS facilities. The groups of Weller and McIndoe recently described a means of minimizing contamination of the feedline leading to the sample loading port, and preventing introduction of oxygen. In this setup, analyte solutions are loaded via a syringe pump housed in a glovebox, and connected to the sample loading inlet by disposable PEEK tubing (Figure 6.1), which is replaced after each use.¹⁰

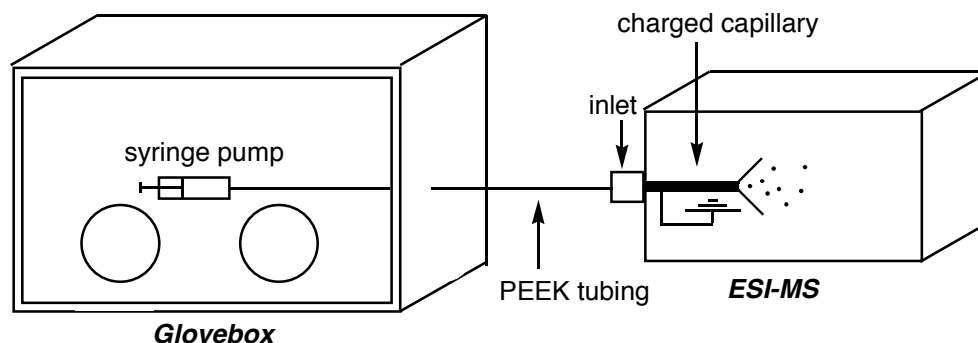


Figure 6.1. Schematic of the inert-atmosphere ESI-MS developed by Weller and McIndoe.¹⁰

Additional challenges in ESI-MS analysis of organometallics emerge from the need for a "suitable" solvent. Most obviously, insoluble molecules are intractable.¹¹ As well, however, some tension exists between the polar nature of the solvents best suited to ESI – most common being H_2O , MeCN, MeOH – and the solubility and reactivity of organometallic analytes. Fortunately, CH_2Cl_2 is also suitable, while the McIndoe group has made headway in adapting hexanes and toluene into "ESI-able" solvents, by doping in small amounts of a lipophilic ionic liquid.¹² The analyte signals are small in comparison to those for the ionic liquid (IL), and unwanted reaction chemistry between the IL and the analyte may be a concern, but this is nevertheless an attractive potential work-around to one of the major limitations of ESI-MS.

A more fundamental issue lies in the fact that ESI-MS is blind to neutral species. While this is true for any mass spectrometric technique, the very gentleness of the method makes ionization of neutral species difficult, unless they contain some readily oxidizable site, or a polar group with which a charged additive can interact.^{13,14} Analysis of charged molecules is of course considerably more straightforward, and one of the standard approaches to ESI-MS analysis of neutral complexes is therefore *ex situ* modification by installation of a charged surrogate ligand.^{2,15,16}

MALDI-TOF MS is highly complementary to ESI-MS (Table 6.1),² in particular for its capacity to expand the scope of analysis to include neutral species. The "matrix" in MALDI serves both as the chromophore required to absorb and transfer energy to the analyte during

ionization, and as the carrier species that escorts the analyte into the gas phase. The method first rose to great prominence as a means of analyzing biopolymers,¹⁷ and the dominant ionization method relies on use of aromatic acid matrices (Chart 6.1) to effect protonation of the polar sites abundant in such structures. This class of matrices contains a UV chromophore chosen for its ability to take up energy from the N₂ lasers in widest use (337 nm); they also afford the requisite acidic (usually phenolic) functionality, and exhibit a high tendency toward crystallinity.¹⁸⁻²⁰

Table 6.1. Characteristics of MALDI and ESI mass spectrometric methods.

	ESI	MALDI
"Soft" ionization	✓	✓
Sensitivity	✓	✓
MS/MS analysis facile	✓	✓ ^[a]
Capacity to analyze neutral species	✗	✓
Unrestricted solvent scope (sample preparation / introduction)	✗	✓
Robust (insensitive to contaminants)	✗	✓
Capacity for quantitation ^[b]	✓	semi-quantitative

^[a]Tandem TOF-TOF instruments are less common. ^[b] Providing that calibration curves can be constructed.

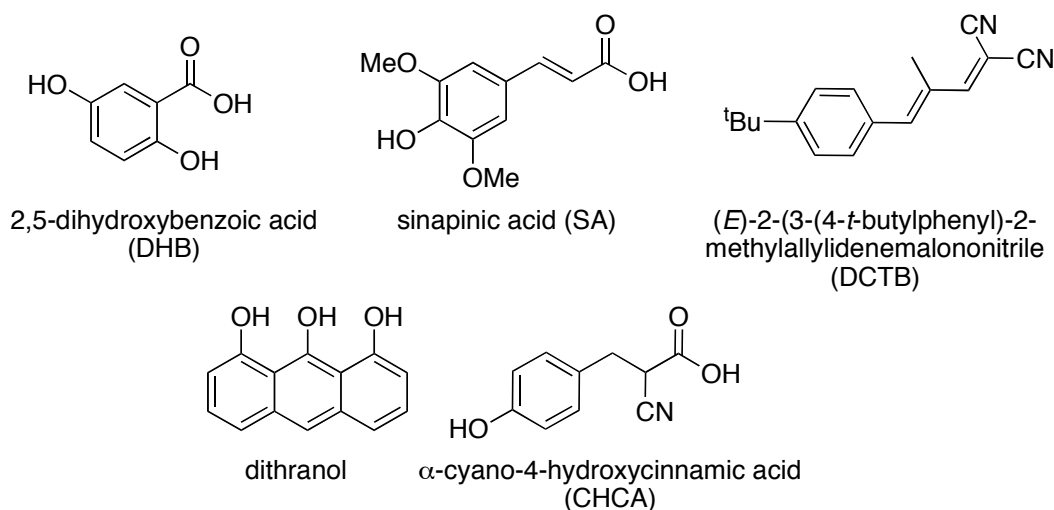


Chart 6.1. Bronsted or Lewis base matrices used for MALDI MS.

Sample preparation in MALDI-MS analysis is very straightforward: at its simplest, it involves simply mixing the analyte and excess matrix in any suitable solvent, spotting microliter aliquots onto the target plate, and allowing them to dry (the "dried-droplet" method). A co-crystallized layer of analyte and matrix is thus formed.^{17,18} Laser irradiation of these spots on the mounted target plate desorbs the matrix and analyte in a plume,²¹ and effects electron-transfer ionization of the matrix. Ensuing proton transfer between the charged matrix species and the analyte generates a cation of the latter, usually of the form $[M+H]^+$ (where M = the molecular ion).

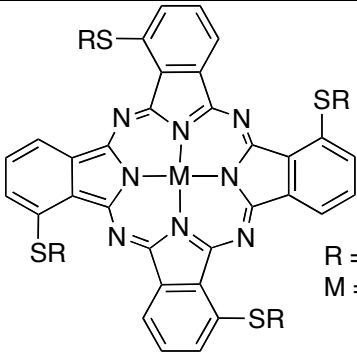
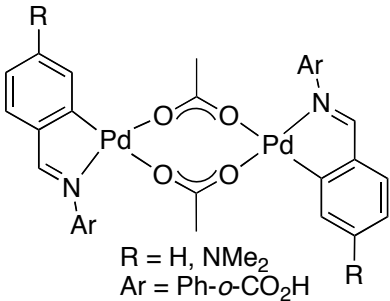
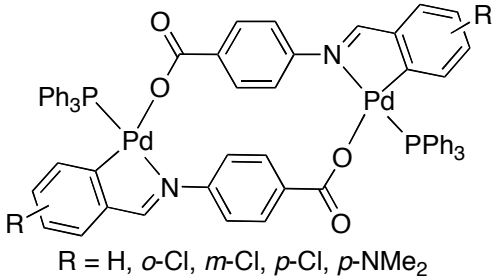
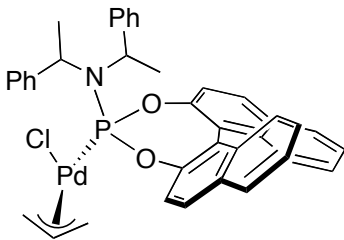
This sample preparation method means that complete solubility is not required for MALDI-MS, and nor are the polar, potentially coordinating, and/or protic solvents that are required in ESI. Furthermore, because the sample is introduced from the solid state, the contamination issues that plague ESI-MS are greatly reduced. A compensating disadvantage lies in the inherent heterogeneity of the sample spots, which contributes to challenges in quantification, and hence kinetic studies (*vide infra*). An additional distinction from ESI-MS lies in the tendency of multiply charged species to undergo reduction or oxidation in the laser plume, which typically results in observation of the singly charged ion (even where the analyte itself is multiply charged). Use of time-of-flight detection means that there is theoretically no mass limit. Resolution is lower, relative to sector instruments (1,000 for linear TOF, vs 100,000 for sector instruments), because smaller ions in later laser pulses are able to "catch up" to heavier ions in the flight tube.² However, reflectron instruments dramatically improve resolution (to 10,000–30,000), ensuring that all ions of the same m/z reach the detector with near-simultaneity.

At the outset of this work, a major challenge with MALDI-MS that is unaddressed in Table 6.1 lay in the extensive fragmentation often observed on attempted analysis of reactive organometallic complexes. This reflects the protic nature of the matrices used (for examples, see Chart 6.1 above), and their tendency to promote ligand protonolysis. MALDI-TOF MS analysis of transition-metal complexes had been successfully applied to characterization of robust cluster compounds and coordinatively saturated, predominantly 18-electron, air-stable compounds.² More reactive species of general interest tended to decompose during sample

preparation, introduction, or analysis.^{2,19} Nevertheless, analysis of coordinatively or electronically unsaturated organometallic complexes has yielded informative results in some cases (Table 6.2). The molecular ion $[M]^+$ is rarely observed, but the protonated complex can sometimes be detected as an $[M+H]^+$ signal (Entry 1).²² Often, however, the highest-mass observable signal arises from ligand loss. Shown in Entries 4-9 are illustrative examples involving protonolysis^{23,24} of an anionic ligand, resulting in an $[M-X]^+$ signal (Entries 4-7 and 9),²⁵⁻²⁹ or $[M-2X]^+$ (Entry 8).³⁰ Labile neutral ligands, such as COD, may also be lost (Entry 7).^{25,27} Bi- or polynuclear complexes may remain intact (Entries 3, 5, 6, 8),^{26,30,31} but in some cases only their monomeric components are observed (Entries 2, 3).³¹ Face-bridged, $M_2(\mu-Cl)_3$ moieties are normally observed intact, where singly- or doubly-bridged $M_2(\text{acetonato})_n$ units are not. In a surprising number of cases, the MALDI matrix employed is not specified (Table 6.2, Entries 1-6), so its potential role in fragmentation cannot be assessed.

Better results are often seen for charged organometallic complexes.^{25,32-36} UV irradiation is then required only for desorption, and laser flux can therefore be tuned to a minimum. Of possibly greater importance is the inherent stability of the charged complex, which extends its lifetime in the gas phase. In the Pd-allyl complex shown in Entry 10;²⁵ the molecular cation is observed as a major signal at m/z 686, despite some fragmentation and aggregation. NMR analysis indicated a 1:1 metal-ligand ratio, suggesting that aggregation is due to gas-phase chemistry.

Table 6.2. Fragmentation products of neutral organometallic complexes analyzed by MALDI-TOF MS.

Entry	Complex	Observed signals			Matrix
		[M] ⁺⁺	[M-X] ⁺	Other	
1 ²²	 R = (CH₂)₇OH M = Cu, Co	—	—	[M+H] ⁺	CHCA
2 ³¹	 R = H, NMe₂ Ar = Ph-<i>o</i>-CO₂H	—	—	[M/2-OAc+DTH] ⁺ , [M/2-OAc] ⁺	DHB
3 ³¹	 R = H, <i>o</i>-Cl, <i>m</i>-Cl, <i>p</i>-Cl, <i>p</i>-NMe₂	—	—	[M+ H-PPh ₃] ⁺ , [M/2+H] ⁺	DHB
4 ²⁵		—	✓	[M-Cl-C ₃ H ₅ +L] ⁺ , [M-Cl-C ₃ H ₅] ⁺	N/A

5 ²⁶		—	✓	—	N/A
6 ²⁶		—	✓	—	N/A
7 ²⁷		—	✓	[M-Cl-COD] ⁺	N/A
8 ³⁰		—	—	[M-Cl ₂] ⁺	N/A
9 ²⁸		—	✓	—	N/A
10 ²⁵		✓	✓	[M-C ₃ H ₅ +L] ⁺	N/A

The foregoing examples illustrate the challenges of unwanted reactions with the matrix that can plague conventional MALDI ionization. A somewhat regressive approach should be

acknowledged, which attempts to address these problems by simply eliminating the matrix altogether.^{29,37-40} Laser desorption is a "harder" ionization method that served as the forerunner to MALDI. Because no matrix is present to absorb, down-regulate, and transfer laser energy, the analyte is subjected to primary ionization.² Recent studies of transition-metal complexes using this technique include the neutral zirconium cyclopentadienyl complex shown in Figure 6.2.²⁹ An absorption band for this species at 350 nm (assigned to a LMCT from Cp to Zr) means that the laser power intended for primary ionization has the potential to populate M-L antibonding levels, and thus to promote fragmentation. The radical molecular cation was not observed (unsurprisingly, as the metal is already in its highest oxidation state). Instead, a major signal is present for $[M-Cl]^+$, accompanied by many others attributed to ligand exchange and aggregation. The latter processes reflect extensive analyte-analyte interactions in the plume: it is just such interactions which the predominance of matrix molecules in MALDI ionization is designed to inhibit.⁴¹

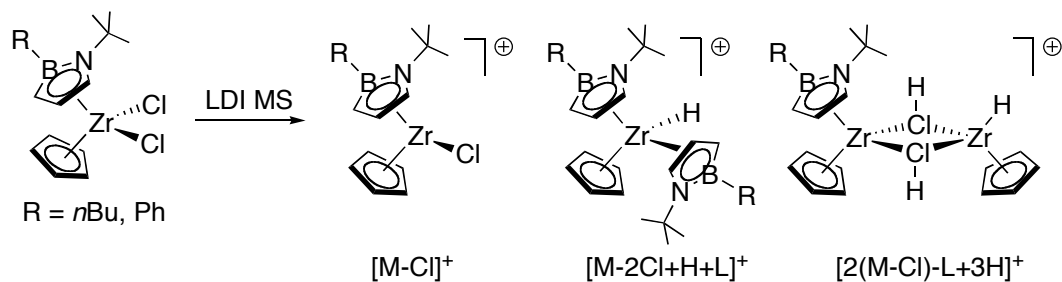


Figure 6.2. Species observed on LDI MS analysis of a neutral zirconium complex.

6.3 Charge-transfer (CT) matrices for MALDI-MS analysis of reactive organometallic complexes.

The incidence of charge-transfer (CT) ionization has long been recognized in the mass spectrometric analysis of transition-metal complexes. Electron-impact mass spectra of highly robust, readily oxidized molecules such as ferrocene are dominated by the signal for the radical molecular cation, and CT ionization is sometimes also seen as a minor contributor along with proton transfer in routine MALDI-MS analysis using protic matrices.²¹ Given the rich redox chemistry and low ionization potentials of many transition metals, we considered that CT ionization could be particularly well suited for analysis of organometallic complexes,

via one-electron oxidation of the matrix by the laser in the primary ionization event, followed by transfer of an electron from the analyte to the matrix (Figure 6.3a). Formation of the desired radical molecular cation requires that the ionization potential of the matrix exceed that of the analyte.⁴²

Polyaromatic hydrocarbons (PAHs) are suitable matrix compounds for this purpose, as one-electron oxidation is facile, relative to proton transfer (Figure 6.3b). McCarley, Limbach and co-workers showed that anthracene worked well as a matrix for the analysis of ferrocenes and other readily oxidized analytes (Table 6.3, Entry 1),⁴³ although this is a highly favourable test case, as indicated by the observation of $[M]^{+\bullet}$ even on EI-MS behaviour of ferrocene (see above). The studies described below, as well as findings from my predecessors in the Fogg group, demonstrate that PAHs can function as highly effective matrices for MALDI MS analysis of organometallic complexes.⁴⁴ In particular, pyrene and anthracene matrices can dramatically reduce the tendency to eliminate anionic ligands from the molecular ion, relative to proton-transfer ionization. The radical molecular cation is commonly observed on charge-transfer ionization of even highly reactive metal complexes using PAH matrices, barring the presence of particularly labile neutral ligands. Selected examples of complexes successfully analyzed by this method, or which present specific problems, will be discussed below, following examination of one further key advance.

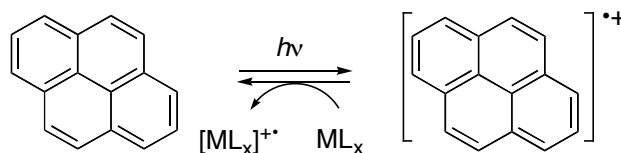


Figure 6.3. Ionization of the PAH pyrene by laser irradiation, followed by one-electron oxidation of a metal complex to generate the radical molecular cation.

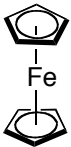
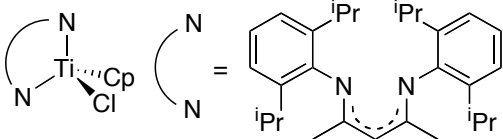
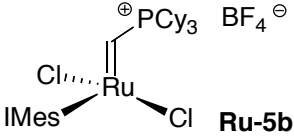
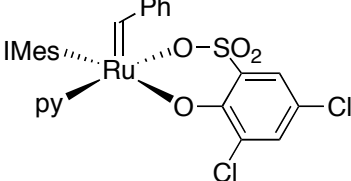
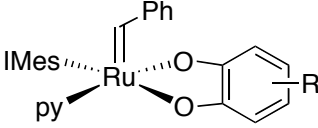
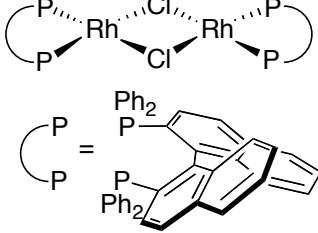
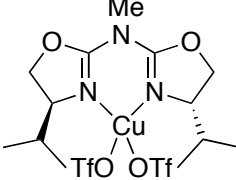
6.4 Charge-transfer MALDI-MS under rigorously anaerobic, anhydrous conditions

While charge-transfer can resolve the ionization problem in MALDI-MS analysis of organometallics, air- and moisture-sensitivity remains an issue. A number of reports have addressed this limitation, with varying degrees of rigour. The Zr complex discussed above (Figure 6.2) is a highly active olefin polymerization catalyst, which rapidly decomposes in

solution on exposure to air.²⁹ Its higher tolerance to air in the solid state permitted satisfactory LDI-MS analysis for samples prepared by pressing the solid onto a target plate, and quickly transferring this to the spectrometer. The absence of any color change in the sample was adduced as evidence of stability, although the complexity characteristic of LDI-MS spectra limits rigorous assessment. In an alternative approach, analyte/matrix solutions are prepared and loaded onto the target plate in a glovebox, and the latter is sealed in a ZiplocTM bag to limit decomposition during transfer to the spectrometer.³⁹ The most sophisticated, rigorous solution involves a direct interface between the sample loading chamber and a glovebox, a setup developed by my predecessors Henrietta Parnas and Maeve Moriarty in the Fogg group.⁴⁴ This instrumentation was used in conjunction with the charge-transfer matrices described in the preceding section, for analysis of a wide range of complexes. A subset of these is illustrated in Table 6.3; other examples that were treated in greater detail are discussed below.

Attesting to the rigorously anaerobic conditions attainable is the successful analysis of the highly air-sensitive Ti(III) complex shown in Entry 2, and the exceedingly reactive, four-coordinate Ru(II) complex of Entry 3 (the Piers olefin metathesis catalyst). No oxidation products were observed, and neither compound exhibited fragments associated with hydrolysis. Excellent isotope matches were observed for $[M]^{+*}$ in both cases.⁴⁴ Other important, commercially available ruthenium metathesis catalysts were examined in greater detail, as noted above: discussion of these is deferred to the next section. It may be noted, however, that all pyridine-containing metathesis catalysts, including catecholate, sulfonato and binaphtholate derivatives, afford $[M\text{-py}]^{+*}$ as the base peak (Table 6.3, Entries 2 and 3; see Chapter 4 and Appendix A for Ru-BINO complexes).^{45,46} Similarly, labile edge-bridged metal dimers are commonly observed as the monomeric units, although the radical molecular cation could be observed for $[\text{RhCl}(\text{COD})]_2$ (Entry 5). Finally, MALDI MS confirmed ligand coordination to a paramagnetic Cu(II) precursor, although observation of $[M]^{+*}$ is precluded by the fact that the metal is already in its highest oxidation state (Entry 7).

Table 6.3. Major signals observed on MALDI-TOF mass spectrometric analysis of organometallic complexes using PAH matrices.

Entry	Complex	Observed signals			Matrix
		$[M]^{+*}$	$[M-X]^+$	Other	
1 ⁴³		✓	—	—	pyrene or anthracene
2 ⁴⁴ [a]		✓	—	$[M-Cl]^+$, $[M-Cp]^+$	pyrene
3 ⁴⁴ [a]		✓	—	—	pyrene
4 ⁴⁵ [a]		—	—	$[M-py]^+$	pyrene
5 ^{45,46} [a]		—	—	$[M-py]^+$	pyrene
6 ⁴⁴ [a]		✓	—	$[M-COD]^{+*}$, $[M/2-COD]^{+*}$ and $[M/2-COD-Cl]^+$	pyrene
7 ⁴⁴ [a]			✓	$[M-CH_3]^+$, $[M-iPr]^+$, $[M-2(OTf)]^+$	pyrene

^[a] Anaerobic analysis carried out by: Dr. Melanie Eelman (Entries 2,3 and 6), Sebastien Monfette (Entries 4 and 5) and myself (Entry 7).

6.4.1 Methodology for CT-MALDI-MS reactions described below.

In all cases, pyrene and anthracene were used as matrices; comparison of both spectra facilitated identification of signals attributed to matrix adducts. For routine analysis of complexes in solution, aliquots of a matrix stock solution and an analyte solution (ca. 100 and 5 mM, respectively) were mixed in an approximately 5:1_{v/v} ratio of matrix to analyte. The resulting solution was spotted on the target plate using a micropipette tip, and the solvent allowed to evaporate. Solid-state samples were analyzed by preparing a Nujol mull of the matrix and analyte, and transferring this to a target plate by use of a clean rubber policeman. Precise matrix:analyte ratios used in the various experiments are given in Chapter 2 (Table 2.1). During signal acquisition, the laser power was kept to a minimum, to maintain satisfactory signal-to-noise ratios. For each sample, at least 300 laser shots were collected. Spectra obtained using pyrene as matrix generally exhibited improved signal-to-noise ratios, and reduced fragmentation, relative to those obtained using anthracene.

All spectra were processed with line broadening set to 1, with base-line subtraction. The presence of seven naturally-occurring, relatively abundant isotopes for ruthenium, and two for chlorine, contributes to the complexity of the signals, and facilitates identification of metal-containing species. Signals and hence molecular composition are assigned based on comparison of predicted and observed (exact) masses and isotope patterns. Spectra were simulated using the Xmass software program.

6.4.2 MALDI mass spectra of common metathesis catalysts: **Ru-1a**, **Ru-2a**, **Ru-1b**, **Ru-1c**, **Ru-4c**.

The ruthenium-benzylidene catalysts **Ru-1a-c** and **Ru-4c** (Chart 6.2) were analyzed by CT-MALDI MS using pyrene as matrix (Figure 6.5). Isolated methyldiene **Ru-2a** (the resting state in RCM and CM reactions using **Ru-1a**) was also analyzed. In all cases, the radical molecular cation ($[M]^{\bullet+}$) is a major signal, with an isotope pattern closely resembling that simulated (Figure 6.5, insets). A slight discrepancy in relative peak heights between the simulated and observed isotope patterns for **Ru-1b-c** is due to overlapping $[M]^{\bullet+}$ and $[M-H]^{\bullet+}$ signals, indicating minor amounts of deprotonation. Notable in the spectra of all of these complexes is a prominent $[M-Cl]^+$ signal, as commonly observed for other neutral

complexes, and a feature of the gas-phase chemistry that does not reflect solution behavior. Loss of the neutral ligands, in comparison, mirrors solution trends. Thus, no $[M-NHC]^{+}$ signals are observed for **Ru-1b**, **Ru-1c** or **Ru-4c**, while the $[M-PCy_3]^{+}$ signal is significant for **Ru-1a-c**. More extensive fragmentation reflects proton abstraction, which may arise from C-H bond activation, a common pathway for stabilization of low-valent ruthenium species. Less well-behaved is styrenyl ether catalyst **Ru-4c**, for which a prominent signal for $[Ru(H_2IMes)-3H]^+$ is observed (Figure 6.5e), signifying extensive fragmentation.

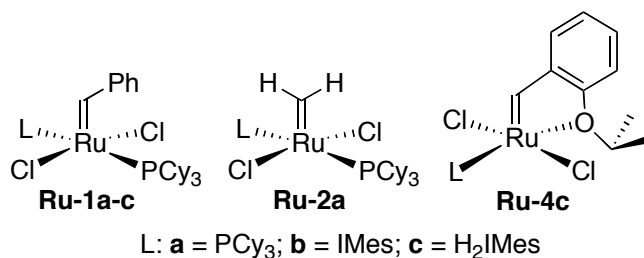


Chart 6.2. Olefin metathesis catalysts analyzed by CT-MALDI MS.

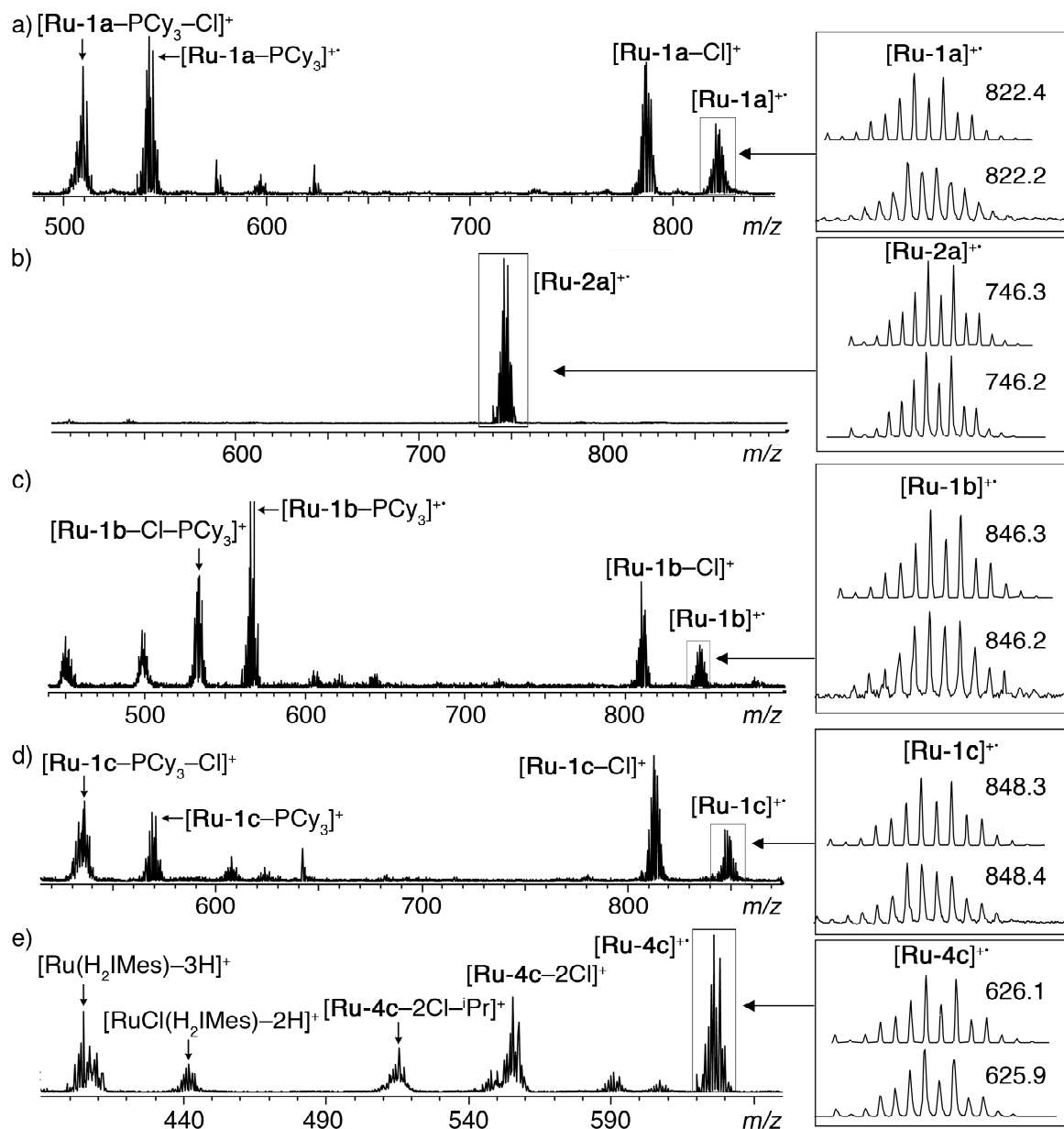


Figure 6.4. CT-MALDI mass spectra of isolated ruthenium-carbene catalysts. a) **Ru-1a**; b) **Ru-2a**; c) **Ru-1b**; d) **Ru-1c**; e) **Ru-4c**. Insets show isotope patterns for the molecular ions with m/z values (top: simulated, bottom: observed), matrix = pyrene.

6.4.3 UV-vis absorption as an indicator for primary ionization of **Ru-1a**, **Ru-2a**, **Ru-1b**, **Ru-4c**.

Kinetic studies by the Grubbs group revealed that loss of PCy_3 from resting state complex **Ru-2a** in solution (a step essential for re-uptake of this species into metathesis) is slower by an order of magnitude than from benzylidene **Ru-1a**. Comparable phosphine lability is

reported for **Ru-2a** and the NHC catalysts **Ru-1b** and **Ru-1c**.⁴⁷ Given this, we were surprised to observe solely $[M]^{++}$ in the MALDI-MS spectrum for **Ru-2a** (Figure 6.5b): that is, no loss of PCy_3 is observed in the gas phase. Loss of L from **Ru-1b-c** may thus reflect laser-induced fragmentation from a primary ionization pathway,²³ rather than simply reporting on solution behavior. To establish the relative tendencies of **Ru-1c**, **Ru-1a**, **Ru-2a** and **Ru-4c** to absorb energy from the 337 nm laser, UV-vis analysis was undertaken (Figure 6.6).

The first-generation methyldiene complex **Ru-2a** absorbs weakly at 337 nm, with an extinction coefficient (ϵ) of $783\text{ M}^{-1}\text{cm}^{-1}$. The presence of one phenyl group on the benzylidene ligand in **Ru-1a**, and of three aryl groups in **Ru-1c** (one phenyl and two mesityl groups) significantly increases ϵ_{337} (to 11,300 for **Ru-1a**, and $43,600\text{ M}^{-1}\text{cm}^{-1}$ for **Ru-1c**). The enhanced molar absorptivity of the benzylidene species, relative to its methyldiene derivative, is expected to promote primary ionization, and thereby to increase the susceptibility of the complex to fragmentation. The much higher molar absorptivity of pyrene ($\epsilon_{337} = 72,700\text{ M}^{-1}\text{cm}^{-1}$)⁴³ should limit this effect, but the low ratios of matrix to analyte employed may reduce contributions from secondary ionization of the analyte.²³

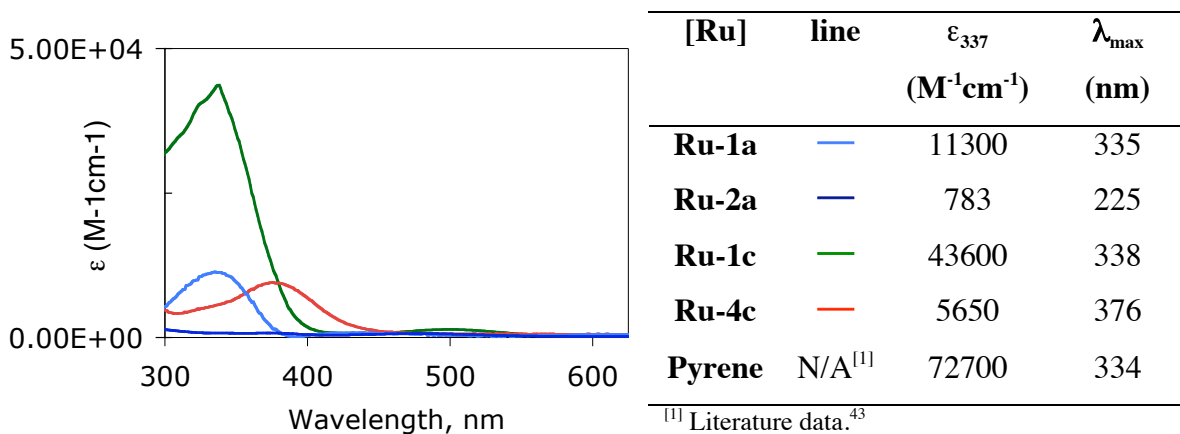


Figure 6.5. UV-vis extinction coefficients (ϵ) for metathesis complexes (C_6H_6).

6.4.4 Analysis of representative, five-coordinate hydride complexes.

While analysis of monohydride complexes by CT-MALDI MS leads to considerable loss of hydride, valuable insight into composition can be obtained. A case in point is the spectrum of dinitrogen complex $RuHCl(N_2)(IMes)_2$ **Ru-8**, the subject of Chapter 3 (Figure 6.7). A major

signal at m/z 744.0 exhibited an excellent isotope match for $[\text{RuCl}(\text{IMes})_2\text{-H}]^+$ (i.e. $[\text{M-N}_2\text{-H}_2]^+$), accompanied by a very small signal for $[\text{M+H}]^+$ at m/z 775.1. Importantly, the MALDI data provided the only evidence to confirm the presence of chloride in the complex, while NMR integration had already confirmed the presence of two IMes ligands per hydride. This underscores the point concerning the complementarity of MALDI and NMR analysis raised above.

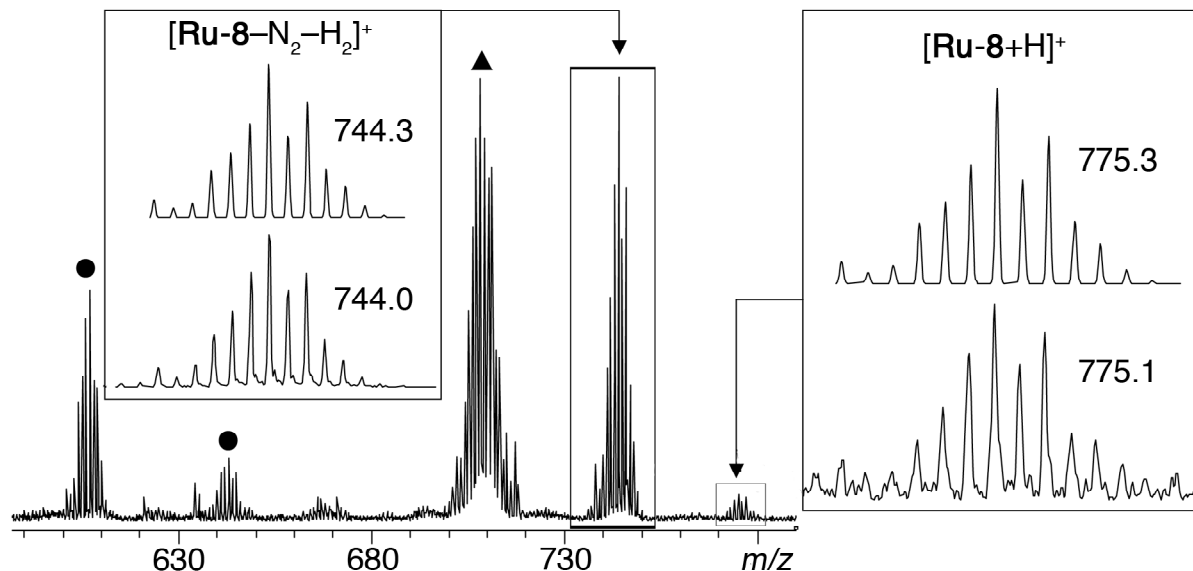


Figure 6.6. CT-MALDI mass spectrum of $\text{RuHCl}(\text{IMes})_2(\text{N}_2)$ **Ru-8**. Insets depict key isotope patterns (top: simulated; bottom: observed). Key for lower-mass fragment peaks: ▲ denotes overlapping signals for $[\text{RuH}(\text{IMes})_2]^+$ (m/z 711.1), $[\text{Ru}(\text{IMes})_2]^+$ (m/z 710.1), $[\text{Ru}(\text{IMes})_2\text{-H}_2]^+$ (m/z 708.1); ● denotes pyrene-matrix adducts: $[\text{Ru}(\text{IMes})(\text{pyr})\text{-H}]^+$ (m/z 607.0), $[\text{Ru}(\text{IMes})(\text{pyr})\text{-Cl}]^+$ (m/z 643.0). Matrix = pyrene.

The related complex $\text{RuHCl}(\text{CO})(\text{IMes})(\text{PCy}_3)$ **Ru-26b** revealed a prominent pattern arising from the overlap of several fragments (Figure 6.8a): while complex, this has diagnostic value for identification of hydridochlorocarbonyl complexes of ruthenium. Loss of the neutral (CO) or anionic (Cl^- , H^-) ligands results in an overlap of signals due to $[\text{M-CO+H}_2]^+$, $[\text{M-HCl}]^+$, $[\text{M-HCl-H}_2]^+$, and $[\text{M-Cl-4H}]^+$, from m/z 708–726. A superposition of simulated isotope patterns is shown in Figure 6.8b (colors correspond to the proposed fragmentation products in Figure 6.8c). Loss of protons prevents observation of clean isotope patterns for

$[\text{Ru-26b-Cl}]^+$ or $[\text{Ru-26b-CO}]^{+*}$. As noted in Section 6.2, MALDI MS customarily gives singly-charged ions.⁴⁸

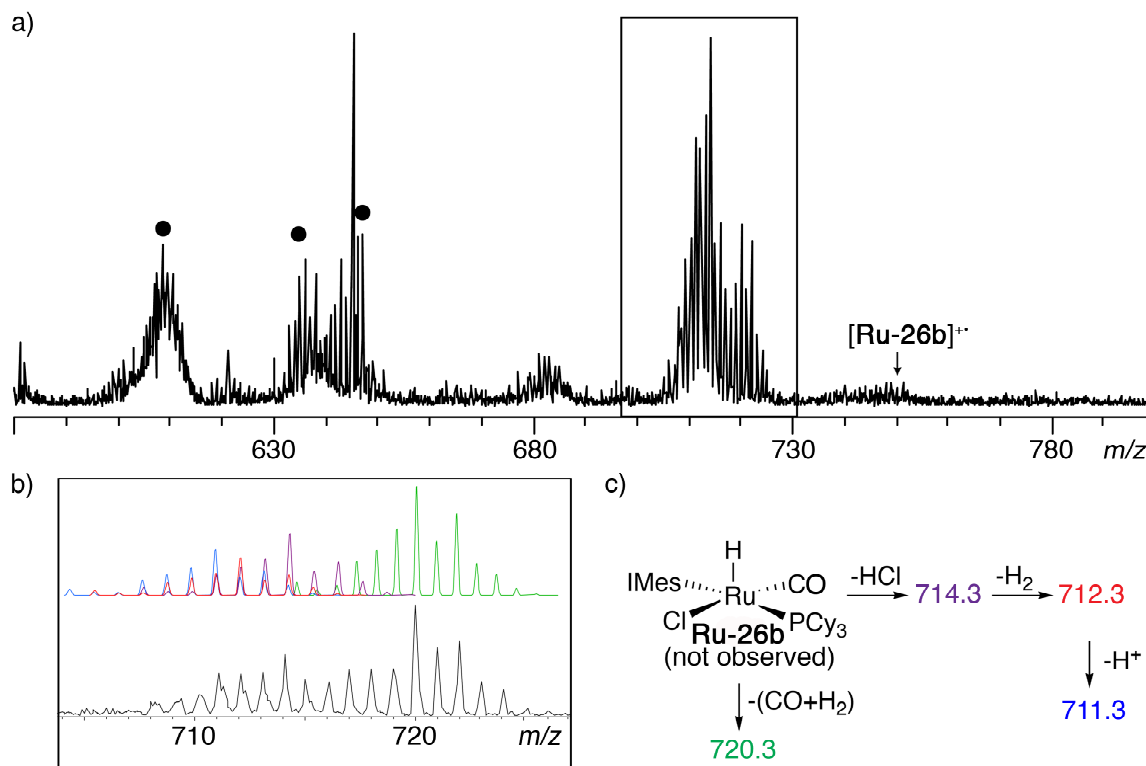


Figure 6.7. CT-MALDI mass spectrum of $\text{RuHCl}(\text{CO})(\text{IMes})(\text{PCy}_3)$ **Ru-26b** (anthracene matrix). a) Major ruthenium-containing signals: ● denotes pyrene matrix adducts; b) Simulated (top) and observed isotope patterns for boxed signals, where colors indicate fragmentation routes outlined in (c).

6.4.5 MALDI MS analysis of solid samples prepared as Nujol mulls.

The capacity to analyze solid samples by MALDI-MS is a major advantage over ESI-MS. This is essential for insoluble complexes, as well as complexes that are unstable in solution, or which differ in composition between the solution and solid state. MALDI-MS analysis of solid samples has been achieved by grinding⁴⁹ or vortex mixing⁵⁰ the sample with solid matrix. Techniques for transferring the sample to the target plate include sticking the solid powder or pressed disc (made with a press generally used for KBr IR analysis) to double-sided tape,^{50,51} pressing the powder on the plate with a spatula²⁹ or by spotting via a slurry (made up in an innocuous solvent).³⁸

The approach utilized here is drawn from the dominant sample preparation method used in IR analysis: that is, preparation of a Nujol mull by grinding the matrix and analyte with a drop of paraffin oil to promote mixing, and applying a thin layer of the amorphous mull to the target plate using a rubber policeman. This preparation method is less time-intensive than some of those outlined above. Increased laser power is generally required (perhaps because the amorphous nature of the mull, as compared to a co-crystallized mixture of analyte and matrix, impedes desorption), but high-quality spectra can nevertheless be obtained. Analysis of methyldiene **Ru-2a** by this method yields a spectrum essentially identical to that observed using the conventional solution preparation method (Figure 6.9a, cf. Figure 6.5b for solution-state analysis).

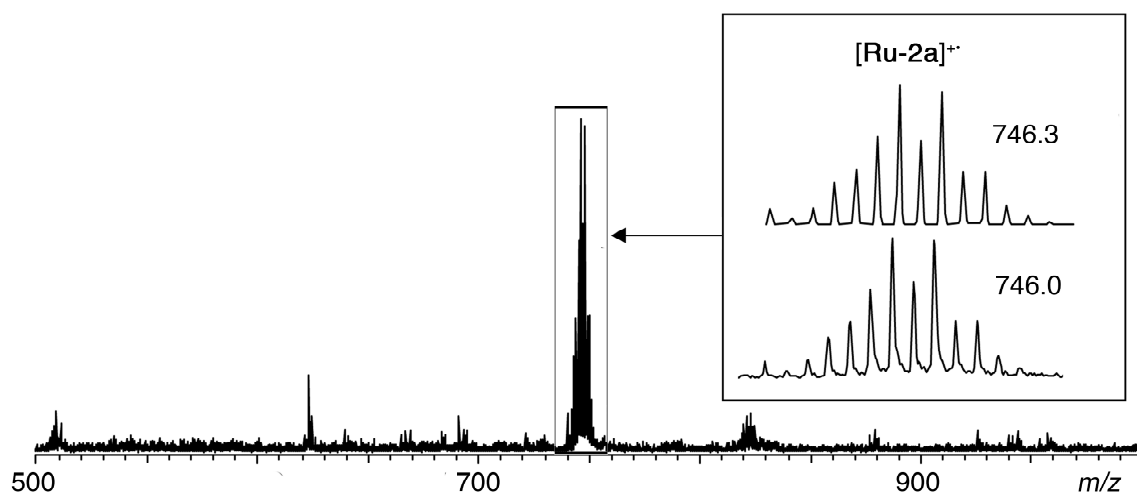


Figure 6.8. CT-MALDI MS analysis of Ru alkylidene catalyst **Ru-2a**, made up as a Nujol mull. Matrix: anthracene.

6.4.6 Accuracy of signal integration for quantification of species ratios.

Quantitative assessment would be highly valuable in applying MALDI MS to the evaluation of reaction rates (*vide infra*). As noted in Section 6.2, the heterogeneity of the crystalline sample spots hinders shot-to-shot reproducibility, and hence quantitative analysis.⁴⁸ Also an issue, however, are differences in ionization efficiency for the different species present. MALDI ionization is not well understood, but is thought to depend on multiple factors, including the relative ionization potentials of the matrix and analyte,⁴³ sample crystallinity,⁵²

and the ratio of matrix to analyte.²³ Different response factors can be anticipated for different species. We considered the possibility that the greater homogeneity achieved in the present system, in which crystallization is limited by the volatility of the solvents (or eliminated, in the case of the Nujol mulls), could permit the construction of calibration curves that could be used to correct for the difference in response factors. We therefore devised a study to answer two questions: (1) Does solution concentration correlate linearly with the integrated MALDI $[M]^{+}$ (and fragment) signal(s), and (2) Do structurally similar complexes (such as **Ru-2a** and **Ru-1a**) exhibit similar ionization efficiencies?

Experiments designed to examine these points utilized samples of the first-generation benzylidene complex **Ru-1a**, and its methylidene analogue **Ru-2a**. Solutions were prepared in which the concentration of **Ru-2a** was held constant at 20 mM, and **Ru-1a** was added in concentrations of 5-50 mM. Each sample was analyzed after mixing these solutions with pyrene or anthracene matrix. The integrated ratio of the signals for **Ru-2a:Ru-1a** (for **Ru-1a**, the sum of $[M]^{+}$, $[M-Cl]^{+}$, $[M-PCy_3]^{+}$ and $[M-PCy_3-Cl]^{+}$ was used) was plotted against the **Ru-2a:Ru-1a** molar ratio in solution.

A crude linear relationship exists between the relative intensities of the signals for **Ru-1a** and **Ru-2a**, and the solution concentrations of these two species (Figure 6.9b), for spectra obtained using both PAH matrices. Almost invariably, however, integration of the signal for **Ru-2a** overestimates the amount of the methylidene complex present. The greatest deviation was found for a 1:1 **Ru-1a:Ru-2a**, for which integration would imply a 4:1 mixture (Figure 6.10a). Clearly, changing the benzylidene phenyl group for a proton to form a methylidene species has a dramatic effect on gas-phase ionization efficiency.

These experiments demonstrate that a semi-quantitative assessment of the proportions of metal species in solution can be gleaned from the MALDI data. While further improvements will undoubtedly add to the scope and rigour of the method, these data can provide useful insight into ligand coordination, catalyst conscription, formation of resting state species, and the onset of decomposition. Each of these will be discussed in detail in the following section (Section 6.5).

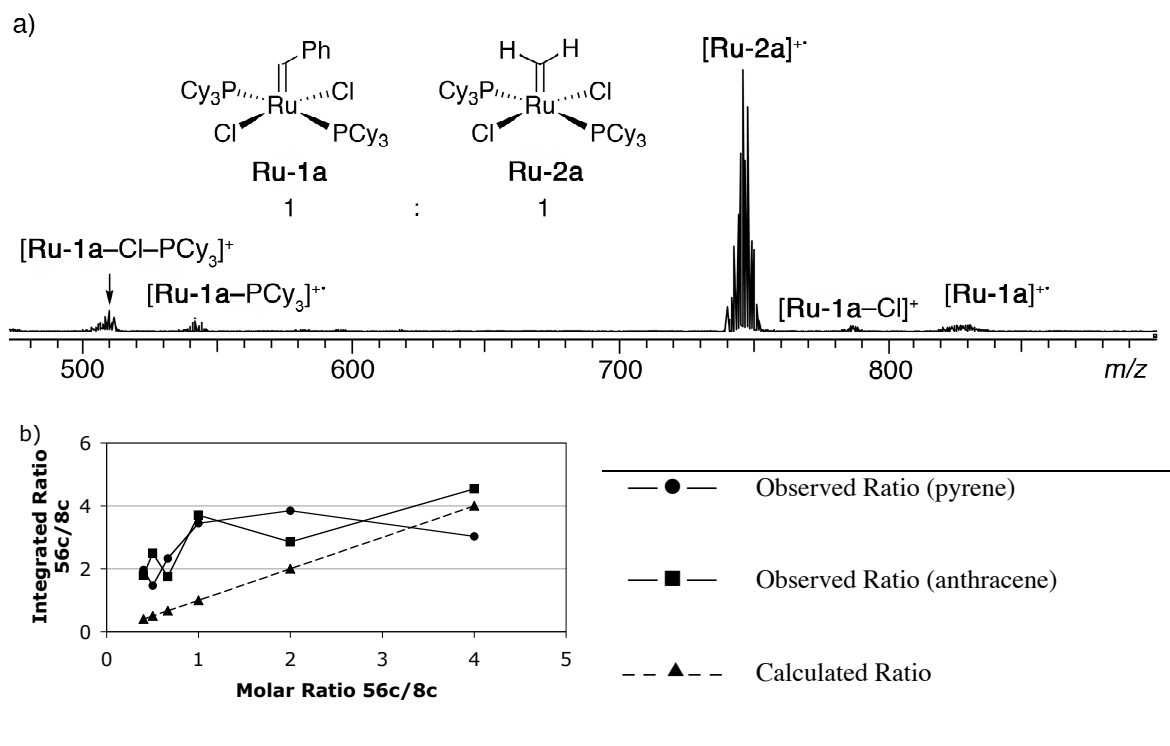


Figure 6.9. Relative MALDI MS response of benzylidene **Ru-1a** and methylidene **Ru-2a**. a) Mass spectrum **Ru-1a** and **Ru-2a** present in equal proportions (20 mM in C₆H₆); b) Observed ratio of integrated signals for **Ru-2a** and **Ru-1a** relative to calculated molar ratios. Matrix = pyrene.

6.5 "Operando" MALDI MS: In situ transformations of ruthenium metathesis catalysts.

These studies examined the evolution in catalyst structure of the first- and second-generation Grubbs catalysts **Ru-1a** and **Ru-1c**, and the Hoveyda catalyst **Ru-4c**, during RCM of benchmark substrates diethyl diallylmalonate **1** and its 2-methylallyl analogue **2**. While **1** is readily cyclized, the higher substitution of the olefinic units in **2** poses a greater challenge. Subsequent studies with the second-generation catalyst **Ru-1b** focused on in situ transformations of the catalyst under a variety of metathesis conditions and substrates. Decomposition was probed during RCM with ether and sulfide substrates. In the context of

tandem metathesis-isomerization catalysis, the efficacy of added K_2CO_3 in transforming metathesis-active **Ru-1b** into a ruthenium hydride target was explored. A final study evaluated the utility of MALDI-MS analysis in assessing catalyst quenching during RCM macrocyclization of lactone **8**.

6.5.1 Methodology.

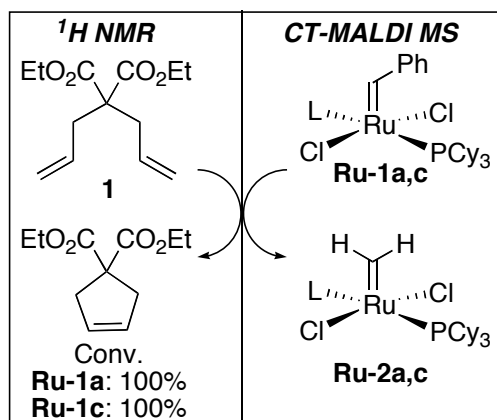
The fate of **Ru-1a-c** under catalytic conditions was examined by removing aliquots from reactions in progress, mixing them with matrix, and immediately spotting them on the target plate for CT-MALDI mass spectrometric analysis (Chapter 2, Section 2.1.8). RCM of **1/2** by **Ru-1a**, **Ru-1c** or **Ru-4c** was analyzed immediately after substrate addition, and again after selected time intervals (1, 4 and 24 h). Control reactions where substrate was not added were performed under identical conditions and analyzed in the same manner. Identification of matrix adducts was facilitated by analyzing each sample with both pyrene and anthracene as the matrix.

For all substrates, except lactone **8**, consumption of diene and formation of the RCM product were quantified by 1H NMR, as discussed in Chapter 2, Section 2.10.3. For **8**, consumption of diene and formation of the RCM product was quantified by GC-FID (Chapter 2, Section 2.10.3): here NMR analysis is misleading, owing to formation of oligomers.⁵³ In the case of **8**, the proportion of oligomer was also quantified.

6.5.2 RCM of diethyl diallyl malonate **1** with **Ru-1a**, **Ru-1c**.

RCM of the benchmark substrate diethyl diallylmalonate **1** was monitored by MALDI-MS to examine the information thus accessible. The first- or second-generation Grubbs catalyst, **Ru-1a** or **Ru-1c**, was added to a solution of **1** in CH_2Cl_2 , and heated for 1 h at 40 °C. Complete conversion of **1** was confirmed by 1H NMR analysis (Scheme 6.1). The expected conversion of the benzylidene to the corresponding methylidene species was readily observed by MALDI MS: in all cases, the spectra are dominated by signals for the methylidene complexes **Ru-2a** or **Ru-2c** (Figure 6.11). Neither the metallocyclobutane intermediate nor the four-coordinate transition state was observed. While the high ionization

efficiency of **Ru-2a** relative to **Ru-1a** (see the semi-quantitative nature of MALDI discussed above) exaggerates the apparent yield of **Ru-2a** and **Ru-2c**, this study indicates that MALDI-MS can be used to monitor catalyst transformations under real catalytic conditions. Key advantages (over, e.g., NMR analysis) are the ease of detecting the metal species without interference by excess substrate, and use of "real" reaction conditions, including standard, low catalyst concentrations, rather than conditions modified to facilitate NMR analysis.



Scheme 6.1. RCM of **1** by **Ru-1a/c**. Organic constituents (left) are analyzed by ¹H NMR and organometallic species (right) by CT-MALDI MS. Conditions: 100 mM **1**, 5 mol% **Ru-1a,c** in CH₂Cl₂ at 40 °C.

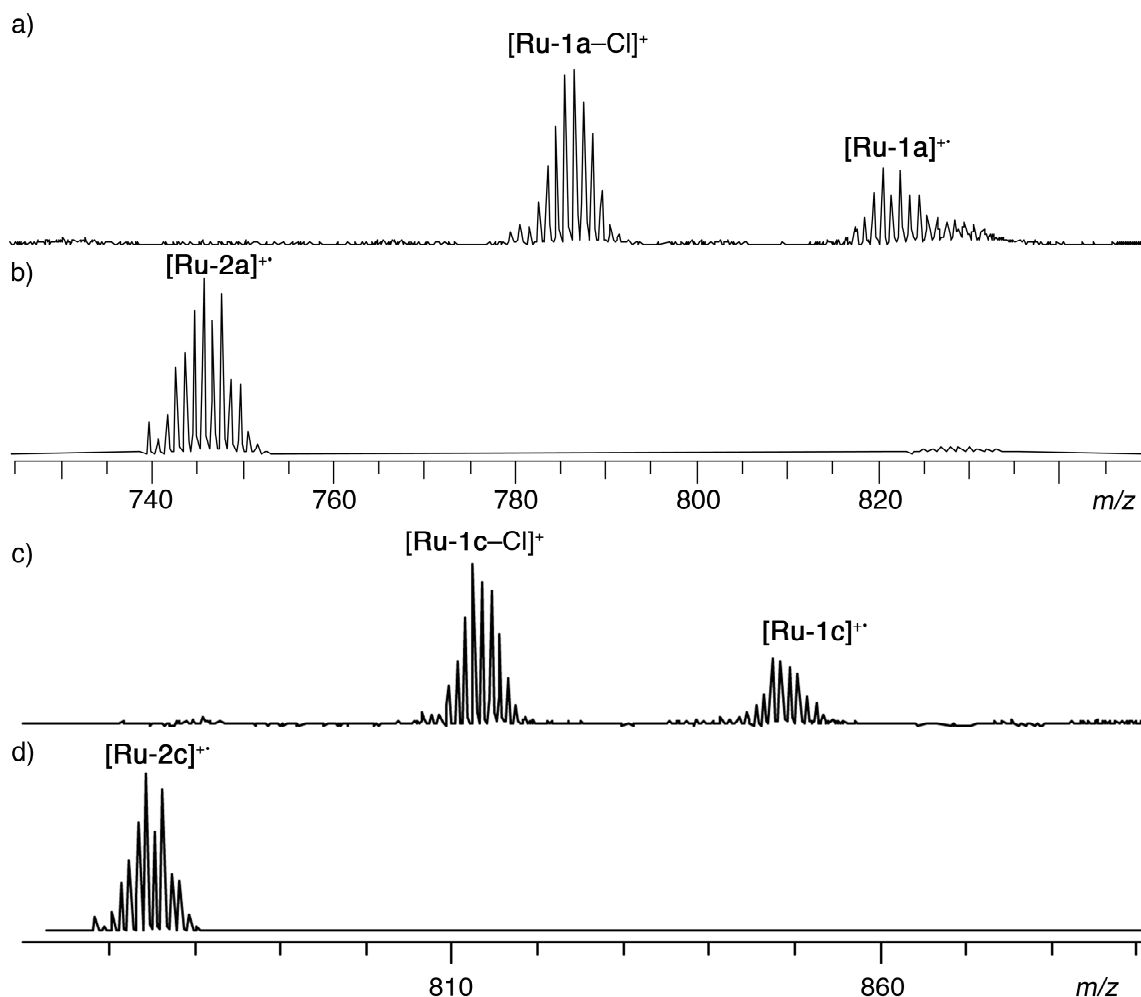


Figure 6.10. In situ transformation of the benzylidene complex to the methylidene resting state during RCM of **1** at 40 °C after 1 h. a) Isolated **Ru-1a** in the absence of **1**; b) Conversion of **Ru-1a** to **Ru-2a**; c) Isolated **Ru-1c** in the absence of **1**; d) conversion of **Ru-1c** to **Ru-2c**. Conditions: 5 mol% **Ru-1a/c**, CH_2Cl_2 .

For comparison, a parallel set of reactions was carried out at ambient temperatures (25 °C in CH_2Cl_2), to evaluate the thermal barrier to RCM. For this experiment, readily-cyclized **1** was again chosen as substrate. The MALDI spectra are dramatically different from those observed at 40 °C. While RCM with **Ru-1a** likewise results in formation of **Ru-2a** as the dominant ruthenium species within 1 h (Figure 6.12a), second-generation **Ru-1c** is only partially converted to **Ru-2c** in either CH_2Cl_2 or C_6H_6 after the same period (Figure 6.12b, c). A higher barrier to phosphine loss in **Ru-1c** than in **Ru-1a** has been reported for experiments

carried out in the absence of substrate.⁴⁷ While the low turnover efficiency of **Ru-1c** is deduced from (e.g.) ROMP studies,^{*1} the present work provides the first direct evidence for the limited conscription of **Ru-1c**, vs. **Ru-1a** – even with a very readily cyclized RCM substrate – into the catalytic cycle at room temperature.

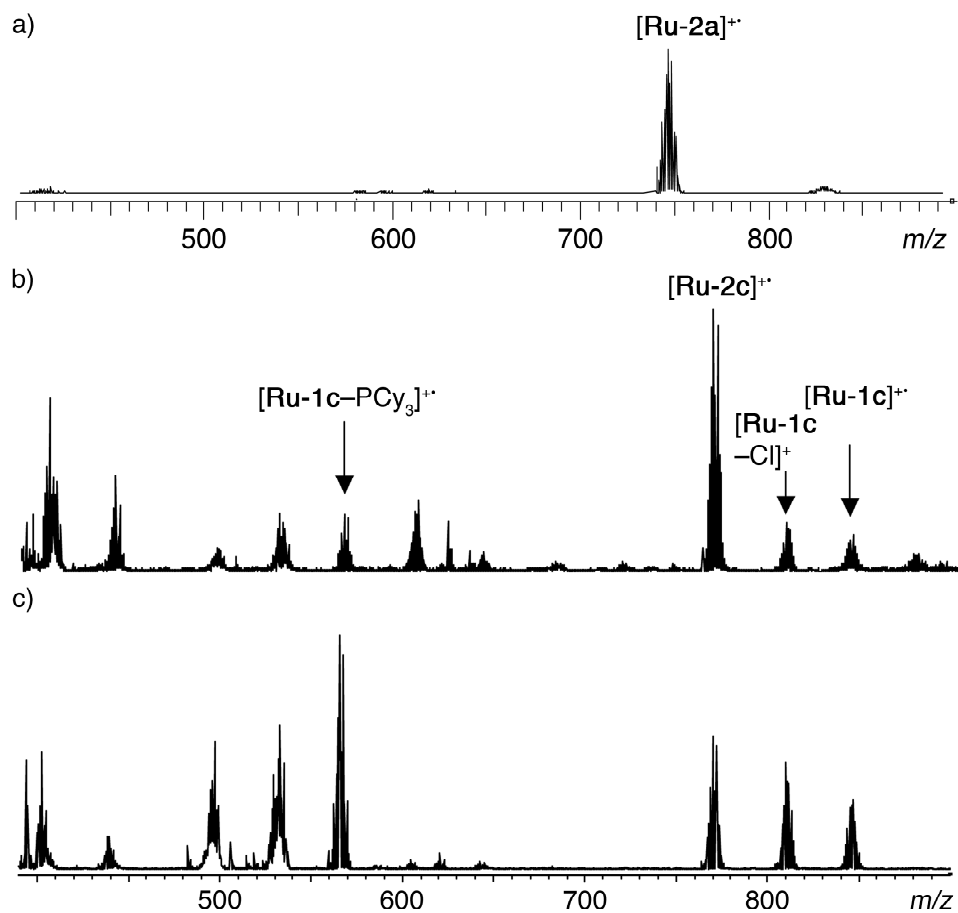


Figure 6.11. In situ transformation of benzylidene precatalysts into their methyldiene resting states during RCM of **1** at 25 °C after 1 h. a) Formation of **Ru-2a** from **Ru-1a** in CH_2Cl_2 ; b) conversion of **Ru-2c** from **Ru-1c** in CH_2Cl_2 ; c) conversion of **Ru-2c** from **Ru-1c** in C_6H_6 .

* Catalyst initiation is readily quantified by ROMP studies by comparing the integrated intensity of the signal for the benzylidene initiator against that the Ru-alkylidene endgroup on the growing polymer chain. This reports on catalyst conscription (as does the average chain length of the polymers), but offers minimal insight into the structure of the Ru endgroup, owing to the relatively low proportion of the latter, and overlap with signals for the growing polymer chain.

6.5.3 RCM of diethyl 2,2-bis(2-methylallyl) malonate **2** with **Ru-1a**, **Ru-1b** and **Ru-4c**.

Metathetical synthesis of tetrasubstituted olefins is highly challenging, and few of the catalysts developed to date are capable of effecting quantitative conversion at low loadings.^{54,55} The most successful ruthenium catalysts used to date have small NHC ligands; the poor reactivity of **Ru-1a** and **Ru-1c** toward tri- and tetra-substituted dienes is thus presumed to be steric in origin. We opted to probe reaction of diethyl 2,2-bis(2-methylallyl) malonate **2** with common metathesis catalysts **Ru-1a**, **Ru-1b** and **Ru-4c**, to establish whether new insights can be gained by directly interrogating the metal complexes during catalysis.

Consistent with earlier reports,⁵⁶ treatment of tetrasubstituted diene **2** with first-generation catalyst **Ru-1a** results in no product formation over 1 h at 40 °C in CD₂Cl₂, or 80 °C in C₇D₈ (¹H NMR analysis; Figure 6.13). The MALDI mass spectrum of the 40 °C sample is dominated by signals for the benzylidene precatalyst **Ru-1a**, with a very small signal for **Ru-2a**. In the 80 °C reactions, only decomposition products were visible (Figure 6.13b), and a control experiment in which benzylidene **Ru-1a** was heated to 80 °C *without* substrate revealed identical signals, indicating that **Ru-1a** itself is the vector for decomposition. It should be recognized that this behaviour reflects not the greater stability of the methyldiene resting state, but the minimal extent to which **Ru-1a** has undergone reaction and turnover with **2**. Thus, RCM to form tetrasubstituted olefins via the first-generation catalyst **Ru-1a** is limited by the low reactivity of the benzylidene species. We presume that the high activation energy to diene coordination, or possibly formation of the metallocyclobutane intermediate, inhibits RCM at 40 °C, while the poor thermal stability of **Ru-1a** prevents conversion under more forcing conditions.

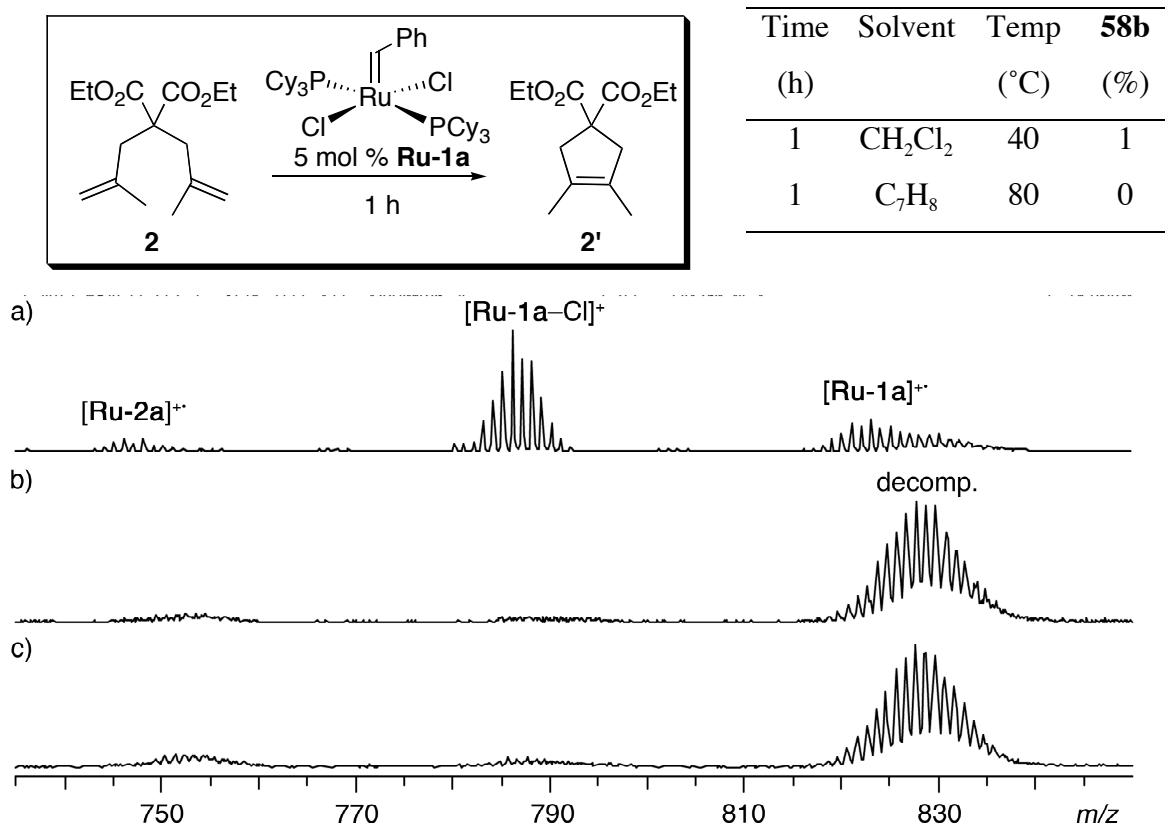


Figure 6.12. Decomposition of benzylidene **Ru-1a** during the formation of tetrasubstituted olefin **2'** from **2**. Reactions evaluated after 1 h in a) CH₂Cl₂ at 40 °C; b) toluene at 80 °C; c) without **2** in toluene at 80 °C. Table provides %RCM product formed as determined by ¹H NMR spectroscopy.

Identical "decomposed **Ru-1a**" signals appear at 40 °C on longer reaction time (4 h), indicating that the window for deactivation is not simply thermal, but temporal. Again, identical signals are observed in the presence or absence of substrate **2** (see Appendix A for additional spectra). As well as the signal highlighted in Figure 6.12 (at m/z 827.5), three additional signals are observed in all cases, at m/z 863.5, 1318.1 and 1353.1 (Figure 6.14). Of these, the signal at m/z 863.5 shows a good isotope-pattern match for dimeric $[\text{Ru}_2(\text{CH})_2\text{Cl}_2\text{PCy}_3)_2+2\text{H}]^+$. Loss of a chloride produces the signal at 827.5, the isotopic distribution of which is less informative, likely due to an overlapping signal for loss (or addition) of a proton. Distinctions in the isotopic distribution are minimal for the two higher-mass species: these are assigned to ruthenium trimers based on their m/z values. The trimeric

species are related to the dimers by loss of a $[\text{RuH}_2\text{Cl}_2(\text{PCy}_3)]^+$ fragment. It remains unclear whether the dimer and trimer are present in solution, or whether they are generated in gas-phase chemistry. It is clear, however, that the benzylidene functionality is cleaved during decomposition.

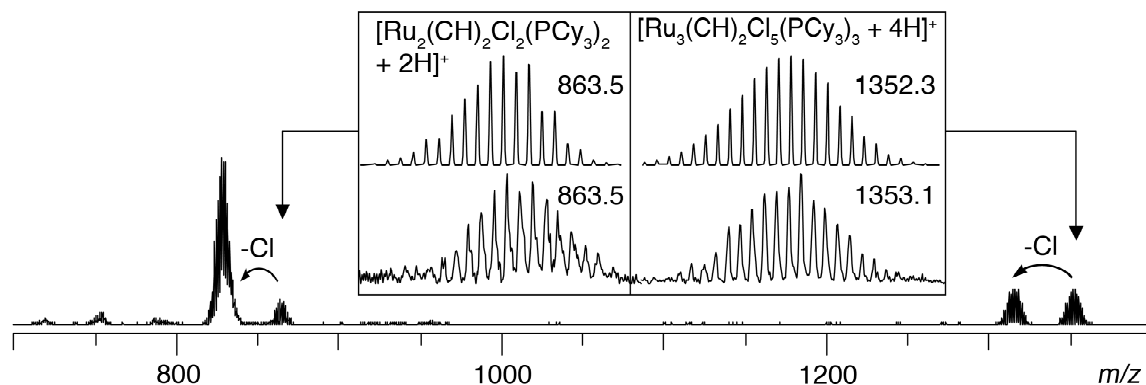


Figure 6.13. Trimeric and dimeric decomposition of **Ru-1a** after heating to 80 °C for 1 h in toluene.

Treatment of tetrasubstituted olefin **2** with second-generation benzylidene **Ru-1c** at 40 °C yielded 14% RCM after 1 h in CH_2Cl_2 and 23% after 24 h. CT-MALDI MS of the 1 h sample is remarkably clean, revealing only a signal for the methyldiene complex **Ru-2c** (Figure 6.14a). Signals due to decomposition products emerge at 24 h (Appendix A, Figure A.11), over which time only ca. 10% further conversion was observed. This contrasts with the behaviour of **Ru-1a**, indicating that in the H_2IMes system, it is the methyldiene species **Ru-2c** that lacks sufficient reactivity to form the tetrasubstituted olefin **58b**, not the inability of the benzylidene precursor to undergo initial reaction with **2**. Product formation increases minimally on raising the temperature to 80 °C in toluene: a maximum conversion of 32% was achieved after 1 h, after which conversion plateaus. MALDI MS analysis of the 1 h sample shows no evidence for **Ru-2c**; a minor signal for $[\text{Ru-1c-Cl}]^+$ indicates that the benzylidene is present, along with significant decomposition (Figure 6.15b). In a control reaction under the same conditions but in the absence of substrate, minimal decomposition of **Ru-1c** is observed, implying that the substrate (i.e. via the methyldiene species) mediates decomposition in this case (Figure 6.15c). The timescale of decomposition is consistent with

the reported half-life of ca. 6 h (55 °C, benzene) reported for methyldiene **Ru-2c** in an earlier NMR study in the absence of substrate.⁵⁷

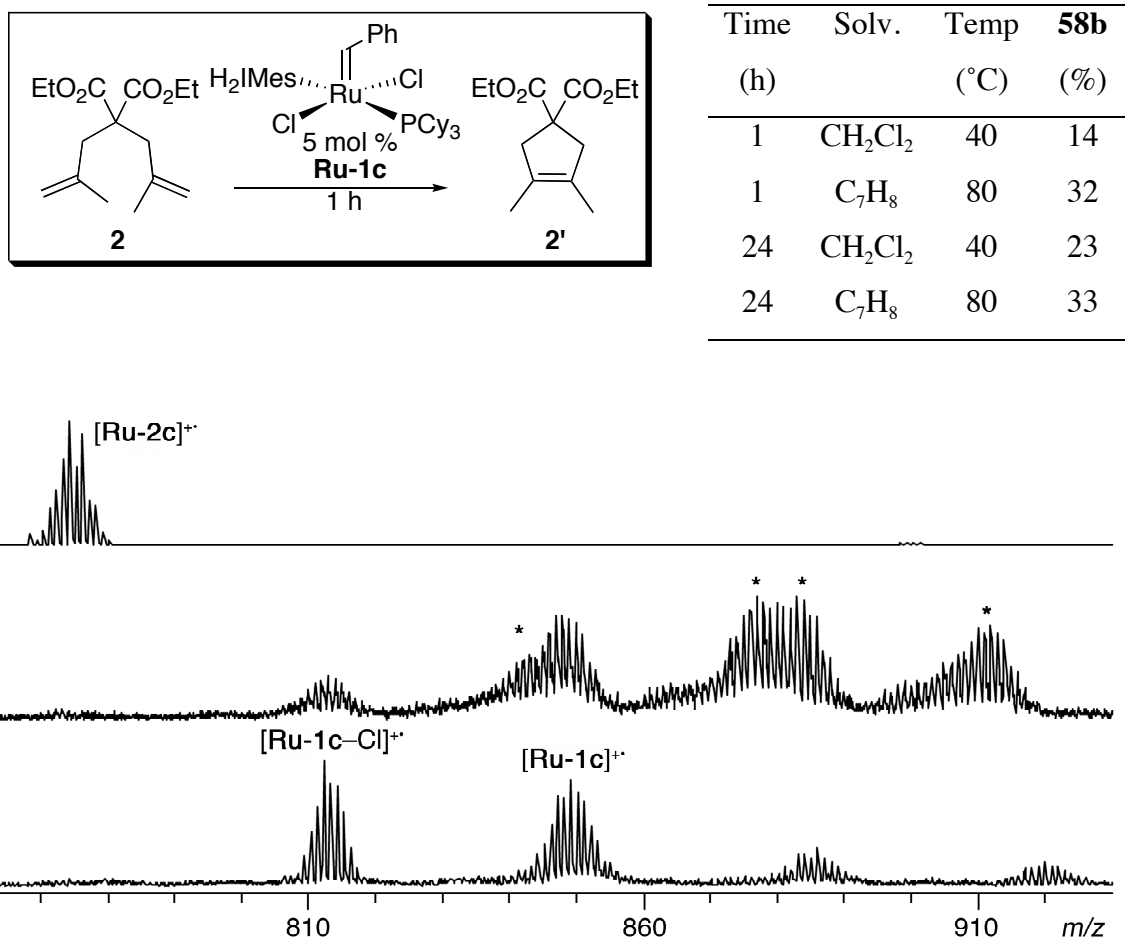


Figure 6.14. Decomposition resulting from reaction of **Ru-1c** with tetrasubstituted olefin **2**. Reactions evaluated after 1 h in a) CH₂Cl₂ at 40 °C; b) toluene at 80 °C; c) without **2**, toluene at 80 °C. The Table shows %RCM product formed as determined by ¹H NMR spectroscopy. [*] Denotes decomposition products.

The data above reveal that it is the stability of the methyldiene intermediate that defines the thermal window for operation using the second-generation Grubbs catalysts, and that the thermal stability of its benzylidene precursor **Ru-1c** is largely immaterial. This is consistent with earlier studies by Grubbs in the presence of the model substrate ethylene.⁵⁷ The contrast in these data to the first-generation catalyst **Ru-1a** underscores the vulnerability of the latter. MALDI MS facilitates pinpointing the timescale and conditions under which

catalyst decomposition occurs, without NMR-imposed restrictions on diamagnetism, solvent scope, concentration, or interference by substrate/product signals.

Literature reports indicate that styrenyl ether catalyst **Ru-4c** effects <10% conversion of the challenging diene **2** under mild conditions even after 4 days (Figure 6.15).^{59,60} At 60 °C, reaction can be induced, but at 5 mol% **Ru-4c** in C₆D₆, a maximum conversion of 30% is reached: on raising the temperature to 70 °C in toluene, 58% conversion is found at 14 h.^{54,59} We monitored the behaviour of **Ru-4c** under similar conditions by MALDI MS; analysis was carried out following reaction at 40 °C in CH₂Cl₂ or at 80 °C in toluene (conditions identical to those used above with **Ru-1a** and **Ru-1c**). Under none of these conditions, with either **2** or the related, readily cyclized substrate **1**, is transformation of **Ru-4c** into its methyldene derivative observed (Appendix A, Figures A.13 and A.14). It may be noted that the active, four-coordinate, methyldene species also goes unobserved with first- or second-generation **Ru-1a** or **Ru-1c**; instead, the PCy₃-stabilized resting state is seen. At 80 °C, decomposition of **Ru-4c** is evident by MALDI MS analysis after just 4 h; these signals dominate the spectrum after 24 h (Figure 6.16). Under identical conditions, but in the absence of **2**, no such signals are present: this suggests that decomposition proceeds through the four-coordinate, Ru-methyldene active catalyst. Hoveyda has proposed that during metathesis of **Ru-4c**, the methyldene complex is trapped and stabilized via recapture by CM with the styrenyl ether coproduct, and that the precatalyst is thus regenerated.^{61,62} While recapture may be occurring here, the evidence for decomposition at 80 °C suggests that it does not compete with the rate of decomposition. This suggests that the high performance of **Ru-4c** observed in other applications (e.g. RCM of vinylic dienes to form the usual disubstituted olefins) is most likely a consequence of slow conscription (which maintains a reservoir of precatalyst), rather than recapture of the styrenyl ether.

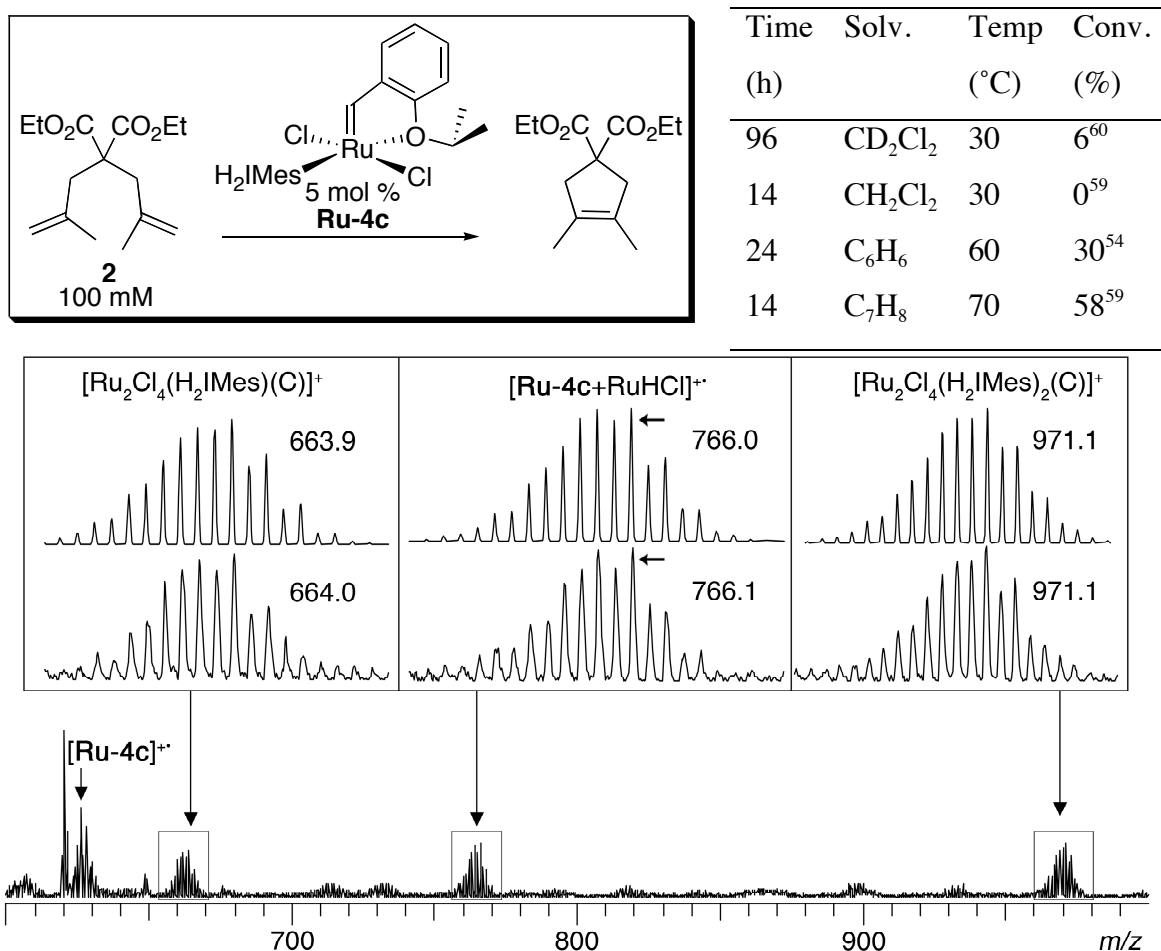


Figure 6.15. Decomposition of **Ru-4c** to a diruthenium species following reaction with **2**. CT-MALDI mass spectrum of this reaction, acquired after 24 h in toluene at 80 °C. The Table shows %RCM product, determined by ¹H NMR spectroscopy.

Decomposition of **Ru-4c** in the reactions above results in the emergence of three dominant MALDI-MS signals, at m/z 971.1, 766.1 and 664.0 (Figure 6.16). These differ from the three species seen in decomposition of the first-generation catalyst. The highest-mass signal is assigned to a methyldiene dimer $[\text{Ru}_2\text{Cl}_4(\text{H}_2\text{IMes})_2(=\text{CH}_2)]^+$, which on gas-phase loss of an NHC ligand and H^+ affords $[\text{Ru}_2\text{Cl}_4(\text{H}_2\text{IMes})(=\text{CH})]^{++}$ (m/z 664.0). The third species (m/z 766.1) contains a styrenyl ether moiety, as judged from its isotope pattern and exact mass, which exhibit an excellent match for $[\text{Ru}_2\text{Cl}_3(\text{IMes})(\text{CHPhO}^i\text{Pr})+\text{H}]^{++}$ or $[\text{Ru-4c}+\text{RuHCl}]^{++}$. Any reasonable structure for these three species contains one or two low-coordinate ruthenium centres, indicating that they arise from gas-phase fragmentation. All might

plausibly be fragments of one unstable parent dimer (m/z 1118) generated by reaction of **Ru-4c** with the four-coordinate methyldiene. Such an initial reaction is strongly suggested by the presence of the styrenyl ether moiety in the species found at m/z 766.1. Structural confirmation of the proposed dimeric decomposition product through complementary analytical methods is desirable.

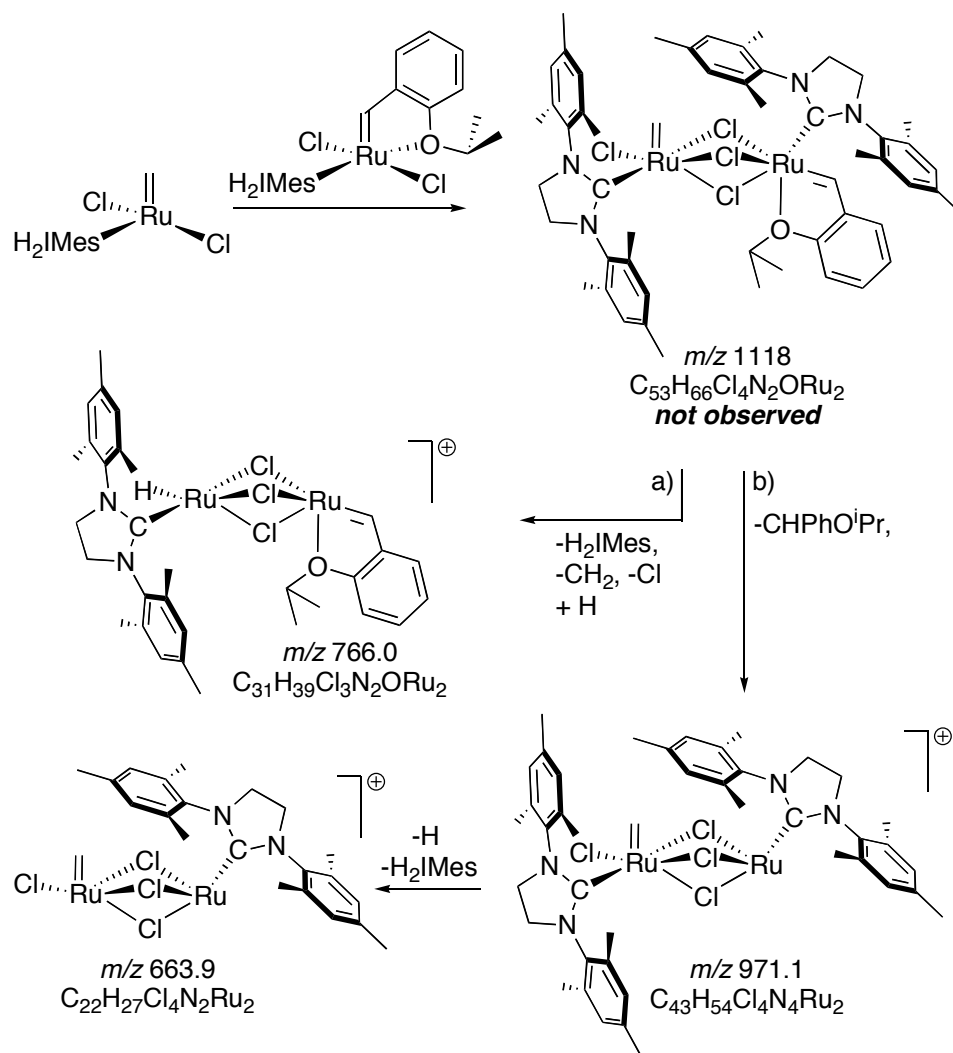


Figure 6.16. Proposed decomposition of **Ru-4c** based on MALDI MS evidence. Fragmentation of the dimeric decomposition species proceeds through a) loss of H₂IMes, CH₂ and HCl or b) loss of the styrenyl ether functionality followed by loss of an NHC.

The preceding study emphasizes the major opportunities that MALDI-MS offers as a guide to reaction chemistry. The MS data give direct insight into the specific conditions associated

with the onset of decomposition – in effect, in the study above, revealing the limits of force – and also offer a glimpse into the nature of the primary decomposition product (in the case of **Ru-4c**, a dimer of as-yet undetermined connectivity). These results help to delineate the experimental parameters under which detailed XRD, NMR and/or kinetic studies should be undertaken.

6.5.4 RCM of diallyl ether **12** and diallyl sulfide **13** with **Ru-1b**.

Decomposition of the Grubbs catalyst **Ru-1b** with substrates known to exhibit incompatibilities with the ruthenium catalysts was also examined. The first of these studies focused on diallyl ether and diallyl sulfide. Diallyl ether is readily cyclized by **Ru-1b**, but can also isomerize to a vinyl ether via an alternative reaction pathway.⁶³ Cross-metathesis of a related vinyl ether with a ruthenium alkylidene complex was shown to generate a Fischer carbene, which on thermolysis underwent partial transformation into a ruthenium hydride complex.⁶⁴ Such hydride species (known isomerization catalysts),⁶⁵ could account for the reported isomerization chemistry. Isomerization may likewise be an issue with diallyl sulfide **13**; as well, however, sulfides are believed to function as poisons for (in particular) soft, late-metal catalysts.^{66,67}

RCM of allyl ether **12** by second-generation catalyst **Ru-1b** (5 mol%) is complete within 15 minutes at 60 °C in C₆H₆, as judged by ¹H NMR analysis. MALDI MS spectra measured at this point indicate that the methyldiene complex **Ru-2b** is the dominant metal species: that is, catalyst recruitment is highly efficient. Given the reported susceptibility of [Ru]=CH₂ species to decomposition (**Ru-2b**, for example, has a reported half-life of ca. 6 h in benzene at 55 °C in the absence of substrate,⁵⁷ see Section 6.5.3), we were interested in examining its ensuing behaviour. Surprisingly, the methyldiene signals show no apparent change over a further hour of heating, with no evidence of decomposition to hydride species (Figure 6.18a). The thermal study of the previous Section demonstrated that methyldiene stability is low at 80 °C: a thermal threshold for deactivation thus appears to exist somewhere between 60 and 80 °C.

Any such threshold can be reduced by the operation of low-energy, substrate-induced decomposition pathways. MALDI-MS analysis of the RCM reaction of diallylsulfide **13** in

benzene reveals extensive decomposition even at 60 °C (Figure 6.18b). This behaviour is consistent with a report from the Nolan group that forcing conditions (80 °C in benzene, with 5 mol% **Ru-1b** – a rather high catalyst loading for such a readily-formed ring size) were required to effect quantitative RCM of **13**, owing to catalyst decomposition.⁶⁶ While assignment of the MALDI signals is complicated by overlap, the low proportions of benzylidene **Ru-1b** and methyldiene **Ru-2b** suggest extensive decomposition: catalyst consumption appears to have been extensive, meaning that a very small reservoir of unreacted catalyst remains to continue metathesis.

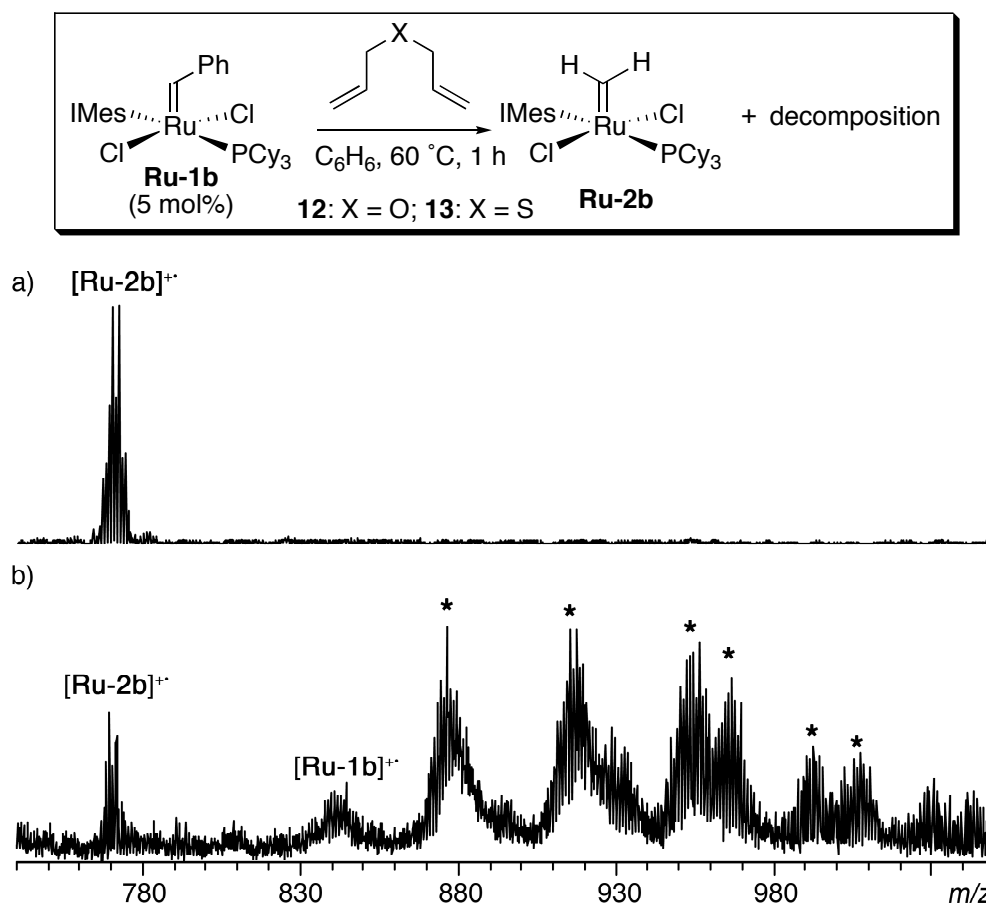


Figure 6.17. Limits of functional group tolerance of **Ru-1b**. In situ formation of a) methyldiene **Ru-2b** following reaction with 100 mM **12**; b) formation of **Ru-2b** and decomposition (*) upon reaction with 100 mM **13**.

6.5.5 In situ generation of $\text{RuHCl}(\text{CO})(\text{IMes})(\text{PCy}_3)$ from **Ru-1b** during tandem RCM-isomerization of **12** with K_2CO_3 .

Tandem catalysis offers potentially high efficiencies in performing consecutive catalytic transformations with a single catalyst dose. Following observations by Jay Conrad from the Fogg group, that in situ addition of K_2CO_3 induced isomerization of the RCM product of diallyl ether **12**, a more detailed study focusing on the catalyst identity was undertaken.

Treatment of diallyl ether **12** with 5 mol% **Ru-1b** in refluxing benzene caused complete conversion to the RCM product within 15 minutes. Solid K_2CO_3 was then added, and the reaction was heated to 65 °C for 4 h. GC-FID analysis of the organic constituents indicated complete isomerization of the RCM product **12'** to the enol **12''**. MALDI-MS analysis revealed several new signals, and complete loss of both **Ru-1b** and **Ru-2b** (Figure 6.19a). The overlapping signals between m/z 705-725 show a fragmentation pattern diagnostic for hydride **Ru-26b**, a known isomerization catalyst (Section 6.4.4, Figure 6.19b). A signal at m/z 780.3 from the reaction mixture exhibits a good isotope-pattern match with $[\text{RuCl}(\text{CO}_3)(\text{IMes})(\text{PCy}_3)\text{-H}]^+$, a potential intermediate in the conversion of **Ru-2b** to **Ru-26b**. This possibility is supported by a decrease in intensity of this signal relative to those for **Ru-26b** over 48 h.

A control reaction with diethyl diallylmalonate **1** was undertaken to assess hydride formation with a substrate not prone to isomerization, under conditions otherwise identical to those above. Signals for hydride **Ru-26b** were accompanied by others consistent with decomposition of the methylidene **Ru-2b**. This suggests that the conversion of **Ru-1b** and/or **Ru-2b** into hydride **Ru-26b** originally observed is due not simply to reaction with K_2CO_3 , but to the presence of both the carbonate and the diallyl ether substrate. The limited scope of K_2CO_3 as a trigger for this transformation inhibits its utility in tandem metathesis-isomerization catalysis. This finding was corroborated by NMR studies by Nicholas Beach from the Fogg group, which found poor conversion to **Ru-2b** with K_2CO_3 , even in the presence of MeOH.

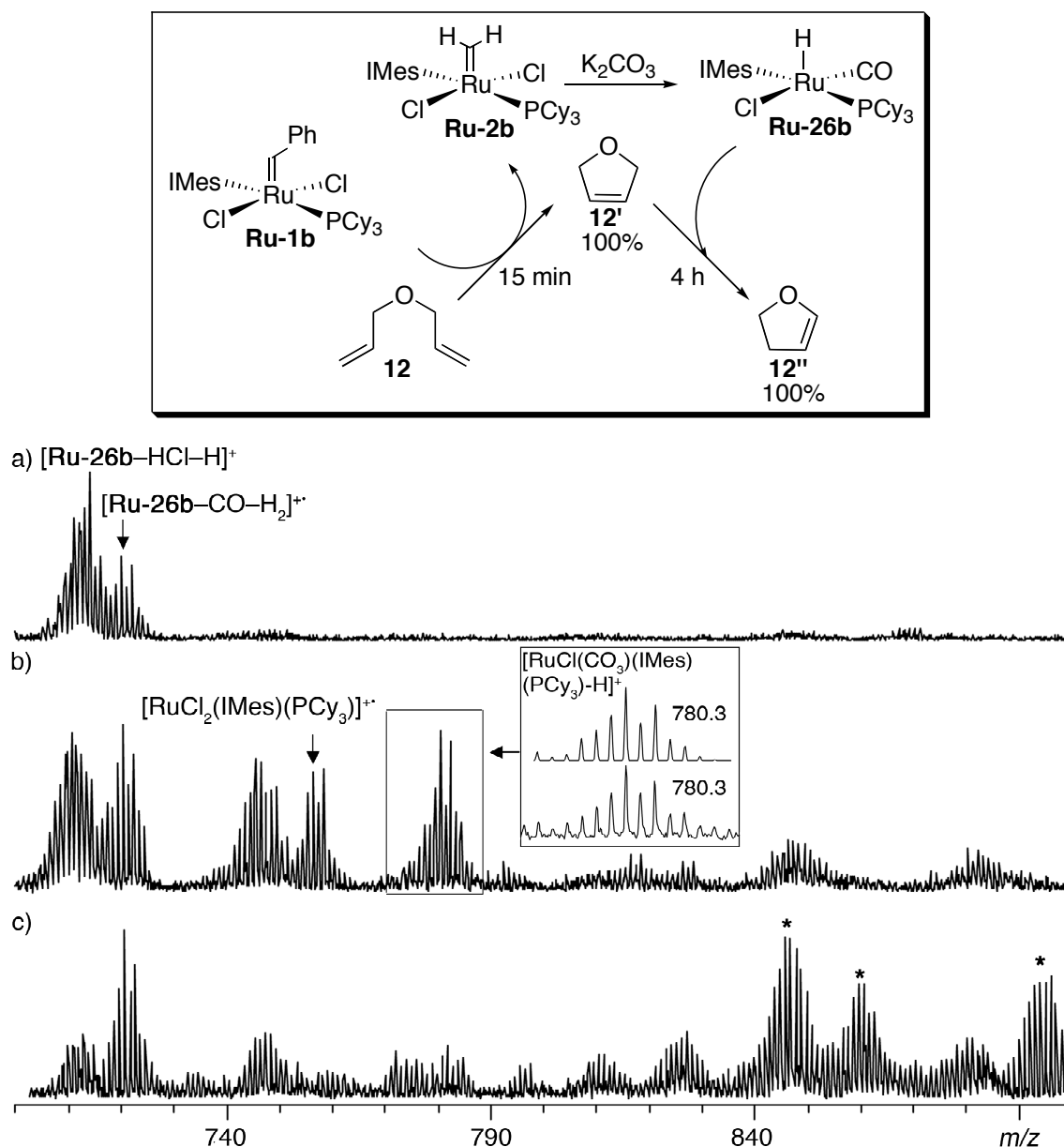


Figure 6.18. Observation of hydride **Ru-26b** during a RCM-isomerization. CT-MALDI mass spectra of a) an authentic sample of **Ru-26b**; b) In situ formation of **Ru-26b** from **Ru-1b** in the presence of diallyl ether **12** and K₂CO₃; c) **Ru-1b** in the presence of diethyl diallylmalonate **1** and K₂CO₃.

6.5.6 Quenching **Ru-1b** with KTp **31** during RCM of lactone **8**.

Chapter 5 (Section 5.2) described the development of a high-throughput quenching protocol that permitted monitoring of HT reactions mediated by a range of ruthenium metathesis catalysts. In particular, KTp **31** proved effective in rapidly and completely arresting catalyst

activity. A post-quenching MALDI-MS study was carried out on the RCM reaction of lactone **8** with **Ru-1b**. No remaining **Ru-1b** was observed, nor was the corresponding methyldiene **Ru-2b**; rather, the major signal is due to $[\text{Ru}(\text{Tp})(\text{IMes})\text{-H}]^+$ (Figure 6.20). Not seen are the expected molecular ions for the known Tp derivative of **Ru-1b**, $[\text{RuCl}(\text{Tp})(\text{IMes})(=\text{CHPh})]^{++}$ (m/z 743), or the corresponding species derived from **Ru-2b**; i.e. $[\text{RuCl}(\text{Tp})(\text{IMes})(=\text{CH}_2)]^{++}$ (m/z 667). The major signal confirms coordination of the Tp ligand to the active catalyst, and we initially presumed that it arises from $[\text{RuCl}(\text{Tp})(\text{IMes})(=\text{CH}_2)]^{++}$ by loss of chloride and the methyldiene, as well as a proton. It may be noted, however, that no such fragmentation pathway emerged in studies of **Ru-2b** itself, while work from several research groups (notably those of Diver,⁶⁸⁻⁷⁰ Johnson,⁷¹ and Piers⁷²) have demonstrated that the alkylidene becomes more susceptible to undesired, non-metathetical reactions when the Ru center is less electron-rich.

Notable in this context is detailed work by Diver describing Buchner insertion of C_α into an adjacent IMes aryl group, promoted by coordination of π -acids trans to the methyldiene or benzyldiene functionality. Intriguingly, a preliminary NMR study of the reaction of preformed **Ru-2a** with Tp, carried out by Justin Lummiss of this research group, reveals immediate loss of signals due to the methyldiene functionality. A more comprehensive study is clearly warranted: specific features worth examining are whether Tp coordination induces Buchner insertion; as well, identification of the Ru species present prior to quenching would establish whether reaction proceeds via the benzyldiene or the methyldiene complex.

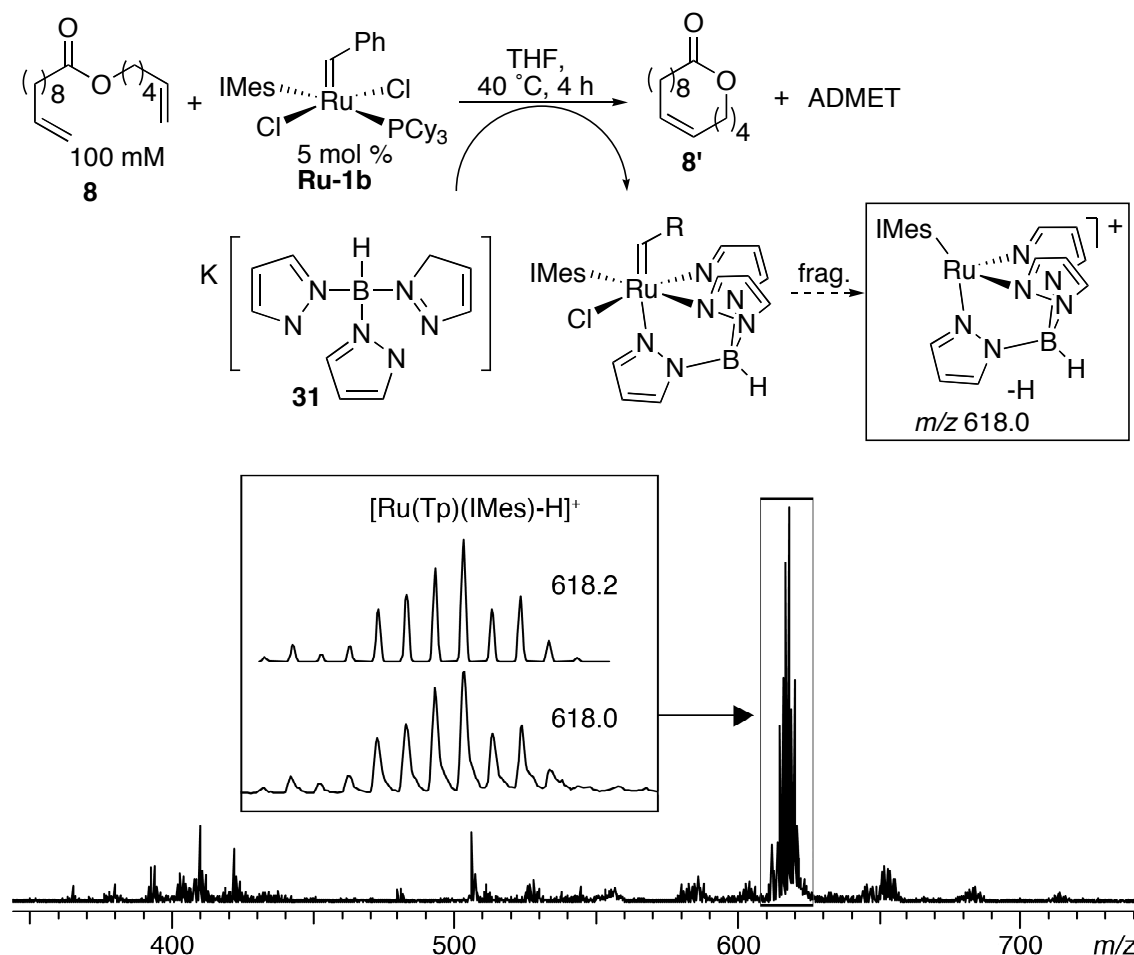


Figure 6.19. Quenched **Ru-1b/Ru-2b** following addition of KTp **31** during reaction with lactone **8**. R = H or Ph, depending if **31** trapped **Ru-2b** or **Ru-1b**.

6.6 Conclusion.

The foregoing describes important advances in the application of MALDI mass spectrometry to analysis of organometallic and inorganic complexes, including reactive transition-metal catalysts. A key breakthrough was the identification of matrices that ionize via charge transfer, rather than protonation, of the analyte. In conjunction with anaerobic sample preparation and introduction, this enabled observation of the intact radical molecular cations for a number of highly reactive, and highly air-sensitive, complexes. Representative examples were presented to showcase the capacity of the technique to cope with coordinatively and electronically unsaturated species, many of which exhibit an excellent match between simulated and observed isotope patterns for $[M]^{+•}$. Where a labile ligand is

present, $[M-L]^{+}$ signals may be observed as the highest-mass peaks, but the core structure can be identified without difficulty. MALDI-MS analysis is highly complementary with NMR methods: NMR analysis typically supports observation of the neutral ligands and evaluation of their number, but often does not enable observation of anionic ligands, such as the halides, and does not give information about the "global nature" of the complexes. Remaining challenges in CT-MALDI ionization include the identification of neutral molecules in their highest oxidation states, observation of which requires the presence of an easily oxidized functionality, or a readily lost anionic ligand. Also valuable would be identification of matrices that promote one-electron reduction of the analyte to afford a radical molecular *anion*, observable in negative-electron mode. Five-coordinate ruthenium hydrides also present problems: it would be worthwhile to clarify whether this is also true for coordinatively saturated hydrides such as $RuHCl(dppe)_2$ ($dppe = 1,2$ -bis(diphenylphosphino)ethane).

These methodologies were extended to the study of dynamic systems, where MALDI-MS offers a unique, powerful guide to structural evolution in transition-metal species in solution during catalytic transformation. Time-dependent sampling reveals signals for catalyst resting states and decomposition products, as well as induced transformations, including those resulting from catalyst quenching. The method also enables identification of threshold conditions that impair catalyst function: this is important, as it reveals the maximally forcing conditions that can be used for operation. Case studies were conducted on the second-generation Grubbs methylenide catalyst, in the context of both thermally-induced and substrate-induced decomposition. Use in conjunction with complementary techniques that quantify organic products (NMR, GC-FID, GC-MS, etc.) offers greatly expanded insight. In bridging the gap between empirical information about catalyst performance (i.e. product formation and selectivity), and direct information about catalyst turnover, speciation, and decomposition, these methodologies offer great promise for the development of more informed structure-activity relationships, and ultimately catalysts operation and redesign.

6.7 References.

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Chapter 7. Conclusions and Future Directions

Efficient exploitation of feedstocks, and reduction of chemical waste, are lofty goals that inspire many people from a breadth of backgrounds in both industrial and academic communities. Organometallic catalysis is one of the major tools that can help us to meet these challenges. Essential to harnessing the powerful catalytic methodologies latent in the transition metals is the discovery and development of new, robust catalyst systems – and, more fundamentally, the invention of better ways to couple catalyst design with catalyst performance. This thesis work targets both of these objectives: that is, the development of synthetic strategies that allow realization of target catalyst structures, and the development of richer means of interrogating their performance. The major catalytic contexts examined are those of nitrogen activation and olefin metathesis, both of which hold great promise for the development of less wasteful, energetically more sustainable chemical processes.

In the context of dinitrogen activation, a chance discovery led to the identification of the first late-metal complex that efficiently binds N_2 , thus overcoming the problem of high N_2 lability that previously limited use of robust, late-metal complexes to carry out N_2 chemistry. Stoichiometric and catalytic reactions of the complex $RuHCl(IMes)_2(N_2)$ reveal a remarkably non-labile dinitrogen ligand. Also of keen interest is the fact that its IR spectrum exhibits the lowest $\nu(N\equiv N)$ band yet reported for a monometallic ruthenium complex. This indicates a high degree of activation relative to other $Ru-N_2$ complexes. It should be recognized that where N_2 *activation* is highly sensitive to the extent of π -back-bonding onto the $N\equiv N$ ligand, N_2 *lability* is much more strongly affected by the strength of σ -donation from N_2 to Ru . A computational study, undertaken to explore the origins of these effects, revealed that the combination of the strongly σ -donating hydride ligand in the apical site of this square-pyramidal complex, and a π -donor chloride trans to the N_2 ligand, maximizes both σ -bonding and π -backbonding. The σ -donor NHC ligands are also important in raising the overall orbital energies to the point that backbonding onto the high-energy N_2 π^* orbitals is energetically accessible. Finally, the unexpected resistance of the bound N_2 to reduction or functionalization was ascribed to steric protection by the bulky mesityl groups. Analogues containing smaller NHC ligands (e.g. with methyl or *iso*-propyl substituents in place of

mesityl) are thus of great interest. Alternatively, NHC ligands with stronger σ -donor capabilities (such as Bertrand's or Crabtree's "abnormal", C5-bound NHCs) could further improve the energetic match between the metal orbitals and $N\equiv N$ π^* orbitals, increasing the reactivity of the N_2 ligand.

In the context of olefin metathesis, a new family of chiral catalysts was developed which bridges the gap between the existing, tunable, but highly sensitive Mo systems, and the more robust but less tunable Ru systems. Routes were developed into previously unattainable $Ru(BINO)(L)(py)(=CHPh)$ complexes, which integrate the best attributes of their predecessors: that is, the robustness of ruthenium and the high modularity of the chiral binaphtholate ligand. While these "first-generation" Ru-BINO catalysts exhibit moderate activity and low selectivity, modifications in catalyst design are expected to have dramatic effects. Striking increases in activity on addition of Lewis acid additives point toward initiation as a limiting factor in catalyst performance. Addition of a weak Lewis acid in sub-stoichiometric amounts may permit slow catalyst conscription, and recoordination of the stabilizing pyridine ligand, features that can increase activity while preventing decomposition. The low selectivities were expected from the earlier Mo systems, in which 3,3'-functionalization of the BINO ligand proved essential to high enantioselectivities; incorporation of 3,3'-substituted BINO ligands in the Ru catalysts is an obvious next step. Preliminary studies suggest that this is challenging, possibly because of steric conflict with the other ancillary ligands present. Unsymmetrically substituted BINO ligands are worth exploring. These synthetic endeavors will benefit from the greater understanding of Ru-BINO coordination modes delineated within both the Ru benzylidene complex, and $Ru(BINO)(PPh_3)_2$. The latter complex is of considerable interest in its own right, as the first entry point into ruthenium binaphtholate complexes. The potentially broad catalytic relevance of the 'Ru(BINO)' moiety is currently under investigation by Carolyn Higman of the Fogg group.

Within the context of expanded insight into catalytic processes, two major avenues were explored. The first involves significant improvements to high-throughput (HT) catalyst screening methodologies. Despite their power, existing HT methods are limited by the need

to work up of the entire reaction wellplate at a single, arbitrary time, without prior knowledge of reaction progress, speciation, catalyst induction periods, or decomposition. A high-throughput quenching method was developed, which offers the most general, powerful means in current use for monitoring HT reactions over time in an array platform. Central to this methodology is the identification of an appropriate quenching agent, for which essential selection criteria are proposed. This approach, as well as single-timepoint screening, was used to benchmark the performance of a range of olefin metathesis catalysts. Future efforts should undertake both comparison of catalysts under standard conditions, and identification of conditions optimal for individual catalysts. HT has the potential to accelerate progress in organometallic catalysis from the discovery stage to understanding, optimization, and implementation. Advocated here is the expanded application of these powerful tools beyond their currently dominant role of optimization, to include the rapid collection of data that will promote mechanistic understanding.

A second, complementary avenue of investigation involved the use of MALDI mass spectrometric methods to expand our capacity to gain insight into catalyst structure and behaviour. Use of polycyclic aromatic hydrocarbons as charge-transfer MALDI matrices, in conjunction with an inert-atmosphere glovebox for sample preparation and introduction, enabled analysis of highly reactive organometallic complexes with minimal decomposition or fragmentation. This work fits within the context of the current drive toward "operando" analysis, aimed at simultaneously assessing catalyst structure and performance under real operating conditions. Direct interrogation of the metal species under relevant catalytic conditions is highly challenging. Charge-transfer MALDI MS was shown to provide powerful insight into reactions *in progress*: it enabled direct observation of catalyst resting states, as well as identification of threshold conditions for catalyst decomposition. It should be emphasized that evaluation of the conditions under which common metathesis catalysts decompose is of considerable interest, but was previously limited in scope and accuracy by the need to tailor the conditions to the analytical tools available (e.g. NMR). Anaerobic, charge-transfer MALDI MS permits, for the first time, direct elucidation of catalyst structure and degradation under real reaction conditions.

Appendices

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A. MALDI MS Spectra

The following are CT-MALDI MS spectra of isolated complexes reported throughout this thesis as well as supplementary spectra for Chapter 6. In all spectra, m/z values are reported with the notation observed value (simulated value), or in insets with the simulated spectrum at the top and the experimental spectrum at the bottom.

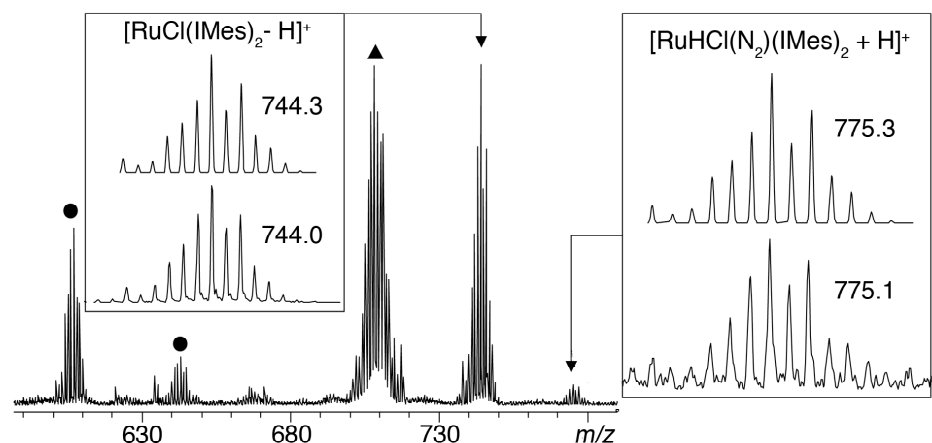


Figure A.1. CT-MALDI mass spectrum of **Ru-8** (pyrene matrix) confirming the presence of one chloride and two IMes ligands. Insets depict key isotope patterns. Key for lower-mass fragment peaks: ▲ denotes overlapping signals for $[\text{RuH}(\text{IMes})_2]^+$, m/z 711.1; $[\text{Ru}(\text{IMes})_2]^{+*}$, m/z 710.1; $[\text{Ru}(\text{IMes})-\text{H}_2]^{+*}$, m/z 708.1. ● denotes pyrene-matrix adducts: $[\text{Ru}(\text{IMes})(\text{pyr})-\text{H}]^+$, m/z 607.0 and $[\text{Ru}(\text{IMes})(\text{pyr})-\text{Cl}]^+$, m/z 643.0.

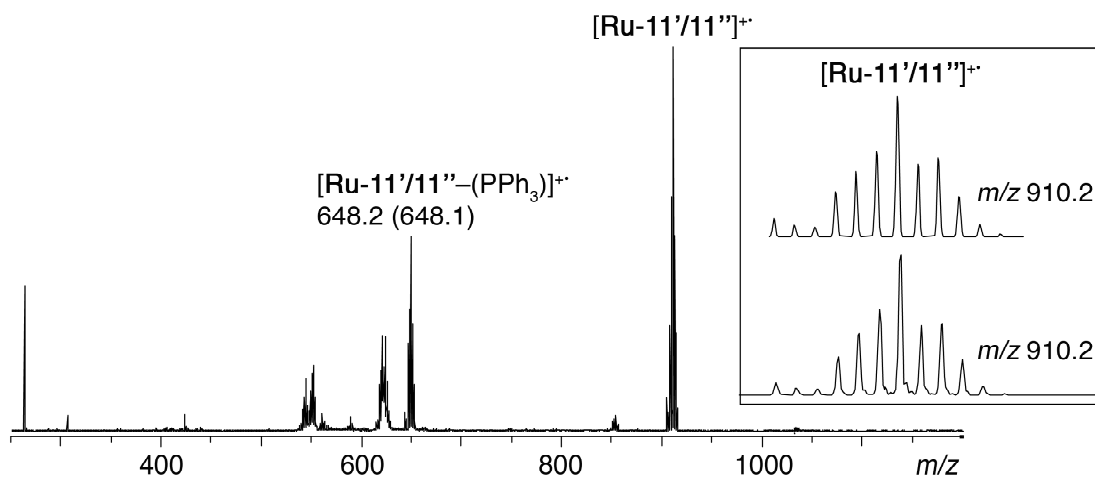


Figure A.2. CT-MALDI MS analysis of $\text{Ru}(\text{BINO})(\text{PPh}_3)_2$ **Ru-11'/11''** with a pyrene matrix.

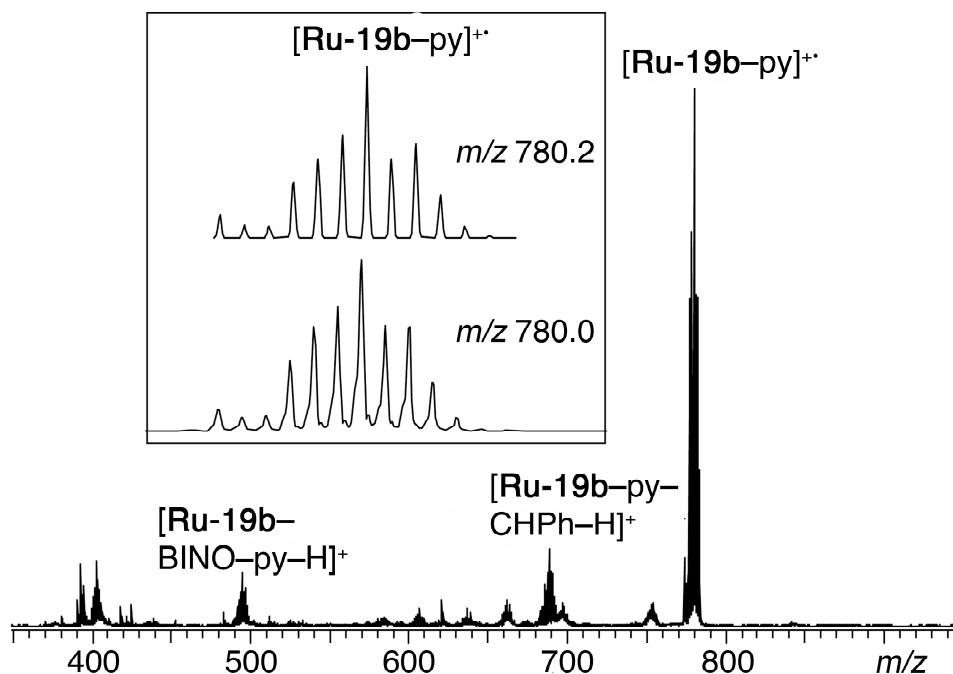


Figure A.3. CT-MALDI MS analysis of Ru(BINO)(IMes)(py)(CHPh) **Ru-19b** (pyrene matrix).

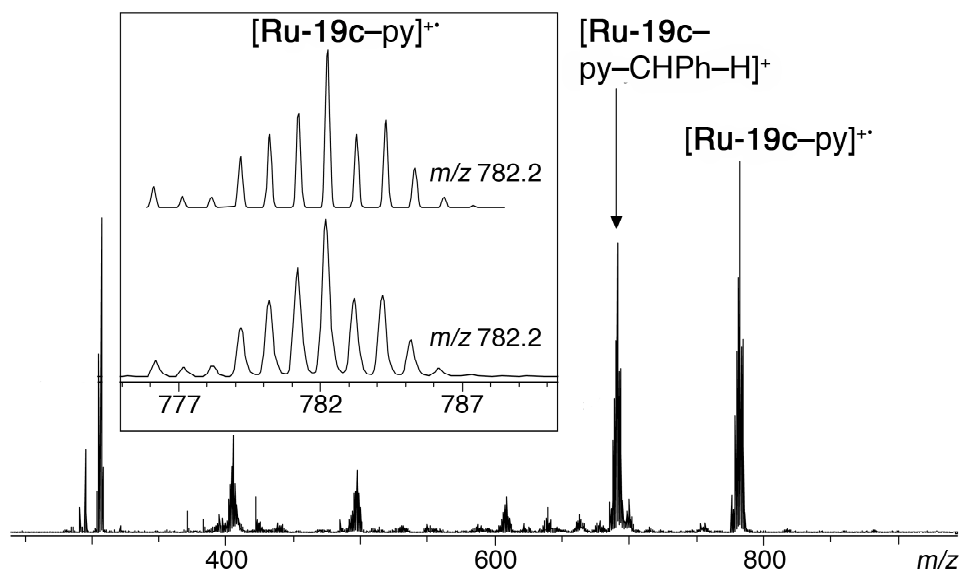


Figure A.4. CT-MALDI MS analysis of Ru(BINO)(H₂IMes)(py)(CHPh) **Ru-19c** (pyrene matrix).

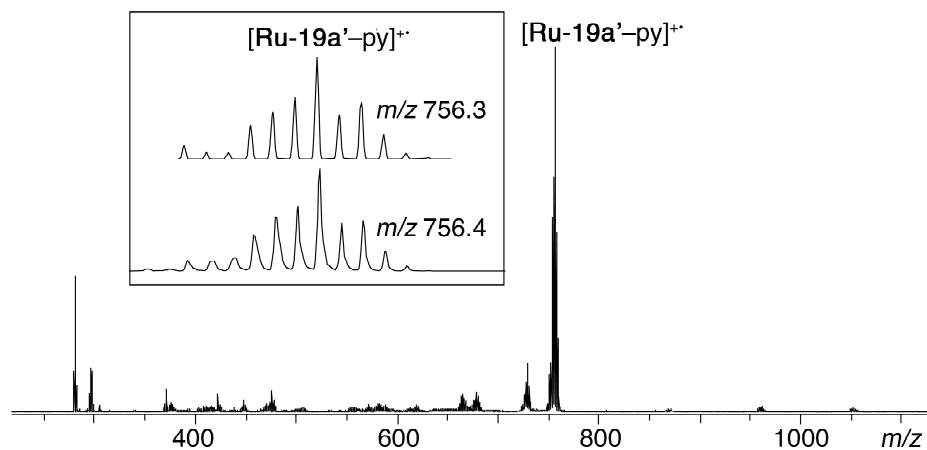


Figure A.5. CT-MALDI MS analysis of Ru(BINO)(PCy₃)(py)(CHPh) **Ru-19a'** (pyrene matrix).

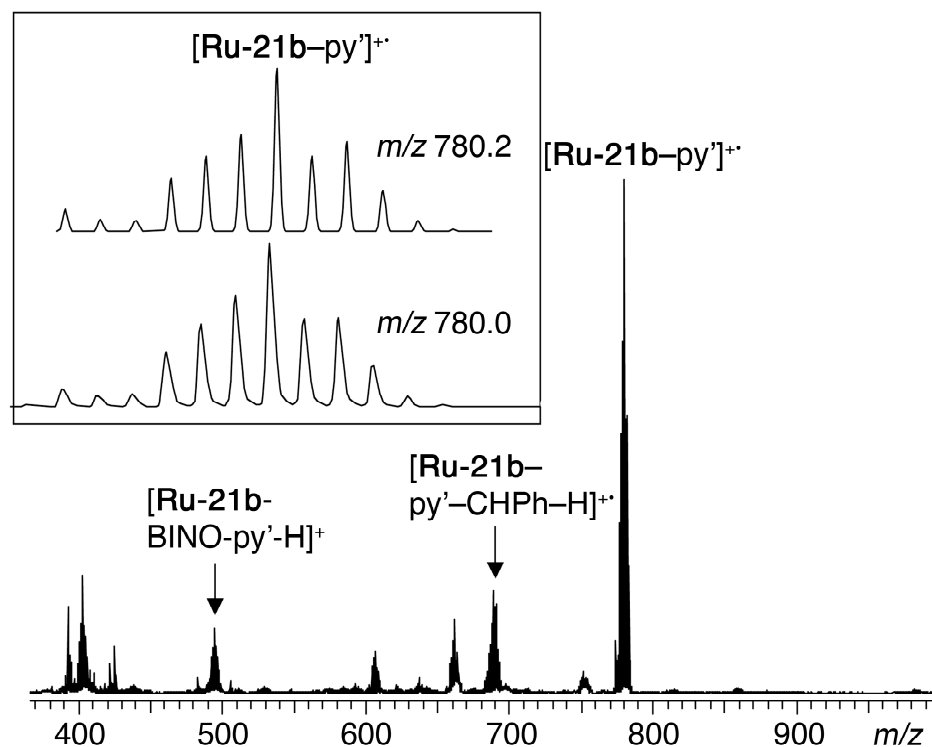


Figure A.6. CT-MALDI MS analysis of (Ru(BINO)(IMes)(py')(CHPh) **Ru-21b** (pyrene matrix). py' = 3-bromopyridine.

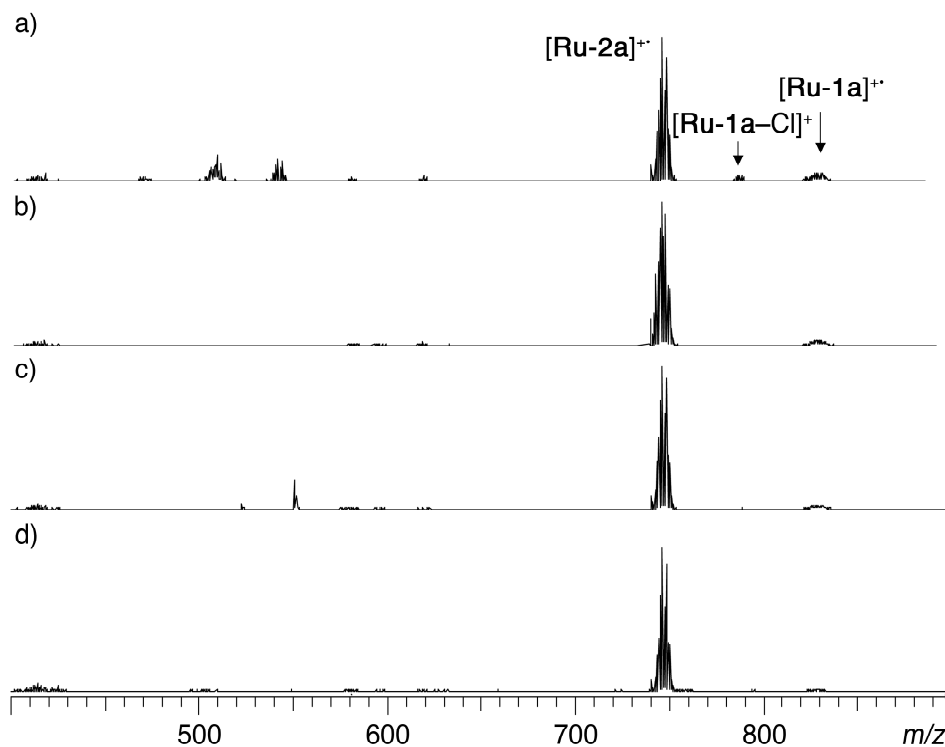


Figure A.7. CT-MALDI MS of the reaction of 100 mM **1** with 5 mol% **Ru-1a** in CH_2Cl_2 at 25 °C. Reaction analyzed a) immediately; b) after 1 h; c) 4 h; d) 24 h.

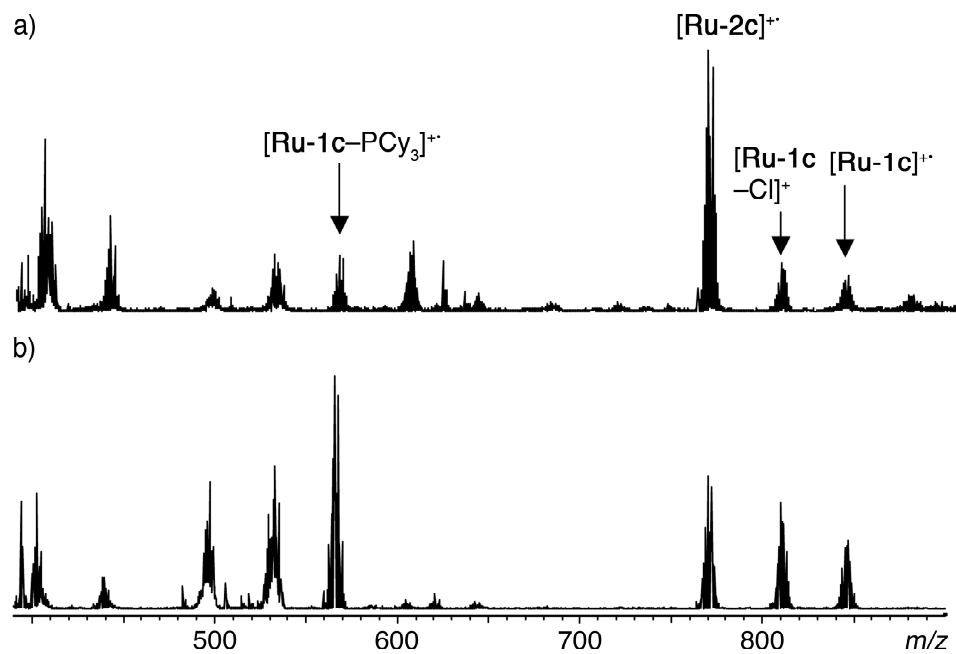


Figure A.8. CT-MALDI MS of the reaction of 100 mM **1** with 5 mol% **Ru-1c** at 25 °C after 1 h. Reaction in a) CH_2Cl_2 ; b) C_6H_6 .

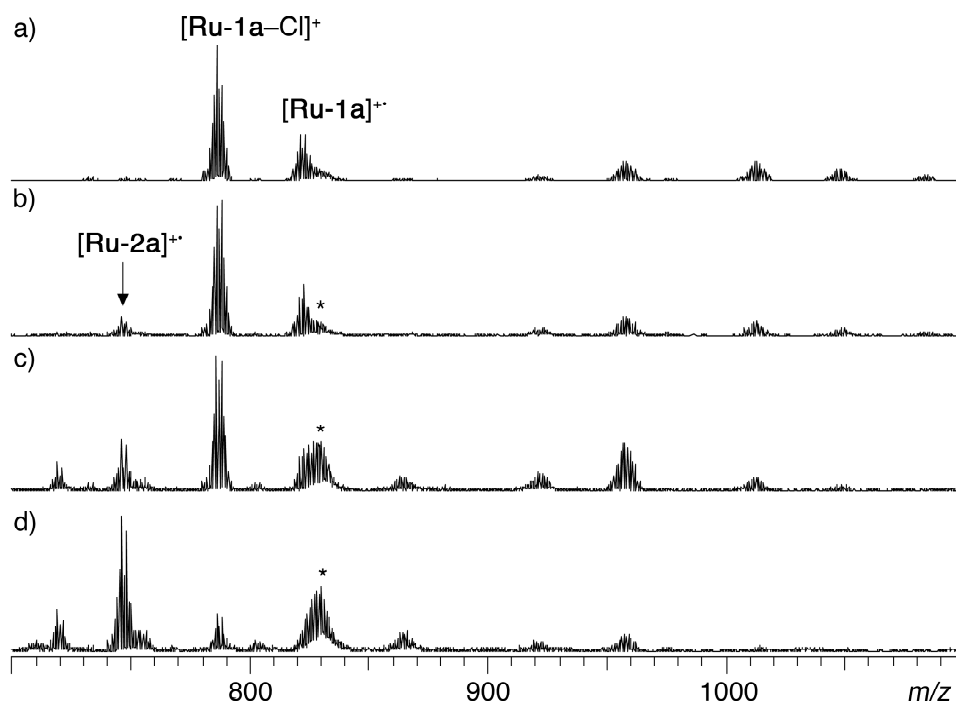


Figure A.9. CT-MALDI MS of the reaction of 100 mM **2** with 5 mol% **Ru-1a** in CH_2Cl_2 at 40 °C. Reaction analyzed a) immediately; b) after 1 h; c) 4 h; d) 24 h. [*] indicates decomposition.

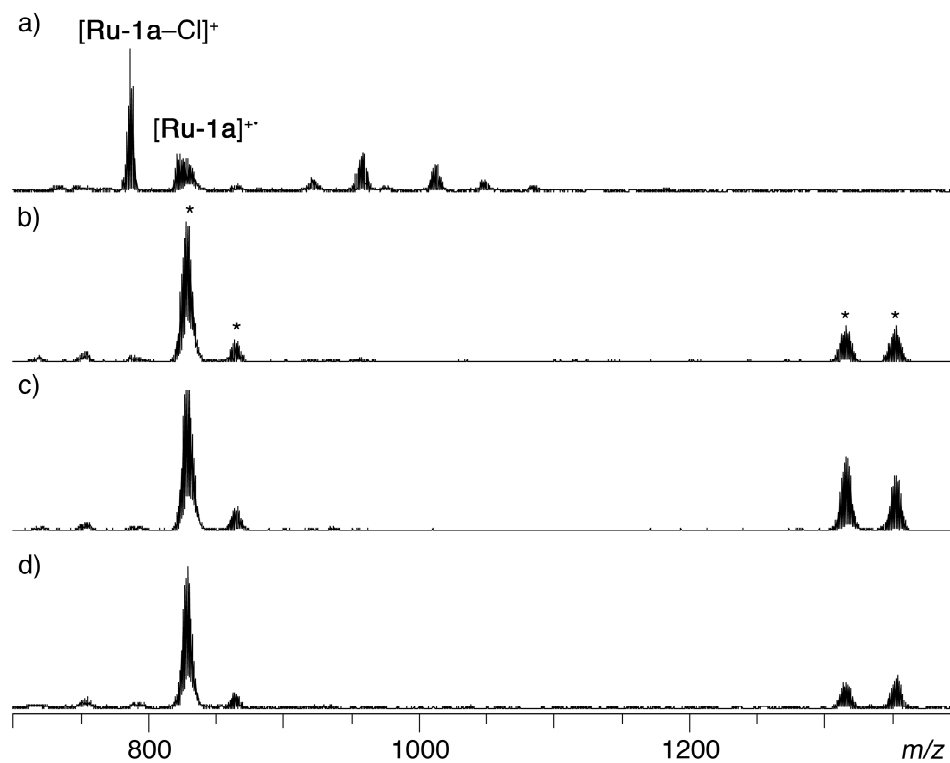


Figure A.10. CT-MALDI MS of the reaction of 100 mM **2** with 5 mol% **Ru-1a** in toluene at 80 °C. Reaction analyzed a) immediately; b) after 1 h; c) 4 h; d) 24 h. [*] indicates decomposition.

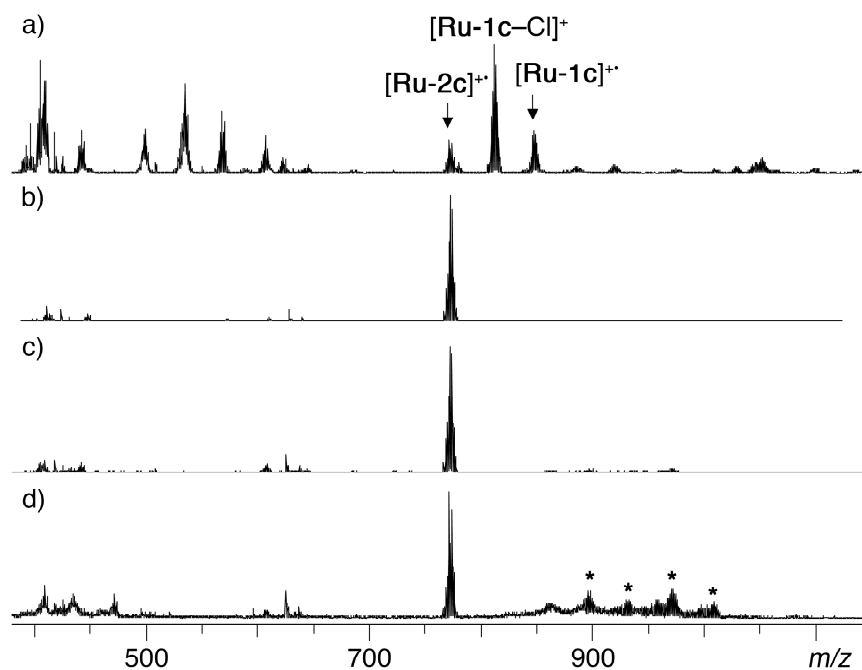


Figure A.11. CT-MALDI MS of the reaction of 100 mM **2** with 5 mol% **Ru-1c** in CH_2Cl_2 at 40 °C. Reaction analyzed a) immediately; b) after 1 h; c) 4 h; d) 24 h. [*] indicates decomposition.

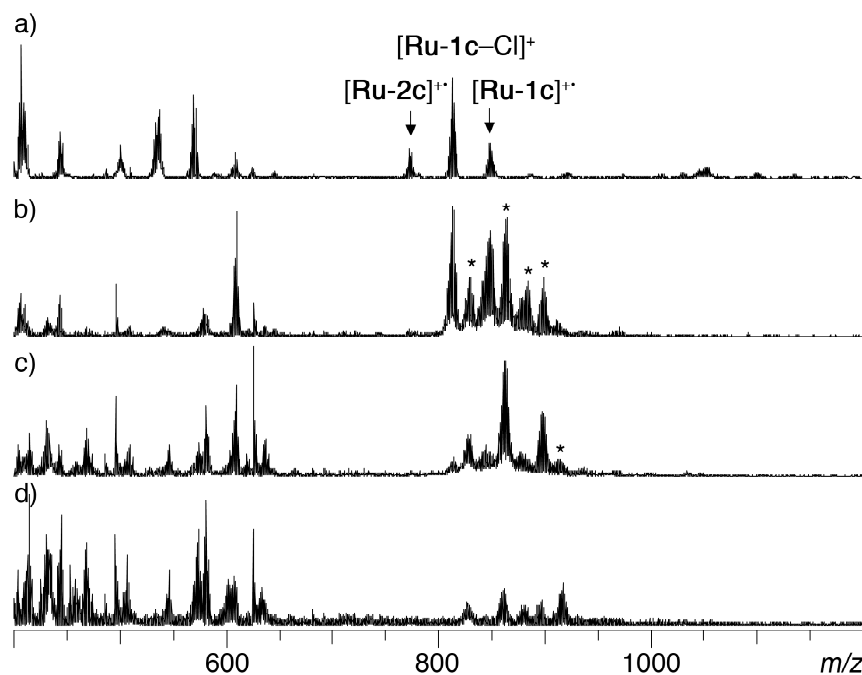


Figure A.12. CT-MALDI MS of the reaction of 100 mM **2** with 5 mol% **Ru-1c** in toluene at 80 °C. Reaction analyzed a) immediately; b) after 1 h; c) 4 h; d) 24 h. [*] indicates decomposition.

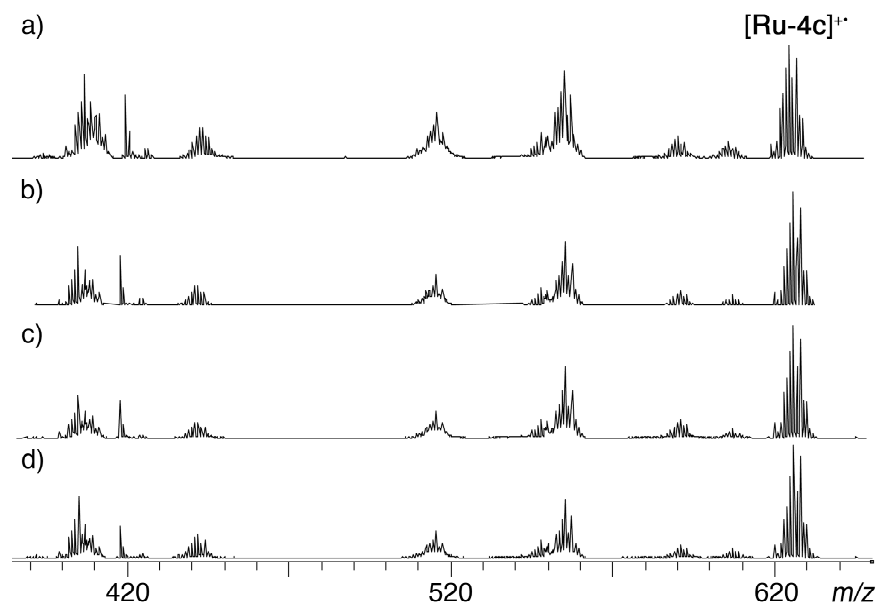


Figure A.13. CT-MALDI MS of the reaction of 100 mM **2** with 5 mol% **Ru-4c** in CH_2Cl_2 at 40 °C. Reaction analyzed a) immediately; b) after 1 h; c) 4 h; d) 24 h.

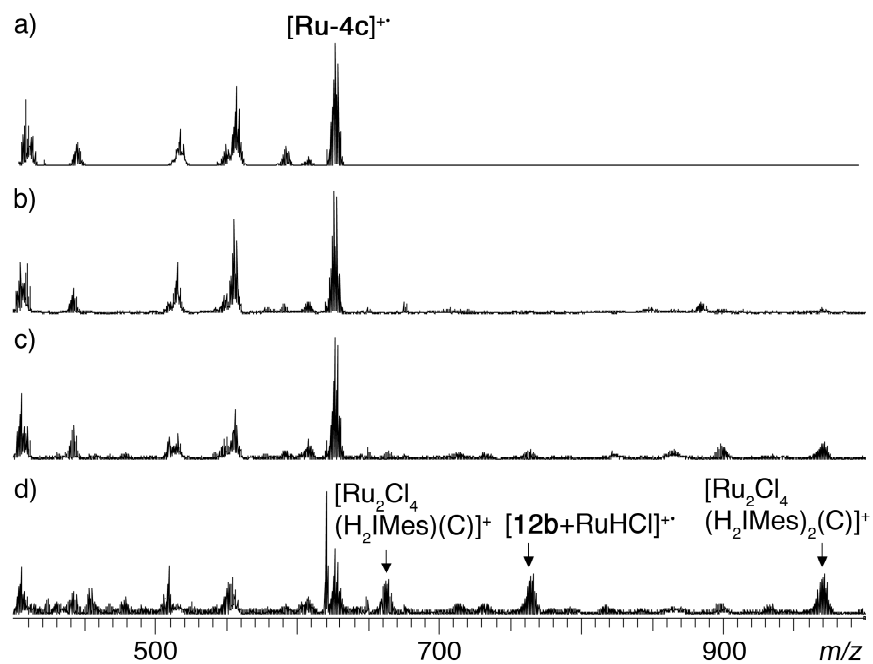


Figure A.14. CT-MALDI MS of the reaction of 100 mM **2** with 5 mol% **Ru-4c** in toluene at 80 °C. Reaction analyzed a) immediately; b) after 1 h; c) 4 h; d) 24 h.

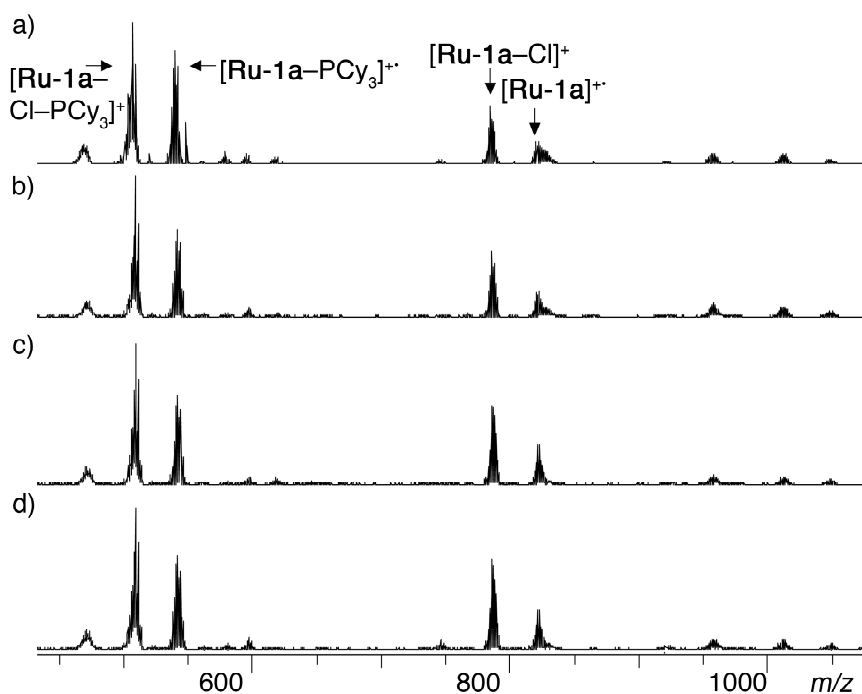


Figure A.15. Stability of **Ru-1a** over time under conditions relevant to catalysis: 5 mM in CH₂Cl₂ at RT. Sample analyzed a) immediately; b) after 1 h; c) 4 h; d) 24 h.

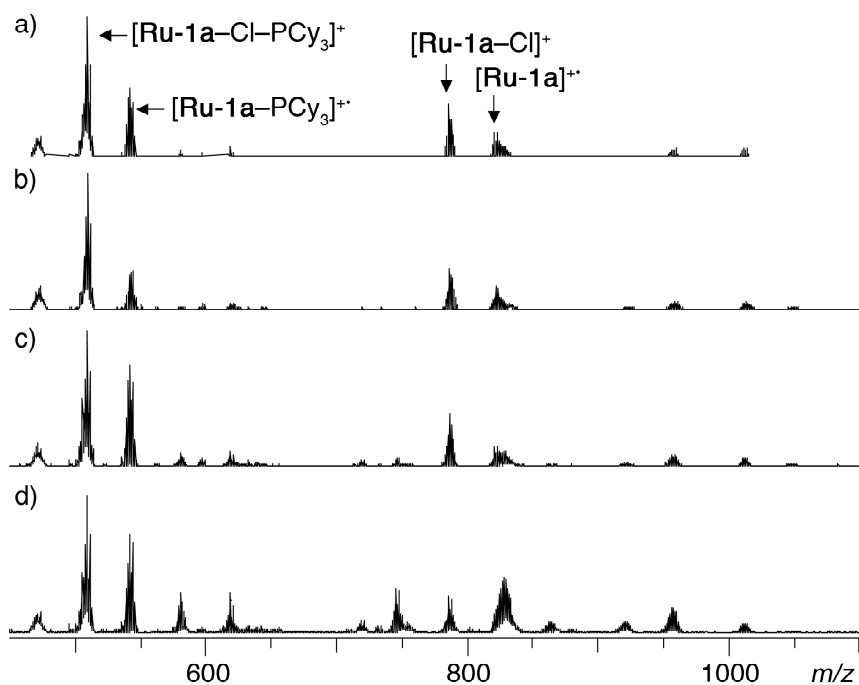


Figure A.16. Stability of **Ru-1a** over time under conditions relevant to catalysis: 5 mM in CH₂Cl₂ at 40 °C. Sample analyzed a) immediately; b) after 1 h; c) 4 h; d) 24 h.

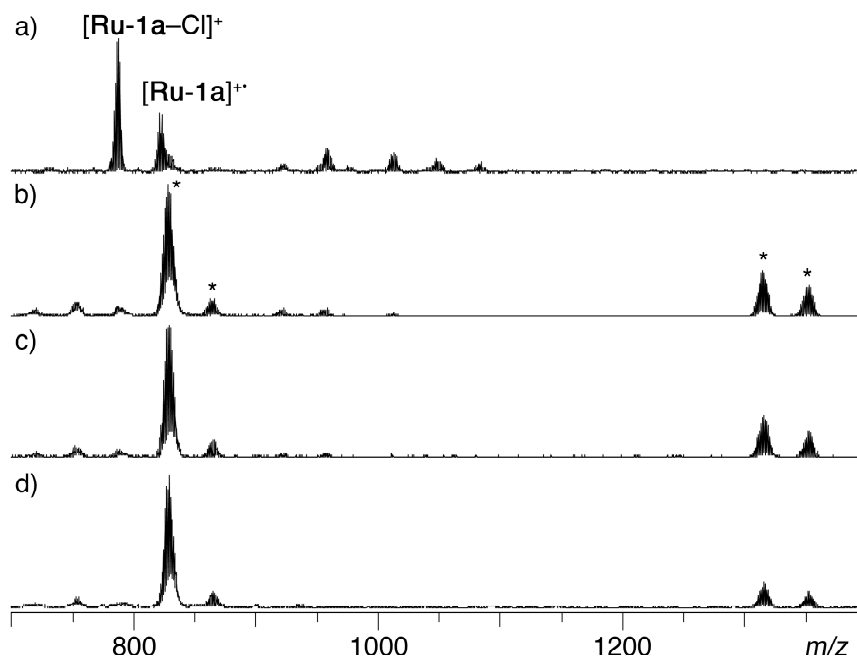


Figure A.17. Stability of **Ru-1a** over time under conditions relevant to catalysis: 5 mM in toluene at 80 °C. Sample analyzed a) immediately; b) after 1 h; c) 4 h; d) 24 h. [*] denotes decomposition, assignments are provided in Chapter 6, Figure 6.13.

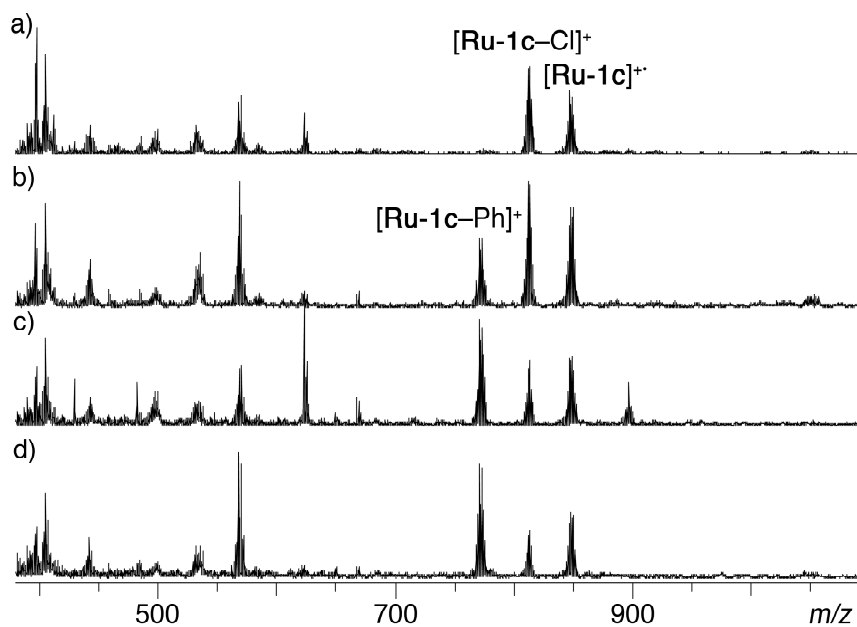


Figure A.18. Stability of **Ru-1c** over time under conditions relevant to catalysis: 5 mM in CH_2Cl_2 at 40 °C. Sample analyzed a) immediately; b) after 1 h; c) 4 h; d) 24 h.

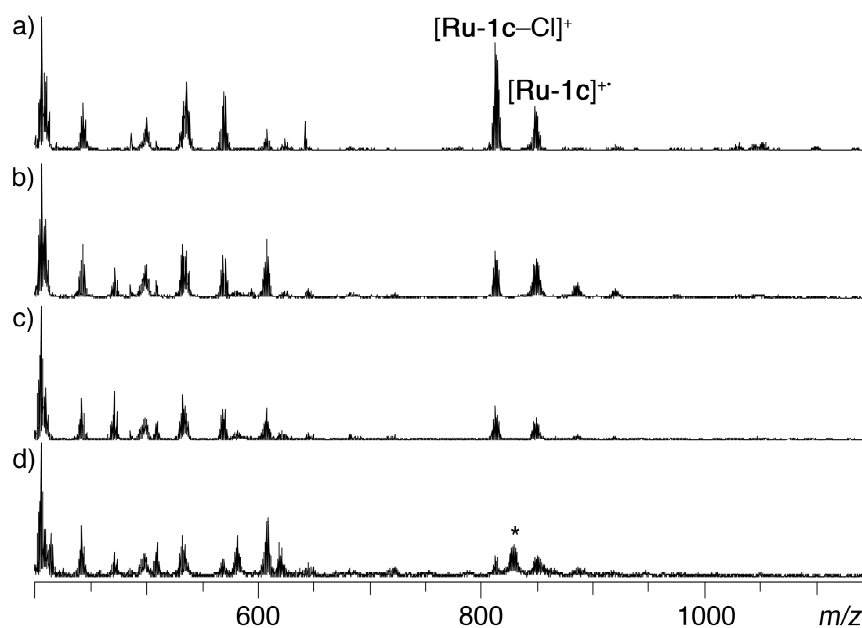


Figure A.19. Stability of **Ru-1c** over time under conditions relevant to catalysis: 5 mM in toluene at 80 °C. Sample analyzed a) immediately; b) after 1 h; c) 4 h; d) 24 h. [*] denotes decomposition.

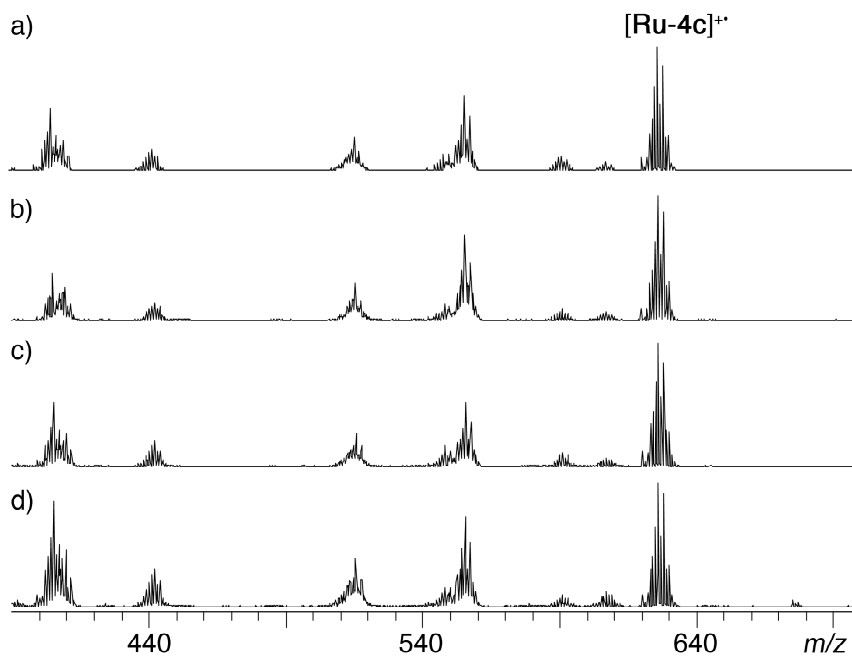


Figure A.20. Stability of **Ru-4c** over time under conditions relevant to catalysis: 5 mM in toluene at 80 °C. Sample analyzed a) immediately; b) after 1 h; c) 4 h; d) 24 h.

B. NMR Probe Reactions

Table B.1. Relevant ^1H NMR benzyldiene signals

Complex	CDCl_3	C_6D_6	CD_2Cl_2	other
Ru-1a	19.98	20.62	20.02	
Ru-1b	19.43		19.40	
Ru-1c			19.16	19.57 ^[a]
Ru-2c			17.81	
Ru-3b	19.44			
Ru-18b	19.34			
Ru-3c				
Ru-3a	19.83 (d, $^3J_{\text{HP}}$ = 9 Hz)			
Ru-3e		19.31		
Ru-3d	19.35			
Ru-4c	16.59			
Ru-19b $\eta^1, \eta^1\text{-BINO}$	18.81		19.18	
Ru-19b' $\eta^3, \eta^1\text{-BINO}$	17.41			
Ru-21b	18.80		19.12	
Ru-19c $\eta^1, \eta^1\text{-BINO}$	18.75		18.93	
Ru-19c' $\eta^3, \eta^1\text{-BINO}$	17.40			
Ru-19a $\eta^1, \eta^1\text{-BINO}$	8.26 (d, $^3J_{\text{HP}}$ = 11.7 Hz)		18.38 (d, $^3J_{\text{HP}}$ = 11.4 Hz)	
Ru-19a' $\eta^3, \eta^1\text{-BINO}$	17.45 (d, $^3J_{\text{HP}}$ = 4.5 Hz)		17.55 (d, $^3J_{\text{HP}}$ = 4.5 Hz)	
Ru-20a $\eta^1, \eta^1\text{-BINO}$			20.16 (d, $^3J_{\text{HP}}$ = 11.4 Hz)	20.46 (d, $^3J_{\text{HP}}$ = 11.5 Hz) ^[b]
Ru-19d ^[c] $\eta^1, \eta^1\text{-BINO}$	17.74	17.82	17.98	
Ru-19d' $\eta^3, \eta^1\text{-BINO}$	17.65	17.81	17.81	
Ru-22c	18.86			
Ru-24b	19.11			

^[a]Toluene- d_8 . ^[b] $\text{C}_5\text{D}_5\text{N}$. ^[c]Ratios of η^1, η^1 : η^3, η^1 : 1.7:1 in CDCl_3 ; 1:1.5 in C_6D_6 ; 1.5:1 in CD_2Cl_2 .

Table B.2. Relevant $^{31}\text{P}\{^1\text{H}\}$ signals^[a]

Complex	CDCl_3	C_6D_6	CD_2Cl_2	THF	$\text{C}_5\text{D}_5\text{N}$
PPh_3	−4.8	−4.7		−4.8	−3.66
OPPh_3	29.7	25.4		24.1	27.5
PCy_3		10.8			10.4

Ru-1a		37.2				
Ru-1c				31.41		
Ru-19a'				46.82		
η^3, η^1 -BINO						
Ru-11' ^[b]	56.5	57.5	56.9	57.3	57.5 ^[c]	
η^3, η^3 -BINO						
Ru-11'		45.0	43.5	44.5	44.9 ^[c]	
η^3, η^1 -BINO			(15 °C: 43.7, 43.3; ABq, $^2J_{PP}$ = 19 Hz)			
Ru-12'	47.8, 46.4	51.6, 50.7	49.1, 48.3			
η^3, η^1 -BINO	(ABq, $^2J_{PP}$ = 23 Hz)	(ABq, $^2J_{PP}$ = 21 Hz) or 47.0 and 45.8 (ABq, $^2J_{PP}$ = 22 Hz) ^[d]	(ABq, $^2J_{PP}$ = 22 Hz)			
Ru-13		49.0 or 45.5 ^[d]				
η^1, η^1 -BINO						
Ru-14'	58.7	59.3 (br)	58.3 (br)			
η^3, η^1 -BINO						
Ru-15	55.2	55.6	56.1		56.0	
η^1, η^1 -BINO						
Ru-16'	65.9, 39.5	64.4, 38.3	64.5, 39.7			
η^3, η^1 -BINO	(ABq, J_{PP} = 28 Hz)	(ABq, J_{PP} = 27 Hz)	(ABq, J_{PP} = 27 Hz)			

^[a] Values referenced externally to 85% H₃PO₄. ^[b] Ratios of η^3, η^3 : η^3, η^1 : 1:0 in CDCl₃; 2.3:1 in C₆D₆; 4:1 in CD₂Cl₂; 1.2:1 in THF; 2.8:1 in toluene-*d*₈. ^[c] Toluene-*d*₈. ^[d] 30%_{v/v} MeCN-*d*₃ in C₆D₆.

Note CDCl₃ was the NMR solvent for all tables below.

Table B.3. Ti₂(BINO) coordination to various precursors in C₆H₆^[a]

Entry	Precursor	t (h)	Conv. (%)	η^1, η^1 -BINO (%)	η^3, η^1 -BINO (%)	other (%)	decomp (%)
1	Ru-1b	17	22	0	0	-	22
2	Ru-3b	15	>99	53	16	-	31
3	Ru-3c	19	98	16	0	-	82
4	Ru-18b	17	99	55	4	11[b]	29
5	Ru-3a	2	>99	7	47	4[b]	47

^[a] Conditions: RT, Ti₂(BINO); NMR spectra measured in CDCl₃. ^[b] Two unidentified alkylidenes at 18.88 (8%) and 19.62 ppm (3 %).

Table B.4. $\text{Ti}_2(\text{BINO})$ coordination to various precursors in pyridine^[a]

Entry	Precursor	t (h)	Conv. (%)	η^1, η^1 - <i>BINO</i> (%)	η^3, η^1 - <i>BINO</i> (%)	other (%)	decomp (%)
1	Ru-3b	20	>99	83	8	-	9
2	Ru-3c	20	95	62	6	6	21
3 ^[b]	Ru-18b	3	>99	75	24	0	1
4	Ru-3a	2	96	23	57	6	10
5	Ru-3e	20	>99	0	0	0	>99
6	Ru-3d	17	97	0	59	0	38
7 ^[c]	Ru-4c	0.75	>99	91	0	0	9

^[a] Conditions: pyridine, $\text{K}_2(\text{BINO})$, RT, 20 h; NMR spectra measured in CDCl_3 . ^[b] Reaction at 40 °C; with 1 equivalent of added AgOTf.

Table B.5. Optimizing the synthesis of $\text{Ru}(\text{BINO})(\text{H}_2\text{IMes})(\text{py})(=\text{CHPh})$ **Ru-19c**^[a]

Entry	Solvent	M	t (h)	Temp (°C)	Conv. (%)	η^1, η^1 - <i>BINO</i> (%)	η^3, η^1 - <i>BINO</i> (%)	decomp (%)
1	C_6H_6	Tl	3	RT	96	31	0	65
2	C_6H_6	Tl	19	RT	98	16	0	82
3	C_6H_6	Tl	3	40	>99	35	0	65
4	$\text{C}_5\text{H}_5\text{N}$	K	3	RT	54	38	2	14
5	$\text{C}_5\text{H}_5\text{N}$	K	20	RT	95	62	6	27 ^[b]

^[a] NMR spectra recorded in CDCl_3 . ^[b] 6 % of this value is an un assigned alkylidene at 18.60 ppm.

Table B.6. Optimizing the synthesis of $\text{Ru}(\text{BINO})(\text{IMes})(\text{py}')(=\text{CHPh})$ **Ru-21b**^[a]

Entry	Solvent	M	t (h)	Temp (°C)	Conv. (%)	η^1, η^1 - <i>BINO</i> (%)	η^3, η^1 - <i>BINO</i> (%)	other (%) ^[b]	decomp (%)
1	C_6H_6	Tl	17	RT	99	55	4	11	29
2	CH_2Cl_2	Tl	17	RT	>99	48	10	3	39
3	C_6H_6	Tl	3	40	96	78	6	5	7
4	CH_2Cl_2	Tl	1	40	97	66	10		21
5 ^[c]	C_6H_6	Tl	3	40	98	32	12		54
6	C_7H_8	Tl	3	40	73	50	7	5	11
7	CH_3CN	Tl	3	40	>99	0	0	0	>99
8	$\text{C}_5\text{H}_5\text{N}$	Tl	3	40	>99	75 ^[d]	24	0	1

^[a] NMR spectra recorded in CDCl_3 . ^[b] Unidentified alkylidenes singlets: entry 1, 18.88 (8%) and 19.62 ppm (3 %); entry 2, 18.88 ppm; entries 3 and 6, 19.61 ppm; ^[c](S)-BINO; ^[d]17 % bis-py', 58% mono-py'.

Table B.7. Optimizing the synthesis of $\text{Ru}(\text{BINO})(\text{PCy}_3)(\text{py})(=\text{CHPh})$ **Ru-19a'**^[a]

Entry	Solvent	M	t (h)	Temp (°C)	Conv. (%)	η^1, η^1 - <i>BINO</i> (%) ^[b]	η^3, η^1 - <i>BINO</i> (%)	other (%) ^[c]	decomp (%)
1	C_6H_6	Tl	2	RT	>99	7	47	4	47
2	$\text{C}_5\text{H}_5\text{N}$	K	2	RT	96	23	57	6	10
3	$\text{C}_5\text{H}_5\text{N}$	K	2	40	98	21	53	13	11

^[a] NMR spectra recorded in CDCl₃. ^[b] Ratio of mono (18.26 ppm, d, ³J_{HP} = 12 Hz) to bis-py (20.14 ppm, d, ³J_{HP} = 11 Hz) complex by entry: 1 (1:0), 2 (1.6:1), 3 (1.1:1); ^[c] unassigned signals by entry: 1, 20.00 ppm (s); 2, 20.41 ppm (s); 3, 20.41 ppm (s, 11%) and 20.00 ppm (s, 2 %).

Table B.8. Conversion of Ru(η^3, η^1 -BINO)(PCy₃)(py)(=CHPh) **Ru-19a'** into Ru(η^1, η^1 -BINO)(PCy₃)(py)₂(=CHPh) **Ru-20a**.^[a]

Entry	Solvent	py (% _{v/v})	η^3, η^1 -BINO Ru-19a' (%)	η^1, η^1 -BINO Ru-19a (%)	η^1, η^1 -BINO 9c (%)	other (%) ^[b]
1	C ₅ D ₅ N	Neat	0	0	95	5
2	CD ₂ Cl ₂	1	58	10	27	5
3	CD ₂ Cl ₂	3	50	5	36	10 ^[c]
4	CD ₂ Cl ₂	5	32	4	55	10 ^[c]
5	CD ₂ Cl ₂	8	26	0	65	10 ^[c]
6	CD ₂ Cl ₂	13	16	0	74	10 ^[c]

^[a] Reactions performed at room temperature and analyzed immediately, except Entry 6 which was analyzed after 12 h; ^[b] Unassigned singlet at 20.68 in pyr-*d*₅ and 20.41 in CD₂Cl₂; ^[c] Combination of the singlet at 20.41 and a doublet at 19.60 (*J*_{HP} = 8.7 Hz), Entry 3: 6% and 4% respectively, Entry 4: 5% and 5%, Entry 5: 6% and 4%, Entry 6: 6% and 4%.

Table B.9. Optimizing the synthesis of Ru(BINO)(IPr)(py)(=CHPh) **Ru-19d**.^[a]

Entry	Add. (1 equiv.)	M	t (h)	Temp (°C)	Conv. (%)	η^1, η^1 -BINO (%) ^[b]	η^3, η^1 -BINO (%) ^[c]	other (%)	decomp (%)
1 ^[d]	-	Tl	3	40	57	0	19	0	38
2	-	K	3	RT	92	0	49	0	43
3	AgOTf	K	3	RT	98	49	7	0	42
4	-	K	17	RT	97	0	59	0	38
5	AgOTf	K	17	RT	98	26	9	14	48
6	AgPF ₆	K	17	RT	94	13	0	26 ^[e]	55

^[a] NMR spectra recorded in CDCl₃. ^[b] Two isomers 18.63 and 18.51 ppm, proportions by entry: 3 (1.6:1); 5, 1.2:1; 6, 3.3:1. ^[c] Two isomers at 17.76 and 17.66 ppm, proportions by entry: 1, 1.7:1; 2, 1.6:1; 3, 1.1:1.3; 4, 1.7:1; 5, 1:0. ^[d] C₆H₆. ^[e] Total integration for four unidentified benzyldiene products.

Table B.10. Optimizing the synthesis of Ru(BINO)(H₂ITol)(py)(=CHPh) **Ru-19e**.^[a]

Entry	Solvent	M	t (h)	Temp (°C)	Conv. (%)	η^1, η^1 -BINO (%)	η^3, η^1 -BINO (%)	other (%)	decomp (%)
1	C ₆ H ₆	Tl	3	40	85	0	0	0	85 ^[b]
2	C ₆ D ₆	Tl	3	40	30	0	0	0	30
3	C ₆ D ₆	Tl	3	40	45	0	0	0	45
4	C ₅ H ₅ N	K	3	40	>99	0	0	0	>99 ^[b]
5	C ₅ H ₅ N	K	20	RT	>99	0	0	0	>99 ^[b]

^[a] NMR spectra were recorded in CDCl₃; ^[b] Several hydride signals are present between -3 and -25 ppm.

Table B.11. Optimizing the synthesis of Ru(BINO)(H₂IMes)(py)(=CHPhOⁱPr) **Ru-22c**^[a]

Entry	Additive (1 equiv)	M	t (h)	Temp (°C)	Conv. (%)	η^1, η^1 -BINO (%)	η^3, η^1 -BINO (%)	other (%)	decomp (%)
1	-	K	20	RT	>99	0	0	52 ^[b]	48
3	AgOTf	K	0.75	RT	>99	91	0	0	9

^[a] NMR spectra recorded in CDCl₃. ^[b] Total integration of seven unidentified benzylidene signals.**Table B.12.** Tl₂(3,3'-dibromo-1,1'-binaphtholate) coordination to various precursors.^[a]

Entry	[Ru]	Solvent	t (h)	Temp (°C)	Conv. (%)	η^1, η^1 -BINO (%)	η^3, η^1 -BINO (%)	other (%)	decomp (%)
1	Ru-3b	C ₆ H ₆	3	40	94	0	33 ^[b]	0	66
2	Ru-3d	C ₆ H ₆	3	40	73	0	10	0	63
3	Ru-3e	C ₆ H ₆	3	40	87	0	0	0	87
4	Ru-3b	C ₅ H ₅ N	20	RT	96	5	26 ^[c]	6 ^[d]	59

^[a] NMR spectra recorded in CDCl₃. ^[b] Two signals 17.36 and 17.02 ppm (1:2.6) ^[c] two signals 17.66 and 17.26 ppm (1:3.9). ^[d] Two signals 21.23 and 21.16 ppm.**Table B.13.** Tl₂(3,3'-diphenyl-1,1'-binaphtholate) coordination to various precursors.^[a]

Entry	[Ru]	Solvent	t (h)	Temp (°C)	Conv. (%)	η^1, η^1 -BINO (%)	η^3, η^1 -BINO (%)	other (%)	decomp (%)
1	Ru-3b	C ₆ H ₆	3	40	>99	0	11	0	89
2	Ru-3d	C ₆ H ₆	3	40	87	0	0	0	87
3	Ru-3e	C ₆ H ₆	3	40	98	0	0	0	98
4	Ru-3b	C ₅ H ₅ N	20	RT	>99	47	1	5	47

^[a] NMR spectra recorded in CDCl₃.

C. Catalytic Data

Table C.1. RCM of **1** with **Ru-19b** and Lewis acids **14** and **15**.^[a]

Time (min)	% Conv.				
	Ru-19b	Ru-19b + 14	Ru-19b + 15	14	15
0	0	0	0	0	0
5	3	7	7		
10	3	21	15		
15	3	36	13		
30	3	41	11		
45	2	35	9		
60	2	40	17	0	0

^[a] Conditions: 10 mM **1** in THF, 5 mol% **Ru-19b**, 10 equiv **14/15**, 50 °C.**Table C.2.** Conditions screen for the ROM/CM of **4**, values after 2 h reaction time.^[a]

[4] Styrene		% Conv.				% ROM/CM				% Polymer			
(mM)	equiv	Ru-19b	Ru-19c	Ru-21b	Ru-19a'	Ru-19b	Ru-19c	Ru-21b	Ru-19a'	Ru-19b	Ru-19c	Ru-21b	Ru-19a'
10	20	72	100	64	33	38	78	33	9	34	22	31	24
10	10	73	100	48	34	40	70	17	9	36	30	31	24
10	5	65	100	0	34	24	57	0	9	41	43	0	25
50	20	77	100	35	33	27	76	3	10	50	24	33	23
50	10	71	100	39	34	21	71	4	11	51	29	35	23
50	5	69	100	50	37	15	63	5	14	55	37	45	23

^[a] Conditions: 2.5 mol% [Ru], THF, 50 °C.**Table C.3.** Conditions screen for the ROM/CM of **4**, values after 6 h reaction time.^[a]

[4] Styrene		% Conv.				% ROM/CM				% Polymer			
(mM)	equiv	Ru-19b	Ru-19c	Ru-21b	Ru-19a'	Ru-19b	Ru-19c	Ru-21b	Ru-19a'	Ru-19b	Ru-19c	Ru-21b	Ru-19a'
10	20	100	100	94	37	68	80	63	15	32	20	30	21
10	10	96	100	84	36	57	71	51	15	39	29	33	21
10	5	85	100	69	36	34	57	25	12	51	43	44	23
50	20	100	100	42	38	42	77	6	17	58	23	36	21
50	10	96	100	44	39	32	72	5	17	64	28	39	22
50	5	89	100	54	36	23	57	5	14	66	43	49	36

^[a] Conditions: 2.5 mol% [Ru], THF, 50 °C.**Table C.4.** *E/Z* selectivity in the ROM/CM conditions screen at 2 and 6 h.^[a]

[4] (mM)		Styrene equiv		2h				6h			
				Ru-19b	Ru-19c	Ru-21b	Ru-19a'	Ru-19b	Ru-19c	Ru-21b	Ru-19a'
10	20			1.3	1.0	1.3	3.4	1.4	1.2	1.2	3.4
10	10			1.3	1.3	1.5	3.5	1.4	1.6	1.3	3.4
10	5			1.5	1.6	0	4.2	1.5	2.5	1.5	3.5
50	20			1.5	0.9	1.9	3.2	1.8	1.0	1.6	3.2
50	10			1.3	1.0	1.5	3.3	1.5	1.0	1.5	3.3

50	5	1.2	1.0	1.4	3.2	1.2	1.1	1.3	3.3
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^[a] Conditions: 2.5 mol% [Ru], THF, 50 °C.

Table C.5. ROM/CM additive screen with **Ru-19b** ^[a]

Additive	% conv	% ROM/CM	E/Z	% missing
16	100	101	1.2	-1.0
17	100	98	1.3	1.6
18	96	93	1.3	2.7
(R)-19	100	99	1.2	1.4
20	100	108	1.5	-8.0
21	58	40	1.5	18
22	68	57	1.2	12
23	3	0	0	3.0
14	100	71	4.9	29
15	100	105	1.2	-4.6
24	100	102	1.0	-1.4
-	88	86	1.3	2.6

^[a] Conditions: 10 mM **4** with 20 equiv styrene and 1 mol% Ru.

Table C.6. ROM/CM additive screen with **Ru-19c** ^[a]

Additive	% conv	% ROM/CM	E/Z	% missing
16	100	106	1.3	-6
17	100	97	1.3	1
18	100	102	1.3	-2
(R)-19	100	95	1.4	5
20	100	96	1.5	34
21	90	91	1.1	-1
22	100	99	1.0	1
23	5	2	0	3
14	100	57	12.1	43
15	100	73	1.5	27
24	100	87	1.4	13
-	100	92	1.3	8

^[a] Conditions: 10 mM **4** with 20 equiv styrene and 1 mol% Ru.

Table C.7. ROM/CM additive screen with **Ru-19a** ^[a]

Additive	% conv	% ROM/CM	E/Z	% missing
16	3	0	0	3
17	2	0	0	2
18	3	0	0	3
(R)-19	5	0	0	5
20	0	0	0	0
21	4	0	0	4
22	3	0	0	3
23	3	0	0	3
14	100	119	3.2	-19

15	53	56	3.2	-3
24	100	120	3.1	-20
-	5	0	0	5

^[a] Conditions: 10 mM **4** with 20 equiv styrene and 1 mol% Ru.

Table C.8. ROM/CM additive screen with **Ru-30b**^[a]

Additive	% conv	% ROM/CM	E/Z	% missing
16	100	104	1.1	-4
17	100	106	1.2	-6
18	94	101	1.1	-7
(R)-19	100	103	1.1	-3
20	100	105	1.3	-5
21	98	105	1.1	-7
22	100	104	1.2	-4
23	4	0	0	4
14	100	62	3.8	38
15	100	94	1.9	6
24	100	83	1.8	17
-	100	101	1.2	-1.1

^[a] Conditions: 10 mM **4** with 20 equiv styrene and 1 mol% Ru.

Table C.9. Primary screen for quenching ability: conversions in RCM of **1** with **Ru-1b** in the presence of high proportions of the quenching agents **Q**.^[a]

Equiv. Q	U	25	26	27	28	29	30	31	32
40	87	24	0.5	43	4	1	3	3	40
60	81	4	0	26	3	0	1	2	30
80	87	3	0	26	2	0	1	2	26
100	85	2	0	25	1	0	1	3	22

^[a] Reactions at 100 mM **1**, 0.5 mol% **Ru-1b** in C₆H₆ at 25 °C and 6 h reaction time.

Table C.10. Secondary screen for quenching ability: conversions in RCM of **1** with **Ru-1b** in the presence of lower proportions of the quenching agents **Q**.^[a]

Equiv. Q	U	26	28	29	30	31
5	94	5	6	18	25	2
12	96	1	4	7	12	2
18	95	0.5	4	3	9	3
25	95	0.5	3	6	6	4

^[a] Reactions at 100 mM **1**, 0.5 mol% **Ru-1b** in C₆H₆ at 25 °C and 6 h reaction time.

Table C.11. Knockdown speed of **31** with **Ru-1a** and **Ru-1b**.^[a]

Cat. (0.5 mol%)	Q	Wait time (h)			
		Immed.	1	4	24
Ru-1a	31	8	8	7	7
Ru-1a	Air	18	22	35	67
Ru-1b	31	44	44	46	47
Ru-1b	Air	52	71	89	98

^[a] RCM of **1** (100 mM) at 25 °C

Table C.12. Validation screen for quenching ability of **31**: conversions in RCM of **1** by various metathesis catalysts in the presence of low proportions of **31**.^[a]

Equiv. Q	Ru-1a	Ru-1b	Ru-1c	Ru-3b	Ru-3c	Ru-21b	Ru-31b	Ru-4c
0	100	99	101	89	101	93	31	100
1	8	4	5	26	58	22	0	101
5	0	0	1	1	3	1	0	2
10	0	0	0	0	1	0	0	1

^[a] Reactions at 100 mM **1**, 0.5 mol% Ru in C₆H₆ at 25 °C and 6 h reaction time.**Table C.13.** Monitoring RCM of **6** by **Ru-1a** with the HT quenching method.^[a]

Time (min)	RCM (%)	error (+/-)
0	0	0.0
10	22	0.9
15	26	0.0
20	30	0.0
25	32	0.2
30	35	0.1
35	36	0.3
50	43	0.5
65	49	0.5

^[a] Conditions: 10 mM **6**, 1 mol% **Ru-1a**, THF, 30 °C.**Table C.14.** Monitoring RCM of **6** by **Ru-1b** with the HT quenching method.^[a]

Time (min)	RCM (%)	error (+/-)
0	0	0.0
8.5	7	0.2
13.5	10	0.5
18.5	14	0.4
23.5	16	0.2
28.5	19	0.1
33.5	22	0.2
48.5	29	0.0
63.5	35	0.1

^[a] Conditions: 10 mM **6**, 1 mol% **Ru-1b**, THF, 30 °C.**Table C.15.** Monitoring RCM of **6** by **Ru-18b** with the HT quenching method.^[a]

Time (min)	RCM (%)	error (+/-)
0	0	0.0
4.5	84	
9.5	88	0.9
14.5	89	0.6
19.5	89	1.0
24.5	89	0.8
29.5	89	0.8
59.5	88	0.9

89.5	89	0.6
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^[a] Conditions: 10 mM **6**, 1 mol% **Ru-18b**, THF, 30 °C.

Table C.16. Monitoring RCM of **6** by **Ru-3b** with the HT quenching method.^[a]

Time (min)	RCM (%)	error (+/-)
0	0	0.0
8	59	1.6
13	88	7.9
23	89	2.1
38	93	1.9
68	94	0.5
128	96	1.2
248	96	1.2
368	97	1.9
548	96	1.2
728	96	1.7
1448	95	1.1

^[a] Conditions: 10 mM **6**, 0.5 mol% **Ru-3b**, C₆H₆, 30 °C.

Table C.17. Monitoring RCM of **6** by **Ru-4c** with the HT quenching method.^[a]

Time (min)	RCM (%)	error (+/-)
0	0	0.0
11.5	57	6.7
16.5	92	8.4
26.5	90	4.1
41.5	96	1.7
71.5	99	1.2
131.5	100	0.8
251.5	100	0.0
371.5	101	0.1
551.5	100	0.6
731.5	100	0.3
1451.5	99	1.4

^[a] Conditions: 10 mM **6**, 0.5 mol% **Ru-4c**, C₆H₆, 30 °C.

Table C.18. Monitoring RCM of **6** by **Ru-1a** with the HT quenching method.^[a]

Time (min)	RCM (%)	error (+/-)
0	0	0.0
13	24	1.9
18	31	32.6
28	33	2.4
43	38	2.1
73	47	2.2
133	61	2.0
253	77	2.1

373	85	1.9
553	92	1.9
733	95	2.8
1453	98	2.4

^[a] Conditions: 10 mM **6**, 0.5 mol% **Ru-1a**, C₆H₆, 30 °C.

Table C.19. Monitoring RCM of **6** by **Ru-1b** with the HT quenching method.^[a]

Time (min)	RCM (%)	error (+/-)
0	0	0.0
9.5	11	
14.5	23	0.0
19.5	35	0.4
24.5	43	0.4
29.5	49	0.7
34.5	55	0.7
64.5	77	1.0
94.5	84	0.7

^[a] Conditions: 180 mM **6**, 0.5 mol% **Ru-1b**, THF, 30 °C.

Table C.20. Monitoring RCM of **6** by **Ru-18b** with the HT quenching method.^[a]

Time (min)	RCM (%)	error (+/-)
0	0	0.0
4.5	57	
9.5	58	0.9
14.5	57	0.6
19.5	54	1.0
24.5	55	0.8
29.5	53	0.8
59.5	56	0.9
89.5	57	0.6

^[a] Conditions: 10 mM **6**, 0.5 mol% **Ru-18b**, THF, 30 °C.

Table C.21. HT reaction monitoring of the RCM of **8** by **Ru-1b** in C₆H₆.^[a]

Time (min)	Diene (%)	error (+/-)	RCM (%)	error (+/-)	ADMET (%)	error (+/-)
0	100	0.0	0	0.0	0	0.0
6	89	3.1	3	3.3	8	0.2
16	38	19.4	61	15.5	1	3.9
31	12	1.4	86	1.1	2	2.5
46	9	0.5	89	3.9	2	3.4
61	8	0.9	88	3.9	3	3.0
91	8	0.6	89	2.3	3	1.7
121	7	0.2	89	3.3	4	3.0
181	6	0.1	88	2.9	5	2.8
241	5	0.1	90	2.6	5	2.5

^[a] Conditions: 5 mM **8**, 0.5 mol% **Ru-1b**, C₆H₆, 40 °C.

Table C.22. HT reaction monitoring of the RCM of **8** by **Ru-1b** in THF.^[a]

Time (min)	Diene (%)	error (+/-)	RCM (%)	error (+/-)	ADMET (%)	error (+/-)
0	100		0.0	0	0.0	0
5	99		4.6	0	0.0	1
15	81		0.1	12	5.7	7
30	56		0.3	36	5.7	8
45	34		0.3	56	6.1	10
60	24		0.7	64	6.2	11
90	15		0.0	73	6.0	13
120	10		0.1	74	5.9	15
180	7		0.5	75	6.9	18
240	5		0.2	78	6.0	17

^[a] Conditions: 5 mM **8**, 0.5 mol% **Ru-1b**, THF, 40 °C.**Table C.23.** HT reaction monitoring of the RCM of **8** by **Ru-1b** in C₆H₆.^[a]

Time (min)	Diene (%)	error (+/-)	RCM (%)	error (+/-)	ADMET (%)	error (+/-)
0	100		0.0	0	0.0	0
7	91		0.6	0	0.0	9
17	49		2.6	6	1.3	45
32	17		0.9	9	2.1	74
47	9		0.3	9	2.1	83
62	6		0.2	9	1.9	85
92	4		0.5	8	1.5	89
122	3		0.4	7	1.4	91
182	2		0.5	6	0.9	92
242	2		0.1	6	1.2	92

^[a] Conditions: 100 mM **8**, 0.5 mol% **Ru-1b**, C₆H₆, 40 °C.**Table C.24.** HT reaction monitoring of the RCM of **8** by **Ru-1b** in THF.^[a]

Time (min)	Diene (%)	error (+/-)	RCM (%)	error (+/-)	ADMET (%)	error (+/-)
0	100		0.0	0	0.0	0
8	88		1.6	0	0.0	12
18	68		1.6	4	0.7	28
33	46		2.2	9	1.5	45
48	35		0.4	11	1.8	54
63	26		0.9	13	2.0	61
93	20		0.2	14	2.5	66
123	17		1.3	14	2.3	69
183	14		3.7	14	1.2	73
243	11		3.3	14	0.3	74

^[a] Conditions: 100 mM **8**, 0.5 mol% **Ru-1b**, THF, 40 °C.**Table C.25.** RCM of **1** (100 mM) with 0.5 mol% **Ru-18b** in C₆H₆ at 25 °C.

Time (min)	diene (%)	error (+/-)	RCM (%)	error (+/-)	missing (%)	error (+/-)
0	100		0.0	0	0.0	0
5	36		5.9	60	2.4	3

10	18	2.9	80	3.0	2	5.9
15	11	1.5	84	2.7	5	1.3
45	3	0.6	98	3.1	0	3.6
90	2	0.2	99	3.6	-1	3.8

Table C.26. RCM of **1** (10 mM) with 0.05 mol% **Ru-18b** at 25 °C.

C₆H₆		THF		(ClCH₂)₂	
Time (min)	RCM (%)	Time (min)	RCM (%)	Time (min)	RCM (%)
0	0	0	0	0	0
8.4	11	7.6	1	6.8	
9.4	23	8.6	2	7.8	
10.4	19	9.6	2	8.8	
11.4	14	10.6	2	9.8	
12.4	8	11.6	1	10.8	
13.4	10	12.6	1	11.8	
18.4	10	17.6	1	16.8	
28.4	12	27.6	2	26.8	16
38.4	11	37.6	2	36.8	10
53.4	15	52.6	2	51.8	11
68.4	16	67.6	2	66.8	10

Table C.27. RCM of **1** (10 mM) with 0.1 mol% **Ru-18b** at 25 °C.

C₆H₆		THF		(ClCH₂)₂	
Time (min)	RCM (%)	Time (min)	RCM (%)	Time (min)	RCM (%)
0	0	0	0	0	0
5.6		4.4	3	3.1	23
6.6		5.4	5	4.1	25
7.6		6.4	5	5.1	23
8.6		7.4	3	6.1	21
9.6		8.4	3	7.1	21
10.6		9.4	4	8.1	20
15.6		14.4	4	13.1	20
25.6	27	24.4	3	23.1	21
35.6	30	34.4	4	33.1	21
50.6	39	49.4	5	48.1	21
65.6	33	64.4	4	63.1	20

Table C.28. RCM of **1** (10 mM) with 0.2 mol% of third generation catalysts at 25 °C in C₆H₆.

[Ru]	Diene (%)	RCM (%)	Missing (%)
None	100	0	0
Ru-3b	20	81	-1
Ru-18b	4	97	-1
Ru-3c	8	92	-1
Ru-18c	2	99	-1
Ru-3d	3	98	-1

Ru-18d	0	101	-1
Ru-3e	68	32	0
Ru-18e	11	90	-1

Table C.29. RCM of **1** (10 mM) with 0.2 mol% of third generation catalysts at 25 °C in (ClCH₂)₂.

[Ru]	Diene (%)	RCM (%)	Missing (%)
None	100	0	0
Ru-3b	59	42	-1
Ru-18b	51	50	-1
Ru-3c	55	48	-3
Ru-18c	53	49	-2
Ru-3d	30	72	-2
Ru-18d	28	76	-4
Ru-3e	90	10	0
Ru-18e	73	27	0

Table C.30. RCM of **16** (10 mM) with 0.2 mol% of third generation catalysts at 25 °C in C₆H₆.

[Ru]	Diene (%)	RCM (%)	Missing (%)
None	100	0	0
Ru-3b	11	93	-3
Ru-18b	3	99	-1
Ru-3c	2	99	-1
Ru-18c	0	93	7
Ru-3d	2	98	1
Ru-18d	1	101	-2
Ru-3e	53	45	2
Ru-18e	2	98	0

Table C.31. RCM of **3** (10 mM) with 0.2 mol% of third generation catalysts at 25 °C in (ClCH₂)₂.

[Ru]	Diene (%)	RCM (%)	Missing (%)
None	100	0	0
Ru-3b	37	62	1
Ru-18b	30	71	-1
Ru-3c	27	75	-2
Ru-18c	30	69	1
Ru-3d	22	78	0
Ru-18d	18	83	-1
Ru-3e	81	17	2
Ru-18e	61	38	1

Table C.32. RCM of **7** (100 mM) with 0.5 mol% **Ru-1a** at 40 °C in CH₂Cl₂.

time (min)	diene (%)	error (+/-)	RCM (%)	error (+/-)	admet (%)	error (+/-)
0	100	0.0	0	0.0	0	0.0
5	45	0.6	54	6.4	1	7.0
10	30	1.2	69	0.9	1	0.3
15	30	0.4	70	1.9	1	2.3
30	20	0.1	79	3.9	1	4.0
60	9	0.0	90	0.5	1	0.5
90	6	0.0	94	1.1	1	1.1

Table C.33. RCM of **7** (100 mM) with 0.5 mol% **Ru-3b** at 40 °C in THF.

time (min)	diene (%)	error (+/-)	RCM (%)	error (+/-)	admet (%)	error (+/-)
0	100	0.0	0	0.0	0	0.0
5	16	0.6	68	1.8	16	2.5
10	3	0.2	79	2.0	18	1.8
15	1	0.0	82	2.9	18	3.0
30	0	0.0	84	1.8	16	1.8
60	0	0.0	89	0.2	11	0.2
90	0	0.0	97	0.8	3	0.8

Table C.34. RCM of **7** (100 mM) with 0.5 mol% **Ru-3b** at 40 °C in CH₂Cl₂.

time (min)	diene (%)	error (+/-)	RCM (%)	error (+/-)	admet (%)	error (+/-)
0	100	0.0	0	0.0	0	0.0
5	25	0.6	56	6.4	19	7.0
10	8	1.2	74	0.9	18	0.3
15	3	0.4	84	1.9	13	2.3
30	1	0.1	83	3.9	16	4.0
60	0	0.0	94	0.5	6	0.5
90	0	0.0	101	1.1	-1	1.1

Table C.35. RCM of **7** (100 mM) with 0.5 mol% **Ru-18b** at 40 °C in THF.

time (min)	diene (%)	error (+/-)	RCM (%)	error (+/-)	admet (%)	error (+/-)
0	100	0.0	0	0.0	0	0.0
5	4	0.6	87	1.8	9	2.5
10	0	0.2	90	2.0	10	1.8
15	0	0.0	93	2.9	7	3.0
30	0	0.0	96	1.8	4	1.8
60	0	0.0	96	0.2	4	0.2
90	0	0.0	96	0.8	4	0.8

Table C.36. RCM of **7** (100 mM) with 0.5 mol% **Ru-18b** at 40 °C in CH₂Cl₂.

time (min)	diene (%)	error (+/-)	RCM (%)	error (+/-)	admet (%)	error (+/-)
0	100	0.0	0	0.0	0	0.0

5	16	0.6	79	6.4	5	7.0
10	2	1.2	89	0.9	9	0.3
15	1	0.4	92	1.9	7	2.3
30	0	0.1	93	3.9	7	4.0
60	0	0.0	94	0.5	6	0.5
90	0	0.0	94	1.1	6	1.1

Table C.37. Phenol additive screen with **Ru-18b** for the RCEYM of **9**

Additive	Equivalents			
	10	20	70	100
16	1	8	8	8
18	9	11	10	8
17	11	11	9	9
35	12	10	10	8
36	7	7	6	6
34	12	14	11	12
33	11	1	12	11
37	9	1	11	9
38	9	10	8	8
<i>(R)</i> - 19	8	9	8	8
none	13	11	13	11

Table C.38 Formation of **10a** in the isomerization of **3** by 2 mol% [Ru] at 60 °C 3 h.

[Ru]	CH ₂ Cl ₂	error (+/-)	CH ₂ Cl ₂		C ₆ D ₆	error (+/-)	C ₆ D ₆	
			+MeOH	error (+/-)			+MeOH	error (+/-)
Ru-25a	6	0.3	10	1.7	7	1.0	8	0.3
Ru-26a	17	2.8	34	5.3	11	3.8	22	3.6
Ru-25b	14	1.3	23	1.6	7	0.7	38	2.7
Ru-26b	11	1.1	31	2.2	11	1.0	41	2.3

Table C.39. Formation of **10b** in the isomerization of **3** by 2 mol% [Ru] at 60 °C 3 h.

[Ru]	CH ₂ Cl ₂	error (+/-)	CH ₂ Cl ₂		C ₆ D ₆	error (+/-)	C ₆ D ₆	
			+MeOH	error (+/-)			+MeOH	error (+/-)
Ru-25a	7	1.2	21	7.0	21	3.7	20	1.7
Ru-26a	12	3.1	12	0.8	6	1.1	10	0.6
Ru-25b	6	0.2	9	0.2	11	0.1	7	0.8
Ru-26b	16	1.2	16	2.8	8	0.2	11	3.7

Table C.40. Formation of **11a** in the isomerization of **3** by 2 mol% [Ru] at 60 °C 3 h.

[Ru]	CH ₂ Cl ₂	error (+/-)	CH ₂ Cl ₂		C ₆ D ₆	error (+/-)	C ₆ D ₆	
			+MeOH	error (+/-)			+MeOH	error (+/-)
Ru-25a	2	1.7	6	0.7	5	0.1	6	0.0

Ru-26a	0	0.0	1	0.6	0	0.0	1	0.7
Ru-25b	2	0.7	3	0.8	3	0.7	3	0.7
Ru-26b	2	0.9	2	1.3	1	0.6	1	1.2

Table C.41. Formation of **11b** in the isomerization of **3** by 2 mol% [Ru] at 60 °C 3 h.

[Ru]	CH ₂ Cl ₂				C ₆ D ₆			
	CH ₂ Cl ₂	error (+/-)	+MeOH	error (+/-)	C ₆ D ₆	error (+/-)	+MeOH	error (+/-)
Ru-25a	14	1.4	0	0.0	2	2.3	0	0.5
Ru-26a	0	0.3	0	0.3	0	0.3	0	0.3
Ru-25b	8	0.2	2	0.4	3	0.5	0	0.0
Ru-26b	0	0.2	0	0.0	0	0.0	0	0.0

Table C.42. RCM of **1** and **2** (100 mM) by 5 mol% **Ru-1a** and **Ru-1c**.

Substrate	Catalyst	Temp (°C)	Solv.	Time (h)	Conv. (%) ^[1]
1	Ru-1a	RT	CH ₂ Cl ₂	1	
1	Ru-1c	RT	CD ₂ Cl ₂	1	>99
1	Ru-1a	40	CD ₂ Cl ₂	1	>99
2	Ru-1a	40	CD ₂ Cl ₂	1	1
2	Ru-1a	80	C ₇ D ₈	1	0
2	Ru-1c	40	CD ₂ Cl ₂	1	14
2	Ru-1c	40	CD ₂ Cl ₂	24	23
2	Ru-1c	80	C ₇ D ₈	1	32
2	Ru-1c	80	C ₇ D ₈	24	33

^[1]Values determined by integration of ¹H NMR signals. Duplicate analysis, within ±3%. (**Ru-1c** with **2** was only done once)

D. Crystallographic Data**Table D.1.** Crystallographic Parameters for RuHCl(N₂)(IMes)₂ **Ru-8.**

	Ru-8
Crystallographer	Dalgarno
CCDC #	792128
empirical formula	C ₄₂ H _{48.75} ClN ₆ Ru
Color, shape	Red Plate
formula wt	774.14
temp. °K	173(2)
wavelength, Å	0.71073
crystal syst, space group	Monoclinic, <i>C2/c</i>
Size (mm)	0.08 × 0.07 × 0.05
<i>a</i> [Å]	20.985(4)
<i>b</i> [Å]	20.967(3)
<i>c</i> [Å]	19.412(3)
α [°]	90
β [°]	109.171(3)°
γ [°]	90
<i>V</i> , Å ³	8068(2)
<i>Z</i> , calcd density, mg/cm ³	8, 1.275
μ , mm ⁻¹	0.491
<i>F</i> (000)	3230
<i>Q</i> range for data collec. Deg	1.41° < θ < 27.11°
limiting indices	-24 ≤ <i>h</i> ≤ 26 -26 ≤ <i>k</i> ≤ 26 -24 ≤ <i>l</i> ≤ 22
no. of rflns collected/unique	28361/ 8841 [<i>R</i> (int) = 0.0306]
abs cor	None
Diffractometer	Bruker SMART 1000 CCD diffractometer
max, min transmission	0.9761–0.9621
refinement method	full-matrix least-squares on <i>F</i> ² (<i>SHELXL-97</i>)
no. of data/restraints/params	8841 / 0 / 494
goodness of fit on <i>F</i> ²	1.03
final <i>R</i> indices	<i>R</i> ₁ = 0.0349, <i>wR</i> ₂ = 0.0956
[<i>I</i> > 2s(<i>I</i>)]	
largest diff peak, hole, e/Å ³	0.82 and -0.271

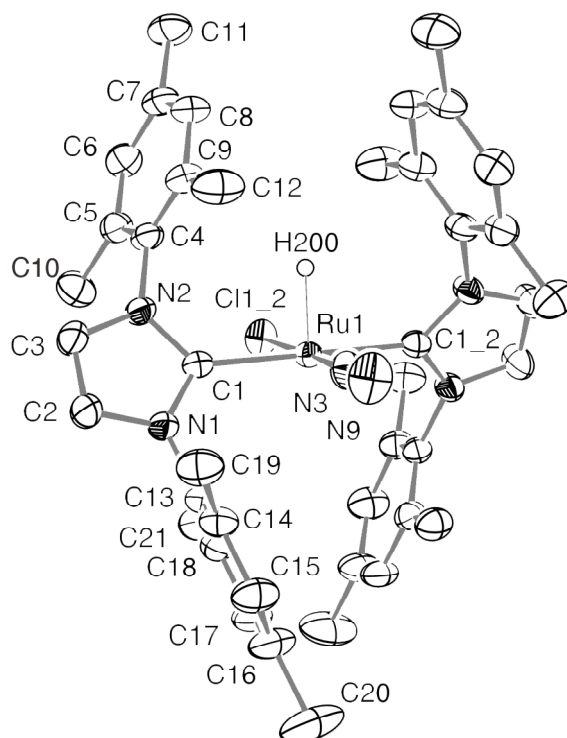


Figure D.1. ORTEP representation of $\text{RuHCl}(\text{N}_2)(\text{IMes})_2$ **Ru-8**. Non-hydrogen ellipsoids at the 50% probability level.

Table D.2. Bond lengths for $\text{RuHCl}(\text{N}_2)(\text{IMes})_2$ **Ru-8** (Å).

Ru(1)-N(3)	1.826(7)	Ru(1)-N(3) ^(a)	1.826(7)
Ru(1)-C(1)	2.076(2)	Ru(1)-C(1) ^(a)	2.076(2)
Ru(1)-Cl(1) ^(a)	2.446(3)	Ru(1)-Cl(1)	2.446(3)
N(1)-C(1)	1.365(3)	N(1)-C(2)	1.387(3)
N(1)-C(13)	1.447(3)	C(1)-N(2)	1.371(3)
Ru(2)-N(7)	1.785(9)	Ru(2)-N(6)	1.855(9)
Ru(2)-C(22) ^(b)	2.073(2)	Ru(2)-C(22)	2.073(2)
Ru(2)-Cl(2)	2.443(3)	Ru(2)-Cl(3)	2.444(4)
N(2)-C(3)	1.383(3)	N(2)-C(4)	1.447(3)
C(2)-C(3)	1.338(4)	N(3)-N(9)	1.102(10)
N(4)-C(22)	1.368(3)	N(4)-C(24)	1.385(3)
N(4)-C(25)	1.451(3)	C(4)-C(5)	1.391(4)
C(4)-C(9)	1.397(3)	N(5)-C(22)	1.369(3)
N(5)-C(23)	1.385(3)	N(5)-C(34)	1.442(3)
C(5)-C(6)	1.386(3)	C(5)-C(10)	1.515(4)
N(6)-N(8)	1.050(13)	C(6)-C(7)	1.391(4)
N(7)-N(10)	1.168(12)	C(7)-C(8)	1.385(4)
C(7)-C(11)	1.518(3)	C(8)-C(9)	1.396(3)
C(9)-C(12)	1.501(4)	C(13)-C(14)	1.395(4)
C(13)-C(18)	1.396(3)	C(14)-C(15)	1.390(4)
C(14)-C(19)	1.508(4)	C(15)-C(16)	1.391(4)
C(16)-C(17)	1.383(4)	C(16)-C(20)	1.517(4)
C(17)-C(18)	1.401(3)	C(18)-C(21)	1.509(4)
C(23)-C(24)	1.338(4)	C(25)-C(26)	1.388(3)
C(25)-C(30)	1.402(3)	C(26)-C(27)	1.394(3)

C(26)-C(31)	1.508(4)	C(27)-C(28)	1.391(4)
C(28)-C(29)	1.386(4)	C(28)-C(32)	1.513(3)
C(29)-C(30)	1.396(4)	C(30)-C(33)	1.504(4)
C(34)-C(39)	1.396(3)	C(34)-C(35)	1.401(3)
C(35)-C(36)	1.394(3)	C(35)-C(40)	1.511(3)
C(36)-C(37)	1.394(4)	C(37)-C(38)	1.385(4)
C(37)-C(41)	1.519(4)	C(38)-C(39)	1.386(4)
C(39)-C(42)	1.510(4)		

Key giving operations for symmetry related atoms: (a) -x, +y, 1/2-z; (b) 1-x, +y, 1/2-z

Table D.3. Bond angles for RuHCl(N₂)(IMes)₂ **Ru-8** (°).

N(3)-Ru(1)-N(3) ^(a)	177.0(5)	N(3)-Ru(1)-C(1)	89.3(3)
N(3) ^(a) -Ru(1)-C(1)	90.7(3)	N(3)-Ru(1)-C(1) ^(a)	90.7(3)
N(3) ^(a) -Ru(1)-C(1) ^(a)	89.3(3)	C(1)-Ru(1)-C(1) ^(a)	179.65(11)
N(3)-Ru(1)-Cl(1) ^(a)	178.6(3)	N(3) ^(a) -Ru(1)-Cl(1) ^(a)	1.6(3)
C(1)-Ru(1)-Cl(1) ^(a)	90.43(9)	C(1) ^(a) -Ru(1)-Cl(1) ^(a)	89.57(9)
N(3)-Ru(1)-Cl(1)	1.6(3)	N(3) ^(a) -Ru(1)-Cl(1)	178.6(3)
C(1)-Ru(1)-Cl(1)	89.57(9)	C(1) ^(a) -Ru(1)-Cl(1)	90.43(9)
Cl(1) ^(a) -Ru(1)-Cl(1)	179.81(13)	C(1)-N(1)-C(2)	112.2(2)
C(1)-N(1)-C(13)	124.99(19)	C(2)-N(1)-C(13)	122.8(2)
N(1)-C(1)-N(2)	102.7(2)	N(1)-C(1)-Ru(1)	128.50(16)
N(2)-C(1)-Ru(1)	128.80(16)	N(7)-Ru(2)-N(6)	180.0000(10)
N(7)-Ru(2)-C(22) ^(b)	89.47(6)	N(6)-Ru(2)-C(22) ^(b)	90.53(6)
N(7)-Ru(2)-C(22)	89.47(6)	N(6)-Ru(2)-C(22)	90.53(6)
C(22) ^(b) -Ru(2)-C(22)	178.93(12)	N(7)-Ru(2)-Cl(2)	180.
C(22) ^(b) -Ru(2)-Cl(2)	90.53(6)	C(22)-Ru(2)-Cl(2)	90.53(6)
N(6)-Ru(2)-Cl(3)	180.	C(22) ^(b) -Ru(2)-Cl(3)	89.47(6)
C(22)-Ru(2)-Cl(3)	89.47(6)	Cl(2)-Ru(2)-Cl(3)	180.
C(1)-N(2)-C(3)	111.7(2)	C(1)-N(2)-C(4)	124.8(2)
C(3)-N(2)-C(4)	123.5(2)	C(3)-C(2)-N(1)	106.4(2)
N(9)-N(3)-Ru(1)	178.0(13)	C(2)-C(3)-N(2)	107.1(2)
C(22)-N(4)-C(24)	112.1(2)	C(22)-N(4)-C(25)	124.4(2)
C(24)-N(4)-C(25)	123.5(2)	C(5)-C(4)-C(9)	122.2(2)
C(5)-C(4)-N(2)	118.7(2)	C(9)-C(4)-N(2)	119.1(2)
C(22)-N(5)-C(23)	111.9(2)	C(22)-N(5)-C(34)	125.0(2)
C(23)-N(5)-C(34)	123.1(2)	C(6)-C(5)-C(4)	118.0(2)
C(6)-C(5)-C(10)	120.6(2)	C(4)-C(5)-C(10)	121.4(2)
N(8)-N(6)-Ru(2)	180.	C(5)-C(6)-C(7)	121.8(2)
N(10)-N(7)-Ru(2)	180.0000(10)	C(8)-C(7)-C(6)	118.6(2)
C(8)-C(7)-C(11)	120.4(2)	C(6)-C(7)-C(11)	121.0(3)
C(7)-C(8)-C(9)	121.8(2)	C(8)-C(9)-C(4)	117.5(2)
C(8)-C(9)-C(12)	120.5(2)	C(4)-C(9)-C(12)	122.0(2)
C(14)-C(13)-C(18)	122.4(2)	C(14)-C(13)-N(1)	118.3(2)
C(18)-C(13)-N(1)	119.3(2)	C(15)-C(14)-C(13)	117.7(2)
C(15)-C(14)-C(19)	120.5(2)	C(13)-C(14)-C(19)	121.7(2)
C(14)-C(15)-C(16)	121.9(3)	C(17)-C(16)-C(15)	118.8(2)
C(17)-C(16)-C(20)	120.4(3)	C(15)-C(16)-C(20)	120.8(3)
C(16)-C(17)-C(18)	121.8(2)	C(13)-C(18)-C(17)	117.4(2)
C(13)-C(18)-C(21)	122.5(2)	C(17)-C(18)-C(21)	120.1(2)
N(4)-C(22)-N(5)	102.5(2)	N(4)-C(22)-Ru(2)	128.96(17)
N(5)-C(22)-Ru(2)	128.45(17)	C(24)-C(23)-N(5)	106.9(2)
C(23)-C(24)-N(4)	106.6(2)	C(26)-C(25)-C(30)	122.5(2)
C(26)-C(25)-N(4)	119.5(2)	C(30)-C(25)-N(4)	118.0(2)

C(25)-C(26)-C(27)	117.9(2)	C(25)-C(26)-C(31)	121.7(2)
C(27)-C(26)-C(31)	120.4(2)	C(28)-C(27)-C(26)	121.8(2)
C(29)-C(28)-C(27)	118.4(2)	C(29)-C(28)-C(32)	121.0(2)
C(27)-C(28)-C(32)	120.6(2)	C(28)-C(29)-C(30)	122.2(2)
C(29)-C(30)-C(25)	117.1(2)	C(29)-C(30)-C(33)	121.4(2)
C(25)-C(30)-C(33)	121.5(2)	C(39)-C(34)-C(35)	122.1(2)
C(39)-C(34)-N(5)	118.5(2)	C(35)-C(34)-N(5)	119.5(2)
C(36)-C(35)-C(34)	118.0(2)	C(36)-C(35)-C(40)	120.0(2)
C(34)-C(35)-C(40)	122.0(2)	C(37)-C(36)-C(35)	121.3(3)
C(38)-C(37)-C(36)	118.6(2)	C(38)-C(37)-C(41)	121.5(3)
C(36)-C(37)-C(41)	119.8(3)	C(37)-C(38)-C(39)	122.5(3)
C(38)-C(39)-C(34)	117.5(2)	C(38)-C(39)-C(42)	120.7(2)
C(34)-C(39)-C(42)	121.7(2)		

Key giving operations for symmetry related atoms: (a) -x, +y, 1/2-z; (b) 1-x, +y, 1/2-z

Table D.4. Crystallographic Parameters for Ru(BINO)(PPh₃)_x(L)_y complexes

	Ru-11''	Ru-12'	Ru-14'
Crystallographer	McDonald	McDonald	McDonald
CCDC #	796872	796870	796871
empirical formula	C ₅₆ H ₄₂ O ₂ P ₂ Ru	C ₆₂ H ₅₃ NO ₃ P ₂ Ru	C ₅₃ H ₄₉ N ₂ O _{3.25} PRu
Color, shape	red, prism	Orange, plate	Orange, prism
formula wt	909.91	1023.06	897.98
temp. °K	173(2)	173(2)	173(2)
wavelength, Å	0.71073	0.71073	0.71073
crystal syst.	Orthorhombic	Orthorhombic	Orthorhombic
space group	<i>P</i> 2 ₁ 2 ₁ 2 ₁ (No. 19)	<i>P</i> 2 ₁ 2 ₁ 2 ₁ (No. 19)	<i>P</i> 2 ₁ 2 ₁ 2 (No. 18)
Size (mm)	0.14 × 0.13 × 0.10	0.44 × 0.11 × 0.03	0.43 × 0.25 × 0.24
<i>a</i> [Å]	13.0968 (6)	13.1015 (5)	18.0557 (4)
<i>b</i> [Å]	14.0641 (7)	13.4592 (5)	19.4773 (5)
<i>c</i> [Å]	23.0032 (11)	28.5044 (10)	12.7568 (3)
α [°]	90	90	90
β [°]	90	90	90
γ [°]	90	90	90
<i>V</i> , Å ³	4237.1 (4)	5026.3 (3)	4486.26 (19)
<i>Z</i> , calcd density, mg/cm ³	4, 1.426	4, 1.352	4, 1.330
μ , mm ⁻¹	0.490	0.424	0.431
<i>F</i> (000)	1872	2120	1864
<i>Q</i> range for data collec.	2.29° < θ < 24.94°	1.43° < θ < 25.69°	1.54° < θ < 27.51°
limiting indices	-16 ≤ <i>h</i> ≤ 16 -17 ≤ <i>k</i> ≤ 17 -28 ≤ <i>l</i> ≤ 28	-15 ≤ <i>h</i> ≤ 15 -16 ≤ <i>k</i> ≤ 16 -34 ≤ <i>l</i> ≤ 34	-23 ≤ <i>h</i> ≤ 23 -25 ≤ <i>k</i> ≤ 25 -16 ≤ <i>l</i> ≤ 16
no. of rflns collected/unique	34014/ 8676 (<i>R</i> _{int} = 0.0496)	37705/9548 (<i>R</i> _{int} = 0.0785)	40159 / 10315 (<i>R</i> _{int} = 0.0195)
abs cor	Gaussian integration (face-indexed)	Gaussian integration (face-indexed)	Gaussian integration (face-indexed)
Diffraction max, min transmission	Bruker D8/APEX II CCD 0.9535–0.9323	Bruker D8/APEX II CCD 0.9891–0.8355	Bruker D8/APEX II CCD 0.9044–0.8377
refinement method	full-matrix least-squares on	full-matrix least-squares on	full-matrix least-squares on

no. of data/restraints/params	F^2 (SHELXL-97) 8676 / 0 / 550	F^2 (SHELXL-97) 9548 / 10 ^[a] / 611	F^2 (SHELXL-97) 10315 / 3 ^[b] / 528
goodness of fit on F^2	1.027	1.023	1.083
final R indices	$R_1 = 0.0268$, $wR_2 = 0.0561$	$R_1 = 0.0380$, $wR_2 = 0.0812$	$R_1 = 0.0316$, $wR_2 = 0.0985$
$R_1 [F_o^2 \geq 2s(F_o^2)]$			
wR_2 [all data]			
largest diff peak, hole, $e/\text{\AA}^3$	0.328 and $-0.316 e \text{\AA}^{-3}$	0.650 and $-0.392 e \text{\AA}^{-3}$	1.028 and $-0.358 e \text{\AA}^{-3}$

[a] O–C distances within the disordered solvent tetrahydrofuran molecule (O1S–C1S, O1S–C4S, O2S–C5S, O2S–C8S) were constrained to be equal (within 0.03 Å) to a common refined value. The same was done for the C–C distances (C1S–C2S, C2S–C3S, C3S–C4S, C5S–C6S, C6S–C7S, C7S–C8S) using a different common refined value. [b] Distances within the solvent tetrahydrofuran molecule were restrained to idealized values during refinement: $d(\text{O10S}–\text{C11S}) = 1.46(1) \text{ \AA}$; $d(\text{C11S}–\text{C12S}) = d(\text{C12S}–\text{C12S}') = 1.52(1) \text{ \AA}$ (C12S' is related to C12S via the crystallographic twofold rotational axis $(0, \frac{1}{2}, z)$, upon which O10S is located).

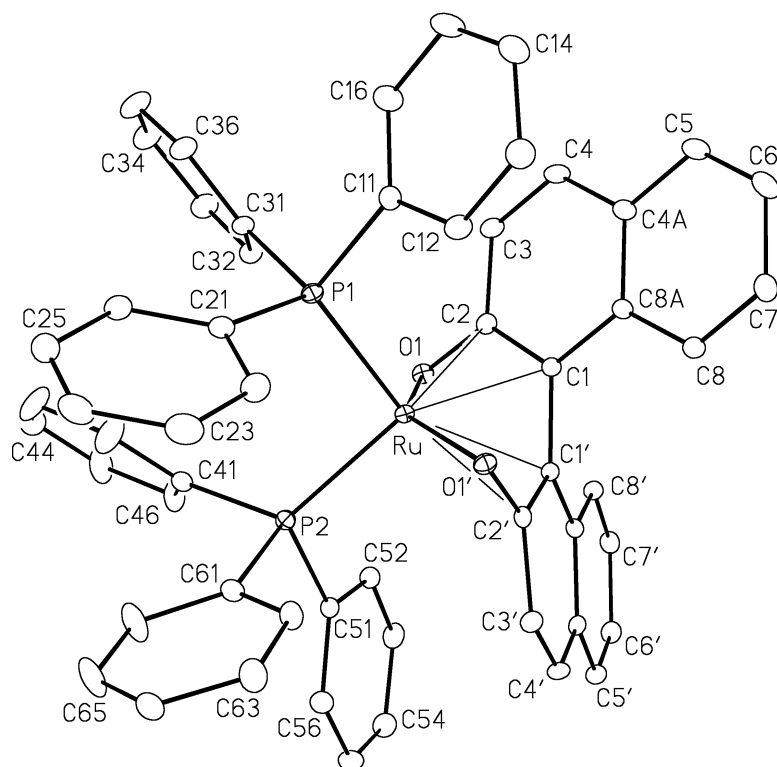


Figure D.2. ORTEP representation of $\text{Ru}(\text{BINO})(\text{PPh}_3)_2$ **Ru-11''**. Non-hydrogen ellipsoids at the 20% probability level.

Table D.5. Bond lengths for $\text{Ru}(\text{BINO})(\text{PPh}_3)_2$ **Ru-11''** (Å).

Ru	P1	2.2613(7)	C8'	C8A'	1.407(3)
Ru	P2	2.2836(7)	C11	C12	1.399(4)
Ru	O1	2.1348(17)	C11	C16	1.389(4)
Ru	O1'	2.1695(16)	C12	C13	1.386(4)
Ru	C1	2.257(2)	C13	C14	1.388(4)
Ru	C2	2.273(2)	C14	C15	1.371(4)

Ru	C1'	2.266(2)	C15	C16	1.388(4)
Ru	C2'	2.310(2)	C21	C22	1.398(4)
P1	C11	1.846(3)	C21	C26	1.393(4)
P1	C21	1.842(3)	C22	C23	1.388(4)
P1	C31	1.830(3)	C23	C24	1.378(4)
P2	C41	1.850(3)	C24	C25	1.364(4)
P2	C51	1.832(2)	C25	C26	1.391(4)
P2	C61	1.828(3)	C31	C32	1.390(3)
O1	C2	1.328(3)	C31	C36	1.397(3)
O1'	C2'	1.321(3)	C32	C33	1.399(3)
C1	C2	1.428(3)	C33	C34	1.376(4)
C1	C8A	1.452(3)	C34	C35	1.377(4)
C1	C1'	1.497(3)	C35	C36	1.385(4)
C2	C3	1.430(3)	C41	C42	1.379(4)
C3	C4	1.351(3)	C41	C46	1.384(4)
C4	C4A	1.431(3)	C42	C43	1.398(5)
C4A	C5	1.411(3)	C43	C44	1.357(5)
C4A	C8A	1.421(3)	C44	C45	1.360(5)
C5	C6	1.360(4)	C45	C46	1.405(4)
C6	C7	1.404(4)	C51	C52	1.397(3)
C7	C8	1.370(3)	C51	C56	1.390(3)
C8	C8A	1.402(3)	C52	C53	1.387(3)
C1'	C2'	1.430(3)	C53	C54	1.390(4)
C1'	C8A'	1.451(3)	C54	C55	1.381(4)
C2'	C3'	1.442(3)	C55	C56	1.393(4)
C3'	C4'	1.353(3)	C61	C62	1.383(4)
C4'	C4A'	1.422(3)	C61	C66	1.394(4)
C4A'	C5'	1.406(3)	C62	C63	1.386(4)
C4A'	C8A'	1.421(3)	C63	C64	1.368(4)
C5'	C6'	1.367(4)	C64	C65	1.363(4)
C6'	C7'	1.395(3)	C65	C66	1.382(4)
C7'	C8'	1.380(3)			

Table D.6. Bond angles for Ru(BINO)(PPh₃)₂ **Ru-11''** (°).

P1	Ru	P2	96.62(2)	C1	C1'	C2'	118.8(2)
P1	Ru	O1	103.43(5)	C1	C1'	C8A'	121.8(2)
P1	Ru	O1'	101.25(5)	C2'	C1'	C8A'	119.4(2)
P1	Ru	C1	113.01(6)	Ru	C2'	O1'	67.12(11)
P1	Ru	C2	96.30(6)	Ru	C2'	C1'	70.12(12)
P1	Ru	C1'	148.05(7)	Ru	C2'	C3'	134.64(17)
P1	Ru	C2'	135.26(6)	O1'	C2'	C1'	120.1(2)
P2	Ru	O1	99.28(5)	O1'	C2'	C3'	121.1(2)
P2	Ru	O1'	105.27(5)	C1'	C2'	C3'	118.7(2)
P2	Ru	C1	148.78(6)	C2'	C3'	C4'	120.7(2)
P2	Ru	C2	134.15(6)	C3'	C4'	C4A'	122.4(2)
P2	Ru	C1'	114.52(6)	C4'	C4A'	C5'	121.7(2)
P2	Ru	C2'	99.18(6)	C4'	C4A'	C8A'	119.0(2)
O1	Ru	O1'	142.64(6)	C5'	C4A'	C8A'	119.2(2)
O1	Ru	C1	65.43(8)	C4A'	C5'	C6'	121.2(2)
O1	Ru	C2	34.88(7)	C5'	C6'	C7'	120.0(2)
O1	Ru	C1'	79.39(7)	C6'	C7'	C8'	120.3(2)
O1	Ru	C2'	114.79(7)	C7'	C8'	C8A'	121.0(2)
O1'	Ru	C1	79.27(8)	C1'	C8A'	C4A'	119.4(2)
O1'	Ru	C2	114.93(8)	C1'	C8A'	C8'	122.3(2)

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O1'	Ru	C1'	64.99(7)	C4A'	C8A'	C8'	118.3(2)
O1'	Ru	C2'	34.12(7)	P1	C11	C12	117.8(2)
C1	Ru	C2	36.75(9)	P1	C11	C16	124.5(2)
C1	Ru	C1'	38.66(8)	C12	C11	C16	117.7(2)
C1	Ru	C2'	66.95(8)	C11	C12	C13	120.8(3)
C2	Ru	C1'	67.57(8)	C12	C13	C14	120.4(3)
C2	Ru	C2'	101.85(8)	C13	C14	C15	119.2(3)
C1'	Ru	C2'	36.41(8)	C14	C15	C16	120.6(3)
Ru	P1	C11	109.86(9)	C11	C16	C15	121.1(3)
Ru	P1	C21	115.32(8)	P1	C21	C22	117.8(2)
Ru	P1	C31	118.97(8)	P1	C21	C26	124.4(2)
C11	P1	C21	102.53(11)	C22	C21	C26	117.5(3)
C11	P1	C31	103.55(12)	C21	C22	C23	121.2(3)
C21	P1	C31	104.80(12)	C22	C23	C24	119.7(3)
Ru	P2	C41	119.35(9)	C23	C24	C25	120.3(3)
Ru	P2	C51	108.19(8)	C24	C25	C26	120.3(3)
Ru	P2	C61	119.58(9)	C21	C26	C25	120.9(3)
C41	P2	C51	100.98(12)	P1	C31	C32	118.16(19)
C41	P2	C61	102.40(13)	P1	C31	C36	123.2(2)
C51	P2	C61	103.86(11)	C32	C31	C36	118.6(2)
Ru	O1	C2	78.26(14)	C31	C32	C33	120.3(2)
Ru	O1'	C2'	78.76(12)	C32	C33	C34	120.2(3)
Ru	C1	C2	72.23(14)	C33	C34	C35	119.9(3)
Ru	C1	C8A	130.77(17)	C34	C35	C36	120.5(3)
Ru	C1	C1'	70.98(12)	C31	C36	C35	120.5(3)
C2	C1	C8A	119.4(2)	P2	C41	C42	119.5(2)
C2	C1	C1'	119.3(2)	P2	C41	C46	123.1(2)
C8A	C1	C1'	121.3(2)	C42	C41	C46	117.4(3)
Ru	C2	O1	66.86(13)	C41	C42	C43	121.3(3)
Ru	C2	C1	71.02(14)	C42	C43	C44	120.8(3)
Ru	C2	C3	133.38(17)	C43	C44	C45	119.0(3)
O1	C2	C1	119.1(2)	C44	C45	C46	121.0(3)
O1	C2	C3	121.4(2)	C41	C46	C45	120.6(3)
C1	C2	C3	119.5(2)	P2	C51	C52	118.42(18)
C2	C3	C4	120.9(2)	P2	C51	C56	123.2(2)
C3	C4	C4A	121.7(2)	C52	C51	C56	118.4(2)
C4	C4A	C5	121.4(2)	C51	C52	C53	121.1(2)
C4	C4A	C8A	119.6(2)	C52	C53	C54	119.5(3)
C5	C4A	C8A	119.0(2)	C53	C54	C55	120.0(3)
C4A	C5	C6	120.7(2)	C54	C55	C56	120.2(3)
C5	C6	C7	120.6(2)	C51	C56	C55	120.5(3)
C6	C7	C8	119.8(3)	P2	C61	C62	118.7(2)
C7	C8	C8A	121.3(2)	P2	C61	C66	124.2(2)
C1	C8A	C4A	118.8(2)	C62	C61	C66	117.2(3)
C1	C8A	C8	122.6(2)	C61	C62	C63	121.3(3)
C4A	C8A	C8	118.6(2)	C62	C63	C64	120.6(3)
Ru	C1'	C1	70.36(12)	C63	C64	C65	119.0(3)
Ru	C1'	C2'	73.47(12)	C64	C65	C66	121.0(3)
Ru	C1'	C8A'	127.83(17)	C61	C66	C65	120.9(3)

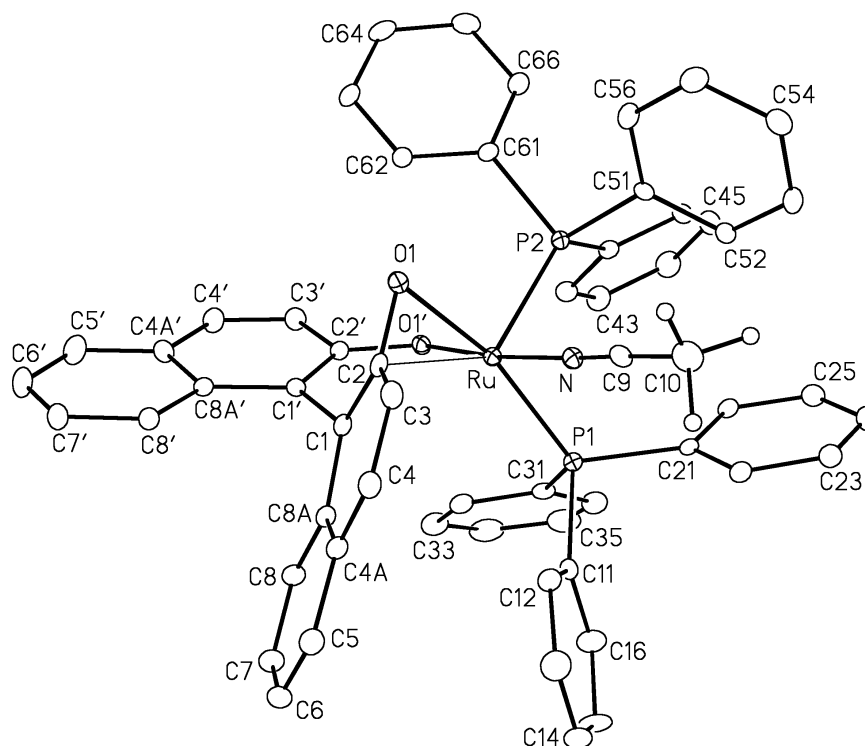


Figure D.3. ORTEP representation of Ru(BINO)(PPh₃)₂(MeCN) **Ru-12'**. Non-hydrogen ellipsoids at the 20% probability level.

Table D.7. Bond lengths for Ru(BINO)(PPh₃)₂(MeCN) **Ru-12'** (Å).

Ru	P1	2.2968(11)	C8'	C8A'	1.409(6)
Ru	P2	2.2793(11)	C9	C10	1.463(6)
Ru	O1	2.159(3)	C11	C12	1.374(5)
Ru	O1'	2.043(2)	C11	C16	1.403(6)
Ru	N	2.017(3)	C12	C13	1.387(6)
Ru	C1	2.592(4) ^[a]	C13	C14	1.361(7)
Ru	C2	2.315(4)	C14	C15	1.375(7)
P1	C11	1.849(4)	C15	C16	1.386(6)
P1	C21	1.848(4)	C21	C22	1.394(6)
P1	C31	1.829(4)	C21	C26	1.390(6)
P2	C41	1.828(4)	C22	C23	1.387(6)
P2	C51	1.825(4)	C23	C24	1.387(7)
P2	C61	1.849(4)	C24	C25	1.380(7)
O1	C2	1.320(5)	C25	C26	1.381(6)
O1'	C2'	1.324(4)	C31	C32	1.390(5)
N	C9	1.136(5)	C31	C36	1.385(6)
C1	C1'	1.501(5)	C32	C33	1.398(6)
C1	C2	1.422(5)	C33	C34	1.382(7)
C1	C8A	1.442(5)	C34	C35	1.372(7)
C1'	C2'	1.384(5)	C35	C36	1.406(6)
C1'	C8A'	1.445(5)	C41	C42	1.392(5)
C2	C3	1.446(5)	C41	C46	1.393(5)
C2'	C3'	1.428(5)	C42	C43	1.398(6)
C3	C4	1.359(5)	C43	C44	1.378(6)

C3'	C4'	1.350(5)	C44	C45	1.367(6)
C4	C4A	1.418(6)	C45	C46	1.387(6)
C4'	C4A'	1.412(6)	C51	C52	1.401(5)
C4A	C5	1.417(5)	C51	C56	1.380(5)
C4A	C8A	1.418(5)	C52	C53	1.386(5)
C4A'	C5'	1.421(6)	C53	C54	1.375(5)
C4A'	C8A'	1.422(5)	C54	C55	1.384(6)
C5	C6	1.371(6)	C55	C56	1.381(6)
C5'	C6'	1.365(6)	C61	C62	1.385(5)
C6	C7	1.391(6)	C61	C66	1.389(5)
C6'	C7'	1.390(6)	C62	C63	1.398(5)
C7	C8	1.372(6)	C63	C64	1.367(6)
C7'	C8'	1.382(6)	C64	C65	1.377(6)
C8	C8A	1.411(5)	C65	C66	1.385(6)

^[a]Nonbonded interaction.

Table D.8. Bond lengths for Ru(BINO)(PPh₃)₂(MeCN) **Ru-12'** (Å).

P1	Ru	P2	99.71(4)	C6	C7	C8	121.0(4)
P1	Ru	O1	164.35(7)	C6'	C7'	C8'	120.3(4)
P1	Ru	O1'	92.21(8)	C7	C8	C8A	120.7(4)
P1	Ru	N	89.96(9)	C7'	C8'	C8A'	121.7(4)
P1	Ru	C2	130.30(10)	C1	C8A	C4A	119.9(3)
P2	Ru	O1	95.65(8)	C1	C8A	C8	121.1(3)
P2	Ru	O1'	83.51(7)	C4A	C8A	C8	118.9(4)
P2	Ru	N	91.70(10)	C1'	C8A'	C4A'	119.1(3)
P2	Ru	C2	129.48(11)	C1'	C8A'	C8'	123.3(4)
O1	Ru	O1'	92.51(10)	C4A'	C8A'	C8'	117.6(4)
O1	Ru	N	86.57(11)	N	C9	C10	178.2(4)
O1	Ru	C2	34.08(11)	P1	C11	C12	120.8(3)
O1'	Ru	N	175.02(12)	P1	C11	C16	120.0(3)
O1'	Ru	C2	99.14(12)	C12	C11	C16	119.0(4)
N	Ru	C2	82.82(13)	C11	C12	C13	121.0(4)
Ru	P1	C11	113.98(13)	C12	C13	C14	120.3(5)
Ru	P1	C21	116.62(13)	C13	C14	C15	119.5(4)
Ru	P1	C31	117.91(14)	C14	C15	C16	121.4(5)
C11	P1	C21	98.77(17)	C11	C16	C15	118.8(4)
C11	P1	C31	99.91(18)	P1	C21	C22	118.7(3)
C21	P1	C31	106.8(2)	P1	C21	C26	123.2(3)
Ru	P2	C41	120.43(13)	C22	C21	C26	118.0(4)
Ru	P2	C51	113.52(13)	C21	C22	C23	121.1(4)
Ru	P2	C61	113.27(13)	C22	C23	C24	119.9(5)
C41	P2	C51	104.68(18)	C23	C24	C25	119.4(4)
C41	P2	C61	98.58(17)	C24	C25	C26	120.4(4)
C51	P2	C61	104.26(18)	C21	C26	C25	121.1(4)
Ru	O1	C2	79.4(2)	P1	C31	C32	114.5(3)
Ru	O1'	C2'	118.9(2)	P1	C31	C36	126.7(3)
Ru	N	C9	177.9(3)	C32	C31	C36	118.7(4)
C1'	C1	C2	118.1(3)	C31	C32	C33	120.7(4)
C1'	C1	C8A	119.5(3)	C32	C33	C34	120.0(5)
C2	C1	C8A	118.8(3)	C33	C34	C35	119.9(5)
C1	C1'	C2'	121.6(3)	C34	C35	C36	120.3(5)
C1	C1'	C8A'	118.8(3)	C31	C36	C35	120.3(5)
C2'	C1'	C8A'	119.5(3)	P2	C41	C42	117.5(3)
Ru	C2	O1	66.49(19)	P2	C41	C46	123.4(3)

Ru	C2	C1	84.2(2)	C42	C41	C46	119.0(4)
Ru	C2	C3	122.3(3)	C41	C42	C43	120.0(4)
O1	C2	C1	120.1(3)	C42	C43	C44	120.2(4)
O1	C2	C3	120.5(4)	C43	C44	C45	119.8(4)
C1	C2	C3	119.3(4)	C44	C45	C46	121.0(4)
O1'	C2'	C1'	122.3(3)	C41	C46	C45	120.0(4)
O1'	C2'	C3'	117.7(3)	P2	C51	C52	120.1(3)
C1'	C2'	C3'	120.0(4)	P2	C51	C56	121.6(3)
C2	C3	C4	120.9(4)	C52	C51	C56	117.9(4)
C2'	C3'	C4'	120.6(4)	C51	C52	C53	121.0(4)
C3	C4	C4A	121.2(4)	C52	C53	C54	120.1(4)
C3'	C4'	C4A'	121.7(4)	C53	C54	C55	119.4(4)
C4	C4A	C5	121.9(4)	C54	C55	C56	120.5(4)
C4	C4A	C8A	119.7(4)	C51	C56	C55	121.1(4)
C5	C4A	C8A	118.4(4)	P2	C61	C62	121.3(3)
C4'	C4A'	C5'	121.7(4)	P2	C61	C66	120.0(3)
C4'	C4A'	C8A'	118.9(4)	C62	C61	C66	118.5(3)
C5'	C4A'	C8A'	119.4(4)	C61	C62	C63	120.2(4)
C4A	C5	C6	121.5(4)	C62	C63	C64	120.3(4)
C4A'	C5'	C6'	121.0(4)	C63	C64	C65	120.1(4)
C5	C6	C7	119.5(4)	C64	C65	C66	119.8(4)
C5'	C6'	C7'	120.1(4)	C61	C66	C65	121.0(4)

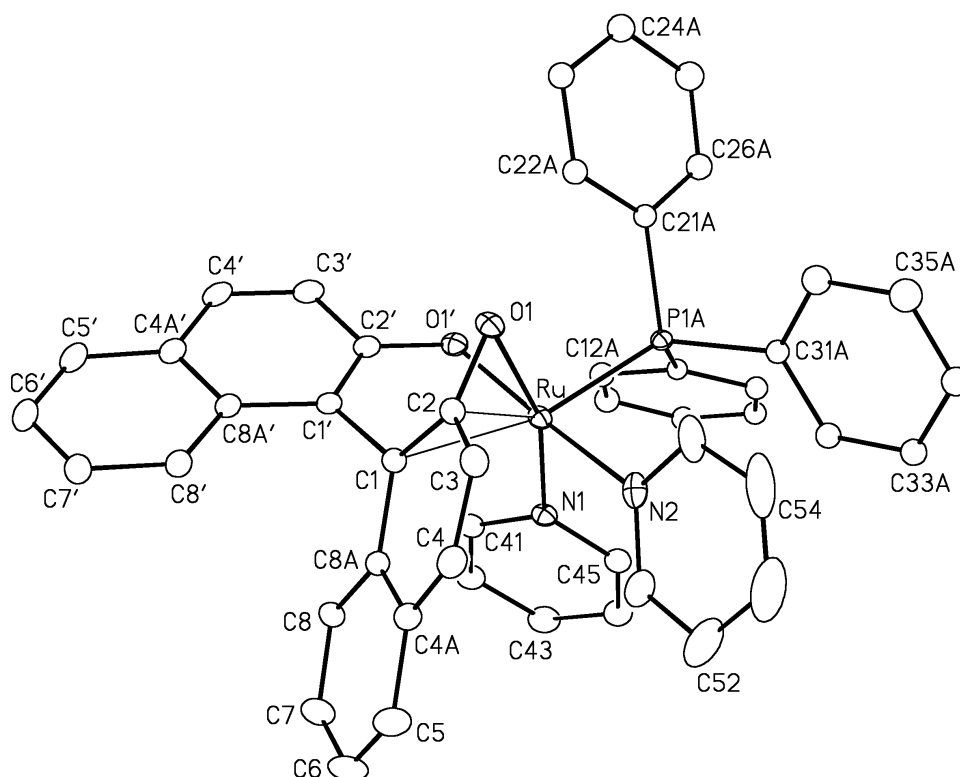


Figure D.4. ORTEP representation of Ru(BINO)(PPh₃)(py)₂ **Ru-14'**. Non-hydrogen ellipsoids at the 20% probability level.

Table D.9. Bond lengths for Ru(BINO)(PPh₃)(py)₂ **Ru-14'** (Å).

Ru	P1A	2.296(5)	C7	C8	1.379(4)
Ru	P1B	2.333(6)	C7'	C8'	1.368(4)
Ru	O1	2.1728(16)	C8	C8A	1.412(4)
Ru	O1'	2.0550(18)	C8'	C8A'	1.421(4)
Ru	N1	2.0853(19)	C11A	C12A	1.397(8)
Ru	N2	2.084(2)	C11A	C16A	1.397(7)
Ru	C1	2.323(2)	C12A	C13A	1.407(8)
Ru	C2	2.256(2)	C13A	C14A	1.389(8)
P1A	C11A	1.835(7)	C14A	C15A	1.359(8)
P1A	C21A	1.838(7)	C15A	C16A	1.405(7)
P1A	C31A	1.821(6)	C21A	C22A	1.391(7)
P1A	C11B	1.847(9)	C21A	C26A	1.386(7)
P1B	C21B	1.830(9)	C22A	C23A	1.414(8)
P1B	C31B	1.850(7)	C23A	C24A	1.392(8)
O1	C2	1.311(3)	C24A	C25A	1.406(8)
O1'	C2'	1.318(3)	C25A	C26A	1.366(8)
N1	C41	1.351(3)	C31A	C32A	1.405(8)
N1	C45	1.351(3)	C31A	C36A	1.423(7)
N2	C51	1.347(4)	C32A	C33A	1.366(9)
N2	C55	1.358(4)	C33A	C34A	1.382(8)
C1	C1'	1.503(4)	C34A	C35A	1.370(8)
C1	C2	1.444(3)	C35A	C36A	1.383(9)
C1	C8A	1.450(3)	C11B	C12B	1.356(11)
C1'	C2'	1.391(4)	C11B	C16B	1.389(9)
C1'	C8A'	1.439(4)	C12B	C13B	1.374(11)
C2	C3	1.444(4)	C13B	C14B	1.397(12)
C2'	C3'	1.435(4)	C14B	C15B	1.334(11)
C3	C4	1.350(4)	C15B	C16B	1.428(10)
C3'	C4'	1.355(4)	C21B	C22B	1.388(8)
C4	C4A	1.439(4)	C21B	C26B	1.395(8)
C4'	C4A'	1.424(4)	C22B	C23B	1.384(9)
C4A	C5	1.409(4)	C23B	C24B	1.376(9)
C4A	C8A	1.419(4)	C24B	C25B	1.411(9)
C4A'	C5'	1.413(4)	C25B	C26B	1.360(9)
C4A'	C8A'	1.420(4)	C31B	C32B	1.414(10)
C5	C6	1.366(5)	C31B	C36B	1.384(9)
C5'	C6'	1.360(5)	C32B	C33B	1.400(10)
C6	C7	1.405(5)	C33B	C34B	1.383(11)
C6'	C7'	1.405(5)	C34B	C35B	1.379(11)

Table D.10. Bond angles for Ru(BINO)(PPh₃)(py)₂ **Ru-14'** (°).

P1A	Ru	O1	104.73(15)	C5'	C4A'	C8A'	119.3(3)
P1A	Ru	O1'	89.05(8)	C4A	C5	C6	121.8(3)
P1A	Ru	N1	91.92(15)	C4A'	C5'	C6'	121.8(3)
P1A	Ru	N2	89.64(9)	C5	C6	C7	119.0(3)
P1A	Ru	C1	165.31(13)	C5'	C6'	C7'	119.2(3)
P1A	Ru	C2	136.44(15)	C6	C7	C8	120.6(3)
P1B	Ru	O1	104.13(18)	C6'	C7'	C8'	120.8(3)
P1B	Ru	O1'	79.59(10)	C7	C8	C8A	121.4(3)
P1B	Ru	N1	91.35(19)	C7'	C8'	C8A'	121.4(3)
P1B	Ru	N2	99.10(11)	C1	C8A	C4A	120.7(2)
P1B	Ru	C1	157.90(13)	C1	C8A	C8	121.7(2)

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P1B	Ru	C2	137.82(19)	C4A	C8A	C8	117.6(2)
O1	Ru	O1'	86.81(7)	C1'	C8A'	C4A'	119.4(3)
O1	Ru	N1	162.41(7)	C1'	C8A'	C8'	123.1(2)
O1	Ru	N2	90.98(9)	C4A'	C8A'	C8'	117.4(2)
O1	Ru	C1	64.12(8)	P1A	C11A	C12A	115.5(4)
O1	Ru	C2	34.37(8)	P1A	C11A	C16A	125.2(4)
O1'	Ru	N1	87.83(8)	C12A	C11A	C16A	119.3(5)
O1'	Ru	N2	177.07(9)	C11A	C12A	C13A	120.4(5)
O1'	Ru	C1	81.05(8)	C12A	C13A	C14A	119.1(6)
O1'	Ru	C2	99.13(9)	C13A	C14A	C15A	120.8(6)
N1	Ru	N2	94.83(9)	C14A	C15A	C16A	121.0(5)
N1	Ru	C1	98.48(8)	C11A	C16A	C15A	119.3(6)
N1	Ru	C2	130.83(9)	P1A	C21A	C22A	119.8(4)
N2	Ru	C1	99.72(9)	P1A	C21A	C26A	120.5(4)
N2	Ru	C2	80.05(9)	C22A	C21A	C26A	119.7(5)
C1	Ru	C2	36.72(8)	C21A	C22A	C23A	119.2(5)
Ru	P1A	C11A	114.3(3)	C22A	C23A	C24A	120.2(6)
Ru	P1A	C21A	113.5(3)	C23A	C24A	C25A	119.1(5)
Ru	P1A	C31A	117.2(2)	C24A	C25A	C26A	120.1(5)
C11A	P1A	C21A	102.0(3)	C21A	C26A	C25A	121.5(5)
C11A	P1A	C31A	104.7(3)	P1A	C31A	C32A	121.6(4)
C21A	P1A	C31A	103.5(4)	P1A	C31A	C36A	120.3(4)
Ru	P1B	C11B	114.5(4)	C32A	C31A	C36A	117.3(5)
Ru	P1B	C21B	116.9(4)	C31A	C32A	C33A	121.9(5)
Ru	P1B	C31B	114.6(3)	C32A	C33A	C34A	119.9(6)
C11B	P1B	C21B	101.3(4)	C33A	C34A	C35A	120.0(5)
C11B	P1B	C31B	104.2(4)	C34A	C35A	C36A	121.3(6)
C21B	P1B	C31B	103.6(4)	C31A	C36A	C35A	119.5(6)
Ru	O1	C2	76.28(13)	P1B	C11B	C12B	117.3(6)
Ru	O1'	C2'	114.76(15)	P1B	C11B	C16B	123.5(6)
Ru	N1	C41	118.08(16)	C12B	C11B	C16B	119.2(7)
Ru	N1	C45	125.25(17)	C11B	C12B	C13B	121.6(8)
C41	N1	C45	116.4(2)	C12B	C13B	C14B	119.4(8)
Ru	N2	C51	122.9(2)	C13B	C14B	C15B	120.4(7)
Ru	N2	C55	119.0(2)	C14B	C15B	C16B	119.9(6)
C51	N2	C55	117.8(3)	C11B	C16B	C15B	119.3(7)
Ru	C1	C1'	101.67(16)	P1B	C21B	C22B	120.4(5)
Ru	C1	C2	69.10(13)	P1B	C21B	C26B	120.6(5)
Ru	C1	C8A	116.13(16)	C22B	C21B	C26B	119.0(6)
C1'	C1	C2	119.1(2)	C21B	C22B	C23B	121.0(6)
C1'	C1	C8A	120.0(2)	C22B	C23B	C24B	118.8(6)
C2	C1	C8A	117.3(2)	C23B	C24B	C25B	120.9(6)
C1	C1'	C2'	119.7(2)	C24B	C25B	C26B	119.0(6)
C1	C1'	C8A'	120.4(2)	C21B	C26B	C25B	121.0(6)
C2'	C1'	C8A'	119.8(2)	P1B	C31B	C32B	118.9(5)
Ru	C2	O1	69.35(12)	P1B	C31B	C36B	123.5(5)
Ru	C2	C1	74.18(13)	C32B	C31B	C36B	117.1(6)
Ru	C2	C3	126.58(18)	C31B	C32B	C33B	121.8(6)
O1	C2	C1	120.3(2)	C32B	C33B	C34B	118.9(7)
O1	C2	C3	120.5(2)	C33B	C34B	C35B	120.3(7)
C1	C2	C3	119.1(2)	C34B	C35B	C36B	120.4(7)
O1'	C2'	C1'	122.4(2)	C31B	C36B	C35B	121.5(6)
O1'	C2'	C3'	118.0(2)	N1	C41	C42	123.1(3)
C1'	C2'	C3'	119.6(2)	C41	C42	C43	119.4(3)
C2	C3	C4	121.3(2)	C42	C43	C44	118.2(2)
C2'	C3'	C4'	120.9(3)	C43	C44	C45	119.2(3)

C3	C4	C4A	121.0(3)	N1	C45	C44	123.5(3)
C3'	C4'	C4A'	121.1(3)	N2	C51	C52	122.2(4)
C4	C4A	C5	121.4(3)	C51	C52	C53	118.6(5)
C4	C4A	C8A	119.0(2)	C52	C53	C54	119.5(4)
C5	C4A	C8A	119.6(3)	C53	C54	C55	119.3(4)
C4'	C4A'	C5'	121.6(3)	N2	C55	C54	122.4(4)
C4'	C4A'	C8A'	119.1(3)				

Table D.11. Crystallographic Parameters for Ru(BINO)(L)(py)(=CHPh) complexes

	Ru-19b	Ru-19c
Crystallographer	McDonald	McDonald
CCDC #	755131	755132
empirical formula	C ₅₇ H ₅₅ N ₃ O ₃ Ru	C ₅₇ H ₅₇ N ₃ O ₃ Ru
Color, shape	Dark green, prism	Green, prism
formula wt	931.11	933.13
temp. °K	173(2)	173(2)
wavelength, Å	0.71073	0.71073
crystal syst.	monoclinic	Monoclinic
space group	<i>P</i> 2 ₁ / <i>c</i> (No. 14)	<i>P</i> 2 ₁ / <i>c</i> (No. 14)
Size (mm)	0.59 × 0.39 × 0.32	0.54 × 0.39 × 0.26
<i>a</i> [Å]	12.6187 (9)	12.7212 (4)
<i>b</i> [Å]	22.5918 (16)	22.4356 (7)
<i>c</i> [Å]	16.7663 (12)	16.7265 (5)
α [°]	90	90
β [°]	106.7799 (8)	106.1806 (3)
γ [°]	90	90
<i>V</i> , Å ³	4576.2 (6)	4584.8 (2)
<i>Z</i> , calcd density, mg/cm ³	4, 1.351	4, 1.352
μ , mm ⁻¹	0.392	0.392
<i>F</i> (000)	1944	1952
<i>Q</i> range for data collecn.	2.20° < θ < 27.58°	1.56° < θ < 27.48°
Deg		
limiting indices	-16 ≤ <i>h</i> ≤ 16 -29 ≤ <i>k</i> ≤ 29 -21 ≤ <i>l</i> ≤ 21	-16 ≤ <i>h</i> ≤ 16 -29 ≤ <i>k</i> ≤ 29 -21 ≤ <i>l</i> ≤ 21
no. of rflns collected/unique	39849/10525 (<i>R</i> _{int} = 0.0165)	40010 / 10464 (<i>R</i> _{int} = 0.0130)
abs cor	Gaussian integration (face-indexed)	Gaussian integration (face-indexed)
Diffractometer	Bruker D8/APEX II CCD	Bruker D8/APEX II CCD
max, min transmission	0.8838–0.8010	0.9037–0.8152
refinement method	full-matrix least-squares on <i>F</i> ² (<i>SHELXL</i> –97)	full-matrix least-squares on <i>F</i> ² (<i>SHELXL</i> –97)
no. of data/restraints/params	10525 [<i>F</i> _o ² ≥ 3 <i>s</i> (<i>F</i> _o ²)] / 0 / 583	10464 [<i>F</i> _o ² ≥ 3 <i>s</i> (<i>F</i> _o ²)] / 0 / 583
goodness of fit on <i>F</i> ²	1.065	1.043
final <i>R</i> indices	<i>R</i> ₁ = 0.0330,	<i>R</i> ₁ = 0.0265,
<i>R</i> ₁ [<i>F</i> _o ² ≥ 2 <i>s</i> (<i>F</i> _o ²)]	<i>wR</i> ₂ = 0.0959	<i>wR</i> ₂ = 0.0767
<i>wR</i> ₂ [all data]		
largest diff peak, hole, e/Å ³	0.528 and –0.314 e Å ⁻³	0.433 and –0.419 e Å ⁻³

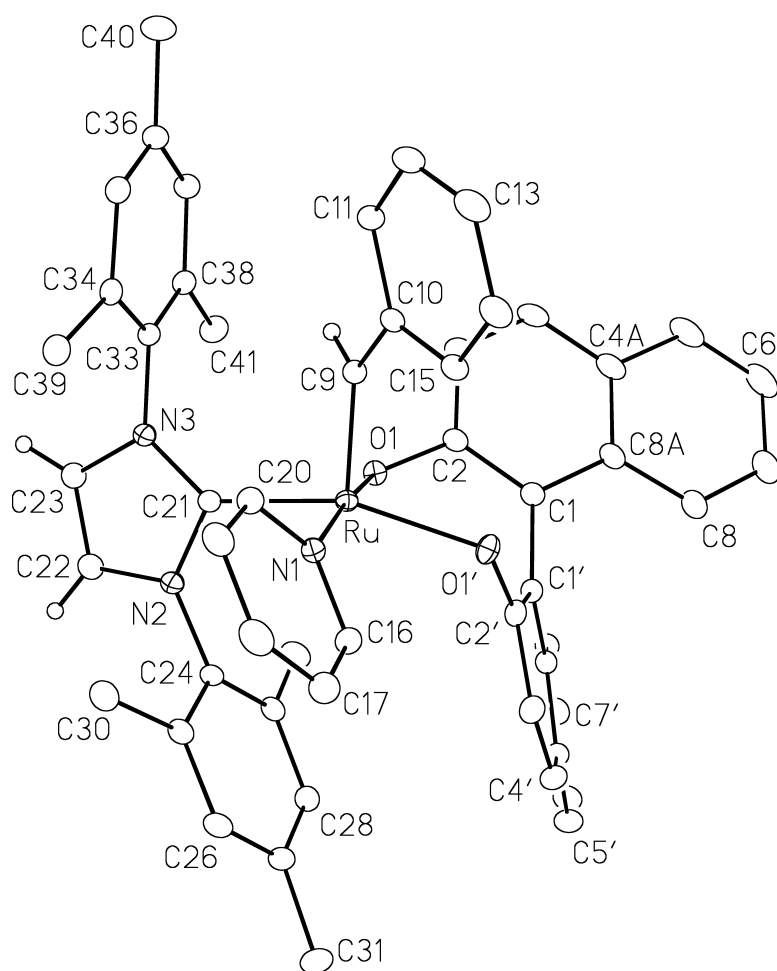


Figure D.5. ORTEP representation of Ru(BINO)(IMes)(py)(=CHPh) **Ru-19b**. Non-hydrogen ellipsoids at the 20% probability level.

Table D.12. Bond lengths for Ru(BINO)(IMes)(py)(=CHPh) **Ru-19b** (Å).

Ru	O1	2.0504(13)	C7	C8	1.373(3)
Ru	O1'	2.0841(13)	C7'	C8'	1.372(3)
Ru	N1	2.0860(15)	C8	C8A	1.424(3)
Ru	C9	1.8302(18)	C8'	C8A'	1.422(3)
Ru	C21	2.0309(17)	C9	C10	1.462(2)
O1	C2	1.337(2)	C10	C11	1.403(2)
O1'	C2'	1.335(2)	C10	C15	1.402(3)
N1	C16	1.343(2)	C11	C12	1.386(3)
N1	C20	1.348(2)	C12	C13	1.379(3)
N2	C21	1.367(2)	C13	C14	1.385(3)
N2	C22	1.388(2)	C14	C15	1.385(3)
N2	C24	1.444(2)	C16	C17	1.385(3)
N3	C21	1.367(2)	C17	C18	1.375(3)
N3	C23	1.392(2)	C18	C19	1.380(3)
N3	C33	1.437(2)	C19	C20	1.379(3)
C1	C1'	1.489(3)	C22	C23	1.341(3)
C1	C2	1.390(3)	C24	C25	1.397(3)
C1	C8A	1.438(2)	C24	C29	1.399(2)

C1'	C2'	1.397(3)	C25	C26	1.391(3)
C1'	C8A'	1.436(3)	C25	C30	1.506(3)
C2	C3	1.428(3)	C26	C27	1.389(3)
C2'	C3'	1.431(3)	C27	C28	1.386(3)
C3	C4	1.362(3)	C27	C31	1.509(3)
C3'	C4'	1.362(3)	C28	C29	1.393(3)
C4	C4A	1.408(3)	C29	C32	1.504(3)
C4'	C4A'	1.414(3)	C33	C34	1.398(3)
C4A	C5	1.421(3)	C33	C38	1.395(3)
C4A	C8A	1.430(3)	C34	C35	1.397(3)
C4A'	C5'	1.417(3)	C34	C39	1.505(3)
C4A'	C8A'	1.433(3)	C35	C36	1.388(3)
C5	C6	1.360(4)	C36	C37	1.392(3)
C5'	C6'	1.366(3)	C36	C40	1.513(3)
C6	C7	1.405(4)	C37	C38	1.391(3)
C6'	C7'	1.410(3)	C38	C41	1.505(3)

Table D.13. Bond angles for Ru(BINO)(IMes)(py)(=CHPh) **Ru-19b** (°).

O1	Ru	O1'	89.57(5)	C1	C8A	C8	123.00(18)
O1	Ru	N1	172.94(5)	C4A	C8A	C8	117.09(18)
O1	Ru	C9	90.89(7)	C1'	C8A'	C4A'	120.16(17)
O1	Ru	C21	84.55(6)	C1'	C8A'	C8'	122.51(17)
O1'	Ru	N1	89.11(5)	C4A'	C8A'	C8'	117.30(17)
O1'	Ru	C9	103.22(7)	Ru	C9	C10	129.73(13)
O1'	Ru	C21	158.68(6)	C9	C10	C11	119.34(17)
N1	Ru	C9	96.16(7)	C9	C10	C15	122.44(16)
N1	Ru	C21	94.22(6)	C11	C10	C15	118.20(17)
C9	Ru	C21	97.36(7)	C10	C11	C12	120.98(19)
Ru	O1	C2	121.62(11)	C11	C12	C13	119.82(19)
Ru	O1'	C2'	116.39(11)	C12	C13	C14	120.27(19)
Ru	N1	C16	119.35(12)	C13	C14	C15	120.3(2)
Ru	N1	C20	123.85(13)	C10	C15	C14	120.44(18)
C16	N1	C20	116.66(16)	N1	C16	C17	123.10(19)
C21	N2	C22	111.92(15)	C16	C17	C18	119.3(2)
C21	N2	C24	124.31(15)	C17	C18	C19	118.47(19)
C22	N2	C24	123.70(15)	C18	C19	C20	119.0(2)
C21	N3	C23	111.02(15)	N1	C20	C19	123.44(19)
C21	N3	C33	127.00(15)	Ru	C21	N2	119.09(12)
C23	N3	C33	121.88(15)	Ru	C21	N3	136.29(13)
C1'	C1	C2	120.07(16)	N2	C21	N3	103.36(14)
C1'	C1	C8A	120.69(16)	N2	C22	C23	106.25(17)
C2	C1	C8A	119.22(17)	N3	C23	C22	107.39(17)
C1	C1'	C2'	119.91(16)	N2	C24	C25	118.35(16)
C1	C1'	C8A'	120.76(16)	N2	C24	C29	119.41(16)
C2'	C1'	C8A'	119.33(17)	C25	C24	C29	122.11(16)
O1	C2	C1	122.26(16)	C24	C25	C26	118.09(17)
O1	C2	C3	117.98(17)	C24	C25	C30	121.81(17)
C1	C2	C3	119.59(17)	C26	C25	C30	120.07(17)
O1'	C2'	C1'	123.85(17)	C25	C26	C27	121.54(18)
O1'	C2'	C3'	117.80(17)	C26	C27	C28	118.64(17)
C1'	C2'	C3'	118.31(17)	C26	C27	C31	120.66(19)
C2	C3	C4	121.57(19)	C28	C27	C31	120.64(19)
C2'	C3'	C4'	122.30(18)	C27	C28	C29	122.27(17)
C3	C4	C4A	120.78(19)	C24	C29	C28	117.30(17)

C3'	C4'	C4A'	120.55(18)	C24	C29	C32	121.93(17)
C4	C4A	C5	121.5(2)	C28	C29	C32	120.69(17)
C4	C4A	C8A	118.88(18)	N3	C33	C34	119.59(16)
C5	C4A	C8A	119.6(2)	N3	C33	C38	117.71(16)
C4'	C4A'	C5'	122.04(18)	C34	C33	C38	122.57(17)
C4'	C4A'	C8A'	118.37(17)	C33	C34	C35	117.04(17)
C5'	C4A'	C8A'	119.58(19)	C33	C34	C39	122.38(17)
C4A	C5	C6	121.3(2)	C35	C34	C39	120.45(17)
C4A'	C5'	C6'	121.4(2)	C34	C35	C36	122.20(18)
C5	C6	C7	119.8(2)	C35	C36	C37	118.52(18)
C5'	C6'	C7'	119.44(19)	C35	C36	C40	120.7(2)
C6	C7	C8	120.6(2)	C37	C36	C40	120.8(2)
C6'	C7'	C8'	120.8(2)	C36	C37	C38	121.73(18)
C7	C8	C8A	121.6(2)	C33	C38	C37	117.81(17)
C7'	C8'	C8A'	121.49(19)	C33	C38	C41	120.60(17)
C1	C8A	C4A	119.90(18)	C37	C38	C41	121.58(18)

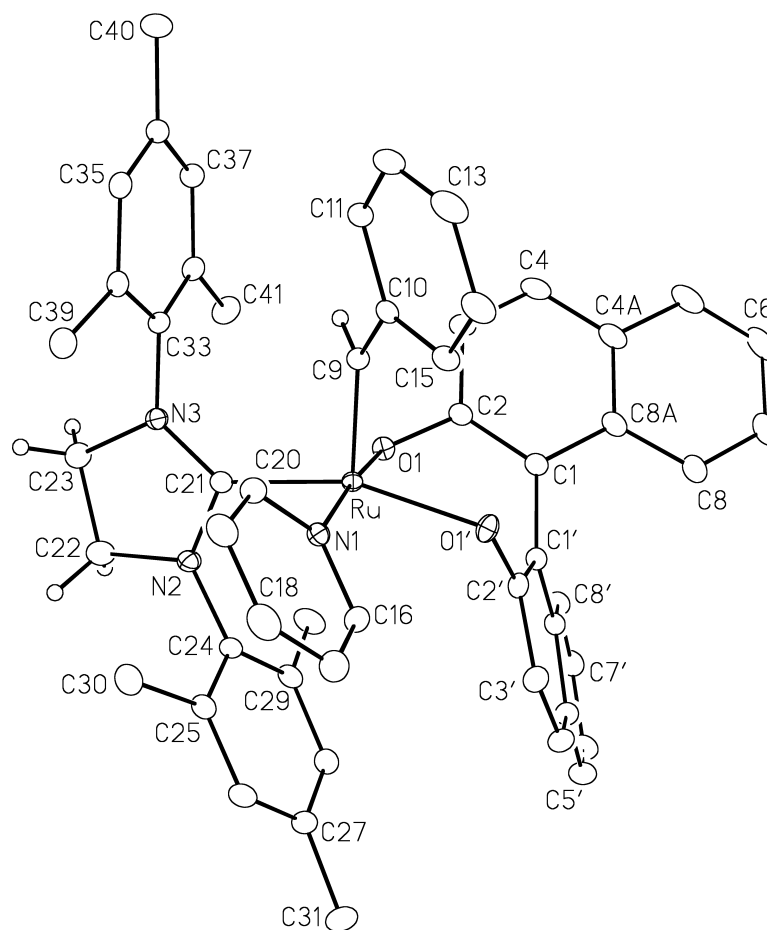


Figure D.6. ORTEP representation of Ru(BINO)(H₂IMes)(py)(=CHPh) **Ru-19c**. Non-hydrogen ellipsoids at the 20% probability level.

Table D.14. Bond lengths for Ru(BINO)(H₂IMes)(py)(=CHPh) **Ru-19c** (Å).

Ru	O1	2.0577(10)	C7	C8	1.375(2)
Ru	O1'	2.0783(11)	C7'	C8'	1.371(2)
Ru	N1	2.0905(12)	C8	C8A	1.422(2)
Ru	C9	1.8274(14)	C8'	C8A'	1.424(2)
Ru	C21	2.0142(14)	C9	C10	1.4632(19)
O1	C2	1.3309(17)	C10	C11	1.400(2)
O1'	C2'	1.3328(18)	C10	C15	1.401(2)
N1	C16	1.3426(19)	C11	C12	1.389(2)
N1	C20	1.350(2)	C12	C13	1.379(3)
N2	C21	1.3504(18)	C13	C14	1.386(3)
N2	C22	1.469(2)	C14	C15	1.385(2)
N2	C24	1.4332(18)	C16	C17	1.385(2)
N3	C21	1.3466(18)	C17	C18	1.375(3)
N3	C23	1.475(2)	C18	C19	1.377(3)
N3	C33	1.4307(19)	C19	C20	1.378(2)
C1	C1'	1.485(2)	C22	C23	1.508(2)
C1	C2	1.391(2)	C24	C25	1.398(2)
C1	C8A	1.438(2)	C24	C29	1.402(2)
C1'	C2'	1.400(2)	C25	C26	1.390(2)
C1'	C8A'	1.433(2)	C25	C30	1.507(2)
C2	C3	1.429(2)	C26	C27	1.385(2)
C2'	C3'	1.433(2)	C27	C28	1.386(2)
C3	C4	1.363(2)	C27	C31	1.509(2)
C3'	C4'	1.359(2)	C28	C29	1.393(2)
C4	C4A	1.408(3)	C29	C32	1.504(2)
C4'	C4A'	1.417(2)	C33	C34	1.395(2)
C4A	C5	1.422(2)	C33	C38	1.401(2)
C4A	C8A	1.428(2)	C34	C35	1.397(2)
C4A'	C5'	1.415(2)	C34	C39	1.508(2)
C4A'	C8A'	1.430(2)	C35	C36	1.386(2)
C5	C6	1.356(3)	C36	C37	1.389(2)
C5'	C6'	1.368(3)	C36	C40	1.510(2)
C6	C7	1.405(3)	C37	C38	1.390(2)
C6'	C7'	1.405(3)	C38	C41	1.504(2)

Table D.15. Bond angles for Ru(BINO)(H₂IMes)(py)(=CHPh) **Ru-19c** (°).

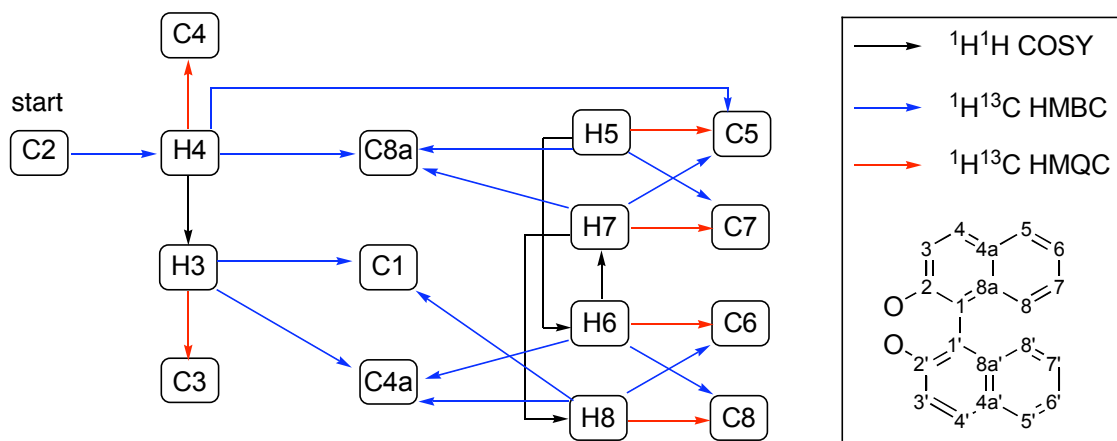
O1	Ru	O1'	89.37(4)	C1	C8A	C8	122.89(15)
O1	Ru	N1	173.74(4)	C4A	C8A	C8	117.20(14)
O1	Ru	C9	90.59(5)	C1'	C8A'	C4A'	120.45(14)
O1	Ru	C21	86.64(5)	C1'	C8A'	C8'	122.18(14)
O1'	Ru	N1	88.66(4)	C4A'	C8A'	C8'	117.34(14)
O1'	Ru	C9	103.45(5)	Ru	C9	C10	130.00(11)
O1'	Ru	C21	158.95(5)	C9	C10	C11	119.21(13)
N1	Ru	C9	95.65(6)	C9	C10	C15	122.37(13)
N1	Ru	C21	93.08(5)	C11	C10	C15	118.40(14)
C9	Ru	C21	97.26(6)	C10	C11	C12	120.65(15)
Ru	O1	C2	121.78(9)	C11	C12	C13	120.08(16)
Ru	O1'	C2'	117.75(9)	C12	C13	C14	120.14(15)
Ru	N1	C16	119.87(10)	C13	C14	C15	120.15(16)
Ru	N1	C20	123.34(10)	C10	C15	C14	120.56(15)
C16	N1	C20	116.74(13)	N1	C16	C17	122.90(15)
C21	N2	C22	113.96(12)	C16	C17	C18	119.43(16)
C21	N2	C24	124.87(12)	C17	C18	C19	118.47(15)

Appendix D. Crystallographic Data

C22	N2	C24	120.71(12)	C18	C19	C20	119.12(16)
C21	N3	C23	113.26(12)	N1	C20	C19	123.32(16)
C21	N3	C33	128.67(12)	Ru	C21	N2	117.04(10)
C23	N3	C33	117.94(12)	Ru	C21	N3	135.77(10)
C1'	C1	C2	120.10(12)	N2	C21	N3	106.91(12)
C1'	C1	C8A	120.49(13)	N2	C22	C23	102.58(13)
C2	C1	C8A	119.38(13)	N3	C23	C22	103.27(13)
C1	C1'	C2'	119.85(13)	N2	C24	C25	118.92(13)
C1	C1'	C8A'	121.03(13)	N2	C24	C29	119.61(13)
C2'	C1'	C8A'	119.11(14)	C25	C24	C29	121.25(13)
O1	C2	C1	122.42(13)	C24	C25	C26	118.65(14)
O1	C2	C3	118.13(13)	C24	C25	C30	122.12(14)
C1	C2	C3	119.31(13)	C26	C25	C30	119.19(14)
O1'	C2'	C1'	123.91(14)	C25	C26	C27	121.44(14)
O1'	C2'	C3'	117.69(13)	C26	C27	C28	118.76(14)
C1'	C2'	C3'	118.37(14)	C26	C27	C31	120.55(15)
C2	C3	C4	121.70(15)	C28	C27	C31	120.63(15)
C2'	C3'	C4'	122.30(14)	C27	C28	C29	122.07(14)
C3	C4	C4A	120.77(15)	C24	C29	C28	117.76(14)
C3'	C4'	C4A'	120.49(15)	C24	C29	C32	122.03(15)
C4	C4A	C5	121.61(17)	C28	C29	C32	120.13(14)
C4	C4A	C8A	118.89(14)	N3	C33	C34	119.70(13)
C5	C4A	C8A	119.49(17)	N3	C33	C38	118.30(13)
C4'	C4A'	C5'	122.13(15)	C34	C33	C38	121.71(13)
C4'	C4A'	C8A'	118.32(14)	C33	C34	C35	117.72(14)
C5'	C4A'	C8A'	119.55(15)	C33	C34	C39	122.46(14)
C4A	C5	C6	121.40(19)	C35	C34	C39	119.68(14)
C4A'	C5'	C6'	121.30(16)	C34	C35	C36	122.02(14)
C5	C6	C7	119.81(17)	C35	C36	C37	118.43(14)
C5'	C6'	C7'	119.61(16)	C35	C36	C40	120.88(15)
C6	C7	C8	120.56(19)	C37	C36	C40	120.67(16)
C6'	C7'	C8'	120.75(16)	C36	C37	C38	121.94(14)
C7	C8	C8A	121.51(18)	C33	C38	C37	117.99(14)
C7'	C8'	C8A'	121.43(15)	C33	C38	C41	120.64(14)
C1	C8A	C4A	119.90(15)	C37	C38	C41	121.35(14)

E. NMR Analysis of Ru-BINO Coordination Modes.

The following is a representative example of the NMR signal assignment for the Ru-BINO complexes. 1D and 2D NMR spectra are provided for complex **Ru-19a'** where relevant correlations and signal assignments are detailed.



Scheme E.1. Schematic representation of the NMR correlations in a BINO ligand.

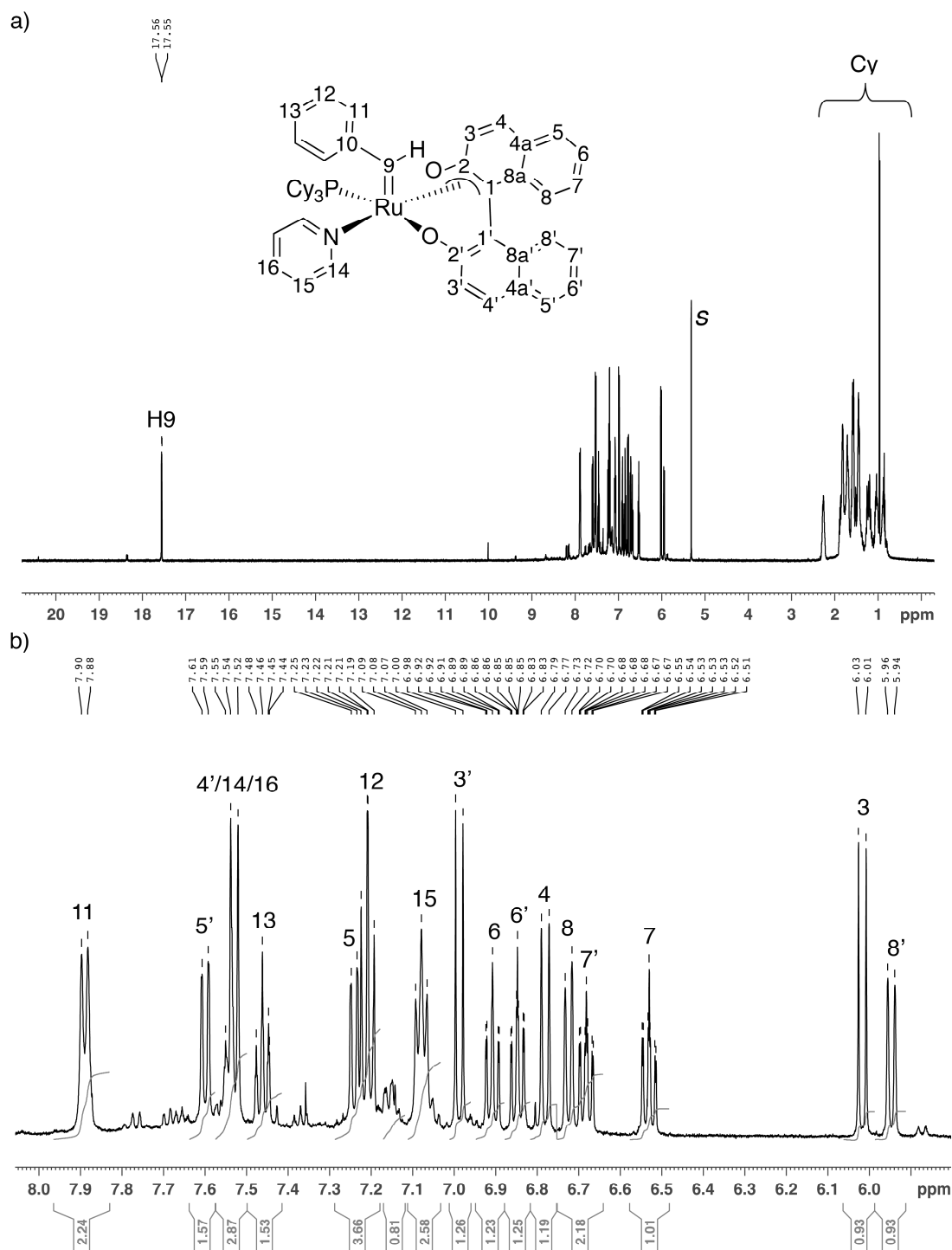


Figure E.1. ^1H NMR spectrum of isolated **Ru-19a'** in CD_2Cl_2 ; S = solvent. a) Full spectrum; b) expanded aromatic region, with peak assignments. Small amounts of a second alkylidene species consistently present are tentatively assigned to a η^1, η^1 -BINO isomer (ca. 10%; 18.39 ppm (d, $^3J_{\text{HP}} = 11.5$ Hz; cf. 4.5 Hz for **Ru-19a'**, and 11.5 Hz for bis-py, η^1, η^1 -BINO **Ru-20**). This doublet correlates (HMBC) with a $^{31}\text{P}\{^1\text{H}\}$ NMR singlet at 49.15 ppm; see Figure E.12 for $^{31}\text{P}\{^1\text{H}\}$ NMR spectrum.

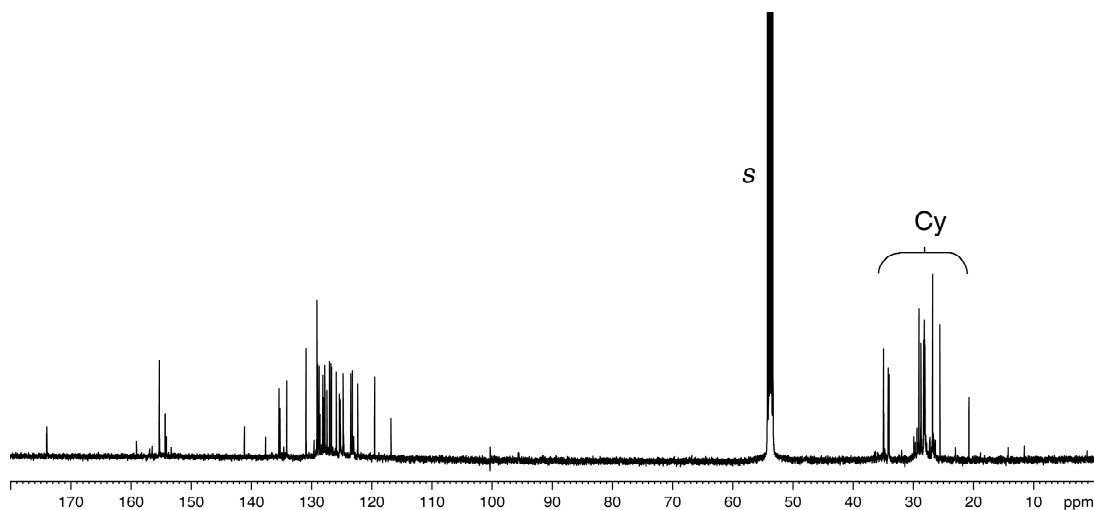


Figure E.2. $^{13}\text{C}\{^1\text{H}\}$ NMR spectrum of isolated **Ru-19a'** in CD_2Cl_2 . The signal for the benzylidene carbon (C^9 : 302.1 ppm; not shown) was located via a ^1H - ^{13}C HMBC experiment. Small amounts of a second alkylidene species consistently present are tentatively assigned to η^1, η^1 -BINO isomer.

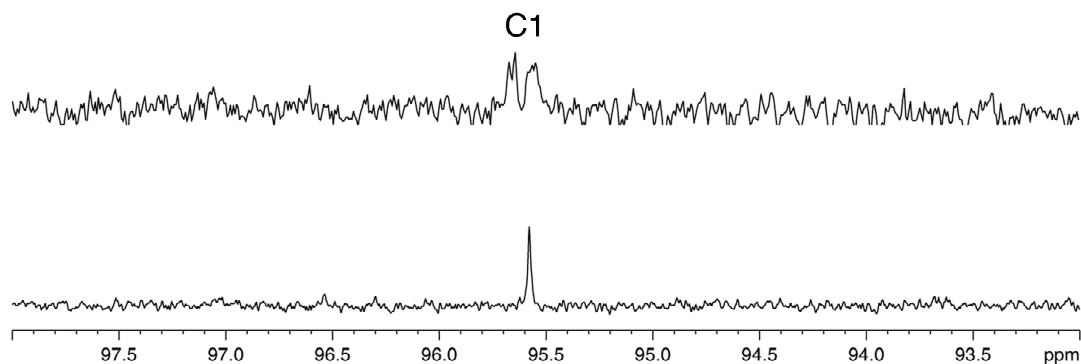


Figure E.3. $^{13}\text{C}\{^1\text{H}\}$ (top) and $^{13}\text{C}\{^{31}\text{P}, ^1\text{H}\}$ (bottom) NMR signals for the C1 carbon in **Ru-19a'**, assigned from its HMBC correlation to H3.

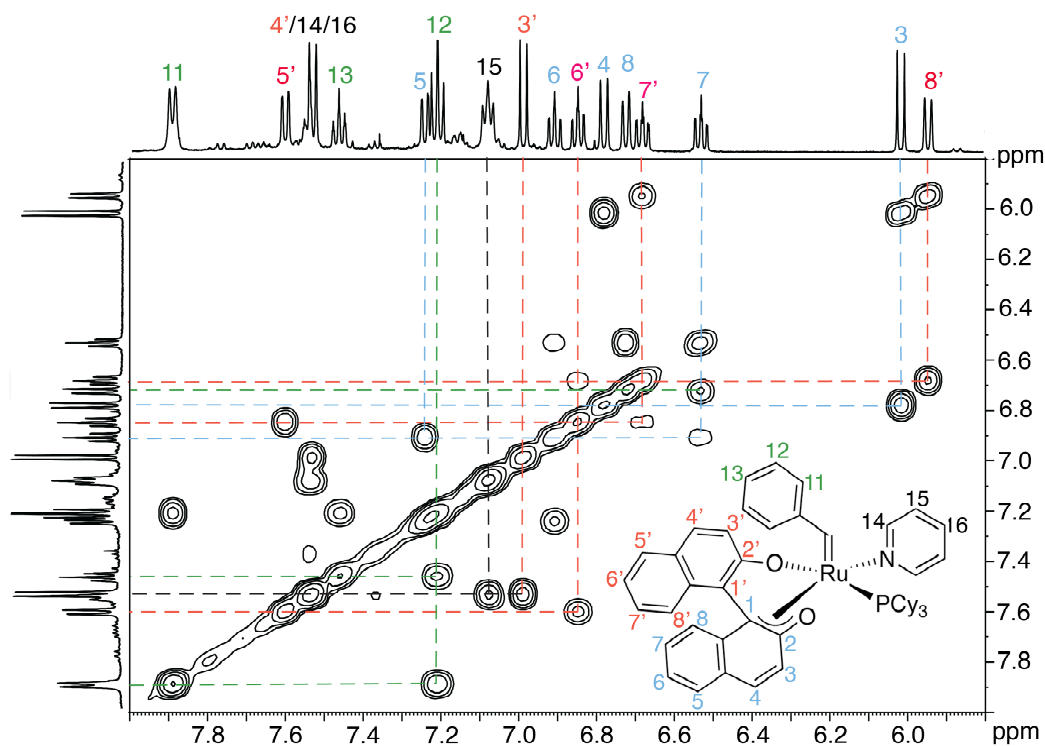


Figure E.4. ^1H - ^1H COSY NMR spectrum of the aromatic region of **Ru-19a'**.

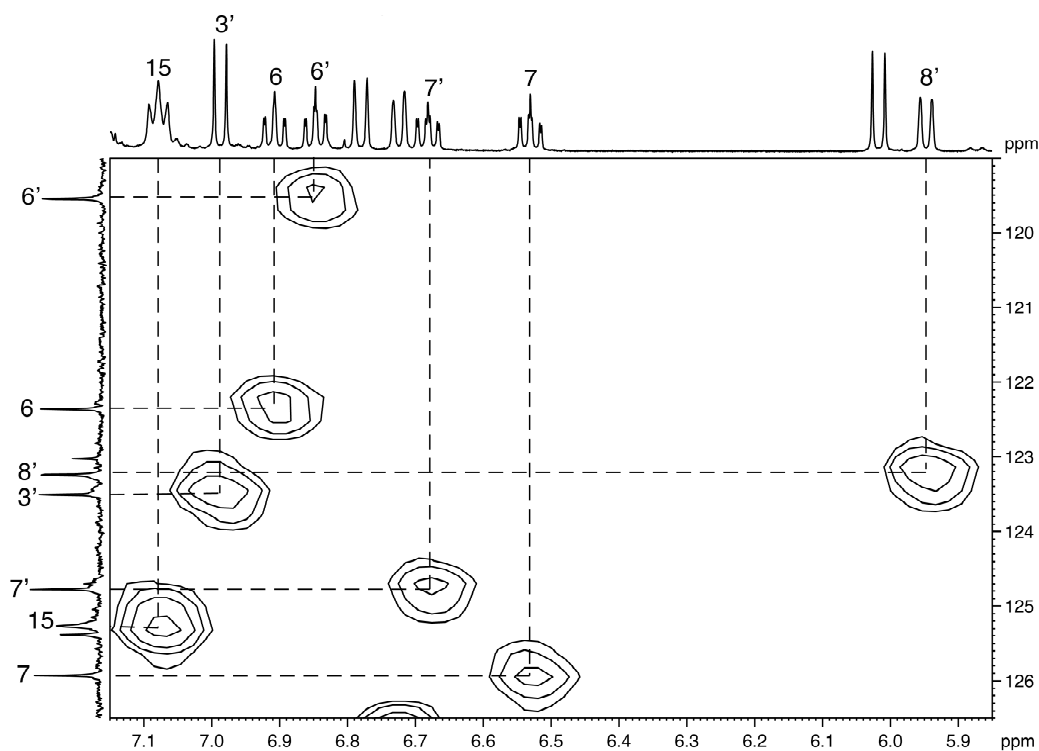


Figure E.5. Expansion of the ^1H - ^{13}C HMQC NMR spectrum of **Ru-19a'**.

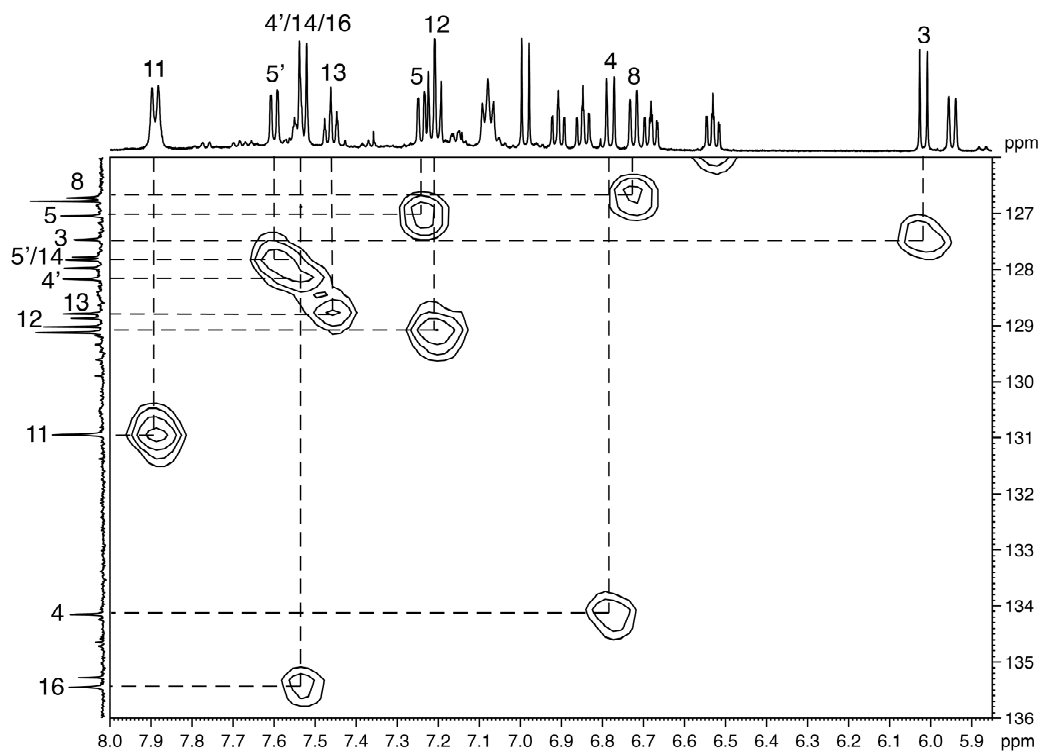


Figure E.6. Expansion of the $^1\text{H}/^{13}\text{C}$ HMQC NMR spectrum of **Ru-19a'**.

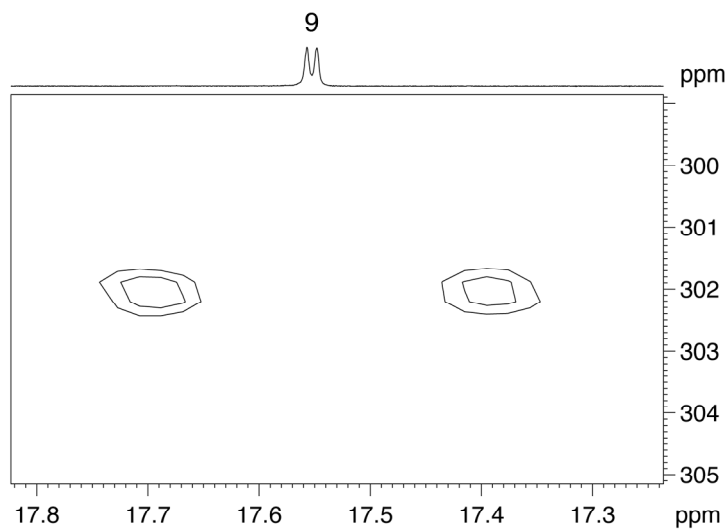


Figure E.7. Location of C9 by a $^1\text{H}/^{13}\text{C}$ HMQC correlation experiment. The decoupler strength is not sufficient at the edge of the sweep width resulting in a splitting of the signal.

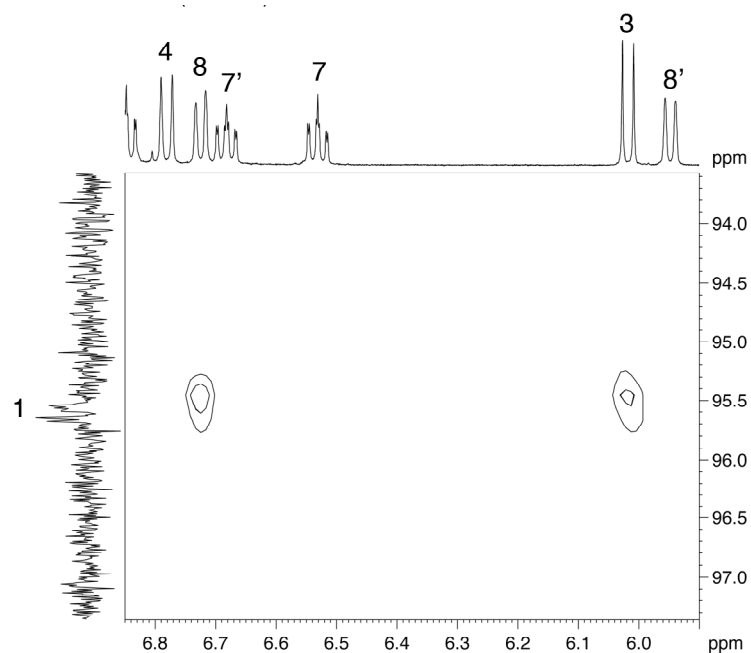


Figure E.8. Expansion of the $^1\text{H}/^{13}\text{C}$ HMBC NMR spectrum identifying the signal for C1.

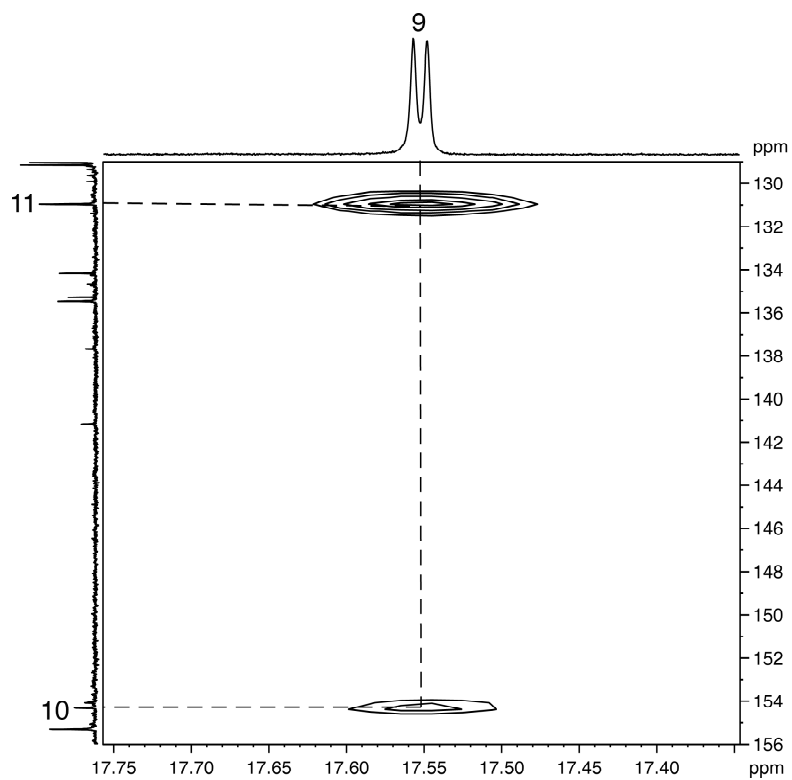


Figure E.9. $^1\text{H}/^{13}\text{C}$ HMBC expansion of the alkylidene correlations of **Ru-19a'**.

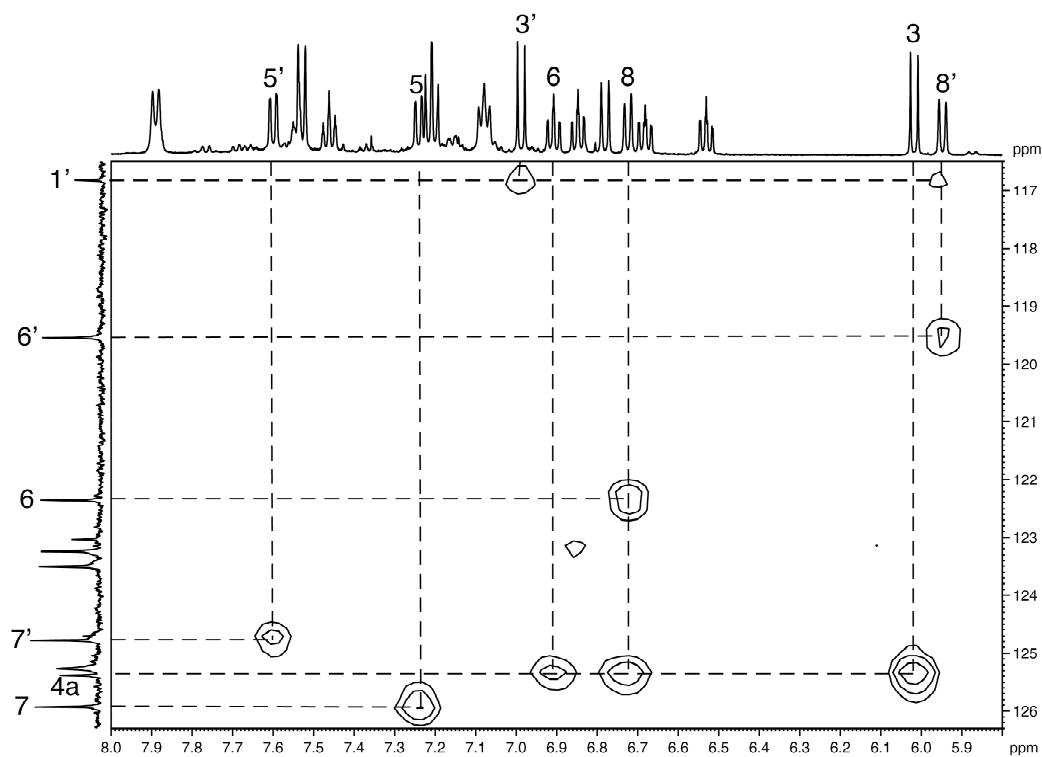


Figure E.10. The aromatic region in a $^1\text{H}/^{13}\text{C}$ HMBC spectrum of **Ru-19a'**.

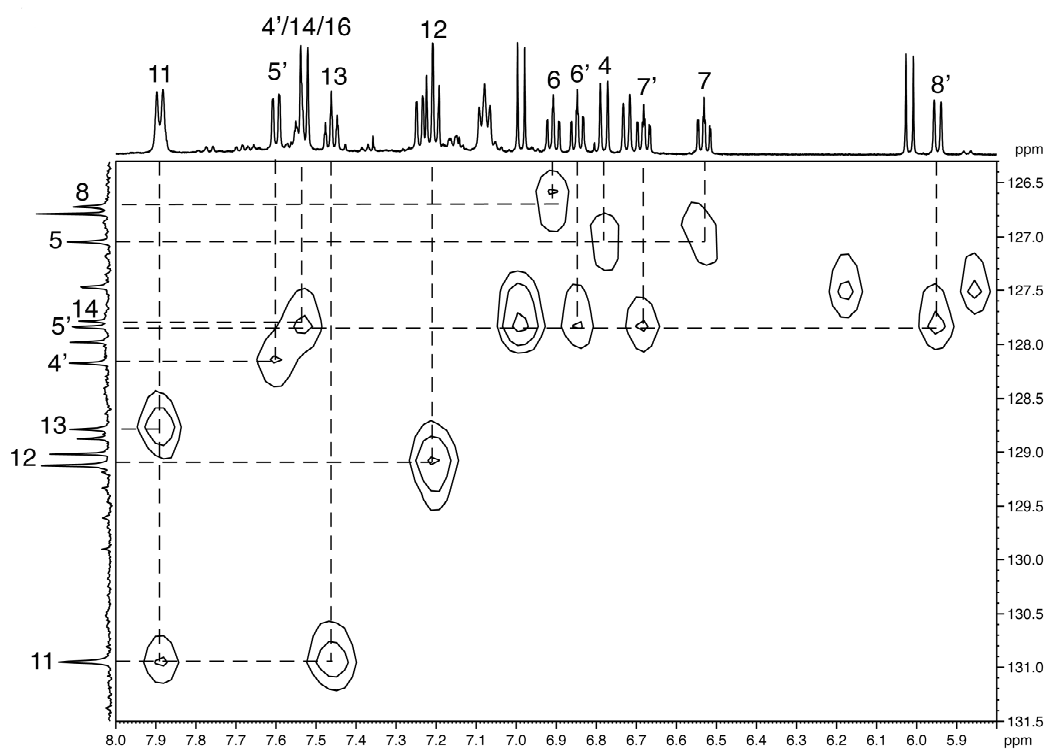


Figure E.11. An expansion of the aromatic region in the $^1\text{H}/^{13}\text{C}$ HMBC spectrum of **Ru-19a'**.

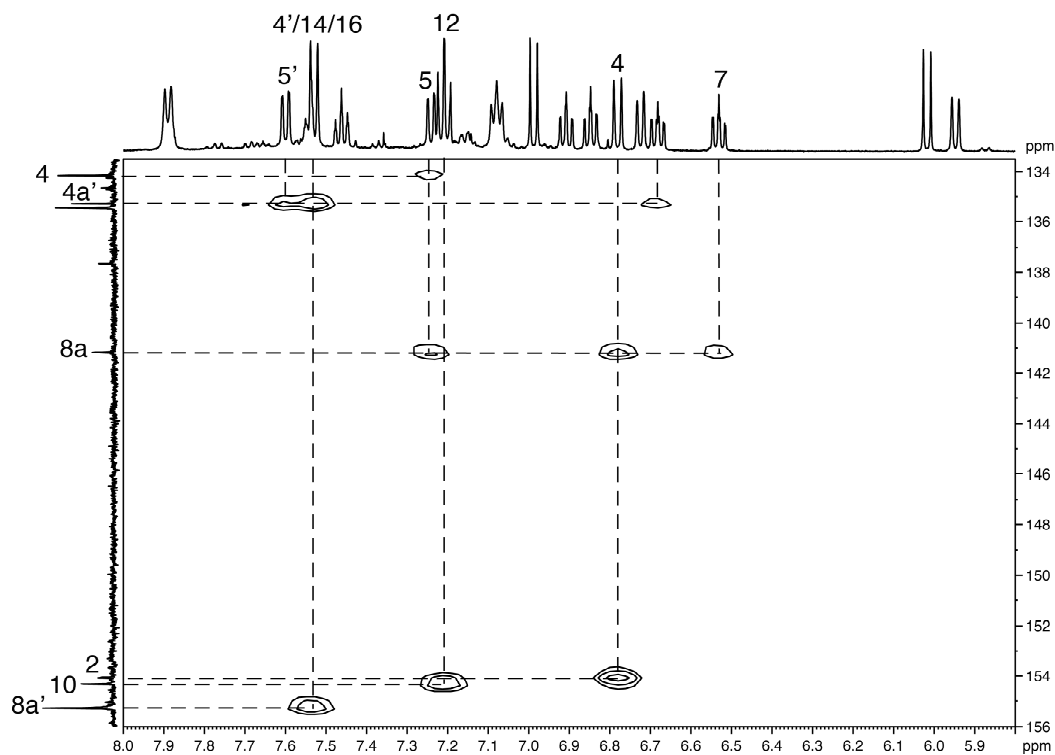


Figure E.12. An expansion of the aromatic region in the $^1\text{H}/^{13}\text{C}$ HMBC spectrum of **Ru-19a'**.

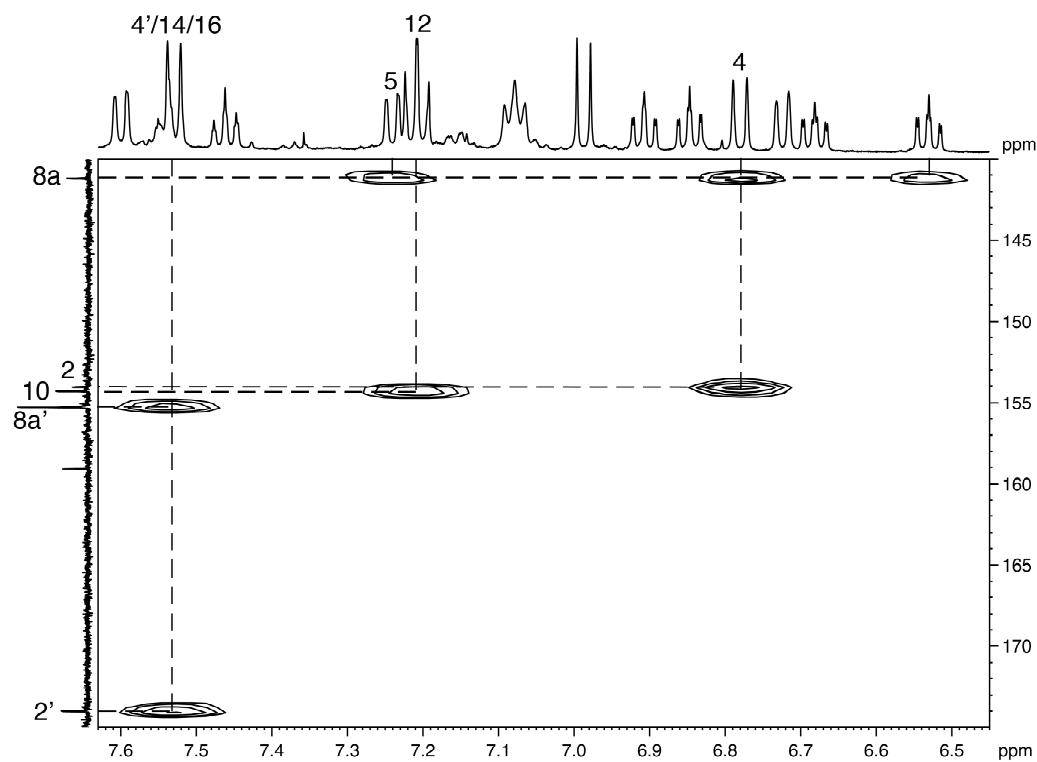


Figure E.13. An expansion of the aromatic region in the $^1\text{H}/^{13}\text{C}$ HMBC spectrum of **Ru-19a'**.

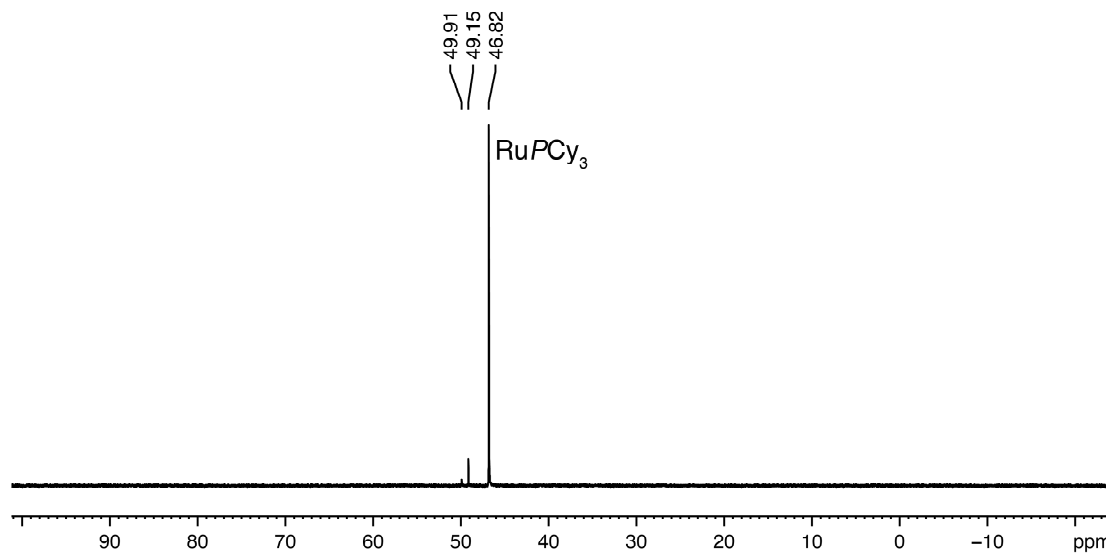


Figure E.14. $^{31}\text{P}\{^1\text{H}\}$ NMR spectrum of **Ru-19a'** in CD_2Cl_2 , referenced externally to H_3PO_4 .

F. Contributions

F.1. Publications

1. J.M. Blacquiere, C.S. Higman, S.I. Gorelsky, N.J. Beach, S.J. Dalgarno, D.E. Fogg* "Unprecedentedly Strong Binding of Dinitrogen at Ruthenium" *Angew. Chem. Int. Ed.*, **2011**, *50*, 916-919.
2. S. Monfette, J.M. Blacquiere, D.E. Fogg* "The Future, Faster: Using High-Throughput Experimentation to Accelerate Discovery in Organometallic Chemistry" *Organometallics*, **2011**, *30*, 36-42; invited article for the Special Issue on the Future of Organometallic Chemistry.
3. J.M. Blacquiere, R. McDonald, D.E. Fogg*. "Integrating the Schrock and Grubbs Catalysts: Ruthenium-Binaphtholate Catalysts for Olefin Metathesis" *Angew. Chem. Int. Ed.*, **2010**, 3807.
4. N.J. Beach, J.M. Blacquiere, S.D. Drouin, and D.E. Fogg*. "Carbonyl-Amplified Catalyst Performance: Balancing Stability against Activity for Five-Coordinate Ruthenium Hydride Hydridocarbonyl Complexes." *Organometallics*, **2009**, *28*, 441.
5. J.M. Blacquiere, T. Jurca, J. Weiss, D.E. Fogg*. "Time as a Dimension in High-Throughput Homogeneous Catalysis" *Adv. Synth. Catal.*, **2008**, *350*, 2849.
6. M.D. Eelman, J.M. Blacquiere, M.M. Moriarty, D.E. Fogg*. "Retooling MALDI Mass Spectrometry for Organotransition-Metal Catalysis" *Angew. Chem. Int. Ed.* **2007**, *47*, 303. (VIP)
7. S. Monfette, J.M. Blacquiere, J.C. Conrad, N.J. Beach, D.E. Fogg* "Ru-Aryloxide Catalysts for Olefin Metathesis" in *Metathesis Chemistry: From Nanostructure Design to Synthesis of Advanced Materials*, NATO Science Series II, Vol 243, Y. Imamoglu, V. Dragutan, Eds. Springer Verlag, Berlin, **2007**, p. 79-89.

F.2. Manuscripts in Preparation

8. J.M. Blacquiere, C.S. Higman, R. McDonald, D.E. Fogg* "A Versatile Source of the Chiral Ru-Binaphtholate Moiety: Synthesis, Structure and Reactivity of Ru(BINO)(PPh₃)₂"
9. J.M. Blacquiere and D.E. Fogg* "Probing the limits of force in olefin metathesis catalysis by CT-MALDI MS"
10. J.M. Blacquiere and D.E. Fogg* "MALDI-TOF Mass Spectrometry for Organometallic Catalysts"
11. J.M. Blacquiere and D.E. Fogg* "Hit or Myth? High-Throughput Experimentation for Applications in Olefin Metathesis"