

Amines in Olefin Metathesis: Ligands and Poisons

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Table of Contents

Abstract	IV
Acknowledgements	V
Lists of Compounds and Abbreviations	VI
Lists of Charts, Schemes, Figures, and Tables	XIV
Chapter 1. Introduction	1
1.1. Catalysis	1
1.2. Olefin metathesis	2
1.2.1. A powerful tool for organic synthesis	2
1.2.2. The history and mechanism of olefin metathesis - highlights	5
1.2.3. Well-defined metal alkylidenes as metathesis catalysts	7
1.2.4. Non-productive metathesis reactions	11
1.3. Catalyst decomposition pathways	13
1.3.1. Inherent decomposition of Ru-alkylidenes and MCB complexes	13
1.3.2. Decomposition induced by chemical additives	14
1.4. Amines in catalyst design - opportunities	17
1.5. Scope of thesis	18
Chapter 2. Experimental Details	23
2.1. General procedures	23
2.1.1. Reaction conditions	23
2.1.2. Reagents and solvents	23
2.1.3. Instrumentation	24
2.1.4. Supplementary data	25
2.2. Experimental data for Chapter 3	25
2.2.1. Stoichiometric reactions of GI, GII, and GII' with N-donors	25
2.2.2. Syntheses of new compounds	26
2.2.3. Characterization data for benzylidene abstraction products	27
2.3. Experimental data for Chapter 4	28
2.3.1. Experimental details for Chapter 4, Sections 4.1-4.3	28
2.3.2. Experimental details for Chapter 4, Section 4.4.	32
2.4. Experimental data for Chapter 5	33
2.4.1. Syntheses of GII adducts of pyrrolidine and morpholine (Section 5.2.1)	33
2.4.2. Syntheses of other new Ru benzylidenes	34
2.4.3. Olefin metathesis	37
2.4.2. Decomposition studies	37
2.4.3. Reactions of Ru alkylidenes with lithium salts	39
2.4.4. Experimental details for Chapter 5, Section 5.6	40
2.6. References	44
Chapter 3. Decomposition of the Grubbs Catalysts by Amines: Benzylidene Abstraction	46
3.1. Introduction	46
3.2. Decomposition of the first-generation Grubbs catalyst GI by benzylidene abstraction	50
3.2.1. Unexpected abstraction of the benzylidene ligand from GI by n-butylamine	50
3.2.2. Benzylidene abstraction from an ethylenediamine (en) derivative of GI	53
3.3. Reactions of GII with primary amines	54
3.3.1. Benzylidene abstraction by n-butylamine: identification of products	54
3.3.2. Benzylidene abstraction from amine adducts of GII as compared with GI	57
3.3.3. Reactions of GII with larger primary amines	58

3.3.4. <i>Proposed mechanism for benzyldiene abstraction by primary amines</i>	60
3.4. <i>Reactions of GII with secondary amines and larger N-donors</i>	62
3.5. <i>Conclusions and future work</i>	63
3.6. <i>References</i>	64
Chapter 4. The Impact of Nitrogen Bases on the Stability and Metathesis Performance of the Hoveyda Catalyst: Alkylidene and Proton Abstraction Pathways	66
4.1. <i>Introduction</i>	66
4.2. <i>Adduct formation on reaction of HII with N-donors</i>	68
4.3. <i>Base-induced decomposition of HII and its active species during metathesis</i>	73
4.4. <i>Subsequent advances</i>	79
4.4.1. <i>C–H activation of the N-heterocyclic carbene during metallacyclobutane decomposition</i>	79
4.4.2. <i>Can GII decompose via deprotonation of the metallacyclobutane?</i>	82
4.4.3. <i>Impact of N-donors on CM yield: GII vs. HII</i>	82
4.4.4. <i>The role of amine basicity in determining the decomposition pathway for GII</i>	84
4.4.5. <i>Metallacyclobutane deprotonation with GII – ethenolysis</i>	85
4.4.6. <i>Alkylidene abstraction from HII during catalysis</i>	86
4.5. <i>Conclusions and future work</i>	90
4.6. <i>References</i>	92
Chapter 5. Amines as Ligands in Olefin Metathesis	95
5.1. <i>Nitrogen ligands in olefin metathesis – design opportunities</i>	95
5.2. <i>Synthesis of Ru benzyldienes with amine ligands</i>	97
5.2.1. <i>Synthesis and characterization of Grubbs benzyldienes with monodentate amine ligands</i>	97
5.2.2. <i>Synthesis and characterization of benzyldiene complexes with chelating diamines.</i>	99
5.3. <i>Olefin metathesis studies with biphenylamine catalysts</i>	104
5.4. <i>Decomposition studies of biphenyldiamine derivatives</i>	106
5.4.1. <i>Impact of aniline derivatives on cross metathesis yield</i>	106
5.4.2. <i>Thermolysis of biphenylamine derivatives</i>	107
5.4.3. <i>Decomposition of Ru-42 during catalysis</i>	110
5.5. <i>Toward N-Anionic ligands in metathesis catalysts</i>	112
5.5.1. <i>Motivation</i>	112
5.5.2. <i>Attempted syntheses of N-Anionic alkylidenes by halogen exchange</i>	113
5.6. <i>Exploring the variable hapticity of the arylamide ligands</i>	116
5.7. <i>Conclusions and future work</i>	122
5.8. <i>References</i>	123
Chapter 6. Conclusions and Future Work	126
6.1. <i>Conclusions</i>	126
6.2. <i>Future Work</i>	128
6.2.1. <i>Studies to expanded relevance and scope</i>	129
6.2.2. <i>Catalyst modifications to mitigate amine-induced decomposition</i>	130
6.2.3. <i>Experimental evidence for bimolecular deactivation during catalysis</i>	131
6.2.4. <i>Amine adducts as a synthetic route to amido complexes</i>	132
6.3. <i>References</i>	132
Appendix 1. NMR Spectra for New Compounds	133
Appendix 2. In Situ Identification of Decomposition Products	151
Appendix 3. Published Contributions	190

Abstract

Olefin metathesis is a powerful tool for assembly of carbon-carbon bonds. Amines and related *N*-donors are problematic functional groups in Ru-catalyzed olefin metathesis - a well-documented, but poorly understood problem.

The first part of this thesis focuses on amine-induced deactivation pathways; two of which are described in depth. Alkylidene abstraction, a previously unknown reaction for nitrogen nucleophiles, was observed for smaller and less Bronsted-basic amines. Deprotonation of the metallacyclobutane intermediate formed during catalysis is prominent for highly Bronsted basic or sterically bulky *N*-donors. Monosubstituted (and, by extension unsubstituted) metallacyclobutanes are particularly vulnerable to deprotonation.

For each pathway, the fate of the alkylidene Ru=CHR functional group proved key in determining the nature of deactivation. Both pathways have been detected during catalysis, as evidenced by formation of diagnostic amine (RCH₂NR₂') or substituted propene products. A combination of quantitative NMR and GC-MS analysis was used to identify these species on loss of the Ru-alkylidene functional group.

The second part of this thesis focuses on incorporating amines into catalyst design – an under-utilized strategy in the context of Ru-catalyzed olefin metathesis. A modified Grubbs-type catalyst was developed featuring a bulky, relatively non-basic biaryldiamine ligand. Metathesis activity for this catalyst was comparable, and in some cases superior to the most widely-used homogeneous catalysts currently available. Several new, related Ru-benzylidenes were also prepared and fully characterized in conjunction with the mechanistic studies described above.

Progress toward development of *N*-anion-containing metathesis catalysts is also discussed. Synthesis of Ru-hydride complexes originally intended for this purpose allowed for a fundamental study of the coordination chemistry and reductive elimination chemistry of the NPh₂⁻ anion.

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For their unconditional love and support, thank you to Mom, Dad, and Rose. Finally, thank you to Faith for always encouraging and believing in me.

List of Compounds

N-donors used as ligands and catalyst poisons

N1		N2	
N3		N4	
N5		N6	
N7		N8	
N9		N10	
N11		N12	
N-13			

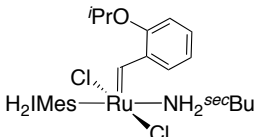
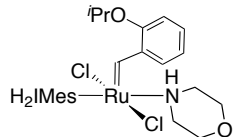
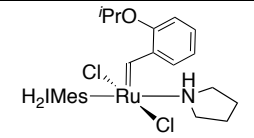
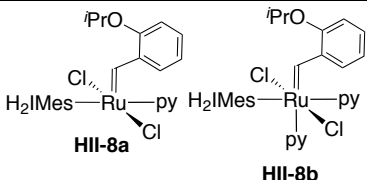
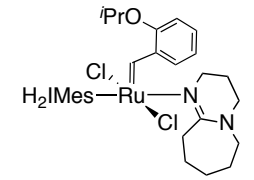
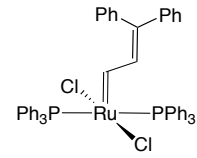
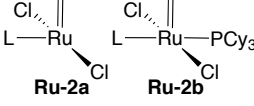
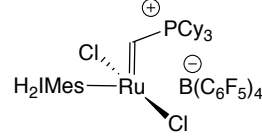
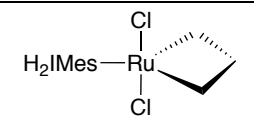
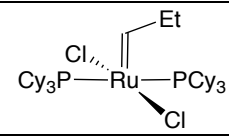
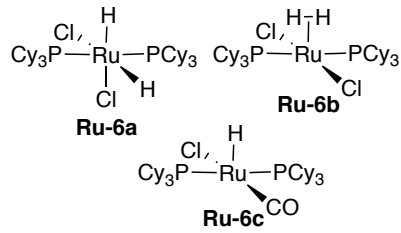
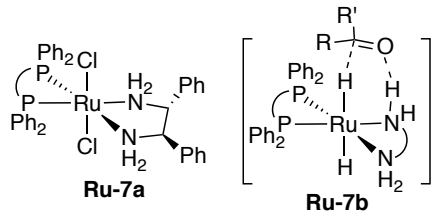
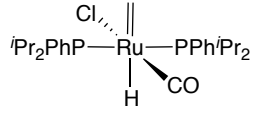
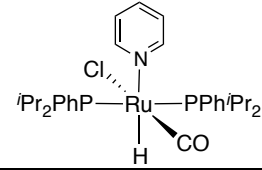
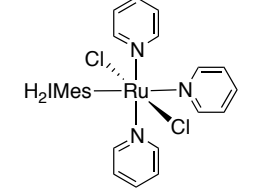
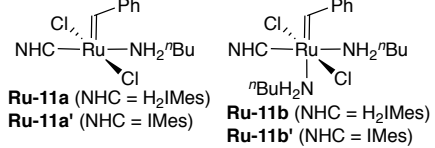
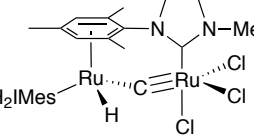
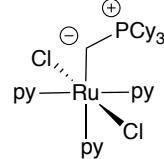
Other organic and main group compounds

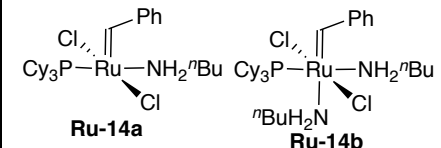
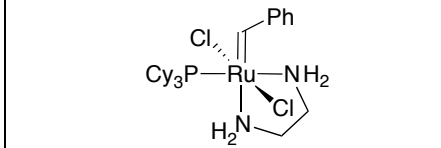
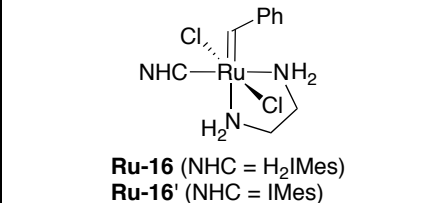
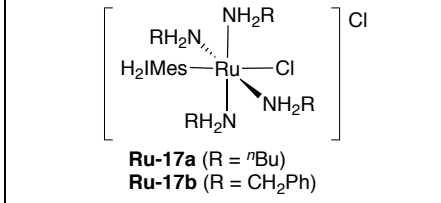
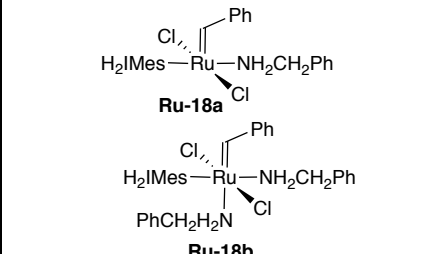
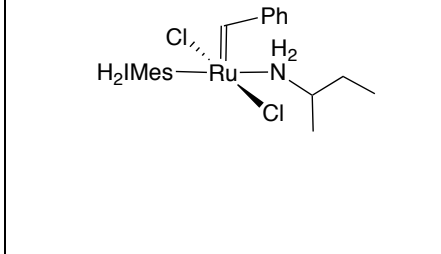
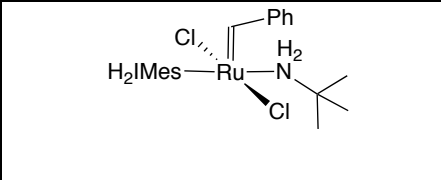
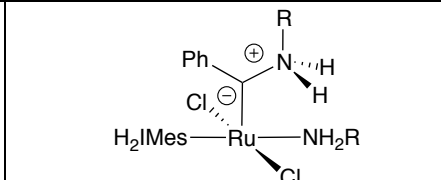
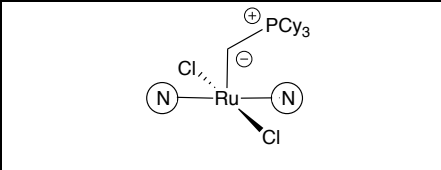
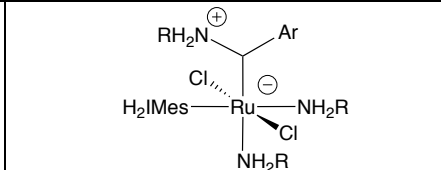
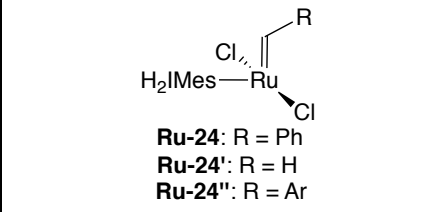
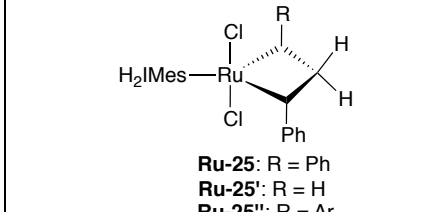
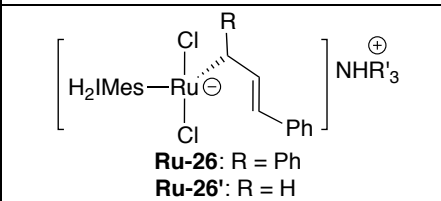
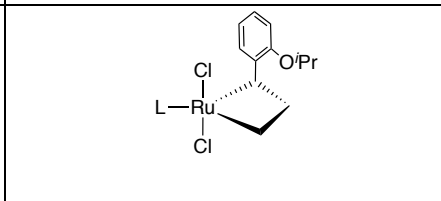
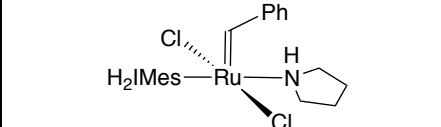
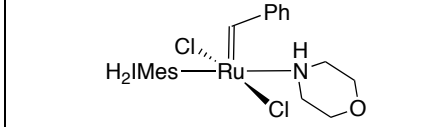
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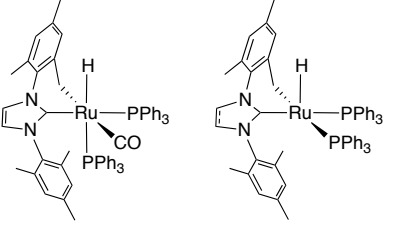
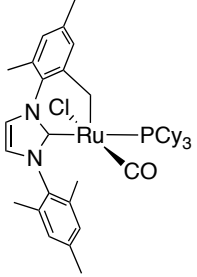
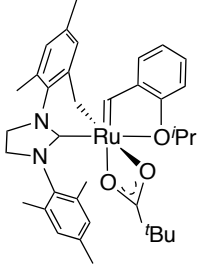
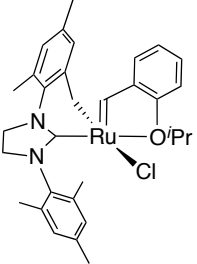
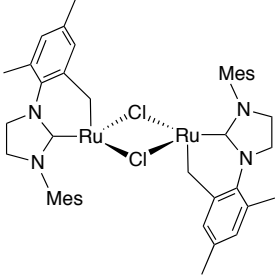
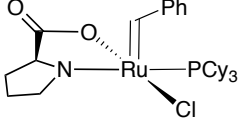
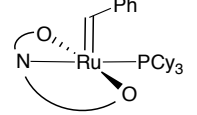
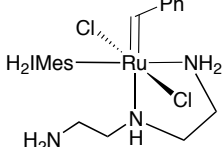
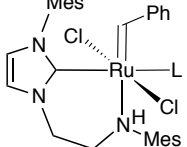
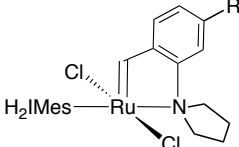
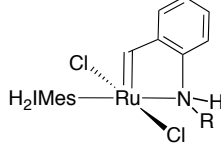
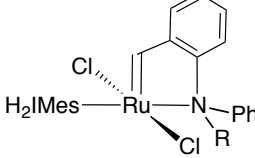
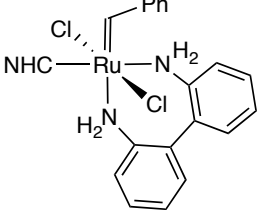
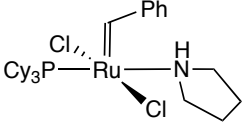
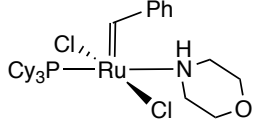
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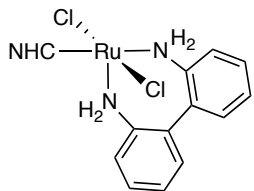
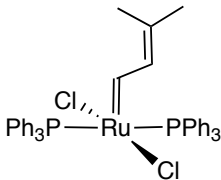
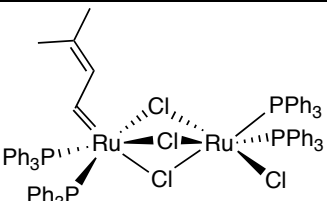
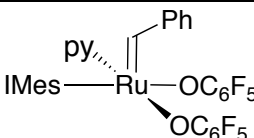
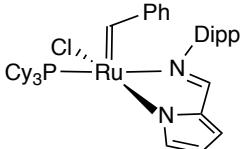
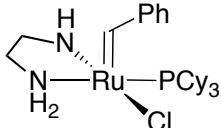
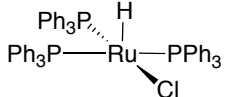
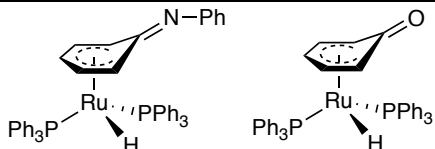
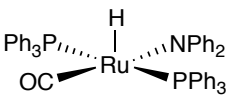
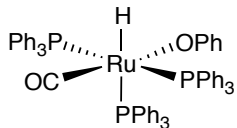
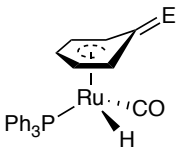
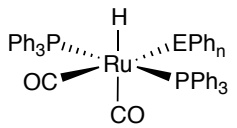
Ruthenium complexes

GI		GIm	
GII/ GII'	 GII (NHC = H ₂ IMes) GII' (NHC = IMes)	GIIIm/ GIIIm'	 GIIIm (NHC = H ₂ IMes) GIIIm' (NHC = IMes)
GIII/ GIII'	 GIII (NHC = H ₂ IMes) GIII' (NHC = IMes)	GIII-Br/ GIII-Br'	 GIII-Br (NHC = H ₂ IMes) GIII-Br' (NHC = IMes)
HII		HII-1 / HII-3	 HII-1a (R = ⁿ Bu) HII-3a (R = CH ₂ Ph) HII-1b (R = ⁿ Bu) HII-3b (R = CH ₂ Ph)

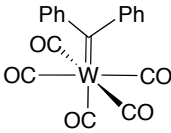
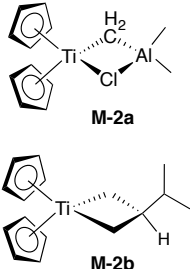
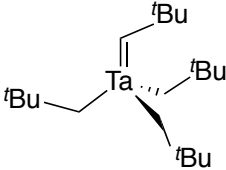
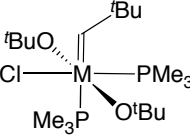
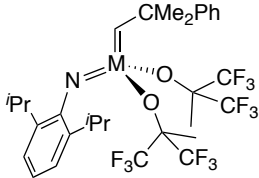
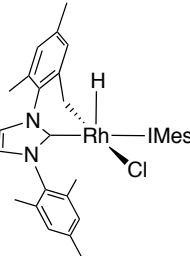
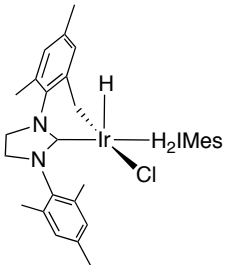
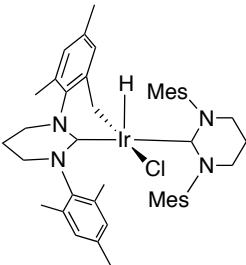
HII-4		HII-6	
HII-7		HII-8	
HII-9		Ru-1	
Ru-2		Ru-3	
Ru-4		Ru-5	
Ru-6		Ru-7	
Ru-8		Ru-9	
Ru-10		Ru-11 / Ru-11'	
Ru-12		Ru-13	

Ru-14	 Ru-14a Ru-14b	Ru-15	
Ru-16	 Ru-16 (NHC = H₂IMes) Ru-16' (NHC = IMes)	Ru-17	 Ru-17a (R = ⁿBu) Ru-17b (R = CH₂Ph)
Ru-18	 Ru-18a Ru-18b	Ru-19	
Ru-20		Ru-21	
Ru-22		Ru-23	
Ru-24	 Ru-24: R = Ph Ru-24': R = H Ru-24'': R = Ar	Ru-25	 Ru-25: R = Ph Ru-25': R = H Ru-25'': R = Ar
Ru-26	 Ru-26: R = Ph Ru-26': R = H	Ru-27	
Ru-28		Ru-29	

Ru-30 / Ru-30'	 Ru-30a Ru-30b (NHC = H₂IMes) Ru-30b' (NHC = IMes)	Ru-31	
Ru-32		Ru-33	
Ru-34		Ru-35	
		Ru-36	
Ru-37		Ru-38	 Ru-38a, L = PCy₃ Ru-38b, PMe₃ Ru-38c, py
Ru-39	 Ru-39a, R = NO₂ Ru-39b, R = H Ru-39c, R = OCH₃	Ru-40	 Ru-40a, R = Me Ru-40b, R = <i>i</i>Pr Ru-40c, R = CH₂Ph
Ru-41	 Ru-41, R = Me Ru-41, R = Et	Ru-42	 Ru-42 (NHC = H₂IMes) Ru-42' (NHC = IMes)
Ru-43		Ru-44	

Ru-45	 Ru-45 (NHC = H₂IMes) Ru-45' (NHC = IMes)	Ru-46	
Ru-47		Ru-48	
Ru-49		Ru-50	
Ru-51		Ru-52	 Ru-52a Ru-52b
Ru-53		Ru-54	
Ru-55		Ru-56	 Ru-56a (E = N, n = 2) Ru-56b (E = O, n = 1)
Ru-57	Ru(CO) ₃ (PPh ₃) ₂		

Other transition metal complexes

M-1		M-2	 M-2a M-2b
M-3		M-4	 M-4a (M = Nb) M-4b (M = Ta)
M-5	 M-5a, (M = W) M-5b (M = Mo)	M-6	
M-7		M-8	

Abbreviations

ADMET	acyclic diene metathesis
Ar	aryl
CM	cross metathesis
COSY	correlation spectroscopy
DBU	1,8-diazabicycloundec-7ene
DDM	diethyl diallylmalonate
DEPT	distortionless enhancement by polarization transfer
Dipp	diisopropylphenyl
EI	electron impact
en	ethylenediamine
EXSY	exchange spectroscopy
FID	flame ionization detector
GC	gas chromatography
HMBC	heteronuclear multiple bond correlation
HMQC	heteronuclear multiple quantum coherence
Hz	Hertz
IR	infrared
IS	internal standard
MCB	metallacyclobutane
Mes	mesityl
MS	mass spectrometry
NHC	<i>N</i> -heterocyclic carbene
NMR	nuclear magnetic resonance
NOE(SY)	nuclear Overhauser effect (spectroscopy)
ppm	parts per million
py	pyridine
RCM	ring closing metathesis
ROMP	ring opening metathesis polymerization
RT	room temperature
SHOP	Shell higher olefins process
THF	tetrahydrofuran
TMB	trimethoxybenzene
TMS	tetramethylsilane
TOF	turnover frequency
TON	turnover number
Tp	hydridotris(pyrazolyl)borate
XRD	X-ray diffraction

List of Charts, Schemes, Figures, and Tables

Chapter 1

Charts

Chart 1.1. Drug targets synthesized by RCM (red indicates RCM site).	4
Chart 1.2. Key advances in development of group 5-6 metal alkylidene catalysts.	7
Chart 1.3. Grubbs catalysts bearing phosphine (first-generation) and NHC (second-generation) ancillary ligands.	8
Chart 1.4. Grubbs catalyst analogues with modified labile L-donor or alkylidene sites.	10

Schemes

Scheme 1.1. Catalyzed carbon-carbon bond forming reactions recently acknowledged with Nobel prizes. (a) olefin metathesis (2005). (b) cross-coupling (2010).	1
Scheme 1.2. Simplified depiction of the types of olefin metathesis reactions. (a) Cross metathesis (CM). (b) Ring-closing metathesis (RCM). (c) acyclic diene metathesis (ADMET). (d) ring-opening metathesis polymerization (ROMP).	2
Scheme 1.3. Sequential (a) cross metathesis and (b) transesterification for conversion of triglycerides to olefin and ester products. ^a	3
Scheme 1.4. RCM as a key step in the synthesis of Ciluprevir (red indicates RCM site).	4
Scheme 1.5. (a) A simplified representation of the Chauvin mechanism. (b) Predicted equilibrium distribution for cross metathesis of cyclopentene with 2-pentene via the mechanism in (a).	5
Scheme 1.6. Reaction of $W(CO)_5(=CPh_2)$ and isobutene to 1,1-diphenylethene.	6
Scheme 1.7. (a) Isolation of titanocyclobutane M-2b from the Tebbe reagent. (b) Isotopic labeling of titanocyclobutane M-2b .	6
Scheme 1.8. Catalytic cycle for the Grubbs catalysts.	8
Scheme 1.9. Direct observation of a Ru-MCB species formed in situ from four-coordinate Ru-3 .	10
Scheme 1.10. Non-productive homodimerization in cross metathesis ^a and strategies for maximizing cross-product yield (5c).	11
Scheme 1.11. Ring/chain equilibrium in ring closing metathesis.	12
Scheme 1.12. Degenerate and productive cross metathesis in a homodimerization reaction.	12
Scheme 1.13. Leading studies illustrating (a) methyldiene abstraction. (b) metallacyclobutane decomposition. (c) bimolecular alkylidene coupling.	14
Scheme 1.14. Decomposition of GI to Ru-hydrides using (a) hydrogen and (b) methanol and base (NEt_3) with proposed mechanism.	15
Scheme 1.15. Decomposition of (a) GII and (b) GI induced by π -acceptor ligands.	16
Scheme 1.16. (a) Structure of an archetypal Noyori binap/diamine catalyst (Ru-7a) and (b) outer-sphere asymmetric hydrogenation involving an “NH” ligand.	17

Chapter 2

Tables

Table 2.1. Crystallographic details for $\text{RuH}(\eta^5\text{-C}_6\text{H}_5\text{-NPh})(\text{PPh}_3)_2$ Ru-52a (CCDC-940549)	44
---	----

Chapter 3

Charts

Chart 3.1. (a) The Grubbs metathesis catalysts, and (b) their methyldiene resting states.	46
--	----

Schemes

Scheme 3.1. (a) Loss of the methyldiene functionality from $\text{RuHCl}(\text{CO})(\text{P}^i\text{Pr}_2\text{Ph})_2(=\text{CH}_2)$ on exposure to pyridine. (b) Rapid decomposition of GIII on exposure to ethylene.	47
Scheme 3.2. Reactions of (a) GI . (b) GII with <i>n</i> -butylamine, reported by the Moore group.	48
Scheme 3.3. Decomposition products reported on thermolysis of GIIIm .	48
Scheme 3.4. Decomposition of Grubbs methyldiene complexes by added py (a) GIIIm . (b) GIIm .	49
Scheme 3.5. Proposed pathway for alkylidene abstraction from GI by <i>n</i> -butylamine N1 to liberate the imine $\text{PhCH}=\text{N}^n\text{Bu}$ (7b).	52
Scheme 3.6. Incomplete decomposition of GI by a single equivalent of <i>n</i> -butylamine N1 .	53
Scheme 3.7. Abstraction of the benzyldiene ligand from Ru-15 , and proposed products. (a) Decomposition of in situ-generated Ru-15 by excess en N2 . (b) Decomposition of Ru-15 with excess <i>n</i> -butylamine N1 .	54
Scheme 3.8. Abstraction of the benzyldiene ligands from GII and GII' by excess <i>n</i> -butylamine N1 .	55
Scheme 3.9. Synthesis of $[\text{RuCl}(\text{H}_2\text{IMes})(\text{NH}_2^n\text{Bu})_4]\text{Cl}$ Ru-17a .	57
Scheme 3.10. Decomposition of Ru-16 with excess <i>n</i> -butylamine N1 .	58
Scheme 3.11. Slow benzyldiene abstraction on reaction of GII with benzylamine N3 . (N.D. = not determined).	59
Scheme 3.12. Adduct formation on reaction of GII with sterically less accessible primary amines, <i>sec</i> -butylamine N4 and <i>t</i> -butylamine N5 .	59
Scheme 3.13. Isolation of mono-amine derivatives of GII by reaction with bulky primary amines.	60
Scheme 3.14. Benzyldiene abstraction requires net transfer of one H (red) from amine: illustrated with NH_2^nBu .	61
Scheme 3.15. a) Proposed mechanism for abstraction of the benzyldiene ligand by primary amines (N1 , N3) and (b) proposed molecular orbital (MO) interaction for the initial nucleophilic attack.	62
Scheme 3.16. Reactions of GII with nitrogen nucleophiles.	63
Figures	
Figure 3.1. ^1H NMR spectra (C_6D_6 , 300.1 MHz) of the reaction of GI with <i>n</i> -butylamine N1 . (a) Spectrum before addition of N1 ; (b) 3 min after amine addition (40% decomposition); (c) 25 min after amine addition (complete decomposition); (d) commercial 7a (Acros) for comparison.	51
Figure 3.2. Reaction profile for decomposition of GI by N1 . (a) Loss in alkylidene signal and formation of $\text{PhCH}_2\text{NH}^n\text{Bu}$ 7a over 30 min. (b) Plot of	52

ln[Ru-14a + Ru-14b] vs. time to 98% decomposition,. % vs. TMB normalized to GI at t_0 (average of two trials, $\pm 2\%$).	
Figure 3.3. Decomposition of RuCl ₂ (L)(PCy ₃)(=CHPh) (L = H ₂ IMes, GII ; IMes, GII') by NH ₂ ⁿ Bu N1 . (a) Loss of total Ru=CHPh signals vs. internal standard. (b) Plot of ln[Ru-11b + GII] and ln[Ru-11b' + GII'] vs. time to >95% decomposition. (c) Rate of formation of PhCH ₂ NH ⁿ Bu 7a over the course of each reaction. % values vs. TMB internal standard normalized to GII or GII' at t_0 ($\pm 2\%$ in replicate runs for GII decomposition. Single-trial results for GII' decomposition and excess amine addition to GII in (c)).	56
Figure 3.4. Benzylidene abstraction from GII with excess N1 : impact of added PCy ₃ and N1 . Values represent total Ru=CHPh integration (vs. TMB, normalized to Ru=CHPh at t_0).	57

Tables

Table 3.1. Summary of kinetic data for benzylidene abstraction from GII by NH ₂ ⁿ Bu N1 .	58
Table 3.2. Equilibrium yields and ¹ H NMR data for new [Ru]=CHAr species formed by reaction of GII with primary amines (10 equiv). Also shown is the proportion of the benzylidene-abstraction product PhCH ₂ NHR observed.	60
Table 3.3. Equilibrium yields and chemical shift of the benzylidene proton for GII -amine adducts (10 equiv amine).	62

Chapter 4

Charts

Chart 4.1. Metathesis catalysts discussed, and the resting-state methyldiene complex for GII .	66
Chart 4.2. Nitrogen bases studied, with binding site shown in blue.	68
Chart 4.3. Exemplary Group 8–9 complexes with C–H activated NHC ligands.	81

Schemes

Scheme 4.1. Amine-induced deactivation of the Grubbs catalysts.	67
Scheme 4.2. Reaction of III with di- or trisubstituted <i>N</i> -donors.	68
Scheme 4.3. Reaction of III with primary amines.	70
Scheme 4.4. Isolation of Ru-17a from the reaction of III or GII with <i>n</i> -butylamine	71
Scheme 4.5. Proposed mechanism for benzylidene abstraction by sterically-accessible primary amines.	72
Scheme 4.6. Reaction of III with styrene and pyrrolidine, and rate plot for loss of alkylidene.	76
Scheme 4.7. Proposed mechanism for base-induced decomposition of the metallacyclobutane.	77
Scheme 4.8. Organic products from base-induced decomposition of III during ethylene metathesis.	78
Scheme 4.9. Origin of the three-carbon marker compounds 13 and 14 . (a) early in catalysis. (b) later in catalysis.	80
Scheme 4.10. Organic products and proposed C–H activated complex Ru-34 from decomposition of III by DBU and styrene.	82
Scheme 4.11. Observed products for base-induced decomposition of GII via metallacyclobutane intermediate Ru-25' .	86
Scheme 4.12. Observed products for ethenolysis of GII .	86

Scheme 4.13. The influence of amine bulk and basicity on the preferred decomposition pathway in metathesis. (a) Methylidene abstraction. (b) Metallacyclobutane deprotonation.	87
Scheme 4.14. Observed major and proposed minor products for decomposition of III in the presence of excess <i>n</i> -butylamine and styrene.	89
Scheme 4.15. Proposed isotopic labeling studies for (a) determining the fate of β -MCB H during metallacyclobutane decomposition. (b) confirming the identity of methylidene abstraction products formed during catalysis.	91
<i>Figures</i>	
Figure 4.1. Impact of <i>N</i> -base on metathesis yields.	73
Figure 4.2. ¹ H NMR spectra (C ₆ D ₆ , 500.1 MHz) of III + 1 DBU + 10 styrene after 0.5 h at 60 °C. Peaks denoted (*) are not assigned.	80
Figure 4.3. Impact of (a) one equivalent and (b) ten equivalents of base on metathesis yields. Grey bars indicate yields for III shown in Section 4.3 above; reproduced here for comparison.	83
Figure 4.4. ¹ H NMR spectra (C ₆ D ₆ , 500.1 MHz) for the reaction of (a) III + 10 morpholine N6 + 10 styrene, after 6 h at 60 °C. Expansion shows olefinic signals for PhHC=CHCH ₂ Ph (minor product) and PhHC=CHCH ₃ (trace quantities) (b) commercial <i>N</i> -methylmorpholine 16 . Peaks denoted (*) not assigned.	88
<i>Tables</i>	
Table 4.1. Key ¹ H NMR data and equilibrium yields for <i>N</i> -adducts of III and GII .	69
Table 4.2. Decomposition rates and products on reaction of III with styrene and base.	75
Table 4.3. NMR data for the complexes of Chart 4.3.	81
Table 4.4. Decomposition Rates and Products Formed on Treating GII with Styrene and Base.	85

Chapter 5

<i>Charts</i>	
Chart 5.1. Grubbs-class metathesis catalysts bearing neutral amine ligands. (a) First-generation; (b) Second-generation catalysts.	95
Chart 5.2. Literature examples of metathesis catalysts with chelating styrenyl-amine ligands.	96
Chart 5.3. En adducts of GI (Ru-15), GII (Ru-16), and GII' (Ru-16').	103
Chart 5.4. Biphenyldiamine N11 and its comparator amines. Note: cf. p <i>K</i> _a 16.6–24.1 for other bases studied in Chapter 4.	106
Chart 5.5. (a) Selected Ru(σ -NRAr) Derivatives. (b) η^5 -Cyclohexadienylimine Complexes of Iron.	116
<i>Schemes</i>	
Scheme 5.1. Prior RCM studies with Ru-42' .	97
Scheme 5.2. Synthesis of morpholine (N6) or pyrrolidine (N7) adducts of (a) GII and (b) GI .	98
Scheme 5.3. Isolation of Ru-42 from GIII .	100
Scheme 5.4. Previously-reported “bimolecular” thermolysis of Ru alkylidenes.	109
Scheme 5.5. Proposed bimolecular decomposition pathways of Ru-42/Ru-42' (a) without involvement from N11 . (b) induced by N11 .	109
Scheme 5.6. Expected “alkylidene abstraction” amine product(s) and proposed Ru product from decomposition of Ru-42 + styrene (bearing an intact N11)	111

ligand).	
Scheme 5.7. Decomposition of Ru-42 under ethylene.	112
Scheme 5.8. Synthesis of Ru-pseudohalide metathesis catalysts by halogen exchange.	113
Scheme 5.9. Reaction of G1 with Li[NHC ₂ H ₄ NH ₂] and proposed Ru-50 , formed in low yield.	114
Scheme 5.10. Prior work demonstrating ruthenium hydride Ru-51 as a synthon for Ru=CHR	115
Scheme 5.11. Piano-Stool products Formed by Reaction of RuHCl(PPh ₃) ₃ with Diphenylamide or Phenoxide.	117
Scheme 5.12. σ -Arylamide and σ -Aryloxide Complexes Accessible from RuHCl(CO)(PPh ₃) ₃	120
Scheme 5.13. Proposed reductive elimination pathway in carbonylation of Ru-52a , Ru-52b to form HEP _n Ru(CO) ₃ (PPh ₃) ₂	120
<i>Figures</i>	
Figure 5.1. ¹ H NMR spectra (CDCl ₃ , 500.1 MHz) of RuCl ₂ (H ₂ IMes)(κ^2 -(H ₂ NC ₆ H ₄) ₂)(=CHPh) Ru-42 . (a) at RT. (b) at -20 °C. (c) at -20 °C with 1 drop D ₂ O. Expansions show region containing N-H signals (5.0–3.5 ppm).	101
Figure 5.2. ¹ H EXSY (500.1 MHz, CDCl ₃ , -20 °C, <i>t</i> ₈ = 0.25 s) of RuCl ₂ (H ₂ IMes)(κ^2 -(H ₂ NC ₆ H ₄) ₂)(=CHPh) Ru-42 showing chemical exchange of NH ₂ (green) and <i>o</i> -CH of biphenyl (red) subunits.	102
Figure 5.3. Metathesis of (a) styrene; (b) pro-lactone 18 by Ru-42 relative to benchmark catalysts GII , GIII , and HII . Conditions: initial olefin concentration 100 mM (styrene) or 5 mM (18); RT, C ₆ H ₆ ; $\pm$ 2.5% in replicate experiments.	104
Figure 5.4. Metathesis of (a) DDM 20 ; (b) styrene by Ru-42 and Ru-42' . Conditions: initial olefin concentration 100 mM, RT, C ₆ H ₆ ; $\pm$ 2.5% in replicate experiments.	105
Figure 5.5. Impact of aniline derivatives (N11 , N12 , N13) on CM yield for homodimerization of styrene by HII . (Results for control and py reactions reproduced from Chapter 4 for comparison.)	107
Figure 5.6. Reaction profile for thermolysis of Ru-42 and Ru-42' (C ₆ D ₆ , 60 °C). Product yields (above) are normalized to decomposed Ru=CHPh against TMB internal standard at 96 h.	108
Figure 5.7. Perspective view of Ru-52a . Non-hydrogen atoms are represented by Gaussian ellipsoids at the 20% probability level. The hydride ligand is shown with an arbitrarily small thermal ellipsoid. Key metrics: C21-N: 1.406(6) Å; C11-N: 1.313(6) Å; C21-N-C11: 120.9(4)°.	118
Figure 5.8. Diagnostic ¹ H NMR locations (C ₆ D ₆ solvent) for the π - and σ -bound N(C ₆ H ₅) ₂ ligand in Ru-52a and Ru-53 .	119
<i>Tables</i>	
Table 5.1. NMR and IR data for derivatives of G1 and GII bearing monodentate amines (morpholine, N6 ; pyrrolidine, N7).	99
Table 5.2. NMR and IR characterization data for second-generation benzylidenes with N,N chelates	103
Table 5.3. Comparison of styrene CM yields and decomposition for Ru-42 vs. HII .	111
Table 5.4. Decomposition of GIII' by N-anionic salts 23 to 25 .	115
Table 5.5. Carbonylation and Reductive Elimination Products from Arylamide and Alkoxy-Containing Ru Hydrides.	121

Chapter 6

Charts

Chart 6.1. Structure of biphenyldiamine adduct Ru-42 .	127
--	-----

Schemes

Scheme 6.1. Abstraction of the benzyldiene group from GII by a primary amine.	126
Scheme 6.2. Organic products attributed to deprotonation of the metallacyclobutane intermediate.	127
Scheme 6.3. Potential involvement of amine in catalyst decomposition via β -CH ₂ transfer.	127
Scheme 6.4. Alkylidene abstraction involving (a) a protic nucleophile, as discussed in Chapter 3. (b) an aprotic nucleophile.	129
Scheme 6.5. Proposed deuterium labeling studies to discern whether C-H activation occurs during metallacyclobutane deprotonation.	130
Scheme 6.6. Proposed addition of steric bulk above and below the basal plane of GII . (a) Potentially improved stability to nucleophilic attack (alkylidene abstraction). (b) Improved selectivity for productive metathesis over MCB deprotonation.	131
Scheme 6.7. Method for detection of “bimolecular” decomposition during catalysis.	132
Scheme 6.8. Deprotonation / halide abstraction as a synthetic route to amido “pseudohalide” catalysts.	132

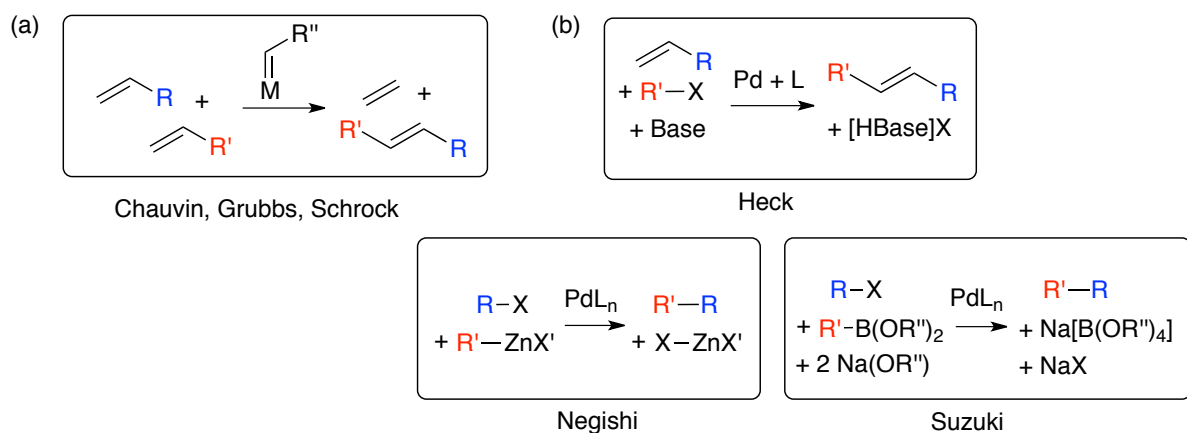
Chapter 1. Introduction

1.1. Catalysis

Catalysts empower the synthetic chemist. The most rudimentary function of a catalyst is to provide a thermodynamically favorable process with a kinetically favorable pathway from reactants to products.¹ A catalyst can also provide selectivity by preferentially lowering the energy of a single transformation where multiple reaction pathways are accessible. With an increase in the number of selective transformations achievable, the chemist is able to design syntheses to achieve a desired product in fewer steps, saving time and materials.² The environmental impact of a synthetic process can therefore be reduced by eliminating solvent and reagent waste from unnecessary reaction steps.³ In practice, these factors can make the difference between an impractical goal and a routine process.

Assembly of carbon-carbon bonds is a core objective of synthetic chemistry. Transition metal catalysis provides powerful methods of targeted C–C bond formation.^{4,5} Indeed, the two most recent Nobel prizes in homogenous catalysis both focus on construction of carbon-carbon molecular frameworks. The pioneers of olefin metathesis (Scheme 1.1a): Chauvin,⁶ Grubbs,⁷ and Schrock⁸ were awarded the Nobel prize in chemistry in 2005. For the development of palladium-catalyzed cross-coupling (Scheme 1.1b), Heck,⁹ Negishi,¹⁰ and Suzuki¹¹ were recognized with the 2010 Nobel prize.

Scheme 1.1. Catalyzed carbon-carbon bond forming reactions recently acknowledged with Nobel prizes. (a) olefin metathesis (2005). (b) cross-coupling (2010).



Cross-coupling has been specifically highlighted as a recent triumph of homogeneous catalysts which has been successfully applied in pharmaceutical, fine chemical, and agricultural industries.^{12,13} The details of this reaction are largely outside the scope of this work (Section 1.5, below), as are the details of organic C–C bond forming reactions (nucleophilic substitution, Diels-

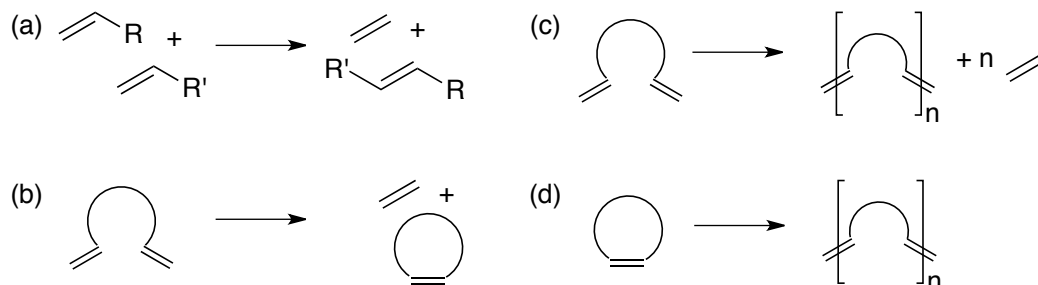
Alder chemistry, etc.).¹⁴ A brief overview of the application, mechanism, and development of olefin metathesis is provided in the following sections.

1.2. Olefin metathesis

1.2.1. A powerful tool for organic synthesis

Olefin metathesis is the exchange of alkene carbon atoms (Scheme 1.1a, above).¹⁵ Cross metathesis (CM) involves reaction of two olefins to produce two new olefin products (Scheme 1.2a). An intramolecular variant of CM results in formation of a ring structure and is referred to as ring-closing metathesis (RCM, Scheme 1.2b). Dienes may also undergo intermolecular cross metathesis to form polymers – referred to as acyclic diene metathesis (ADMET, Scheme 1.2c). Alternatively, polymers may form by intermolecular metathesis of cyclic olefins – known as ring-opening metathesis polymerization (ROMP, Scheme 1.2d).

Scheme 1.2. Simplified depiction of the types of olefin metathesis reactions. (a) Cross metathesis (CM). (b) Ring-closing metathesis (RCM). (c) acyclic diene metathesis (ADMET). (d) ring-opening metathesis polymerization (ROMP).



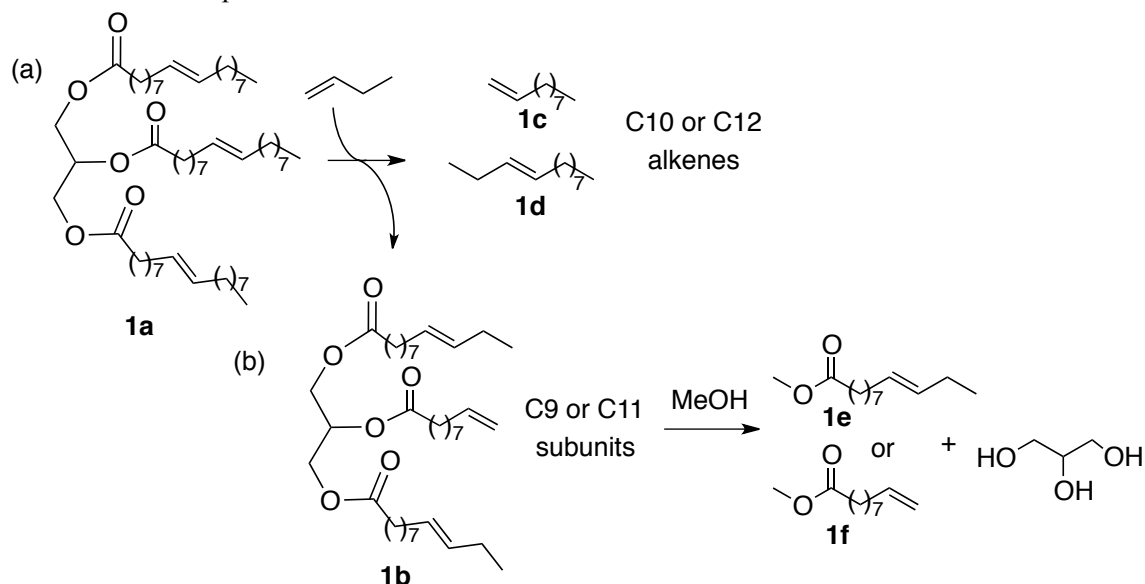
Olefin metathesis has been used industrially for decades.¹⁶ For example, the shell higher olefins process (commercialized in 1977) uses CM in conjunction with oligomerization and isomerization processes to convert ethylene into C11-C14 alkenes.¹⁷ Synthesis of some commodity polymers (for example, polynorbornenes) is also achieved by metathesis (ROMP).¹⁶ Industrial processes have historically relied on ill-defined heterogeneous catalysts, formed in situ by treatment of a transition metal oxide or halide with a reducing agent.¹⁸ The heterogeneous systems are advantageous in that they are inherently amenable to removal and are often thermally and chemically robust. In contrast, opportunity for rational study and design is limited by the ill-defined nature of the active species.

Examples of homogeneous catalysis in industrial olefin metathesis have emerged only in the last two years. The first example employing cross metathesis, a bio-oils refinery in Indonesia, began

shipping products in 2013. This facility, a joint venture between Elevance Renewable Sciences and Wilmar International, produces specialty oleochemicals by sequential cross metathesis and transesterification of triglycerides from vegetable oils (palm, soybean, and canola). These products have applications as lubricants, synthetic oils, fuels, surfactants, and synthetic precursors to fine chemicals.¹⁹ Four additional production facilities are claimed to be in current development.²⁰

In bio-oils refinement, the presence of various triglycerides in vegetable oils give rise to a mixture of products. These species may then be separated based on their physical properties (i.e. boiling point) and sold as commodities in their own right, or subjected to further refinement. As an illustrative example of the underlying chemistry, synthesis of surfactants from the triglyceride of oleic acid (the most common fatty acid ester in canola oil) is shown in Scheme 1.3.

Scheme 1.3. Sequential (a) cross metathesis and (b) transesterification for conversion of triglycerides to olefin and ester products.^a



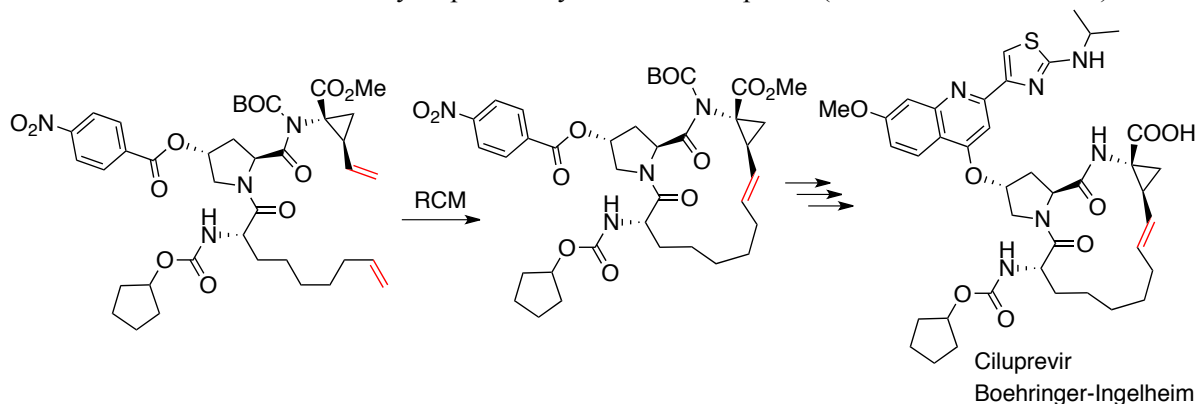
^a Triglyceride intermediate **1b** has been arbitrarily depicted as bearing one central C9 substituent and two C11 subunits. A statistical distribution of C9 and C11 subunits is obtained in the reaction mixture.

Cross metathesis of the triglyceride with an inexpensive, short-chain alkene (1-butene) converts each C17 subunit of triglyceride **1a** into two subunits – one C9 or C11 bound to the glyceride backbone (**1b**) and one C10 or C12 alkene (**1c** and **1d**).²¹ The decene **1c** and dodecene **1d** co-products may then be separated for use as lubricants or synthetic oils, or hydrogenated for use as fuels. The glyceride subunits are then separated by transesterification, affording a mixture of the C13 (**1e**) and C11 (**1f**) products, both of which are sold commercially as surfactants.¹⁹

The pharmaceutical industry has also implemented olefin metathesis into commercial processes as of 2014,²² following a long and arduous campaign of optimization. Boehringer-

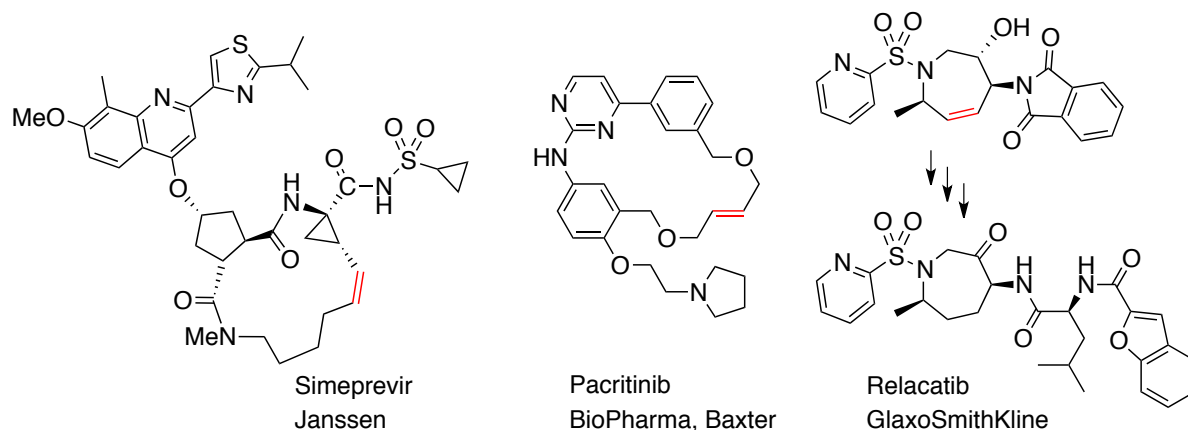
Ingelheim described pilot-scale implementation of Ciluprevir,²³ an antiviral compound for treatment of hepatitis C beginning in 2005. This was the first reported large-scale pharmaceutical process using olefin metathesis (Scheme 1.4), which was aimed at developing amounts of material sufficient to support clinical trials. Ciluprevir was ultimately unsuccessful in phase I clinical trials due to cardiac toxicity.²⁴ Its development did, however, demonstrate the utility of olefin metathesis in RCM macrocyclization for the assembly of complex, biologically-active molecules.

Scheme 1.4. RCM as a key step in the synthesis of Ciluprevir (red indicates RCM site).



A subsequent, structurally-related hepatitis C antiviral, Simeprevir, was developed by Janssen Pharma and successfully completed clinical trials in 2013.²⁵ Simeprevir has been distributed globally, with sales amounting to \$234 million USD in the first quarter of 2015 alone.²⁶ Other emerging pharmaceuticals employing RCM include Pacritinib (a kinase inhibitor in development for treatment of myelofibrosis)²⁷ and Relacatib (a cathepsin K inhibitor for treatment of osteoporosis) (Chart 1.1).^{19,28}

Chart 1.1. Drug targets synthesized by RCM (red indicates RCM site).



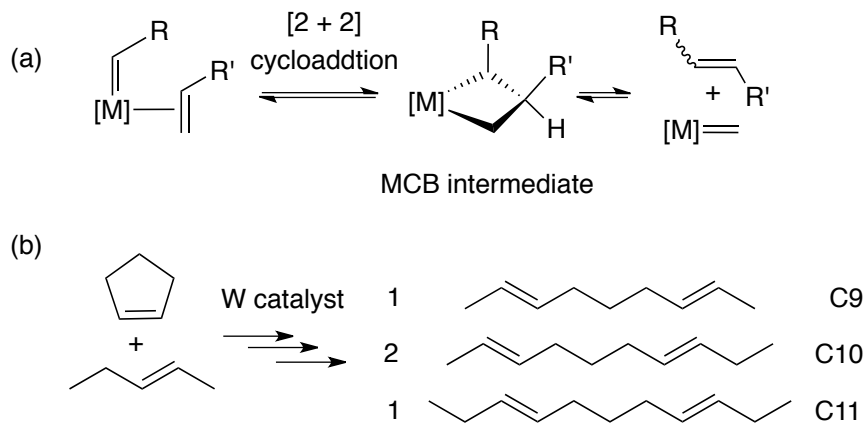
The recent industrial uptake of olefin metathesis, particularly for pharmaceutical synthesis, is enabled by the development of robust homogeneous catalysts. The state-of-the-art catalysts in use today are the product of decades of research into the underlying organometallic chemistry of olefin metathesis. Highlights of this research process are discussed in the following section.

1.2.2. The history and mechanism of olefin metathesis - highlights

A DuPont patent filed in 1955 described titanium-catalyzed polymerization of a norbornene monomer.²⁹ Though the details were not known at the time, this was the first reported instance of olefin metathesis. Cross metathesis (CM) using molybdenum and tungsten catalysts was observed by chemists at Phillips Petroleum in the early 1960s.³⁰ This report described disproportionation of propene into ethylene and 2-butene. Cleavage and re-formation of carbon-carbon double bonds was identified as the underlying phenomenon by the late 1960s though at the time, the active catalyst structures and mechanism were not known.³¹

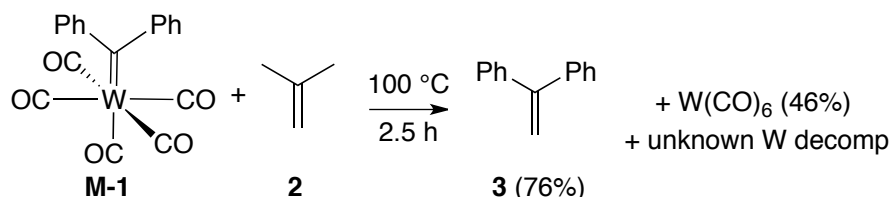
In a seminal report in 1971, Chauvin correctly identified the mechanism of olefin metathesis (Scheme 1.5a). An initial [2+2] cycloaddition between a metal alkylidene and an olefin results in formation of a metallacyclobutane (MCB) intermediate. Subsequent cycloreversion affords an equilibrium mixture of olefin products.³² Key evidence in the Chauvin study was observation of a mixture of C9, C10, and C11 species (1:2:1 ratio) as the major products from cross metathesis of cyclopentene and 2-pentene (Scheme 1.5b). The observed product distribution was inconsistent with other leading hypotheses involving cyclic alkane³¹ or metallacyclopentane intermediates.³³ Kinetic^{34,35} and isotopic labeling studies³⁶ in following years provided early support for the Chauvin mechanism.

Scheme 1.5. (a) A simplified representation of the Chauvin mechanism. (b) Predicted equilibrium distribution for cross metathesis of cyclopentene with 2-pentene via the mechanism in (a).



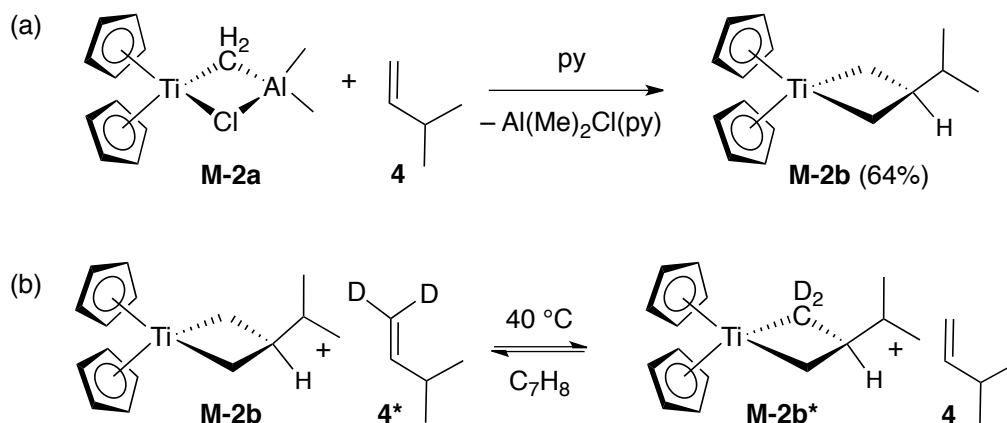
The Chauvin mechanism pointed to involvement of two key types of organometallic species in olefin metathesis – a metal alkylidene and a metallacyclobutane intermediate. Early support for the former was provided in a 1974 study by Casey et al. Formation of 1,1-diphenylethene **3** on reaction of $\text{W}(\text{CO})_5(=\text{CPh}_2)$ **M-1** with isobutene **2** was observed, confirming transfer of the alkylidene substituent to the olefin (Scheme 1.6). The corresponding $[\text{W}]=\text{CMe}_2$ product was not identified, however as an unidentified decomposition mechanism resulted in formation of $\text{W}(\text{CO})_6$ and other unidentified tungsten species.³⁷

Scheme 1.6. Reaction of $\text{W}(\text{CO})_5(=\text{CPh}_2)$ and isobutene to 1,1-diphenylethene.³⁷



The Tebbe reagent³⁸ **M-2a** provided an early model for studying the metallacyclobutane intermediate formed during catalysis (above, Scheme 1.5a). The now-iconic complex has been known for over 30 years, though the crystal structure was not reported until 2014.³⁹ In 1980, Grubbs reported that reaction of **M-2a** with 3-methyl-1-butene **4** afforded titanacyclobutane **M-2b**.⁴⁰ In a subsequent study, isolated **M-2b** underwent isotopic exchange with deuterium-labeled **4*** (Scheme 1.7b), confirming that metallacyclobutane complexes are capable of exchanging substituents with olefins.^{41,42}

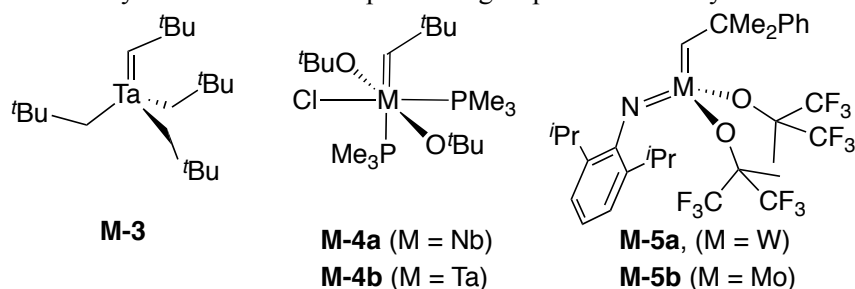
Scheme 1.7. (a) Isolation of titanacyclobutane **M-2b** from the Tebbe reagent. (b) Isotopic labeling of titanacyclobutane **M-2b**.



1.2.3. Well-defined metal alkylidenes as metathesis catalysts

The first well-defined metathesis catalysts were reported shortly following Chauvin's study. A discrete, isolable tantalum carbene (**M-3**, Chart 1.2a)⁴³ was reported by Schrock in 1974. The metathesis activity of this class of carbene was later demonstrated for related **M-4a**, which induced self-metathesis of Z-2-pentene at RT.⁴⁴ Modification of the Schrock complexes led to successful preparation of tungsten⁴⁵ and molybdenum^{46,47} catalysts (**M-5**, Chart 1.2).⁸ The Mo and W catalysts exhibit exceptional activity and tunability, and were later applied to development of commercially-available enantioselective molybdenum catalysts.^{48,49} The group 6 catalysts are, however highly oxophilic and unstable in the presence of air, moisture, protic functional groups, carboxylic acids, and aldehydes.⁵⁰ By comparison to the robust ruthenium alkylidene catalysts (Chart 1.3, below), group 6 catalysts have not been as widely adopted in synthetic organic chemistry.^{50,51}

Chart 1.2. Key advances in development of group 5-6 metal alkylidene catalysts.

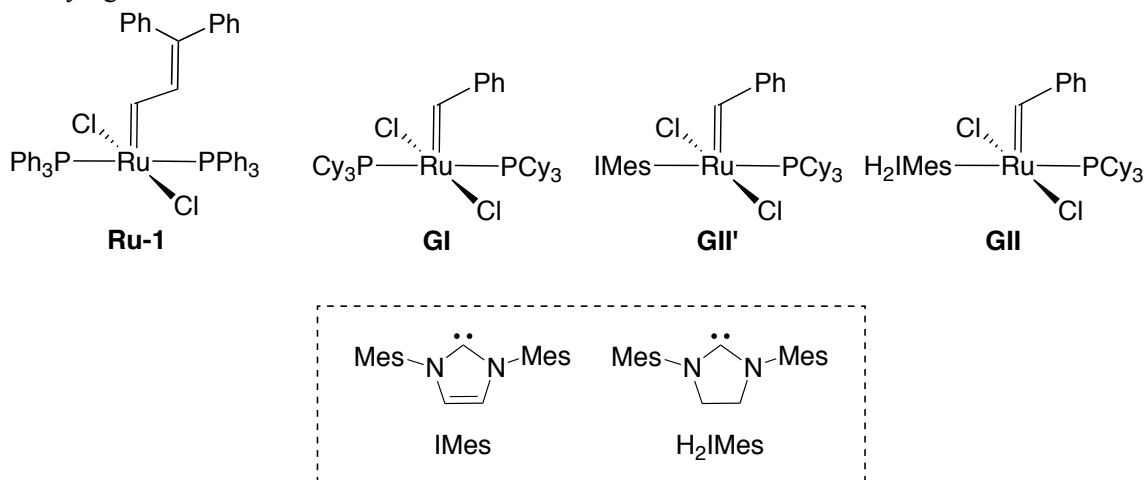


In contrast to the group 6 catalysts, Ru alkylidenes, pioneered by Grubbs,⁷ are less sensitive to air and moisture. As a result of their lower oxophilicity, Ru alkylidenes react preferentially with olefins, even in the presence of carbonyl-containing functional groups.⁴² The first well-defined olefin metathesis catalyst based on Ru (**Ru-1**, Chart 1.3) was reported by Grubbs et al. in 1992.⁵² This complex was the basis for development of the so-called “first-generation” Grubbs catalyst **GI** (Chart 1.3).⁵³ Replacement of one PCy₃ ligand in **GI** by an *N*-heterocyclic carbene (NHC) ligand affords the “second-generation” catalyst **GII**. The IMes derivative was reported almost simultaneously by the groups of Grubbs⁵⁴ and Nolan⁵⁵ in 1999. Shortly thereafter, Grubbs reported an analogue bearing a saturated NHC, H₂IMes (**GII**, Chart 1.3).⁵⁶ The second-generation catalysts exhibit higher metathesis activity than does **GI**.⁵⁷ The saturated NHC analogue **GII** is more widely-used than **GII**.

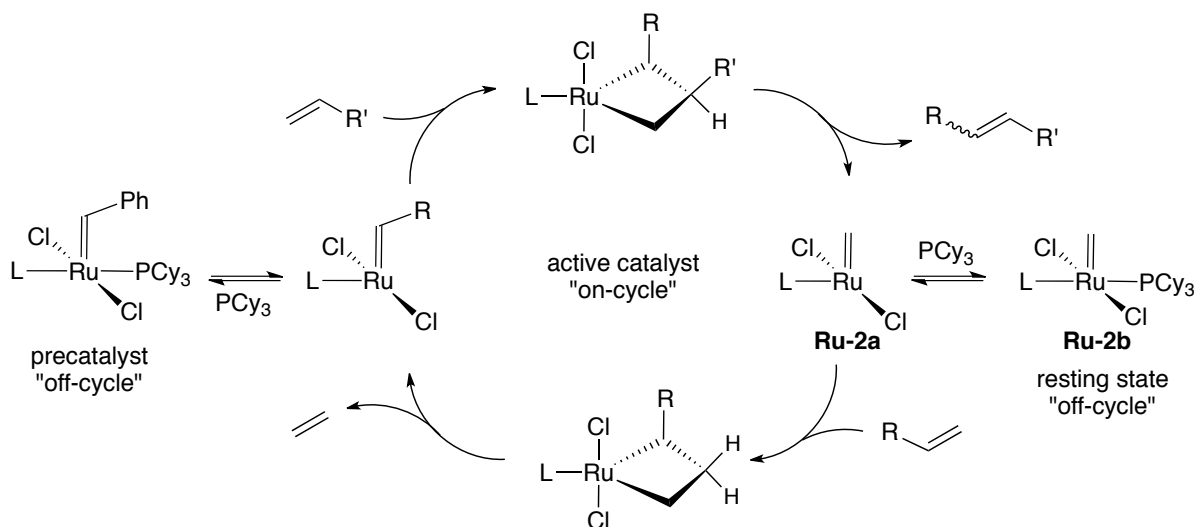
While the oxidation state of the group 6 catalysts is clear-cut, the oxidation state of Ru in the Grubbs catalysts remains controversial. X-ray absorption data^[125] are most consistent with an oxidation state of +2 for Ru. Following computational modeling of the Ru=CHPh bond, however, the Jensen group suggested that this moiety is more appropriately described as a Schrock carbene than a

Fischer carbene (albeit one that is more polarized toward the metal than in a classic Schrock carbene).^[126]

Chart 1.3. Grubbs catalysts bearing phosphine (first-generation) and NHC (second-generation) ancillary ligands.



Scheme 1.8. Catalytic cycle for the Grubbs catalysts.



The Ru species discussed above (**Ru-1**, **GI**, **GI'**, and **GI**) are able to participate in catalysis only following phosphine dissociation to form a four-coordinate Ru complex. The four-coordinate species then binds an olefin substrate and undergoes [2+2] cycloaddition. Competitive recoordination of the phosphine ligand generates a methylidene species **Ru-2b** as the thermodynamic resting state outside the catalytic cycle ("off-cycle").⁵⁸

The strong σ -donor character of NHC ligands has been well-established.⁵⁹⁻⁶¹ On this basis, Grubbs assigned the high activity of the second-generation catalysts to the lability of the PCy_3 ligand

trans to the NHC. In a subsequent kinetics study, the Grubbs group indicated that **GII** in fact initiates slowly relative to **GI**.⁵⁸ This “inverse trans-effect” was subsequently attributed to hindered benzylidene rotation (proposed as a trigger for PCy₃ loss) because torsional barriers for **GII** exceed those of **GI**.^{62,63} A recent study within our research group proposed that the strong σ -donor effect of the NHC ligand enforces π -donation to the PCy₃ ligand, and this plays a key role in inhibiting phosphine loss.⁶⁴ Catalyst longevity was shown to be explicitly related to PCy₃ non-lability. Importantly, however, the same four-coordinate intermediate mediates both metathesis and deactivation, so longer lifetime does not translate into higher productivity.

Many variations on the Grubbs catalyst design have been reported. Much attention has been devoted to alteration of the NHC ligand of the second-generation catalysts.^{15,65} Replacement of chloride ligands by bromide, iodide, or pseudohalide ligands (e.g. alkoxide) has also been explored, albeit to a lesser extent.⁶⁶ Both strategies sensibly focus on ancillary ligands that are retained throughout the catalyst cycle (Scheme 1.8), and are therefore capable of directly modulating catalysis.

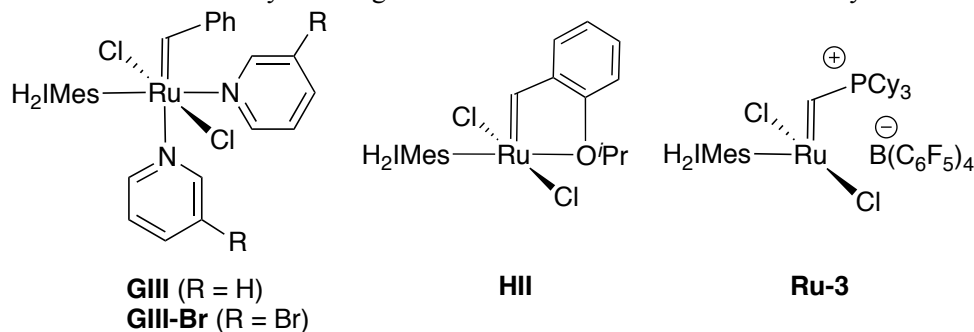
Interestingly, some highly successful Grubbs catalyst variants utilize a very different design strategy. The “placeholder” ligand and/or alkylidene ligand (PCy₃ and benzylidene for **GII**, respectively) cannot directly influence the active catalyst as both are lost within the first turnover cycle (in all cases forming **Ru-2a**, Scheme 1.8, above). Instead, these sites may be used to modulate initiation rates and the stability of off-cycle species. Catalyst “commitment” (that is, the proportion of time spent on-cycle vs. off)^{58,67} can likewise be modulated by these ligands, since recapture of the four-coordinate active catalyst reduces time spent in the active catalyst cycle. These alterations can have a dramatic impact on catalyst performance, despite making no structural change to the “on-cycle” species.

Replacing the phosphine ligand of **GII** with pyridine or 3-bromopyridine affords adducts **GIII** or **GIII-Br**; so-called “third-generation” Grubbs catalysts (Chart 1.4). The py adducts initiate at much higher rates than **GII** (up to 1.2×10^6 times faster).⁶⁸ The third-generation complexes are ideal for ROMP where rapid initiation vs. chain propagation is key in controlling polydispersity.⁶⁹ They have been less successful in CM and RCM applications, however. This is due in part to their instability in the presence of ethylene (a usual by-product of CM and RCM reactions).⁷⁰

Arguably the most successful Ru metathesis catalyst to date has been the second-generation Hoveyda catalyst: **III**.⁷¹ In this design, the benzylidene group and placeholder phosphine are replaced by a chelating styrenyl ether.^{72,73} The styrenyl ether ligand can react with **Ru-2a**, regenerating **III** as the off-cycle resting state species.⁷⁴ Unlike **GII**, a substrate-associative initiation pathway is accessible for **III** where olefinic substrates are sufficiently small.^{75,76} As a result, for

sterically unencumbered substrates, activity scales with substrate concentration, and **HII** outperforms **GII** at high substrate concentration.⁷⁷⁻⁸¹

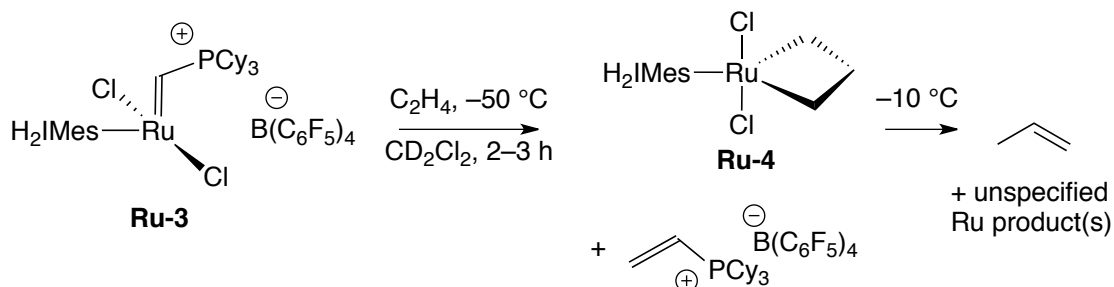
Chart 1.4. Grubbs catalyst analogues with modified labile L-donor or alkylidene sites.



Modification of “placeholder” and alkylidene sites has also facilitated mechanistic study of the Grubbs catalysts. The metallacyclobutane (MCB) intermediate of the Chauvin mechanism plays a crucial role in olefin metathesis (above). The first isolable MCB (a titanacyclobutane, **M-3**) was reported in 1980,⁴⁰ and several Mo and W examples developed in the following years.⁸²⁻⁸⁵ In contrast, the MCB corresponding to the Grubbs Ru catalysts was not observed until 2005.⁸⁶ In the archetypal Grubbs catalyst, the presence of a phosphine ligand renders a five-coordinate methylidene species (**Ru-2b**, Scheme 1.8, above) the most thermodynamically stable entity during catalysis. Reversion to a methylidene is thus favored over a build-up of MCB in solution, which renders the latter unobservable.⁵⁸

The four-coordinate Piers “pre-activated” catalyst **Ru-3** does not contain a placeholder ligand analogous to PCy_3 . Under C_2H_4 , **Ru-3** cleanly and quantitatively forms an unsubstituted metallacyclobutane **Ru-4** at $-50\text{ }^\circ\text{C}$ (Scheme 1.9). The MCB **Ru-4** was stable for several hours in solution, facilitating NMR identification, but decomposed on warming to $-10\text{ }^\circ\text{C}$ to form propene and unidentified Ru product(s).⁸⁷ Treatment of **Ru-3** with RCM substrate DDM likewise permitted observation and mechanistic study of substituted Ru-MCB complexes in situ.⁸⁸⁻⁹⁰

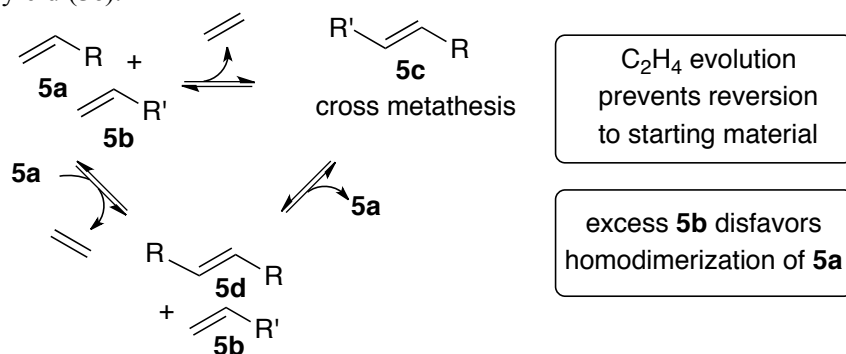
Scheme 1.9. Direct observation of a Ru-MCB species formed in situ from four-coordinate **Ru-3**.



1.2.4. Non-productive metathesis reactions

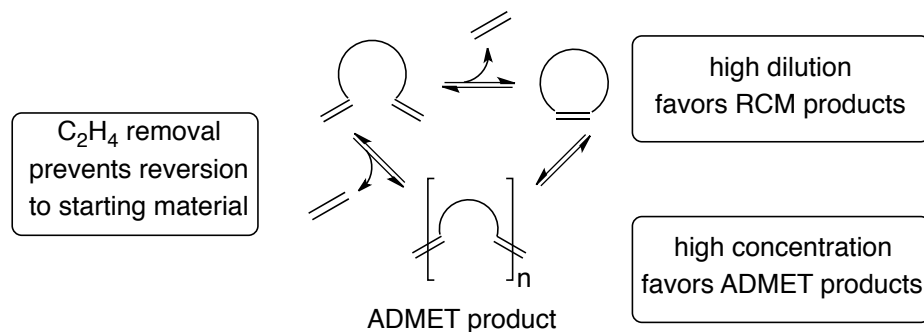
The equilibrium nature of the olefin metathesis reaction presents inherent challenges in implementation. Metathesis normally produces an equilibrium mixture of cross products, precursors, and self-metathesis products (i.e. “RHC=CHR” **5d**, Scheme 1.10). These issues represent a challenge to purification. To maximize substrate conversion, CM and RCM are often performed using terminal olefins to produce gaseous ethylene as a by-product. Evolution of ethylene from the reaction mixture prevents reversion to starting materials. Depending on the nature of the cross metathesis substrates, CM yield can be maximized by manipulating the reaction stoichiometry. Where homodimerization of one reactant is kinetically less favorable, it may be used in excess to promote CM over non-productive self-metathesis.⁹¹

Scheme 1.10. Non-productive homodimerization in cross metathesis^a and strategies for maximizing cross-product yield (**5c**).

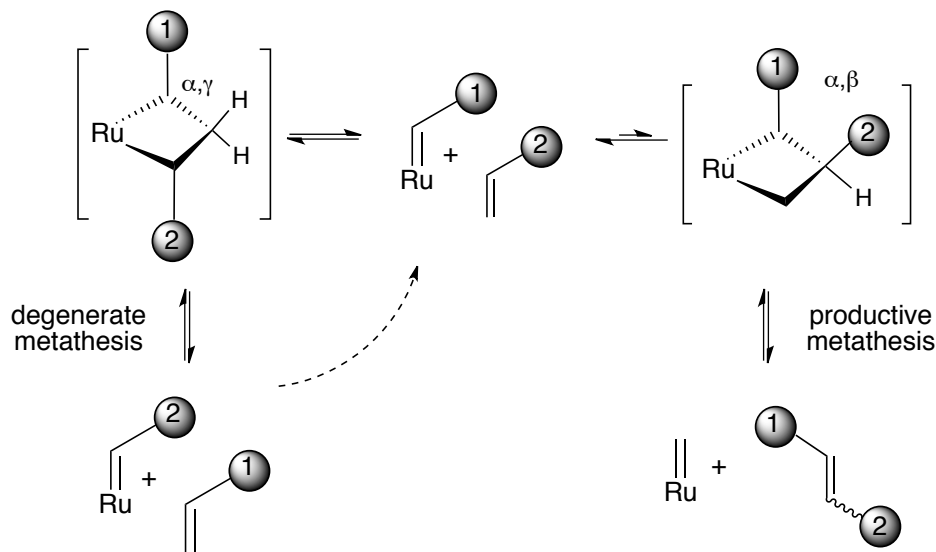


^a homodimerization of **5b** (not shown) is presumed to be the less favorable self-metathesis reaction. Olefin types exhibiting slow homodimerization with **GI**, **GII**, or **M-5b** as catalyst have been previously categorized.⁹¹

In the context of RCM, competitive ADMET leads to the formation of oligomer or polymer products. ADMET can indeed be the kinetically-dominant process,⁹² though RCM yields may still be optimized using the reaction conditions. Decreasing the reaction concentration via dilution shifts the ring/chain equilibrium in favor of monomeric cyclic olefins (Scheme 1.11).⁹³

Scheme 1.11. Ring/chain equilibrium in ring closing metathesis.

Not every instance of metallacyclobutane formation and cycloreversion results in a net change of product distribution. Even for a simple homodimerization CM reaction, α,β - and α,γ -substituted MCB structures may form. One outcome (α,β) corresponds to the formation of a desired homocoupling product, whereas the other (α,γ) is a degenerate process, ultimately re-forming starting materials (Scheme 1.12).

Scheme 1.12. Degenerate and productive cross metathesis in a homodimerization reaction.

The proportion of each process depends on the stability of the corresponding metallacyclobutane intermediate, as established in prior studies of Mo and W MCB complexes.^{94,95} Though not inherently detrimental to product distribution, degenerate metathesis causes the catalyst to spend non-productive time “on-cycle” where it is vulnerable to decomposition, and can therefore reduce yields.⁹⁶

1.3. Catalyst decomposition pathways

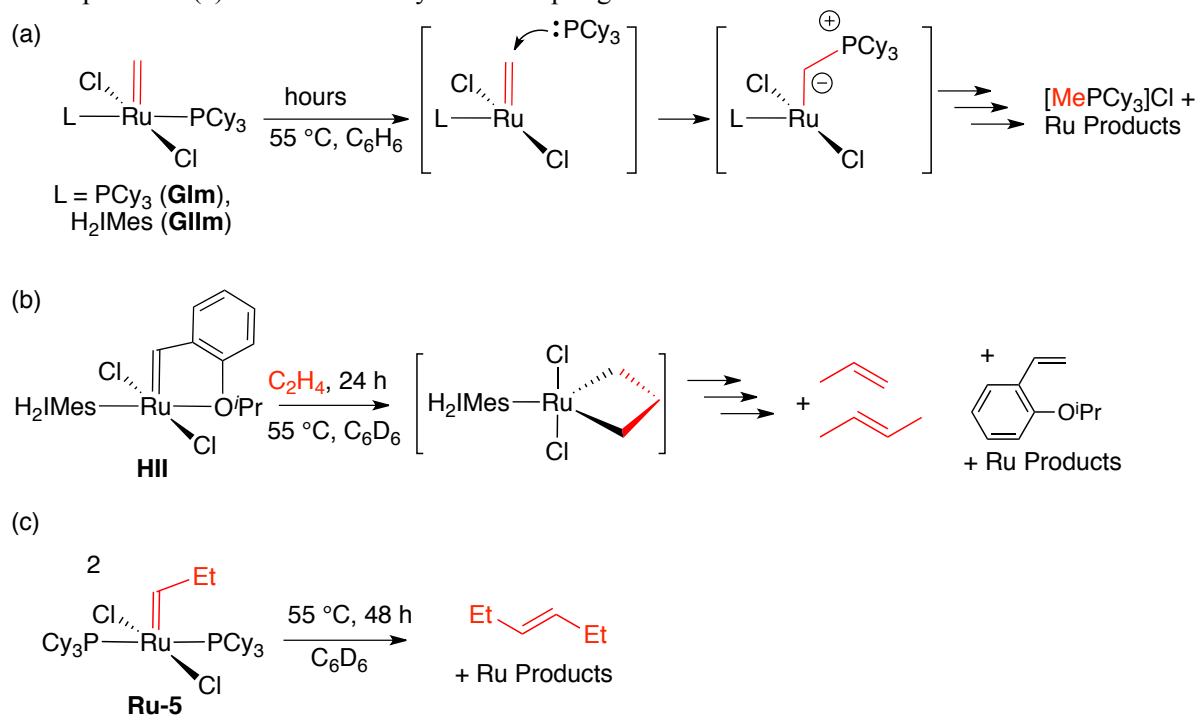
1.3.1. Inherent decomposition of Ru-alkylidenes and MCB complexes

Because a metal alkylidene or metallacyclobutane functional group is required for olefin metathesis, loss of these groups corresponds to a loss of catalyst activity. Understanding the nature of catalyst deactivation is crucial to advancing the current state-of-the-art for homogeneous catalysts.⁹⁷ Several leading studies provided insight into the decomposition chemistry of Ru metathesis catalysts at the outset of the studies described herein. In each case, identification of the fate of the Ru=CHR or MCB functional group has provided clues to the nature of the deactivation processes.

Grubbs and Hong reported that thermolysis of resting-state species **GIm**/**GIIm** ultimately leads to formation of [MePCy₃]Cl (Scheme 1.13a). Nucleophilic attack by PCy₃ was proposed as the mechanism of deactivation, leading to abstraction of the Ru=CH₂ functional group by phosphine.⁷⁰ Similarly, Piers reported formation of [MePCy₃]Cl on thermal decomposition of pre-activated species **Ru-3**.⁹⁸ Formation of a σ -alkyl [Ru]–CH₂–PCy₃ intermediate was suggested in each case. ¹³C-Labeling studies from our group confirmed that the methyl group of the phosphonium salt originates in the methylidene ligand,⁹⁹ and presented crystallographic evidence for the σ -alkyl species in the first-generation system.¹⁰⁰

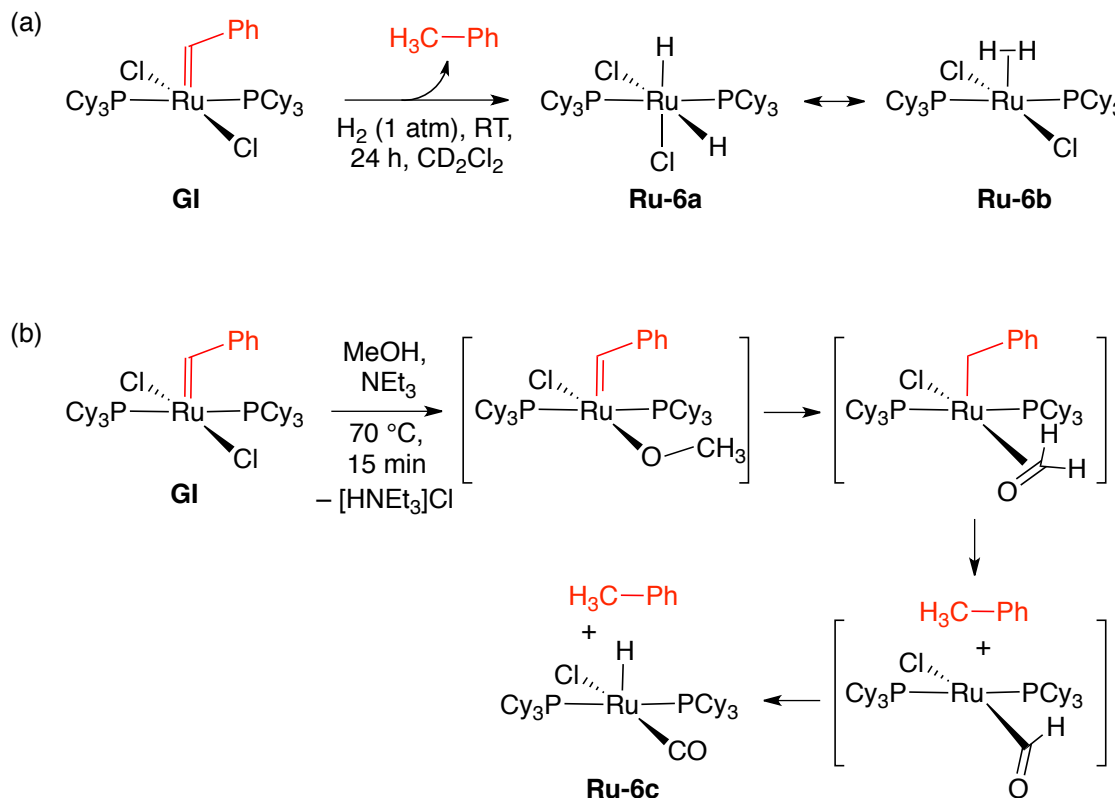
The above decomposition pathway relies on the presence of a phosphine nucleophile. Phosphine-free catalysts (most importantly **III**) have gone almost wholly unexamined. A computational study by van Rensberg et al. suggested that the unsubstituted metallacyclobutane of the second-generation Grubbs catalysts might decompose to propene via a β -H elimination pathway.¹⁰¹ In a rare experimental study, Bessalova et al. reported that propene and 2-butene are formed on thermolysis of **III** under C₂H₄ (Scheme 1.13b).¹⁰² (Butene would be expected to form from CM of propene under metathesis conditions.) Piers likewise found that pre-activated **Ru-3** decomposed to form propene on exposure to ethylene (Scheme 1.9, above).⁸⁷

Leading reports from Grubbs^{103,104} and Fogg^{105,106} have also noted the possibility of a bimolecular deactivation pathway. Thermolysis of Ru=CHR (e.g. **Ru-5**, below) complexes may result in form RHC=CHR and non-alkylidene Ru products (Scheme 1.13c). This process is thought to proceed via a four-coordinate alkylidene intermediate, though the mechanistic details have not been elucidated.

Scheme 1.13. Leading studies illustrating (a) methyldiene abstraction. (b) metallacyclobutane decomposition. (c) bimolecular alkylidene coupling.

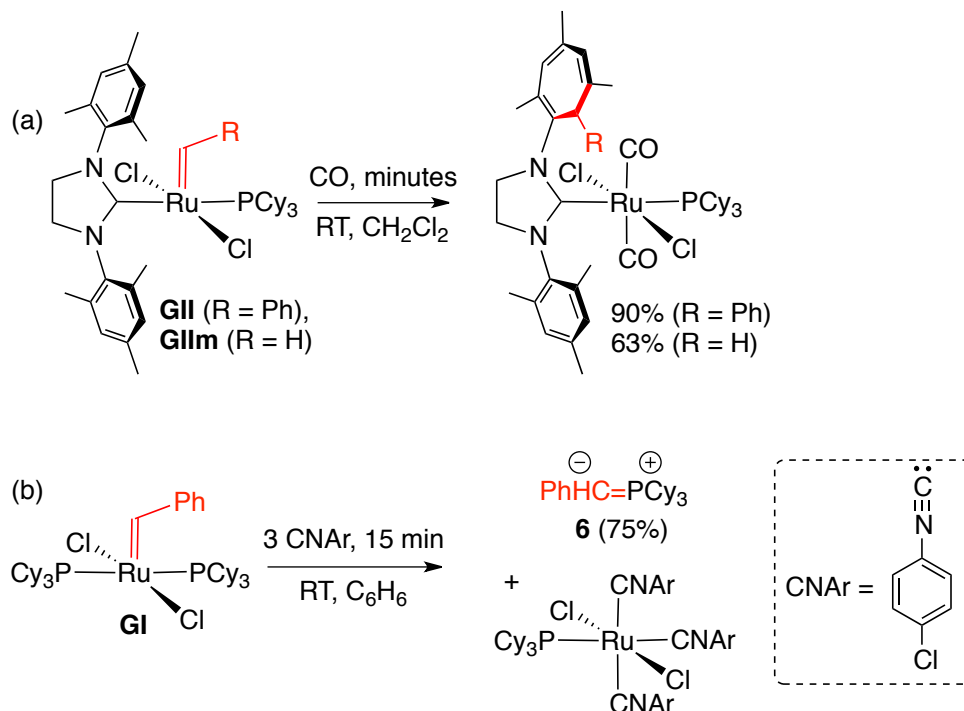
1.3.2. Decomposition induced by chemical additives

Decomposition of the Grubbs catalysts may also be induced by various chemical additives. Under hydrogen, Fogg et al. demonstrated that the benzylidene ligand of **GI** is lost as toluene, resulting in formation of a mixture of Ru-hydride tautomers **Ru-6a** and **Ru-6b** (Scheme 1.14a).¹⁰⁷ In subsequent reports, Mol et al. observed that treatment of **GI** with a primary alcohol and a Bronsted base similarly results in formation of a non-alkylidene hydride **Ru-6c** and loss of the benzylidene ligand predominantly as toluene (Scheme 1.14b), though they noted the presence of several unidentified organic and Ru-hydride products.¹⁰⁸ In the latter study, toluene was proposed to form by sequential hydride and proton migration to eventually produce the observed CO ligand of **Ru-6c**. Formation of a mixture of hydrides has been noted for **GII** under similar conditions.^{109,110}

Scheme 1.14. Decomposition of **GI** to Ru-hydrides using (a) hydrogen and (b) methanol and base (NEt₃) with proposed mechanism.

Strong π -acceptor ligands are likewise detrimental to Ru alkylidenes. Diver et al. noted that treatment of **GII** or **GIIIm** with CO or isocyanide triggers insertion of the alkylidene into the H₂IMes mesityl group via a Buchner ring expansion in minutes at RT (Scheme 1.15a).^{111,112} For **GI**, which lacks an analogous ligand aryl group, decomposition by isocyanide instead affords a phosphorus ylide **6** in 75% yield within 15 min (Scheme 1.15b). A related phosphonium salt was reported on decomposition of **GI** by CO (again, within minutes at RT), though yield was limited to 27%.¹¹³ The formation of phosphorus ylide or phosphonium salt products from **GI** was in line with the alkylidene abstraction mechanism shown above for **GIm/GIIIm** thermolysis (Scheme 1.13a). Though the same chemistry is not established for **GI** itself (presumably for steric reasons), it appears to be induced by the presence of π -acid ligands, which would be expected to render the benzylidene more electrophilic inductively. It is noteworthy that benzylidene abstraction by phosphine was also reported by Hoffman in the absence of π -acceptor ligands; though for a system with a highly-strained 4-membered metallacycle (RuCl₂(^tBu₂PCH₂P^tBu₂)(=CHPh)).¹¹⁴ Presumably, relief of ring strain acts as a driving force in this case.

Scheme 1.15. Decomposition of (a) **GII** and (b) **GI** induced by π -acceptor ligands.



Amines and related *N*-donors are also detrimental to Ru-catalyzed olefin metathesis.¹¹⁵ Protecting group strategies enable metathesis on amine-containing substrates;¹¹⁶ though the underlying sensitivity cannot be considered a “solved problem.” Adventitious amine poisons are an ongoing concern in the industrial implementation of olefin metathesis. For example, reduced reaction yields and undesired product isomerization have been linked to contamination of metathesis reactions by *N*-donors including morpholine and 1,8-diazabicycloundec-7-ene (DBU) in the recent industrial syntheses of Ciluprevir^{23,117} and Relacatib¹¹⁸ (Section 1.2.1, above). The resulting cost of additional materials, purification, or even protection / deprotection steps ultimately detracts from the economic viability of olefin metathesis in industrial settings.

Primary and secondary amines are particularly detrimental, though high metathesis yields can often be obtained in the presence of sterically bulky tertiary amines.¹¹⁹ Further, electron-withdrawing groups near nitrogen generally improve metathesis performance.¹²⁰ In line with these observations, poisoning via coordinative saturation is generally cited as a source of deactivation for reactions containing amine poisons.¹¹⁹⁻¹²¹

On coordination of an amine ligand to a metathesis catalyst, the key alkylidene functional group would be retained. Such poisoning by coordinative saturation is a plausible, but fundamentally

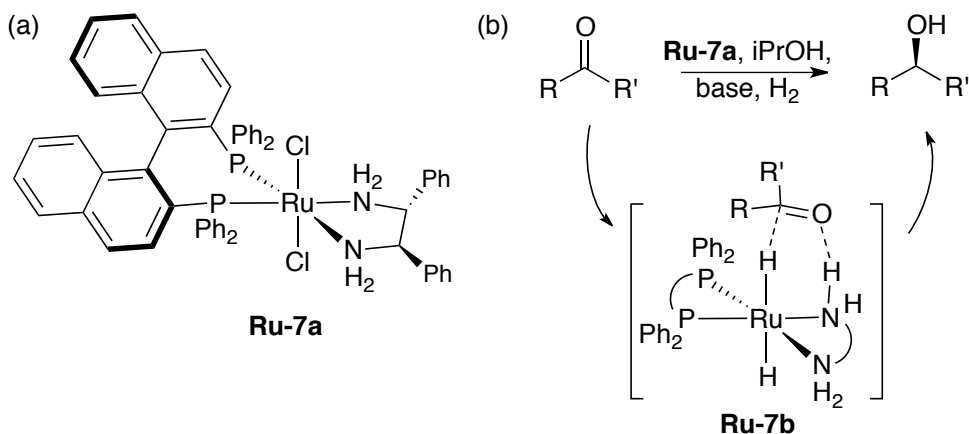
incomplete description of amine poisoning. At the outset of this work, the mechanistic basis for these pathways was unexamined.

1.4. Amines in catalyst design - opportunities

Amines are not widely successful in the design of Ru catalysts for olefin metathesis, and only a limited number of leading examples are known (see Chapter 5 for details). This is undoubtedly influenced by well-known compatibility issues in the specific context of Ru-catalyzed olefin metathesis. We speculated that a more complete understanding of the nature of amine-induced decomposition might enable development of highly active catalysts employing amine ligands as a design feature.

In the broader context of coordination chemistry and catalysis, amine ligands have indeed been extraordinarily useful. Coordination complexes of amines were the earliest known species containing metal-organic bonds. Alfred Werner correctly described the structures of metal-ammonia complexes of Co^{3+} , Cr^{3+} , and Pt^{3+} in the mid 1890s; the beginning three decades of research which laid the groundwork for modern coordination chemistry and culminated in a Nobel prize in 1913.¹²²

Scheme 1.16. (a) Structure of an archetypal Noyori binap/diamine catalyst (**Ru-7a**) and (b) outer-sphere asymmetric hydrogenation involving an “NH” ligand.



Given their prominence in coordination chemistry, it is no surprise that many useful organometallic catalysts employ nitrogen ligands in their structure. The Ru-binap/diamine complexes (**Ru-7a** and related structures) developed by Noyori in the 1980s–90s are a highly-successful example.¹²³ The Noyori catalysts are extraordinarily useful for asymmetric transfer hydrogenation reactions. This process is achieved via an outer-sphere hydrogenation mechanism, which is enabled by the “NH” ligand (**Ru-7b**, Scheme 1.16).

1.5. Scope of thesis

Activity, selectivity, and stability are all crucial aspects of rational catalyst design.¹²⁴ In the study of homogeneous catalysis, increased reactivity and selectivity are common short-term goals. The nature of catalyst deactivation in “failed” reactions is less widely studied.¹²⁴ In a recent review, Crabtree described catalyst deactivation as having “attracted less academic attention in homogenous catalysis than is justified by its importance.”⁹⁷ Indeed, in the search for better-performing catalysts, it seems intuitive that systematic examination of deactivation should be seen as a prerequisite for rational catalyst or process redesign. Such an approach is at the heart of this work.

There are two major portions to the research described in this thesis. The first focuses on the mechanism of catalyst deactivation, in the specific context of amine-poisoned olefin metathesis. The second is an exploration of the coordination chemistry of related amine and amido complexes. The goal of this research is to understand, and ideally improve upon the weaknesses of the most successful and widely-used olefin metathesis catalysts.

Chapter 3 describes the in situ coordination and decomposition chemistry of the Grubbs catalyst with amines and related nitrogen ligands. Chapter 4 extends the scope of the study to decomposition of catalytic intermediates, with a particular focus on the widely-used second-generation Hoveyda catalyst. Chapter 5 applies the concepts developed in Chapters 3 and 4 to a working catalyst and also describes the synthesis, isolation, characterization, and decomposition chemistry of a family of related amine and amido compounds. New insights and suggestions for future work are collected in Chapter 6.

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Chapter 2. Experimental Details

2.1. General procedures

2.1.1. Reaction conditions

Reactions were carried out using standard double-manifold Schlenk or glovebox (MBraun Labmaster 130) techniques¹ at room temperature (RT; 20–23 °C) under N₂ unless otherwise indicated. Reactions above RT were carried out using a thermostatted silicone oil bath with independent thermometer confirmation. Those below RT were carried out using an ice or acetone-dry ice bath (0 °C or –78 °C, respectively).

2.1.2. Reagents and solvents

Caution: n-butyllithium is pyrophoric and air-sensitive, and was handled only under inert atmosphere.

The following materials were prepared according to literature procedures: RuCl₂(PPh₃)₃,² RuCl₂(PCy₃)₂(=CHPh) **GI**,³ RuCl₂(H₂IMes)(PCy₃)(=CHPh) **GII**,⁴ RuCl₂(IMes)(PCy₃)(=CHPh) **GII'**,⁵ RuCl₂(H₂IMes)(py)₂(=CHPh) **GIII**,⁶ RuCl₂(CH(C₆H₄-O^{*i*}Pr))(H₂IMes) (**IIII**),⁴ RuCl₂(IMes)(2,2-biphenyldiamine)(=CHPh) (**Ru-42'**),⁷ RuHCl(PPh₃)₃ (**Ru-51**),⁸ RuHCl(CO)(PPh₃)₃,⁹ RuHCl(CO)₂(PPh₃)₂,¹⁰ biphenyldiamine **N11**,¹¹ *o*-isopropoxybenzaldehyde,¹² *o*-isopropoxystyrene **12**,¹² hex-5-enylundec-10-enoate **18**,¹³ LiNPh₂,¹⁴ and KOPh.¹⁵ Lithium amide salts LiNHPh, Li(en), and Li(NC₄H₉) were prepared analogously to LiNPh₂ by substituting aniline, ethylenediamine, or pyrrole for HNPh₂.

Amines previously stored under air (triethylamine **N10**, pyridine **N8**, *sec*-butylamine **N4**, *t*-butylamine **N5**, and 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU **N9**)) were distilled over CaH₂ and freeze-pump-thaw degassed prior to use. Other liquid amines (*n*-butylamine **N1**, pyrrolidine **N7**, morpholine **N6**, benzylamine **N3**, ethylenediamine **N2**, aniline **N13**; 98 to >99.5%) were shipped under N₂ or degassed by a minimum of three consecutive freeze-pump-thaw cycles and stored under N₂ on receipt. Their purity was confirmed by ¹H NMR analysis prior to use. Ethylene (Linde grade 3.0) and CO (BOC grade 2.8) were used as received. Styrene and diethyl diallylmalonate were degassed as described above and stored over 4 Å molecular sieves under N₂ prior to use. Other reagents (PCy₃, 1,3,5-trimethoxybenzene, decane, phenol, diphenylamine, *o*-phenylaniline) were obtained from commercial sources (Strem, Sigma-Aldrich, Acros Organics, Alfa Aesar) were used as received.

Dry, oxygen-free C₆H₆, C₇H₈, CH₂Cl₂, Et₂O, THF, and hexanes were obtained using a Glass Contour or Anhydrous Engineering solvent purification system. Methanol, acetone, and pentane were purified by distillation from appropriate drying agents¹⁶ and stored over activated 4 Å molecular

sieves in amber bottles in a glovebox prior to use. CDCl_3 (Cambridge Isotopes) dried by distillation over CaH_2 and stored in a glovebox prior to use. D_2O was freeze-pump-thaw degassed prior to use. All other NMR solvents (C_6D_6 , C_7D_8 , THF-d_8 , and CD_2Cl_2 ; Cambridge Isotopes) were stored under N_2 over 4 Å molecular sieves for at least 24 h before use.

2.1.3. Instrumentation

NMR Spectroscopy. Samples were referenced to the residual proton or carbon signals of the deuterated solvent (^1H , ^{13}C), or to external 85% H_3PO_4 (^{31}P). Signals are reported relative to TMS (^1H and ^{13}C) or 85% H_3PO_4 (^{31}P) at 0 ppm. All nuclear magnetic resonance (NMR) spectra of organometallic compounds were collected under anaerobic conditions using Teflon-sealed NMR tubes (J. Young or screw-cap NMR tubes). Data was collected using a Bruker Avance 300, Avance 400, or Avance 500 NMR spectrometer at RT (20–23 °C) unless otherwise indicated. For variable-temperature NMR experiments, reported temperatures are those of the internal thermocouple of the spectrometer probe.

Infrared Spectroscopy. Infrared (IR) spectra were collected by attenuated total reflectance (ATR) using a Varian 640 Infrared Spectrometer or Nicolet Nexus 550-FTIR.

GC-FID analysis. Metathesis conversions and yields were measured on a GC (Agilent 7890A) equipped with a flame ionization detector (FID) and polysiloxane column (Agilent HP-5) at an inlet split ratio of 10:1 and inlet temperature of 250 °C. Retention times were confirmed by comparison to pure samples. Reactant conversion and product yield were quantified from integrated peak areas vs. decane internal standard, corrected for response factors of decane and analyte. Calibration curves (peak areas vs. concentration) were constructed in the relevant concentration regime to account for the dependence on detector response for all analytes.

GC-MS Analysis. Gas chromatography (GC) coupled to electron ionization mass spectrometry (EI-MS) was performed using an Agilent Technologies 5975B inert XL EI/CL MSD equipped with a CTC analytics auto-sampler and a polysiloxane column. Samples were diluted to ca. 1 mg/mL using CH_2Cl_2 under N_2 and kept sealed in 1.5 mL sample vials equipped with rubber septa prior to analysis. No calibration for ionization efficiency was applied. Analytes were identified by comparison of mass spectra to literature sources (as cited), and/or by comparison to authentic samples.

X-Ray Crystallography. Single-crystal X-ray diffraction (XRD) data for $\text{RuH}[(\eta^5\text{-C}_6\text{H}_5)\text{NPh}](\text{PPh}_3)_2$ was carried out by Dr. Robert McDonald of the University of Alberta Crystallography Laboratory (Edmonton, AB). Data were collected using a Bruker Platform diffractometer equipped with an Apex II CCD area detector at 173 K using Mo $\text{K}\alpha$ radiation. The

structure was resolved by Patterson location of heavy atoms followed by structure expansion and full-matrix least-squares refinement on F^2 .

Elemental Analysis. Elemental analyses for new compounds were obtained externally by Guelph Chemical Laboratories (Guelph, ON) up to late 2013. Subsequent analyses were carried out by MHW Laboratories (Phoenix, AZ).

2.1.4. Supplementary data

NMR spectra for isolated, new compounds appear in Appendix 1. NMR spectra and GC-MS data for crude reaction mixtures appear in Appendix 2. XRD data for $\text{RuH}[(\eta^5\text{-C}_6\text{H}_5)\text{NPh}](\text{PPh}_3)_2$ were deposited as CCDC 940549 with the Cambridge Crystallographic Data Centre (www.ccdc.cam.ac.uk/data_request/cif).

2.2. Experimental data for Chapter 3

2.2.1. Stoichiometric reactions of **GI**, **GII**, and **GII'** with *N*-donors

Procedure for single timepoint reactions: In the glovebox, a J. Young NMR tube was charged with **GII** (10 mg, 0.012 mmol), TMB (ca. 1.0 mg), and 0.60 mL C_6D_6 , to give a solution 20 mM in Ru. The sample was removed from the glovebox and a ^1H NMR spectrum measured to establish the **GII**: TMB ratio at t_0 . The NMR tube was returned to the glovebox and DBU **N9** (19.0 μL , 0.127 mmol, 10 equiv) was added. The sample was shaken vigorously and ^1H and $^{31}\text{P}\{^1\text{H}\}$ NMR spectra were collected after 1 h. The sample was then placed in a 60 °C oil bath (thermocouple-equipped; ± 1.5 °C). After 24 h, ^1H and ^{31}P NMR spectra were again collected. For RT experiments, samples were stored at ambient temperature (20–23 °C) for 24 h. Equilibrium positions were inferred from relative integration of alkylidene (δ_{H} 19.9–19.5, $\text{Ru}=\text{CHPh}$) signals against **GII** (δ_{H} 19.65), and corroborated by $^{31}\text{P}\{^1\text{H}\}$ NMR integration of free PCy_3 (δ_{P} 10.4) against **GII** (δ_{P} 30.1). Decomposition was quantified against TMB internal standard and normalized to t_0 .

Procedure for kinetic studies: A sample of **GII** and TMB was prepared as above, in 0.51 mL C_6D_6 . In a screw-cap Rotoflo NMR tube, the initial ratio of **GII** : TMB was measured by integrating the ^1H NMR signals for the $[\text{Ru}]=\text{CH}$ and TMB $\text{sp}^2\text{-CH}$ protons. A solution of 12 μL NH_2^tBu **N1** (8.9 mg, 0.12 mmol, 10 equiv) in 80 μL C_6D_6 was injected using a gas-tight syringe. The pierced septum was immediately protected with Parafilm, a stopwatch was started, and the mixture was shaken vigorously for 30 s. The sample was returned to the NMR spectrometer (internal temperature 20–23 °C) and collection of the first ^1H NMR spectrum began within 4 min of amine injection. Loss of the alkylidene signals was monitored at 20 min intervals over 12 h. Timepoints given are midpoints of ^1H

NMR data collection (ca. 2 min). For reactions that did not reach >95% decomposition within 12 h, a “final” timepoint was taken at 20–24 h.

2.2.2. Syntheses of new compounds

$RuCl_2(H_2IMes)(NH_2^{sec}Bu)(=CHPh)$ **Ru-19**. $NH_2^{sec}Bu$ **N4** (20 μ L, 14 mg, 0.20 mmol) was added to a dark green solution of **GIII** (74 mg, 0.10 mmol) in 5 mL CH_2Cl_2 . A colour change to pale green was observed over 30 min, at which point volatiles were removed in vacuo. The residue was dissolved again in 5 mL CH_2Cl_2 and treated again with $NH_2^{sec}Bu$ **N4** (20 μ L, 14 mg, 0.20 μ mol), stirred 30 min and again dried in vacuo. This process was repeated until 1H NMR analysis of the crude reaction mixture indicated full conversion to the product (δ_H 19.58 in C_6D_6 , $Ru=CHPh$). A total of five iterations (100 μ L, 72, 1.0 mmol $NH_2^{sec}Bu$) were required. A pale green solid was isolated following reprecipitation from hexanes (2 mL, $-30^\circ C$). Yield after drying: 50 mg (77%). 1H NMR (C_6D_6 , 500.1 MHz): δ 19.58 (s, 1H, $Ru=CHPh$), 8.30 (d, $^3J_{HH} = 8$ Hz, 2H, *o*-CH of Ph), 7.35 (t, $^3J_{HH} = 7$ Hz, 1H, *p*-CH of Ph), 7.11 (t, $^3J_{HH} = 8$ Hz, 2H, *m*-CH of Ph), 6.98 (s, 2H, *m*-CH of Mes), 6.54 (s, 1H, *m*-CH of Mes), 6.50 (s, 1H, *m*-CH of Mes), 3.49–3.37 (m, 2H, CH_2 H_2IMes), 3.33–3.22 (m, 2H, CH_2 of H_2IMes), 3.05–2.86 (m, 1H, α -CH of ^{sec}Bu), 2.85 (s, 3H, *o*-CH₃ of Mes), 2.81 (s, 3H, *o*-CH₃ of Mes), 2.36 (s, 3H, *o*-CH₃ of Mes), 2.28 (s, 3H, *o*-CH₃ of Mes), 2.21 (s, 3H, *p*-CH₃ of Mes), 2.13 (dd, $^2J_{HH} = 10$ Hz, $^3J_{HH} = 8$ Hz, 1H, NH), 2.04 (s, 3H, *p*-CH₃ of Mes), 1.92 (apparent t, $J_{HH} = 10$ Hz, 1H, NH), 0.85–0.59 (m, 2H, β -CH₂ of ^{sec}Bu), 0.47 (d, $^3J_{HH} = 7$ Hz, 3H, β -CH₃ of ^{sec}Bu), 0.41 (t, $^3J_{HH} = 8$ Hz, 3H, γ -CH₃ of ^{sec}Bu). $^{13}C\{^1H\}$ NMR (C_6D_6 , 75.53 MHz): δ 309.5 ($Ru=CHPh$), 220.1 (C_{NHC} of H_2IMes), 152.2 (C_i of Ph), 140.3 (Mes), 138.6 (Mes), 137.91 (Mes), 137.86 (Mes), 137.3 (Mes), 135.4 (Mes), 129.8 (br, *m*-CH of Mes + *p*-Ph), 129.73 (*m*-CH of Mes), 129.69 (*m*-CH of Mes), 129.65 (*m*-CH of Mes), 129.57 (*o*-CH of Ph), 129.0 (*m*-CH of Ph), 51.4 (CH_2 of H_2IMes), 50.5 (CH_2 of H_2IMes), 49.2 (α -CH of ^{sec}Bu), 31.4 (β -CH₂ of ^{sec}Bu), 21.2 (*o*-CH₃ of Mes), 21.0 (*o*-CH₃ of Mes), 20.8 (br, *o*-CH₃ of Mes $\times$ 2), 20.7 (β -CH₃ of ^{sec}Bu), 18.6 (*p*-CH₃ of Mes), 18.5 (*p*-CH₃ of Mes), 10.1 (γ -CH₃ of ^{sec}Bu). IR (ATR, cm^{-1}): $\nu(N-H)$ 3282, 3209 cm^{-1} . Satisfactory elemental analysis could not be obtained, as indicated by these representative values. Anal. Calc'd. for $C_{32}H_{43}N_3Cl_2Ru$: C, 59.90; H, 6.75; N, 6.55. Found: C, 57.65; H, 6.58; N, 6.63. Despite the absence of impurities by NMR analysis (see Appendix 1), combustion analysis was consistently low in carbon even when V_2O_5 was added to promote complete combustion. While spectroscopic analysis supports the assignment, paramagnetic, fluxional, or otherwise NMR-invisible impurities may be present.

$RuCl_2(H_2IMes)(NH_2^tBu)(=CHPh)$ **Ru-20**. NH_2^tBu **N5** (1 mL, 0.7 g, 9 mmol) was used to dissolve **GIII** (80 mg, 0.11 mmol). After 1 h, the pale green solution was dried in vacuo to afford a green residue. The residue was dissolved again in 1 mL NH_2^tBu **N5**, and again dried in vacuo two

times. A pale green solid was isolated and washed three times with cold hexanes (3 mL). Yield after drying: 52 mg (73%). ^1H NMR (C_6D_6 , 500.1 MHz): δ 19.63 (s, 1H, Ru=CHPh), 8.38 (d, $^3J_{\text{HH}} = 8$ Hz, 2H, *o*-Ph), 7.35 (t, $^3J_{\text{HH}} = 7$ Hz, 1H, *p*-Ph), 7.12 (t, $^3J_{\text{HH}} = 8$ Hz, 2H, *m*-Ph, overlaps w $\text{C}_6\text{D}_5\text{H}$), 6.96 (s, 2H, *m*-CH of Mes), 6.50 (s, 1H, *m*-CH of Mes), 3.42 (t, $^3J_{\text{HH}} = 9$ Hz, 2H, CH_2 of H_2IMes), 3.26 (t, $^3J_{\text{HH}} = 9$ Hz, 2H, CH_2 of H_2IMes), 2.84 (s, 6H, *o*- CH_3 of Mes), 2.32 (s, 6H, *o*- CH_3 of Mes), 2.28 (s, 2H, NH), 2.21 (s, 3H, *p*- CH_3 of Mes), 2.03 (s, 3H, *p*- CH_3 of Mes), 0.83 (s, 9H, β - CH_3 of ^tBu). $^{13}\text{C}\{^1\text{H}\}$ NMR (C_6D_6 , 75.53 MHz): δ 310.8 (Ru=CHPh), 219.8 (C_{NHC} of H_2IMes), 152.2 (C_i of Ph), 140.2 (*o*-C of Mes), 138.7 (*p*-C of Mes), 137.9 (br, *o*-C + *p*-C of Mes), 137.2 (C_i of Mes), 135.4 (C_i of Mes), 129.9 (*m*-CH of Mes), 129.8 (*o*-Ph), 129.7 (*p*-Ph), 129.6 (*m*-CH of Mes), 129.0 (*m*-Ph), 52.1 (α -C of ^tBu), 51.3 (CH_2 of H_2IMes), 50.5 (NHC CH_2 of H_2IMes), 31.0 (β - CH_3 of ^tBu), 21.1 (*p*- CH_3 of Mes), 21.0 (*p*- CH_3 of Mes), 20.8 (*o*- CH_3 of Mes), 18.6 (*o*- CH_3 of Mes). IR (ATR, cm^{-1}): $\nu(\text{N-H})$ 3367, 3299. Satisfactory elemental analysis was not obtained for this molecule, as noted above for **Ru-19**. Representative values: Anal. Calc'd. for $\text{C}_{32}\text{H}_{43}\text{N}_3\text{Cl}_2\text{Ru}$: C, 59.90; H, 6.75; N, 6.55. Found: C, 54.18; H, 6.10; N, 6.24.

Attempted synthesis of Ru-19 from GII: $\text{NH}_2^{\text{sec}}\text{Bu}$ **N4** (140 μL , 101 mg, 1.39 mmol) was added to a stirred pink suspension of **GII** (110 mg, 0.133 mmol) in 6 mL hexanes. The mixture was stirred for 24 h and a pink solid was isolated by filtration. The isolated material contained only **GII** by ^1H and ^{31}P NMR analysis. An aliquot of the reaction supernatant was dried in vacuo and ^1H NMR analysis indicated the presence of **GII** and the desired adduct in a 6 : 1 ratio. Reversion to **GII** may have been induced on exposure to vacuum. Unsuccessful synthesis of the desired adduct from **GII** is attributed to relatively high solubility of **Ru-19** in hexanes, which inhibits selective precipitation of the adduct (as in **Ru-28** and **Ru-29**, below).

Attempted synthesis of Ru-20 from GII: This reaction was attempted as described above for **Ru-19** from **GII** using $^t\text{BuNH}_2$ **N5** in place of **N4**. Solely **GII** was observed in the isolable solid after 24 h, and on drying the reaction supernatant in vacuo.

2.2.3. Characterization data for benzylidene abstraction products

PhCH₂NHⁿBu 7a: Key ^1H NMR (C_6D_6 , 500.1 MHz): δ 3.62 (s, 2H, PhCH_2N). $^{13}\text{C}\{^1\text{H}\}$ NMR (C_6D_6 , 125.8 MHz): δ 54.4 (PhCH_2N), 49.5 (α - CH_2 of ^nBu), 32.8 (β - CH_2 of ^nBu), 20.8 (γ - CH_2 of ^nBu), 14.3 (CH_3). Ph (^1H and ^{13}C) and ^nBu (^1H) NMR signals are obscured in solution by styrene and excess $\text{NH}_2^{\text{sec}}\text{Bu}$, respectively. EI-MS, $[\text{M}^+]$: m/z calc'd for $\text{C}_{11}\text{H}_{17}\text{N}$, 163.1; found, 163.1. ^1H NMR and GC-MS data for *N*-butylbenzylamine ($\text{PhCH}_2\text{NH}^n\text{Bu}$) were identical to those of an authentic sample (Acros Organics).

PhCH=NⁿBu **7b**: Key ¹H NMR (C₆D₆, 300.3 MHz): δ 8.04 (HC=N). (CDCl₃, 300.3 MHz): δ 8.27 (HC=N); ¹³C{¹H} NMR (CDCl₃, 75.5 MHz): δ 161.2. EI-MS, [M⁺]: *m/z* calc'd for C₁₁H₁₅N, 161.1; found, 161.1. NMR data (CDCl₃) and EI-MS data were in good agreement with literature values.¹⁷

NH(CH₂Ph)₂ **9**: ¹H NMR data could not be resolved from excess benzylamine reactant (C₆D₆). EI-MS, [M⁺]: *m/z* calc'd for C₁₄H₁₅N, 197.1; found, 197.1 GC-MS data for *N,N'*-dibenzylamine (NH(CH₂Ph)₂) **9** were identical to those of an authentic sample (Sigma Aldrich).

2.3. Experimental data for Chapter 4

2.3.1. Experimental details for Chapter 4, Sections 4.1-4.3

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*Stoichiometric reactions of **III** with nitrogen bases.* To a solution of **III** (15 mg, 0.024 mmol) in 1.00 mL C₆D₆ was added TMB (ca. 1 mg) as an internal integration standard. This solution was divided into two portions (0.012 mmol **III**), half being treated with amine or pyridine, and the other half being used as a control reaction. In a screw-cap Rotoflo NMR tube, the initial ratio of **III** : TMB was measured by integrating the ¹H NMR signals for the [Ru]=CH and TMB sp²-CH protons. A solution of 12 μL NH₂ⁿBu **N1** (8.9 mg, 0.12 mmol, 10 equiv) in 80 μL C₆D₆ was injected using a gas-tight syringe. The pierced septum was immediately protected with Parafilm, a stopwatch was started, and the mixture was shaken vigorously for 30 s. The first ¹H NMR spectrum was collected within 4 min. Loss of the alkylidene signals was monitored at 20 min intervals over 12 h.[†]

For the corresponding reaction of benzylamine **N3**, the first spectrum was measured at 15 min and 24 h (ca. 50% loss in total alkylidene at 24 h). Spectra were measured at 24 h intervals for a further 72 h. For all other amines (morpholine **N6**, pyrrolidine **N7**, pyridine **N8**, DBU **N9**, NEt₃ **N10**, *sec*-butylamine **N4**), spectra were measured at 1 h and again at 24 h. For pyridine and *sec*-butylamine, spectra were recorded at –20 °C (C₇D₈) to reduce the breadth of the alkylidene signal. Reactions of morpholine, pyrrolidine, pyridine, DBU, NEt₃, and *sec*-butylamine showed no change after 24 h at RT, or after heating to 60 °C for an additional 24 h.

* Compound numbers have been modified for consistency throughout the thesis. For a Table of Compound Numbers and Structures, see p. VII.

[†] Note added subsequent to publication: A heterogeneous mixture formed from the reaction with NH₂ⁿBu **N1** on deposition of [RuCl(H₂IMes)(NH₂ⁿBu)₄]Cl **Ru-17a** as a yellow solid. The reaction mixture was fully solubilized with CDCl₃ (ca 1:1 w C₆D₆) to confirm quantitation of ArCH₂NHⁿBu **10**. No change to the analyte: internal standard ratio was observed. The reaction mixture was then spiked with an authentic sample of **10** to verify the chemical shifts of the analyte in the mixed-solvent system. All other reactions produced a homogenous orange or red solution upon decomposition of **III**.

*Confirmation of **III**–(**III-7**) equilibrium.* A sample was prepared as above, with collection of an ^1H NMR spectrum after 1 h. The sample was then dried under vacuum (ca. 50 mTorr) for 20 min, and re-dissolved for analysis. ^1H NMR (C_6D_6 , 500.1 MHz): δ 20.25 (Ru=CHAr for **III-7**, 53%), 16.72 (Ru=CHAr for **III**, 47%).

*Synthesis of $[\text{RuCl}(\text{H}_2\text{IMes})(\text{NH}_2^t\text{Bu})_4]\text{Cl}$, **Ru-17a**.* To a pink solution of **GII** (175 mg, 0.206 mmol) in 13 mL C_6H_6 was added NH_2^tBu **N1** (0.200 mL, 2.02 mmol, 10 equiv). The solution turned green immediately, and yellow over 24 h. A pale yellow precipitate deposited over this time. The solvent was stripped off, and the residue was washed with hexanes (3×5 mL). Yield after drying under vacuum: 128 mg (81%). The corresponding reaction of **III** likewise afforded $[\text{RuCl}(\text{H}_2\text{IMes})(\text{NH}_2^t\text{Bu})_4]\text{Cl}$, **Ru-17a** in 69% isolated yield. ^1H NMR (CD_2Cl_2 + 1% NH_2^tBu , 500.1 MHz): δ 7.00 (s, 4H, *m*-CH of Mes), 3.96 (s, 4H, CH_2 of H_2IMes), 2.69–2.59 (m, 8H, NH_2), 2.56 (s, 12H, *o*- CH_3 of Mes), 2.29 (s, 6H, *p*- CH_3 of Mes), 1.99–1.88 (m, 8H, α - CH_2 of ^tBu), 1.33 (t of t, $^3J_{\text{HH}} = 7$ Hz, 8H, β - CH_2 of ^tBu), 1.14 (q of t, $^3J_{\text{HH}} = 7$ Hz, 8H, γ - CH_2 of ^tBu), 0.86 (t, $^3J_{\text{HH}} = 7$ Hz, 12H, CH_3 of ^tBu). $^{13}\text{C}\{^1\text{H}\}$ NMR (CD_2Cl_2 + 1% NH_2^tBu **N1**, 125.8 MHz): δ 224.6 (C_{NHC} of H_2IMes), 139.9, 138.5, 137.7, 130.7 (*m*-CH of Mes), 53.6 (CH_2 of H_2IMes), 45.2 (α - CH_2 of ^tBu), 35.8 (β - CH_2 of ^tBu), 20.9 (*p*- CH_3 of Mes), 20.4 (γ - CH_2 of ^tBu , detected from HMQC correlation with γ - CH_2 of ^tBu), 20.3 (*o*- CH_3 of Mes), 14.0 (CH_3 of ^tBu). IR (ATR, cm^{-1}): $\nu(\text{N-H})$ 3361–3134. Anal. Calc'd. for $\text{C}_{37}\text{H}_{70}\text{N}_6\text{Cl}_2\text{Ru}$: C, 57.64; H, 9.15; N, 10.90. Found: C, 57.52; H, 9.00; N, 10.79. *Note:* The NH , β - CH_2 , and CH_3 signals are obscured by added NH_2^tBu **N1**. The integration values and multiplicities for these signals were confirmed from the spectrum for the dominant species $[\text{RuCl}(\text{H}_2\text{IMes})(\text{NH}_2^t\text{Bu})_4]\text{Cl}$ **Ru-17a** in CD_2Cl_2 . The chemical shifts for β - CH_2 , and CH_3 signals were confirmed by COSY correlation with γ - CH_2 .

Preparation of $\text{NH}(\text{R})(\text{CH}_2\text{Ar})$; $\text{Ar} = o\text{-C}_6\text{H}_4\text{-O}^i\text{Pr}$: Isopropoxy-substituted benzylamines were prepared by modification of a reported reductive amination procedure.¹⁸ These reactions were carried out in air with non-dried solvents.

$\text{R} = n\text{-Bu}$, **10**. NH_2^tBu (1.1 mL, 0.80 g, 11 mmol) and excess Na_2SO_4 (ca. 4 g) were added to a stirred, colorless solution of *o*-isopropoxybenzaldehyde (1.2 g, 7.1 mmol) in 30 mL THF. After 2 h, the mixture was filtered to remove excess Na_2SO_4 . The filtrate was treated with sodium borohydride (1.1 g, 29 mmol) and 15 mL CH_3OH , and stirring was continued for 2 h. The reaction was then quenched with 20 mL saturated aq. NH_4Cl , extracted with CH_2Cl_2 , washed with brine, dried with Na_2SO_4 , and stripped of solvent. Chromatography on silica gel (3% MeOH + 0.5% NH_4OH in CH_2Cl_2) afforded **1** as a colorless liquid. Yield 1.37 g (88%). *Note:* for compound numbering, see SI. ^1H NMR (C_6D_6 , 300.3 MHz): δ 7.45 (dd, $^3J_{\text{HH}} = 7$ Hz, $^4J_{\text{HH}} = 1$ Hz, 1H, C_3H of Ar), 7.11 (ddd, $^3J_{\text{HH}} =$

8 Hz, $^4J_{\text{HH}} = 1$ Hz, 1H, C_5H of Ar), 6.90 (ddd, $^3J_{\text{HH}} = 7$ Hz, $^4J_{\text{HH}} = 1$ Hz, 1H, C_4H of Ar), 6.65 (d, $^3J_{\text{HH}} = 8$ Hz, 1H, C_6H of Ar), 4.20 (septet, $^3J_{\text{HH}} = 6$ Hz, 1H, CH of ^iPr), 3.93 (s, 2H, ArCH_2N), 2.59 (t, $^3J_{\text{HH}} = 7$ Hz, $\alpha\text{-CH}_2$ of ^nBu), 2.46 (br s, 1H, NH), 1.57–1.39 (m, 2H, $\beta\text{-CH}_2$ of ^nBu), 1.37–1.20 (m, 2H, $\gamma\text{-CH}_2$ of ^nBu), 1.10 (d, $^3J_{\text{HH}} = 6$ Hz, 6H, CH_3 of ^iPr), 0.85 (t, $^3J_{\text{HH}} = 7$ Hz, CH_3 of ^nBu). $^{13}\text{C}\{^1\text{H}\}$ NMR (C_6D_6 , 75.53 MHz): δ 156.5 (C_1 of Ar), 130.4 (C_3H of Ar), 130.0 (C_2 of Ar), 128.1 (C_5H of Ar, by HMQC correlation with C_5H), 120.6 (C_4H of Ar), 112.9 (C_6H of Ar), 69.7 (CH of ^iPr), 49.2 (ArCH_2N), 49.1 ($\alpha\text{-CH}_2$ of ^nBu), 32.5 ($\beta\text{-CH}_2$ of ^nBu), 22.1 (CH_3 of ^iPr), 20.8 ($\gamma\text{-CH}_2$ of ^nBu), 14.2 (CH_3 of ^nBu). GC-MS m/z : $[\text{M}^+]$ calc'd for $\text{C}_{14}\text{H}_{23}\text{NO}$, 221.2; found, 221.2. IR (ATR, cm^{-1}): $\nu(\text{N-H})$ 3365. Anal. Calc'd. for $\text{C}_{14}\text{H}_{23}\text{NO}$: C, 75.97; H, 10.47, 6.33. Found: C, 75.63; H, 10.20; N, 6.56.*

$R = \text{CH}_2\text{Ph}$, **11**. Synthesis as for $R = ^n\text{Bu}$, using $\text{NH}_2\text{CH}_2\text{Ph}$ in place of NH_2^iBu . Yield: 61%. ^1H NMR (C_6D_6 , 300.3 MHz): δ 7.37 (d, $^3J_{\text{HH}} = 8$ Hz, 2H, $o\text{-Ph}$), 7.31 (dd, $^3J_{\text{HH}} = 8$ Hz, $^4J_{\text{HH}} = 2$ Hz, 1H, C_3H of Ar), 7.20 (t, $^3J_{\text{HH}} = 8$ Hz, 2H, $m\text{-Ph}$), 7.14–7.07 (overlapping m, 2H, $p\text{-Ph} + \text{C}_5\text{H}$ of Ar), 6.89 (ddd, $^3J_{\text{HH}} = 7$ Hz, $^4J_{\text{HH}} = 1$ Hz, 1H, C_4H of Ar), 6.64 (d, $^3J_{\text{HH}} = 8$ Hz, 1H, C_6H of Ar), 4.16 (septet, $^3J_{\text{HH}} = 6$ Hz, 1H, CH of ^iPr), 3.89 (s, 2H, NCH_2Ar), 3.71 (s, 2H, NCH_2Ph), 1.50 (br s, 1H, NH), 1.04 (d, $^3J_{\text{HH}} = 6$ Hz, 6H, CH_3 of ^iPr). $^{13}\text{C}\{^1\text{H}\}$ NMR (C_6D_6 , 75.53 MHz): δ 156.4 (C_1 of Ar), 141.6 ($ipso\text{-Ph}$), 130.4 (C_3H of Ar), 130.3 (C_2 of Ar), 128.53, 128.52, 128.4, 127.0 ($p\text{-Ph}$), 120.6 (C_4H of Ar), 112.9 (C_6H of Ar), 69.7 (CH of ^iPr), 53.4 (NCH_2Ph), 49.1 (NCH_2Ar), 22.1 (CH_3 of ^iPr). GC-MS m/z : $[\text{M}^+]$ calc'd for $\text{C}_{17}\text{H}_{21}\text{NO}$, 255.2; found, 255.2. IR (ATR, cm^{-1}): $\nu(\text{N-H})$ 3337. Anal. Calc'd. for $\text{C}_{17}\text{H}_{21}\text{NO}$: C, 79.96; H, 8.29, 5.49. Found: C, 79.77; H, 8.09; N, 5.36.†

Assessing impact of base on maximum turnover numbers (TON) in self-metathesis of styrene.

A stock solution of styrene and decane was prepared (0.275 M and 0.215 M, respectively) and an aliquot (ca. 50 μL) was taken to measure the initial ratio of substrate to internal standard. A Schlenk tube equipped with a stir bar was charged with 2.0 mL of this stock solution (0.55 mmol styrene, 0.43 mmol decane) and diluted to 4.9 mL with C_6H_6 . Pyrrolidine **N7** was then added (0.10 mL of a 0.55 M stock solution in C_6H_6 ; 0.055 mmol; 10 equiv vs. **III**). Finally, **III** (0.50 mL of a 0.011 M stock solution, 5.5 μmol) was added. Final volume: 5.5 mL C_6H_6 , $[\text{styrene}] = 100$ mM, $[\text{base}] = 10$ mM, $[\text{III}] = 1$ mM). The reaction vessel was transferred to a Schlenk line and heated to 60 $^\circ\text{C}$ within 10 min. After stirring for 24 h and 48 h, aliquots were removed against a flow of N_2 , quenched with excess KTp (ca. 1 mg, >10 equiv vs. Ru) in 1 mL CH_2Cl_2 , and analyzed by GC-FID. Values are averages of two independent trials ($\pm 2.5\%$).

* Bernadette T. Dobigny is acknowledged for assistance in optimizing the purification protocol for this compound under supervision from Benjamin J. Ireland and Prof. Deryn E. Fogg.

† Bernadette T. Dobigny is acknowledged for synthesis of this molecule under supervision from Benjamin J. Ireland and Prof. Deryn E. Fogg.

Identifying catalyst decomposition products formed by metathesis in the presence of base.

(a) *During Self-Metathesis of Styrene.* A solution of **III** (15 mg, 0.024 mmol) and TMB (ca. 1 mg, 0.006 mmol) was prepared in 1.20 mL C₆D₆. An aliquot (0.60 mL, 0.012 mmol **III**) was transferred to a J. Young NMR tube. Pyrrolidine **N7** (10 μ L, 0.12 mmol, 10 equiv) was added, and a ¹H NMR spectrum was collected to determine the initial integration ratio of **III** relative to TMB. Styrene (14 μ L, 0.12 mmol, 200 mM, 10 equiv) was then added. The remaining solution was likewise treated with styrene, and used as a control reaction. Both reactions were heated to 60 °C, and monitored at 2 h intervals. At 10 h: 90% loss of alkylidene; 99% at 18 h. Additional experiments utilized 10 equiv DBU **N9** or NEt₃ **N10**. No alkylidene signals were evident for either of these bases after 30 min. For additional experiments at 21 °C: complete loss of alkylidene after 1 h for NEt₃ **N10**. With DBU **N9**: 88% loss at 10 h, complete decomposition by 18 h. With pyrrolidine: 78% loss of alkylidene at 7 d (NMR data collected at 24 h intervals). Under all conditions, <4% stilbene was formed (GC-FID analysis). The organic decomposition products were (*E*)-PhCH=CHCH₂Ph **13** (major) and (*E*)-PhCH=CHCH₃ **14** (minor). Alkylidene signal for RuCl₂(H₂IMes)(HNC₄H₈)(=CHPh) **Ru-28** intermediate: δ 19.67 ppm.

Characterization data for (E)-PhCH=CHCH₂Ph, 13: ¹H NMR (C₆D₆, 500.1 MHz): δ 6.31 (d, ³J_{HH} = 16 Hz, 1H, PhHC=), 6.19 (dt, ³J_{HH} = 16 Hz, ³J_{HH} 7 Hz, 1H, =CHCH₂Ph), 3.25 (d, ³J_{HH} = 7 Hz, 2H, =CHCH₂Ph). ¹H and ¹³C{¹H} NMR signals for the Ph group were incompletely resolved from those for styrene and styrenyl ether *o*-PrO-C₆H₄-HC=CH₂. Key ¹³C{¹H} NMR data (C₆D₆, 125.8 MHz): δ 131.5 (PhHC=), 129.4 (=CHCH₂Ph), 39.6 (=CHCH₂Ph). DEPT-135 experiments support assignment of the key olefin and methylene signals; ¹H-COSY experiments confirm connectivity (for spectra, see SI). EI-MS, [M⁺]: *m/z* calc'd for C₁₅H₁₄, 194.1; found, 194.1. NMR¹⁹ and EI-MS²⁰ data agree with literature values for PhHC=CHCH₂Ph.

Characterization data for (E)-PhCH=CHCH₃, 14: ¹H NMR (C₆D₆, 500.1 MHz): δ 6.29 (d, ³J_{HH} = 16 Hz, 1H, PhHC=C), 6.03 (d of q, ³J_{HH} = 16 Hz, ³J_{HH} = 7 Hz, 1H, C=CHCH₃), 1.64 (d, ³J_{HH} = 7 Hz, ³J_{HH} = 3H, C=CHCH₃). EI-MS, [M⁺]: *m/z* calc'd for C₉H₁₀, 118.1; found, 118.1.

(b) *During degenerate metathesis of ethylene.* A solution of **III** (15 mg, 0.024 mmol) and TMB (ca. 2 mg, 0.012 mmol) was prepared in 1.20 mL C₆D₆. An aliquot (0.60 mL, 0.012 mmol **III**) was transferred to a J. Young NMR tube, and pyrrolidine **N7** (10 μ L, 0.12 mmol, 10 equiv) was added. The remaining solution was used as a control reaction. A ¹H NMR spectrum was collected to determine the integration ratio of **III** relative to TMB. To saturate the solutions in ethylene, each sample was freeze-pump-thaw degassed (5 x), then thawed under static vacuum. 1 atm of C₂H₄ was introduced at RT, samples were shaken vigorously, and a timer was started. ¹H NMR spectra were collected after 2 h and 16 h (when full decomposition was evident).

*Characterization data for ArCH₂CH=CH₂, **15**:* ¹H NMR (C₆D₆, 500.1 MHz): δ 6.09–5.97 (m, 1H, CH=CH₂), 5.12–5.00 (m, 2H, CH=CH₂), 4.24–4.13 (m, 1H, CH of ⁱPr, overlaps with ArCH=CHCH₃), 3.48 (d, ³J_{HH} = 6 Hz, 2H, ArCH₂CH=CH₂), 1.09 (d, ³J_{HH} = 6 Hz, 6H, CH₃ of ⁱPr). Aromatic signals not assigned due to overlap with signals from Ru species present. EI-MS, [M⁺]: *m/z* calc'd for C₁₂H₁₆O, 176.1. Found: 176.1.

*Characterization data for (E)-ArCH=CHCH₃, **15'**:* ¹H NMR (C₆D₆, 500.1 MHz): δ 6.17 (d of q, ³J_{HH} = 16 Hz, ³J_{HH} = 6 Hz, 1H, =CHCH₃), 4.24–4.13 (m, 1H, CH of ⁱPr, overlaps with ArCH₂CH=CH₂), 1.75 (dd, ³J_{HH} = 7 Hz, ⁴J_{HH} = 3 Hz, ⁴J_{HH} = 3H, C=CHCH₃), 1.10 (d, ³J_{HH} = 6 Hz, 6H, CH₃ of ⁱPr). Aromatic signals not assigned due to overlap with signals from Ru species present. EI-MS, [M⁺]: *m/z* calc'd for C₁₂H₁₆O, 176.1. Found: 176.1.

2.3.2. Experimental details for Chapter 4, Section 4.4.

*Attempted isolation of **III-7**:* Pyrrolidine **N7** (150 μL, 130 mg, 1.83 mmol) was added to a stirred green suspension of **III** (107 mg, 0.171 mmol) in 5 mL hexanes. The suspension was stirred vigorously for 24 h, after which the solid was filtered off and washed with hexanes (3 × 3 mL) and allowed to dry for several hours under N₂ at ambient pressure. A sample (ca. 10 mg / 0.6 mL C₆D₆) was analyzed by ¹H NMR spectroscopy indicating a mixture of the desired adduct and **III** starting material (key data for Ru=CHPh: 20.25 (**III-7**), 16.72 (**III**)) in a 2:1 ratio. An additional ca. 0.6 mL C₆D₆ was added to the NMR sample and ¹H NMR data was collected after 30 min. Following dilution, a 1:1 ratio of **III-7** and **III** was inferred from the relative integration of the corresponding Ru=CHAr signals. Extensive overlap of signals in the aliphatic region precluded integration of HNC₄H₈ signals independently from Mes (18H) and ⁱPr (6H) CH₃ signals at 3.9–0.3 ppm. Several broad signals integrating to 5H total were observed at 4.6–3.9, and are assigned collectively as H₂IMes (CH₂) and OiPr (CHMe₂). Both before and after dilution, the total integration from 3.9–0.3 ppm corresponded to ca. 33H, indicative of one equivalent HNC₄H₈ per Ru in the original isolated solid. It is plausible that the desired *mono*-amine adduct precipitates cleanly from hexanes, but reverts partially to **III** on dissolution, though contamination of the isolated solid by **III** and excess pyrrolidine **N7** could not be conclusively ruled out.

*Decomposition studies of **GII** and **III**:* Experiments were performed analogously to the procedure described above for “Identifying catalyst decomposition products formed by metathesis in the presence of base,” above (Section 2.3.1). For decomposition of **III** by excess NH₂ⁿBu **N1** + styrene, amine and substrate stock solutions were mixed and added simultaneously to a solution of **III** with TMB internal standard. A heterogeneous mixture formed on decomposition of **III** with 10

equiv. $\text{NH}_2^{\text{n}}\text{Bu}$ **N1** and styrene. The reaction mixture was fully solubilized with CDCl_3 to confirm quantitation of key products. For all other experiments (*N*-donors known to form stable adducts with **GII** or **III**), the *N*-donor was added prior to substrate addition and homogeneous orange or red solutions were obtained following alkylidene decomposition. Characterization data for organic products, other than those already described in Section 2.3.1, are provided in Section 2.2.4 (for $\text{PhCH}_2\text{NH}^{\text{n}}\text{Bu}$) and below:

*Characterization data for $\text{PhCH}_2\text{CH}=\text{CH}_2$, **14'**:* ^1H NMR (C_6D_6 , 500.1 MHz): δ 5.90–5.78 (m, 1H, $\text{HC}=\text{CH}_2$), 5.00–4.91 (m, 2H, $\text{HC}=\text{CH}_2$), 3.17 (d, $^3J_{\text{HH}} = 7$ Hz, 2H, PhCH_2). ^1H NMR signals for the Ph group were incompletely resolved from those of $\text{PhHC}=\text{CHCH}_3$. EI-MS, $[\text{M}^+]$: m/z calc'd for C_9H_{10} , 118.1; found, 118.1. ^1H NMR data were identical to those of an authentic sample (Sigma-Aldrich) and GC-MS data for allylbenzene ($\text{PhCH}_2\text{CH}=\text{CH}_2$) matched literature values.²⁰

*Characterization data for *N*-methylmorpholine, **16**:* ^1H NMR (C_6D_6 , 500.1 MHz): δ 3.58 (dd, $^3J_{\text{HH}} = 4$ Hz, 5 Hz, 4H, NCH_2), 2.00 (s). OCH_2 signals not assigned due to overlap with unknown decomposed Ru. $^{13}\text{C}\{^1\text{H}\}$ NMR (C_6D_6 , 125.8 MHz): δ 67.0 (NCH_2), 55.7 (NCH_3), 46.5 (OCH_2). EI-MS, $[\text{M}^+]$: m/z calc'd for $\text{C}_5\text{H}_{11}\text{NO}$, 101.1; found, 101.1. NMR and GC-MS data for *N*-methylmorpholine were identical to those of an authentic sample (Sigma-Aldrich).

2.4. Experimental data for Chapter 5

2.4.1. Syntheses of **GII** adducts of pyrrolidine and morpholine (Section 5.2.1)

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$\text{RuCl}_2(\text{H}_2\text{IMes})(\text{HNC}_4\text{H}_8)(=\text{CHPh})$ **Ru-28**. Pyrrolidine **N7** (150 μL , 130 mg, 1.83 mmol) was added to a stirred pink suspension of **GII** (150 mg, 0.177 mmol) in 10 mL hexanes. The suspension turned brown within 5 min, and dark green over 18 h. At 18 h, the suspension was filtered off, and the resulting green solid was washed with hexanes (3×3 mL). Yield after drying in vacuo: 76 mg (67%). ^1H NMR (C_6D_6 , 300.3 MHz): δ 19.67 (s, 1H, $[\text{Ru}]=\text{CH}$), 8.33 (d, $^3J_{\text{HH}} = 7$ Hz, 2H, Ph, *o*-CH), 7.31 (t, $^3J_{\text{HH}} = 7$ Hz, 1H, Ph, *p*-CH), 7.10 (t, $^3J_{\text{HH}} = 7$ Hz, 2H, Ph, *m*-CH), 6.98 (s, 2H, Mes *m*-CH), 6.43 (s, 2H, Mes *m*-CH), 3.53–3.41 (m, 2H, NHC CH_2), 3.41–3.21 (m, 3H, *NH*; NHC CH_2), 2.81 (s, 6H, Mes *o*-CH₃), 2.49–2.36 (m, 2H, NCH_2), 2.32 (s, 6H, Mes *o*-CH₃), 2.19 (s, 3H, Mes *p*-CH₃), 2.15–2.03 (m, 2H, NCH_2), 1.98 (s, 3H, Mes *p*-CH₃), 1.22–1.05 (m, 2H, NCH_2CH_2), 0.81–0.63 (m, 2H, NCH_2CH_2). $^{13}\text{C}\{^1\text{H}\}$ NMR (C_6D_6 , 75.5 MHz): δ 302.1 (s, $\text{Ru}=\text{CH}$), 222.9 (s, C_{NHC}), 152.7 (s, Ph, *C_i*),

* Compound numbers have been modified for consistency throughout the thesis. For a Table of Compound Numbers and Structures, see p. VII.

140.8 (s, Mes, *o*-C), 138.7 (s, Mes, *p*-C), 137.8 (s, Mes, *p*-C), 137.6 (s, Mes, *o*-C), 137.0 (s, Mes, *i*-C), 135.1 (s, Mes, *i*-C), 130.1 (s, Ph *o*-CH), 129.6 (s, Mes *m*-CH), 129.5 (s, Mes *m*-CH), 128.8 (s, Ph *p*-CH), 128.5 (s, Ph *m*-CH), 51.4 (s, NHC CH₂), 50.3 (s, NHC CH₂), 46.7 (s, HNCH₂), 24.8 (s, NCH₂CH₂), 21.0 (br, Mes *o*-CH₃, *p*-CH₃), 18.5 (s, Mes, *o*-CH₃). IR (ATR, cm⁻¹): ν(N-H) 3242. Anal. Calc'd. for C₃₂H₄₁N₃Cl₂Ru: C, 60.09; H, 6.46; N, 6.57. Found: C, 59.83; H, 6.22; N, 6.49.

RuCl₂(H₂IMes)(HNC₄H₈O)(=CHPh), **Ru-29**. Prepared as for **Ru-28**. Yield: 78%. ¹H NMR (C₆D₆, 500.1 MHz): δ 19.74 (s, 1H, [Ru]=CH), 8.33 (d, ³J_{HH} = 8 Hz, 2H, Ph, *o*-CH), 7.30 (t, ³J_{HH} = 8 Hz, 1H, Ph, *p*-CH), 7.09 (t, ³J_{HH} = 8 Hz, 2H, Ph, *m*-CH), 6.86 (s, 2H, Mes, *m*-CH), 6.41 (s, 2H, Mes, *m*-CH), 3.47-3.39 (m, 2H, NHC CH₂), 3.33-3.24 (m, 2H, NHC CH₂), 3.19 (d, ³J_{HH} = 12 Hz, 2H, OCH₂), 3.14 (t, ³J_{HH} = 12 Hz, 1H, NH), 3.05-2.91 (m, 2H, NCH₂), 2.76 (s, 6H, Mes, *o*-CH₃), 2.58 (td, ³J_{HH} = 12 Hz, ²J_{HH} = 3 Hz, 2H, OCH₂), 2.30 (s, 6H, Mes, *o*-CH₃), 2.06 (s, 3H, Mes, *p*-CH₃), 1.97 (s, 3H, Mes, *p*-CH₃), 1.76 (d, 2H, ³J_{HH} = 12 Hz, NCH₂). ¹³C{¹H} NMR (C₆D₆, 125.8 MHz): δ 304.2 ([Ru]=CH), 221.9 (C_{NHC}), 152.1 (s, Ph, C_i), 140.9 (s, Mes, *o*-C), 138.8 (s, Mes, *p*-C), 137.9 (s, Mes, *p*-C), 137.6 (s, Mes, *o*-C), 136.8 (s, Mes, *i*-C), 134.7 (s, Mes, *i*-C), 130.2 (s, Ph, *o*-CH), 129.6 (s, Mes, *m*-CH), 129.5 (s, Mes, *m*-CH), 129.1 (s, Ph, *p*-CH), 128.7 (s, Ph, *m*-CH), 67.4 (OCH₂), 51.4 (NHC CH₂), 50.2 (NHC CH₂), 45.0 (HNCH₂), 21.0 (s, Mes, *o*-CH₃), 20.9 (br s, Mes, *p*-CH₃), 18.5 (s, Mes, *o*-CH₃). IR (ATR, cm⁻¹): ν(N-H) 3213. Anal. Calc'd. for C₃₂H₄₁N₃OCl₂Ru: C, 58.62; H, 6.30; N, 6.41. Found: C, 58.84; H, 6.37; N, 6.28.

2.4.2. Syntheses of other new Ru benzylidenes

RuCl₂(PCy₃)(HNC₄H₈)(=CHPh), **Ru-43**. Pyrrolidine **N7** (200 μL, 173 mg, 2.44 mmol) was added to a purple suspension of **GI** (203 mg, 0.247 mmol) in 10 mL hexanes. A colour change to brown occurred within 5 min, with a gradual change to dark green over 1 h. After 5 h, product was filtered off affording a green solid and light brown supernatant. The solid was washed with hexanes (3 × 3 mL) and dried in vacuo to afford a pale green powder (104 mg, 0.169 mmol, 69%). ³¹P{¹H} NMR (C₆D₆, 121.6 MHz): δ 42.9. ¹H NMR (C₆D₆, 300.3 MHz): δ 20.16 (d, 1H, ³J_{PH} = 12 Hz, [Ru]=CHPh), 8.39 (d, ³J_{HH} = 8 Hz, 2H, *o*-CH of Ph), 7.32 (t, ³J_{HH} = 7 Hz, 1H, *p*-CH of Ph), 7.16 (apparent t, overlaps w solvent, ³J_{HH} = 7 Hz, 2H, *m*-CH of Ph), 3.89 (br s, 1H, NH of amine), 2.83–2.59 (m, 2H, NCH₂ of amine), 2.59–2.36 (m, 5H, NCH₂ of amine + CH of PCy₃), 2.31–2.07 (m, 6H, CH₂ of PCy₃), 2.07–1.67 (m, 12 H, CH₂ of PCy₃), 1.67–1.47 (m, 3H, CH₂ of PCy₃), 1.41–1.07 (m, 11H, CH₂ of PCy₃ + NCH₂CH₂ of amine), 0.95–0.77 (m, 2H, NCH₂CH₂ of amine). ¹³C{¹H} NMR (C₆D₆, 75.5 MHz): δ 304.1 (d, ²J_{PC} = 15 Hz, [Ru]=CHPh), 155.6 (s, *ipso*-C of Ph), 129.7 (s, *m*-CH of Ph), 129.4 (s, *p*-CH of Ph), 126.0 (s, *o*-CH of Ph), 47.9 (s, NCH₂ of amine), 35.1 (d, ¹J_{PC} = 20 Hz, CH of PCy₃), 30.6 (s, CH₂ of PCy₃), 28.1 (d, ²J_{CP} = 10 Hz, CH₂ of PCy₃), 26.8 (s, CH₂ of PCy₃), 25.2 (s,

NCH₂CH₂ of amine). IR (ATR, cm⁻¹): ν(N-H) 3254. Anal. Calc'd. for C₂₉H₄₈NCl₂PRu: C, 56.76; H, 7.88; N, 2.28. Found: C, 56.92; H, 7.62; N, 2.55.

RuCl₂(PCy₃)(HNC₄H₈O)(=CHPh), **Ru-44**. Morpholine **N6** (200 μL, 200 mg, 2.31 mmol) was added to a purple suspension of **GI** (206 mg, 0.250 mmol) in 10 mL hexanes. A colour change to brown occurred within 15 min, and to dark green/brown over 1 h. After 3 h, a green solid was filtered off, leaving a red/brown filtrate. The solid was reprecipitated from CH₂Cl₂/hexanes to remove the equilibrium proportion of **GI** remaining (ca. 5%), washed with hexanes (3 x 3 mL) and dried in vacuo to afford a pale green powder (84 mg, 0.13 mmol, 53%). ³¹P{¹H} NMR (C₆D₆, 121.6 MHz): δ 43.8. ¹H NMR (C₆D₆, 500.1 MHz): δ 20.13 (d, 1H, ³J_{PH} = 12 Hz, [Ru]=CHPh), 8.36 (d, 2H, ³J_{HH} = 8 Hz, *o*-CH of Ph), 7.28 (t, 1H, ³J_{HH} = 8 Hz, *p*-CH of Ph), 7.12 (t, 2H, ³J_{HH} = 8 Hz, *m*-CH of Ph), 3.53 (br t, 1H, ³J_{HH} = 13 Hz, NH of amine), 3.22 (d, 2H, ³J_{HH} = 11 Hz, OCH₂ of amine), 3.10 (q, 2H, ³J_{HH} = 13 Hz, NCH₂ of amine), 2.80 (t, 2H, ³J_{HH} = 11 Hz, OCH₂ of amine), 2.51–2.39 (m, 3H, CH of PCy₃), 2.31 (d, 2H, ³J_{HH} = 13 Hz, NCH₂ of amine), 2.23–2.08 (m, 6H, CH₂ of PCy₃), 1.96–1.91 (m, 6H, CH₂ of PCy₃), 1.91–1.68 (m, 6H, CH₂ of PCy₃), 1.68–1.53 (m, 3H, CH₂ of PCy₃), 1.35–1.13 (m, 9H, CH₂ of PCy₃). ¹³C{¹H} NMR (C₆D₆, 125.8 MHz): δ 303.4 (Ru=CHPh, by HMQC), 154.5 (*ipso*-C of Ph), 129.8, 129.7, 126.0, 67.8 (OCH₂ of amine), 46.0 (NCH₂ of amine), 35.1 (d, ¹J_{PC} = 21 Hz, CH of PCy₃), 30.5 (CH₂ of PCy₃), 28.1 (d, ²J_{CP} = 10 Hz, CH₂ of PCy₃), 26.8 (s, CH₂ of PCy₃). IR (ATR, cm⁻¹): ν(N-H) 3217. Anal. Calc'd. for C₂₉H₄₈NOCl₂PRu: C, 55.32; H, 7.68; N, 2.22. Found: C, 54.99; H, 7.84; N, 2.41.

RuCl₂(PCy₃)(en)(=CHPh) **Ru-15**. Ethylenediamine (en, 41 μL, 0.61 mmol) was diluted into 4 mL CH₂Cl₂ and the resulting solution was added drop-wise to a stirred purple solution of **GI** (495 mg, 0.598 mmol) in 60 mL CH₂Cl₂. An immediate colour change to light green was observed. After 30 min, the solvent was removed under vacuum and the resulting green residue was washed with hexanes (5 x 10 mL) affording a pale green powder (284 mg, 0.472 mmol, 79%). ³¹P{¹H} NMR (C₆D₆, 121.6 MHz): δ 35.3 (s). ¹H NMR (C₆D₆, 300.3 MHz): δ 20.29 (d, 1H, ³J_{HP} = 11 Hz, Ru=CHPh), 8.73 (d, ³J_{HH} = 7 Hz, 2H, *o*-CH of Ph), 7.47 (t, ³J_{HH} = 8 Hz, 1H, *p*-CH of Ph), 7.25 (apparent t, ³J_{HH} = 8 Hz, 2H, *m*-CH of Ph), 3.54 (br t, ³J_{HH} = 6 Hz, 2H, NH₂), 2.43–2.21 (m, 5H, *ipso*-CH of PCy₃ + CH₂ of en), 2.20–2.04 (m, 6H, CH₂ of PCy₃), 1.96 (br s, 2H, NH₂ of en), 1.85–1.55 (m, 18H, CH₂ of PCy₃ + CH₂ of en), 1.38–1.14 (m, 8H, CH₂ of PCy₃). ¹³C{¹H} NMR (C₆D₆, 75.5 MHz): δ 317.8 ([Ru]=CHPh, by HMQC), 156.3 (*ipso*-C of Ph), 130.1 (*m*-CH of Ph), 129.6 (*p*-CH of Ph), 128.5 (*o*-CH of Ph, by HMQC), 42.5 (CH₂ of en), 42.0 (CH₂ of en), 35.6 (d, ¹J_{CP} 19 Hz, *ipso*-CH of PCy₃), 29.8 (CH₂ of PCy₃), 28.2 (d, ²J_{CP} 9.8 Hz, CH₂ of PCy₃), 27.1 (CH₂ of PCy₃). IR (ATR, cm⁻¹): ν(N-H) 3377, 3300, 3234. Anal. Calc'd for C₂₇H₄₇N₂Cl₂PRu: C, 53.81; H, 7.86; N, 4.65. Found: C, 53.57; H, 7.62; N, 4.47.

RuCl₂(H₂IMes)(en)(=CHPh) **Ru-16**. Ethylenediamine (18 μ L, 16 mg, 0.27 μ mol) was added to a pink suspension of **GII** (151 mg, 0.18 μ mol) in 10 mL hexanes. The suspension turned green within 15 min. The product was filtered off and the resulting green solid was washed with hexanes (3 x 5 mL). Yield after drying in vacuo: 101 mg (88%). ¹H NMR (C₆D₆, 500.1 MHz): δ 19.09 (s, 1H, [Ru]=CHPh), 8.47 (d, ³J_{HH} = 8 Hz, 2H, *o*-CH of Ph), 7.40 (t, ³J_{HH} = 8 Hz, 1H, *p*-CH of Ph), 7.19 (d, ³J_{HH} = 8 Hz, 2H, *m*-CH of Ph), 6.88 (s, 2H, *m*-CH of Mes), 6.52 (s, 2H, *m*-CH of Mes), 3.30 (s, 4H, CH₂ of NHC), 2.77 (br s, 6H, *o*-CH₃ of Mes), 2.64 (t, ³J_{HH} = 6 Hz, 2H, NH), 2.43 (br s, 6H, *o*-CH₃ of Mes), 2.18 (s, 3H, *p*-CH₃ of Mes), 2.09–1.93 (m, 5H, *p*-CH₃ of Mes + H₂NCH₂), 1.59 (br s, 4H, H₂NCH₂ + NH). ¹³C{¹H} NMR (C₆D₆, 125.8 MHz): δ 312.0 ([Ru]=CH), 221.9 (*Ci* of NHC), 154.5 (*Ci* of Ph), 139.8 (br s, *C* of Mes), 139.2 (br s, *C* of Mes), 138.4 (br s, *C* of Mes), 138.1 (br s, *C* of Mes), 137.4 (br s, *C* of Mes), 130.7 (s, *o*-CH of Ph), 130.1 (*m*-CH of Mes), 129.6 (*m*-CH of Mes), 129.0 (*m*-CH of Ph), 128.7 (*p*-CH of Ph), 51.5 (CH₂ of NHC), 50.6 (CH₂ of NHC), 41.9 (H₂NCH₂), 41.7 (H₂NCH₂), 21.1 (br s, *p*-CH₃ of Mes), 19.7 (*o*-CH₃ of Mes), 18.9 (*o*-CH₃ of Mes). IR (ATR, cm⁻¹): ν (N-H) 3368, 3346, 3299, 3274. Anal. Calc'd. for C₃₀H₄₀N₄Cl₂Ru: C, 57.32; H, 6.41; N, 8.91. Found: C, 57.18; H, 6.52; N, 9.17.

RuCl₂(IMes)(en)(=CHPh) **Ru-16'**. Ethylenediamine (11 μ L, 9.9 mg, 0.17 mmol, 1.1 equiv.) was added to a dark green solution of RuCl₂(CHPh)(IMes)(py)₂ (112 mg, 0.154 mmol) in 8 mL C₆H₆. After 30 min, the solvent was removed under vacuum and the dark green residue was washed with hexanes (5 x 3 mL) affording RuCl₂(CHPh)(IMes)(en) as a pale green solid (85 mg, 0.14 mmol, 88%). ¹H NMR (C₆D₆, 300.3 MHz): δ 19.41 (s, 1H, [Ru]=CHPh), 8.52 (d, ³J_{HH} = 7 Hz, 2H, *o*-CH of Ph), 7.45 (t, ³J_{HH} = 7 Hz, 1H, *p*-CH of Ph), 7.21 (apparent t, ³J_{HH} = 8 Hz, 2H, *m*-CH of Ph), 6.68 (br s, 4H, *m*-CH of Mes), 6.25 (s, 2H, CH of NHC), 2.84 (t, ³J_{HH} = 6 Hz, 2H, NH₂), 2.42 (br s, 12H, *o*-CH₃ of Mes), 2.11 (br s, 8H, *p*-CH₃ of Mes + H₂NCH₂), 1.68–1.65 (m, 4H, NH₂ + H₂NCH₂). ¹³C{¹H} NMR (C₆D₆, 75.5 MHz): δ 312.8 (Ru=CHPh), 189.1 (*Ci* of NHC), 155.0 (*Ci* of Ph), 138.7, 138.1, 130.5, 129.4, 129.1, 128.6, 124.2 (CH of NHC), 42.0 (H₂NCH₂), 41.9 (H₂NCH₂), 21.1 (*p*-CH₃ of Mes), 19.1 (br s, *o*-CH₃ of Mes). One quaternary Mes ¹³C signal was not located by ¹³C{¹H} or HMBC NMR experiments. IR (ATR, cm⁻¹): ν (N-H) 3368, 3329, 3298, 3238. Anal. Calc'd. for C₃₀H₃₈N₄Cl₂Ru: C, 57.50; H, 6.11; N, 8.94. Found: C, 57.32; H, 5.93; N, 9.22.

RuCl₂(H₂IMes)(2,2-biphenyldiamine)(=CHPh) **Ru-42**. Biphenyldiamine **N11** (55 mg, 0.30 mmol) was dissolved in 1 mL C₆H₆ and added to a green solution of **GIII** (218 mg, 0.300 mmol) in 4 mL C₆H₆. After 15 min, the reaction mixture was dried in vacuo to afford a mixture of the desired product with **GIII** and biphenyldiamine **N11**. The mixture was dissolved in fresh C₆H₆ and stirred an additional 15 min before drying again in vacuo. The process was repeated until >99% consumption of **GIII** was evident by ¹H NMR (10 iterations). The resulting green solid was reprecipitated from

CH₂Cl₂ / hexanes and washed with hexanes (3 × 3 mL). Yield after drying in vacuo: 180 mg (80%). ¹H NMR (CDCl₃, 500.1 MHz, 253 K): δ 18.49 (s, 1H, [Ru]=CHPh), 8.73 (br s, *o*-CH of Ph), 7.56 (t, ³J_{HH} = 6 Hz, 1H, *p*-CH of Ph), 7.40 (br s, 1 H, *o*-CH of Ph) 7.37 (s, 1 H, *m*-CH of Mes), 7.32–7.16 (m, 3H, *m*-CH of Ph + CH of amine), 7.15–6.79 (m, 6 H, *m*-CH of Mes + 5 × CH of amine), 6.78 (s, 1 H, *m*-CH of Mes), 6.58 (d, ³J_{HH} = 9 Hz, 1H, *o*-CH of amine), 6.19 (s, 1H, CH of Mes), 5.93 (br s, 1H, *o*-CH of amine), 4.69 (br s, 1H, NH), 4.44 (br s, 1H, NH), 4.32 (br s, 1H, NH), 4.17–4.02 (m, 1H, CH₂ of NHC), 4.02–3.89 (m, 2H, CH₂ of NHC), 3.89–3.67 (m, 2H, NH + CH₂ of NHC), 2.75 (s, 3H, *o*-CH₃ of Mes), 2.67 (s, 3H, *o*-CH₃ of Mes), 2.55 (s, 3H, *p*-CH₃ of Mes), 2.35 (s, 3H, *p*-CH₃ of Mes), 2.02 (s, 3H, *o*-CH₃ of Mes), 1.90 (s, 3H, *o*-CH₃ of Mes). ¹³C{¹H} NMR (CDCl₃, 125.8 MHz, 253 K): δ 307.5 ([Ru]=CH), 215.7 (C_i of NHC), 151.7 (C_i of Ph), 141.0, 139.4, 139.2, 138.9, 138.4, 138.0, 137.9, 137.6, 136.7, 130.3, 130.1, 129.9, 129.7, 129.6, 129.3, 129.0, 128.8, 128.6, 128.3, 128.2, 127.5, 127.4, 127.1 (*o*-C of amine), 126.3 (*o*-C of amine), 123.8 (*m*-CH of amine), 122.3 (CH of amine), 121.1 (CH of amine), 120.8, 51.3 (CH₂ of NHC), 50.8 (CH₂ of NHC), 21.2 (*p*-CH₃ of Mes), 20.9 (*o*-CH₃ of Mes), 19.5 (*o*-CH₃ of Mes), 19.4 (*o*-CH₃ of Mes), 18.8 (*p*-CH₃ of Mes), 18.2 (*o*-CH₃ of Mes). Selected data in C₆D₆: ¹H NMR (CD₆D₆, 500.1 MHz): δ 18.98 (s, 1H, [Ru]=CHPh), 4.51 (br s, 4H, NH). IR (ATR, cm⁻¹): ν(N-H) 3346 (s), 3324 (m), 3258 (m). Anal. Calc'd. for C₄₀H₄₄N₄Cl₂Ru: C, 63.82; H, 5.89; N, 7.44. Found: C, 63.81; H, 6.06; N, 7.66.

2.4.3. Olefin metathesis

Olefin metathesis experiments in Chapter 5 (Section 5.3 and 5.4) were performed as described in Section 2.3.1, at 60 °C or RT. For benchmarking studies in Section 5.3, no additional base was added. Stock solutions of **GII**, **GIII**, **Ru-42**, or **Ru-42'** were used in place of **HII**, and diethyl diallylmalonate **20** or hex-5-enylundec-10-enoate **18** were used in place of styrene where indicated. Reactions of styrene and diethyl diallylmalonate **20** were carried out at an initial substrate concentration of 100 mM, a Ru concentration of 1.0 mM or 0.05 mM, and total reaction volumes of 5.0–5.5 mL. RCM macrolactonization of **18** were carried out at an initial substrate concentration of 5 mM, a Ru concentration of 0.05 mM, and total reaction volumes of 15–20 mL.

2.4.2. Decomposition studies

Thermolysis. A solution of RuCl₂(H₂IMes)(2,2-biphenyldiamine)(=CHPh) **Ru-42** (10 mg) and ca. 1 mg TMB (0.006 mmol) in 0.65 mL C₆D₆ was subjected to ¹H NMR analysis to determine the initial ratio of Ru=CHPh to TMB. The sample was heated to 60 °C in an oil bath and ¹H NMR spectra were collected after 2 h, then at 24 h intervals until 96 h. Depletion of **Ru-42** was quantified

by diminution of the Ru=CHPh signal at 18.97 ppm against CH of TMB at 6.25 ppm. Formation of *E*-stilbene was quantified by integration of the well-resolved *o*-CH signal at 7.32 (d, $^3J_{\text{HH}} = 8$ Hz, 4H). GC-MS analysis of a small portion of the crude reaction mixture, removed after 96 h, confirmed the identity of *E*-stilbene. Note that for this experiment, one CH Mesityl signal (1H) of **Ru-42** overlaps with CH of TMB at 6.25 ppm in C₆D₆ in the “initial” NMR spectrum. A correction corresponding to the total integration of Ru=CHPh (1 : 1 with the overlapping signal) was applied to integration values for TMB internal standard for experiments with **Ru-42**.

Characterization data for (*E*)-stilbene: ^1H NMR (C₆D₆, 500.1 MHz): δ 7.32 (d, $^3J_{\text{HH}} = 8$ Hz, 4H, *o*-CH of Ph), 7.00 (s, 2H, =CHPh). ^1H NMR signals for the *m*-CH and *p*-CH of the Ph group were incompletely resolved from those of **Ru-45** and unreacted **Ru-42** or **Ru-42'**. EI-MS, [M⁺]: *m/z* calc'd for C₁₄H₁₂, 180.1; found, 180.1. ^1H NMR and GC-MS data matched those of an authentic commercial sample (Sigma Aldrich).

At 96 h, loss of benzylidene reached 55%. Present in 52% yield (95% vs. decomposed Ru) was RuCl₂(H₂IMes)(κ^2 -(H₂NC₆H₄)₂) **Ru-45**. This compound gives rise to four NH doublets between 4.8 and 3.3 ppm. The same species was formed in higher yield for decomposition experiments with styrene and C₂H₄. In situ characterization data for **Ru-45** is provided below. The NHC and **N11** (CH) signals of **Ru-45** were incompletely resolved from those of unreacted **Ru-42**.

Thermolysis of the IMes complex **Ru-42'** was performed as described above for **Ru-42**, except GC-MS analysis at 96 h indicated 90% loss of Ru=CHPh. Four doublets (4.75, 4.64, 4.37, and 3.44 ppm; $^2J_{\text{HH}} = 10$ Hz) were assigned to the NH groups of **Ru-45'**.

Decomposition of Ru-42: (a) During self-metathesis of styrene. A solution of **Ru-42** and TMB in C₆D₆ was prepared as above. Following collection of an initial ^1H NMR spectrum, styrene (12 μL , 13 mg, 0.13 mmol) was added and a timer was started. ^1H NMR spectra were collected after 2 h and again after 20 h. After 20 h (>95% decomposition), a small portion of the sample was removed for GC-MS analysis. The sample was then heated to 60 °C to collect ^1H NMR and COSY data (see discussion), then cooled to RT and 1 drop of degassed D₂O was added under N₂. ^1H NMR data was again collected at RT and 60 °C.

Partial characterization data for RuCl₂(H₂IMes)(κ^2 -(H₂NC₆H₄)₂) **Ru-45** (compound not isolated; data limited to VT ^1H NMR, COSY, and EXSY experiments): ^1H NMR (C₆D₆, 500.1 MHz): δ 4.76 (d, $^3J_{\text{HH}} = 10$ Hz, NH), 4.46 (d, $^3J_{\text{HH}} = 10$ Hz, NH), 4.30 (d, $^3J_{\text{HH}} = 10$ Hz, NH), 3.48–3.32 (m, 5H, CH₂ of H₂IMes + NH), 3.09–1.45 (m, overlapping, 18H, *o/p*-CH₃ of Mes). ^1H NMR (C₆D₆, 500.1 MHz, 333 K): δ 4.86 (s, 1H, NH), 4.47 (s, 1H, NH), 4.29 (s, 1H, NH), 3.70–3.41 (m, 5H, CH₂ of H₂IMes + NH), 2.74 (s, 6H, *o*-CH₃ of Mes), 2.55 (s, 6H, *o*-CH₃ of Mes), 2.10 (s, 6H, *p*-

CH_3 of Mes). (CH_3 and CH of Mes signals are broad, poorly resolved at RT.) Signals assigned as “NH” exchanged with added D_2O . CH of Mes and **N11** subunits were incompletely resolved from styrene and stilbene in the crude reaction mixture.

(b) *During degenerate metathesis of ethylene.* A solution of **Ru-42** and TMB in C_6D_6 was prepared as above. Following collection of an initial ^1H NMR spectrum, the solution was freeze-pump-thaw degassed (5 x), then thawed under static vacuum. 1 atm of C_2H_4 was introduced at RT, the sample was shaken vigorously, and a timer was started. ^1H NMR spectra were collected after 30 min (when full decomposition was evident). Formation of ca. 70% (vs. **Ru-42** at t_0) $\text{RuCl}_2(\text{H}_2\text{IMes})(\kappa^2\text{-(H}_2\text{NC}_6\text{H}_4)_2)$ **Ru-45** was inferred by observation of four doublets between 4.8 and 3.3 ppm (NH), in good agreement with in situ characterization described for styrene self-metathesis (above). A small portion of the sample was removed and analyzed by GC-MS to confirm the identity of styrene.

Characterization data for styrene: ^1H NMR (C_6D_6 , 500.1 MHz): δ 6.57 (dd, $^3J_{\text{HH}} = 17$ Hz, 1H, $\text{PhHC}=\text{CH}_2$), 5.59 (d, $^3J_{\text{HH}} = 17$ Hz, 1H, $\text{PhHC}=\text{C(H)H}$), 5.06 (d, $^3J_{\text{HH}} = 11$ Hz, 1H, $\text{PhHC}=\text{C(H)H}$). ^1H NMR signals for the Ph group were incompletely resolved from those of **Ru-45**. EI-MS, $[\text{M}^+]$: m/z calc'd for C_8H_8 , 104.1; found, 104.1. ^1H NMR and GC-MS data matched those of an authentic sample (Sigma Aldrich).

2.4.3. Reactions of Ru alkylidenes with lithium salts

*Attempted synthesis of $\text{RuCl}(\kappa^2\text{-HNC}_2\text{H}_4\text{NH}_2)(=\text{CHPh})(\text{PCy}_3)$ **Ru-50** from **GI**:* A solution of $\text{Li}[\text{HNC}_2\text{H}_4\text{NH}_2]$ (12 mg, 0.18 mmol) was prepared in 1.00 mL THF. An aliquot (0.235 mL, 2.8 mg, 0.042 mmol, 1.2 equiv) was added to a stirred solution of **GI** (28 mg, 0.034 mmol) in 2.0 mL C_6H_6 attached to a Schlenk line. After 30 min, a colour change from purple to red-brown was observed and a ca 0.2 mL aliquot was taken for $^{31}\text{P}\{^1\text{H}\}$ NMR analysis (by syringe against positive N_2 pressure) and transferred to a screw cap NMR tube with a Teflon septum, pre-charged with 0.3 mL C_6H_6 and a few drops of C_6D_6 . A second aliquot was taken after 3 h and no changes were observed. The solvent was then removed under vacuum of the reaction mixture and the red-brown residue was solubilized in C_6D_6 for ^1H and ^{31}P NMR analysis. *Key data for the minor alkylidene product:* $^{31}\text{P}\{^1\text{H}\}$ NMR (C_6D_6 , 121.6 MHz): δ 49.6 (s). ^1H NMR (C_6D_6 , 300.1 MHz): δ 15.84 (d, $^3J_{\text{HP}} = 11$ Hz). Excess free PCy_3 and minor quantities of **GI** and $\text{RuCl}_2(\text{PCy}_3)(\text{en})(=\text{CHPh})$ **Ru-15** (above) were apparent by ^1H and $^{31}\text{P}\{^1\text{H}\}$ NMR analysis. A low in situ yield of the alkylidene product was inferred from the ratio of its $^{31}\text{P}\{^1\text{H}\}$ NMR signal to free PCy_3 . The corresponding non-alkylidene Ru product was not identified due to signal overlap in the organic region of the ^1H NMR spectrum.

*Reactions and **GIII'** with Li[NRR'] salts.* A solution of **GIII'** (11 mg, 0.015 mmol) and TMB (ca. 3 mg, 0.018 mmol) was prepared in 1.00 mL C₆D₆. An aliquot (0.50 mL, 0.0075 mmol **GIII'**) was transferred to a J. Young NMR tube and a ¹H NMR spectrum was collected to determine the initial integration of **GIII'** relative to TMB internal standard. A solution of Li[NPh₂] **24** (10 mg, 0.057 mmol) in THF (0.100 mL) was prepared and a aliquot (0.015 mL, 1.5 mg, 0.0086, 1.1 equiv vs. Ru) was added. An aliquot of THF (0.015 mL) was added to the remaining **GIII'** solution, which was then used as a control reaction. ¹H NMR spectra were collected after 30 min and again after 1 h (ca 90% decomposition for the test reaction) at RT. *Ru=CHPh signal for unstable intermediate* (C₆D₆/THF, 300.1 MHz): δ_H 19.59 (29% against IS at 30 min, not observed at 1 h).

Reactions of **GIII'** with Li[NC₄H₄] **23** and Li[NHPh] **25** were performed analogously, except no data points were collected at 0.5 h and 3 h (no change). After 3 h, minimal changes were observed and fresh stock solutions of **23** and **25** in THF were prepared. An additional 3 equiv of each Li salt was added to the corresponding reaction and ¹H NMR data were collected after 30 min. *Ru=CHPh signal for minor product of Li[NC₄H₄] reaction* (30 min, RT, C₆D₆/THF, 300.1 MHz) δ_H 19.31 (9% w 1.1 equiv Li salt, 35% after addition of 4 equiv total Li salt).

2.4.4. Experimental details for Chapter 5, Section 5.6

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Syntheses. *RuH[(η⁵-C₆H₅)NPh](PPh₃)₂ **Ru-52a**.* A solution of Li[NPh₂] **24** (64 mg, 0.37 mmol, 1.1 equiv) in 0.8 mL THF was added to a purple suspension of RuHCl(PPh₃)₃ **Ru-53** (300 mg, 0.325 mmol) in 30 mL C₆H₆ in a Schlenk flask. A dark orange solution was obtained within 15 min on stirring at 45 °C. After a total reaction time of 45 min, the solvent was stripped to dryness. The residue was taken up in C₆H₆ and filtered through Celite to remove LiCl and excess LiNPh₂. The filtrate was concentrated to ca. 1 mL, and the product was precipitated by addition of pentane (5 mL). The orange solid was filtered off and washed with pentane (3 × 2 mL) and Et₂O (3 × 1 mL). Yield 189 mg (73%). X-ray quality crystals were obtained by layering a saturated solution of RuH[(η⁵-C₆H₅)NPh](PPh₃)₂ in toluene with hexanes, and chilling at -30 °C overnight. ³¹P{¹H} NMR (C₆D₆, 121.6 MHz): δ 59.6 (d, ²J_{PP} = 29 Hz, 1P), 55.6 (d, ²J_{PP} = 29 Hz, 1P). ¹H NMR (C₆D₆, 300.1 MHz): δ 7.63-7.25 (m, 12H, Ph), 7.08 (t, ³J_{HH} = 7.6 Hz, 2H, Ph; overlap with residual proton of deuterated solvent), 6.95-6.70 (m, 21H, Ph), 5.22 (br s, 1H, η⁵-C₆H₅), 5.01 (br s, 1H, η⁵-C₆H₅), 4.77 (br s, 1H,

* Compound numbers have been modified for consistency throughout the thesis. For a Table of Compound Numbers and Structures, see p. VII.

$\eta^5\text{-C}_6\text{H}_5$), 4.37 (br s, 1H, $\eta^5\text{-C}_6\text{H}_5$), 4.04 (t, $^3J_{\text{HH}} = 4.74$ Hz, 1H, $\eta^5\text{-C}_6\text{H}_5$), -11.94 (t, $^2J_{\text{PH}} = 33$ Hz, 1H, Ru-H). $^{13}\text{C}\{^1\text{H}\}$ NMR (C_7D_8 , 125.8 MHz):* δ 153.0, 152.5, 139.1 (d, 40 Hz), 138.7 (d, 40 Hz), 134.4 (d, 11 Hz), 128.9, 128.7, 127.6 (d, 9 Hz), 127.5 (d, 9 Hz), 123.2, 120.6, 101.5 ($\eta^5\text{-C}_6\text{H}_5$), 97.2 ($\eta^5\text{-C}_6\text{H}_5$), 80.7 ($\eta^5\text{-C}_6\text{H}_5$), 73.9 ($\eta^5\text{-C}_6\text{H}_5$), 70.8 ($\eta^5\text{-C}_6\text{H}_5$). IR (ATR, cm^{-1}): $\nu(\text{Ru-H})$ 1967, $\nu(\text{C=N})$ not observed: either weak or shifted below the aromatic envelope. Anal. Calc'd. for $\text{C}_{48}\text{H}_{41}\text{NP}_2\text{Ru}$: C, 72.53; H, 5.20; N, 1.76. Found: C, 72.30; H, 4.94; N, 1.49.

RuH($\sigma\text{-NPh}_2$)(CO)(PPh₃)₂ **Ru-53**. A solution of LiNPh_2 **24** (53 mg, 0.30 mmol, 1.3 equiv) in 10 mL THF was added to a Schlenk flask containing a white suspension of $\text{RuHCl(CO)(PPh}_3)_3$ (225 mg, 0.236 mmol) in 40 mL THF. A dark red solution formed within 15 min on stirring at RT. After a total reaction time of 1 h, the solvent was stripped to dryness. The residue was taken up in C_7H_8 and filtered through Celite to remove Li salts. The Celite was rinsed with C_7H_8 (3×20 mL) and the combined filtrate was stripped to dryness. The resulting red residue was washed with hexanes (3×20 mL) and filtered off to yield a red powder. Yield 148 mg (76%). $^{31}\text{P}\{^1\text{H}\}$ NMR (C_6D_6 , 121.6 MHz): δ 41.7 (s). ^1H NMR (C_6D_6 , 300.1 MHz): δ 7.87-7.54 (m, 12H, Ph), 7.51-7.29 (m, 3H, Ph), 7.08-6.79 (m, 21H, Ph), 6.56 (br s, 2H, NPh), 6.04 (br s, 2H, NPh), -17.19 (t, $^2J_{\text{PH}} = 22$ Hz, 1H, Ru-H). $^{13}\text{C}\{^1\text{H}\}$ NMR (C_6D_6 , 125.8 MHz): δ 202.2 (Ru-CO; located by HMBC), 135.0 (vt, 20 Hz), 134.6 (vt, 6 Hz), 132.1, 129.9, 128.3 (vt, 4.3 Hz), 127.8, 120.3, 117.8, 116.2, 104.2. IR (ATR, cm^{-1}): $\nu(\text{Ru-H})$ 2099 (m); $\nu(\text{CO})$ 1927 (s). Anal. Calc'd. for $\text{C}_{49}\text{H}_{41}\text{NOP}_2\text{Ru}$: C, 71.52; H, 5.02; N, 1.70. Found: C, 71.27; H, 4.85; N, 1.99.

RuH($\sigma\text{-OPh}$)(CO)(PPh₃)₃ **Ru-54**. A solution of KOPh (36 mg, 0.27 mmol, 1.2 equiv) in 10 mL THF was added to a stirred white suspension of $\text{RuHCl(CO)(PPh}_3)_3$ (216 mg, 0.226 mmol) in 35 mL THF in a Schlenk flask. A yellow solution formed within 15 min at RT. After a total of 2 h, the solvent was stripped off to yield a yellow residue, which was taken up in C_6H_6 , filtered through Celite, and rinsed through with additional C_6H_6 (2×3 mL). The solvent was removed, and the residue was reprecipitated from CH_2Cl_2 -hexanes to yield a white powder, which was filtered off and dried under vacuum. Yield 207 mg (91%). $^{31}\text{P}\{^1\text{H}\}$ NMR (C_6D_6 , 121.6 MHz): δ 38.1 (br s, 2P), 16.3 (br s, 1P). $^{31}\text{P}\{^1\text{H}\}$ NMR (C_7D_8 , 263 K): δ 38.5 (d, $^2J_{\text{PP}} = 17$ Hz, 2P), 16.0 (t, $^2J_{\text{PP}} = 17$ Hz, 1P). ^1H NMR (C_6D_6 , 300.1 MHz): δ 7.62-7.25 (m, 18H, Ph), 7.10-6.74 (m, 31H, Ph), 6.47 (t, $^3J_{\text{HH}} = 6.9$ Hz, 1H, Ph), -6.63 (dt, $^2J_{\text{PH}} = 112$ Hz, $^2J_{\text{PH}} = 24$ Hz, 1H, Ru-H). $^{13}\text{C}\{^1\text{H}\}$ NMR (CD_2Cl_2 , 125.8 MHz):[†] δ 204.6 (t, 18 Hz, Ru-CO), 168.1, 136.2 (vt, 22 Hz), 135.9 (d, 21 Hz), 134.8 (d, 6 Hz), 134.7 (vt, 6 Hz),

* $^{13}\text{C}\{^1\text{H}\}$ and DEPT NMR data reported in C_7D_8 due to poor solubility in C_6D_6 . Other nuclei reported in C_6D_6 to allow comparison between **Ru-52a**, **Ru-53**, and **Ru-54**.

[†] $^{13}\text{C}\{^1\text{H}\}$ and DEPT NMR reported in CD_2Cl_2 due to the poor solubility in C_6D_6 . Other nuclei reported in C_6D_6 to allow comparison between **Ru-52a**, **Ru-53**, and **Ru-54**.

129.6, 129.5, 129.3, 128.0 (vt, 5 Hz), 127.8 (d, 5 Hz), 120.2, 110.9. IR (ATR, cm^{-1}): $\nu(\text{Ru-H})$ 2000 (m), $\nu(\text{CO})$ 1901 (s). Anal. Calc'd. for $\text{C}_{61}\text{H}_{51}\text{O}_2\text{P}_3\text{Ru}$: C, 72.54; H, 5.09. Found: C, 72.19; H, 4.85.

General procedure for carbonylation reactions: $\text{RuH}[(\eta^5\text{-C}_6\text{H}_5)\text{O}](\text{PPh}_3)_2$ **Ru-52b** (10 mg, 0.013 mmol) and TMB (2 mg, 1.3 equiv) were dissolved in 1.0 mL C_6D_6 , and a ^1H NMR spectrum was measured to establish the initial ratio of RuH to TMB. The orange sample was freeze-pump-thaw degassed five times, then stirred under 1 atm CO.

*Characterization data for $\text{Ru}(\text{CO})_3(\text{PPh}_3)_2$ **Ru-57** and HNPh_2 from $\text{RuH}[(\eta^5\text{-C}_6\text{H}_5)\text{NPh}](\text{PPh}_3)_2$, **Ru-52a**:* (a) After 2 h at 50 °C: $^{31}\text{P}\{^1\text{H}\}$ NMR (C_6D_6 , 121.6 MHz): δ 56.4 (s, 92%, $\text{Ru}(\text{CO})_3(\text{PPh}_3)_2$), 47.5 (s, 5%), 25.6 ppm (s, 3%). ^1H NMR (C_6D_6 , 300.3 MHz; NH signal only): δ 5.01 (br s, HNPh_2 , 0.8 equiv vs. TMB). $^{13}\text{C}\{^1\text{H}\}$ NMR (C_6D_6 , 75.5 MHz; amine signals only): δ 143.7, 129.6, 121.2, 118.2. IR (ATR, cm^{-1}): $\nu(\text{CO})$ 1898 (s). The spectroscopic data for $\text{Ru}(\text{CO})_3(\text{PPh}_3)_2$ agreed with literature values: δ_{P} 56.0 ppm (C_7D_8); $\nu(\text{CO})$ 1900 (s).²¹

(b) After 40 h at RT: $^{31}\text{P}\{^1\text{H}\}$ NMR (C_6D_6 , 121.6 MHz): δ 56.4 (s, 58%, $\text{Ru}(\text{CO})_3(\text{PPh}_3)_2$), 47.5 (s, 20%), 39.3 (s, 1%), 25.6 (s, 5%), -5.0 ppm (s, 16%, PPh_3). ^1H NMR (C_6D_6 , 300.3 MHz, NH signal only): δ 5.01 (br s, HNPh_2 , 0.9 equiv vs. TMB).

*Characterization data for $\text{Ru}(\text{CO})_3(\text{PPh}_3)_2$ **Ru-57** and HOPh from **Ru-52b**:*

(a) After 6 h at 90 °C in C_7D_8 : $^{31}\text{P}\{^1\text{H}\}$ NMR (C_7D_8 , 121.6 MHz): δ 56.2 (s, 93%, $\text{Ru}(\text{CO})_3(\text{PPh}_3)_2$), 26.2 (s, 2%) -5.0 ppm (s, 5%, PPh_3). ^1H NMR (C_7D_8 , 300.3 MHz; phenol signals only): δ 4.87 ppm (s, HOPh , 0.9 equiv vs. TMB). $^{13}\text{C}\{^1\text{H}\}$ NMR (C_7D_8 , 75.5 MHz; phenol signals only): δ 157.5, 130.0, 120.1, 115.9.

(b) After 24 h 50 °C in toluene: No reaction.

Characterization data for $\text{Ru}(\text{CO})_3(\text{PPh}_3)_2$ and HNPh_2 from $\text{RuH}(\sigma\text{-NPh}_2)(\text{CO})(\text{PPh}_3)_2$:

(a) After 2 h at 50 °C: $^{31}\text{P}\{^1\text{H}\}$ NMR: δ 56.4 (s, sole signal, $\text{Ru}(\text{CO})(\text{PPh}_3)_2$ **Ru-57**).

(b) After 20 min at RT: $^{31}\text{P}\{^1\text{H}\}$ NMR (C_6D_6 , 121.6 MHz): 56.4 (s, 52%,), 47.5 (s, 26%), -5.0 ppm (s, 23%). ^1H NMR (C_6D_6 , 300.3 MHz; amine signals only): δ 5.01 (br s, HNPh_2 , 0.9 equiv vs. TMB).

*Attempted Synthesis of $\text{RuH}(\sigma\text{-NPh}_2)(\text{CO})_2(\text{PPh}_3)_2$ **Ru-56**:* A pale yellow solution of $\text{RuHCl}(\text{CO})_2(\text{PPh}_3)_2$ (10 mg, 0.014 mmol, 14 mM) with trimethoxybenzene (TMB) as internal standard (1 mg, 0.4 equiv) in 1.00 mL C_6D_6 was treated with a stock solution of LiNPh_2 **24** in THF (1.1 equiv). A color change from yellow to red occurred over 24 h at RT. $^{31}\text{P}\{^1\text{H}\}$ NMR (C_6D_6 , 121.6

MHz): 56.4 (s, 42%, $\text{Ru}(\text{CO})_3(\text{PPh}_3)_2$), 50.7 (5%), 41.7 (s, 52%, $\text{RuH}(\sigma\text{-NPh}_2)(\text{CO})(\text{PPh}_3)_2$) **Ru-53**. ^1H NMR (500.1 MHz): 5.38 (br s, HNPh_2 , 50% vs. IS), -17.19 (t, $^2J_{\text{PH}} = 22$ Hz, 52% vs. IS, $\text{RuH}(\sigma\text{-NPh}_2)(\text{CO})(\text{PPh}_3)_2$). The sample was freeze-thaw degassed, then thawed under CO and heated for 2 h at 50 °C. Over this time the solution became colorless. $^{31}\text{P}\{^1\text{H}\}$ NMR analysis indicated only $\text{Ru}(\text{CO})_3(\text{PPh}_3)_2$ and ^1H NMR analysis showed an increase to 90% in situ yield of HNPh_2 vs. TMB internal standard.

*Crystallographic Details for $\text{RuH}[(\eta^5\text{-C}_6\text{H}_5)\text{O}](\text{PPh}_3)_2$ **Ru-52a**:** Single crystals of $\text{RuH}[(\eta^5\text{-C}_6\text{H}_5)\text{O}](\text{PPh}_3)_2$ were analyzed using a Bruker PLATFORM diffractometer equipped with an APEXII CCD area detector. Diffraction measurements were made using graphite-monochromated Mo K_α radiation, with the crystal cooled to 173 K under a cold nitrogen gas stream (see Table 2.1 for crystallographic details). Programs for diffractometer operation, data collection, data reduction, and absorption correction were those supplied by Bruker. The structure was solved using Patterson location of heavy atoms followed by structure expansion (*DIRDIF-2008*) and refined using full-matrix least-squares on F^2 in (*SHELXL-97*). CCDC 940549 contains the supplementary crystallographic data for this Article. These can be obtained free of charge from the Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

* Dr. Robert McDonald of the University of Alberta Crystallography Laboratory is credited for collection and refinement of XRD data for this molecule.

Table 2.1. Crystallographic details for RuH(η^5 -C₆H₅-NPh)(PPh₃)₂ **Ru-52a** (CCDC-940549)

diffractometer	Bruker PLATFORM/APEX II CCD ^b
radiation (λ [Å])	graphite-monochromated Mo K α (0.71073)
temperature (°C)	–100
scan type	ω scans (0.3°) (20 s exposures)
data collection 2θ limit (deg)	52.92
total data collected	29797 ($-15 \leq h \leq 15$, $-12 \leq k \leq 12$, $-37 \leq l \leq 37$)
independent reflections	7815 ($R_{\text{int}} = 0.0557$)
number of observed reflections (NO)	6189 [$F_o^2 \geq 2s(F_o^2)$]
structure solution method	Patterson/structure expansion (<i>DIRDIF-2008</i> ^c)
refinement method	full-matrix least-squares on F^2 (<i>SHELXL-97</i> ^d)
absorption correction method	Gaussian integration (face-indexed)
range of transmission factors	0.9708–0.8712
data/restraints/parameters	7815 / 0 / 473
goodness-of-fit (S) ^e [all data]	1.070
final R indices ^f	
R_1 [$F_o^2 \geq 2s(F_o^2)$]	0.0605
wR_2 [all data]	0.1672
largest difference peak and hole	3.011 and –0.898 e Å ^{–3}

^aObtained from least-squares refinement of 8433 reflections with $4.90^\circ < 2\theta < 48.18^\circ$.

^bPrograms for diffractometer operation, data collection, data reduction and absorption correction were those supplied by Bruker.

^cBeurskens, P. T.; Beurskens, G.; de Gelder, R.; Smits, J. M. M.; Garcia-Granda, S.; Gould, R. O. (2008). The *DIRDIF-2008* program system. Crystallography Laboratory, Radboud University Nijmegen, The Netherlands.

^dSheldrick, G. M. *Acta Crystallogr.* **2008**, *A64*, 112–122.

^e $S = [Sw(F_o^2 - F_c^2)^2 / (n - p)]^{1/2}$ (n = number of data; p = number of parameters varied; $w = [s^2(F_o^2) + (0.0889P)^2 + 10.3480P]^{-1}$ where $P = [\text{Max}(F_o^2, 0) + 2F_c^2]/3$)

^f $R_1 = \sum |F_o| - |F_c| / \sum |F_o|$; $wR_2 = [Sw(F_o^2 - F_c^2)^2 / Sw(F_o^4)]^{1/2}$

2.6. References

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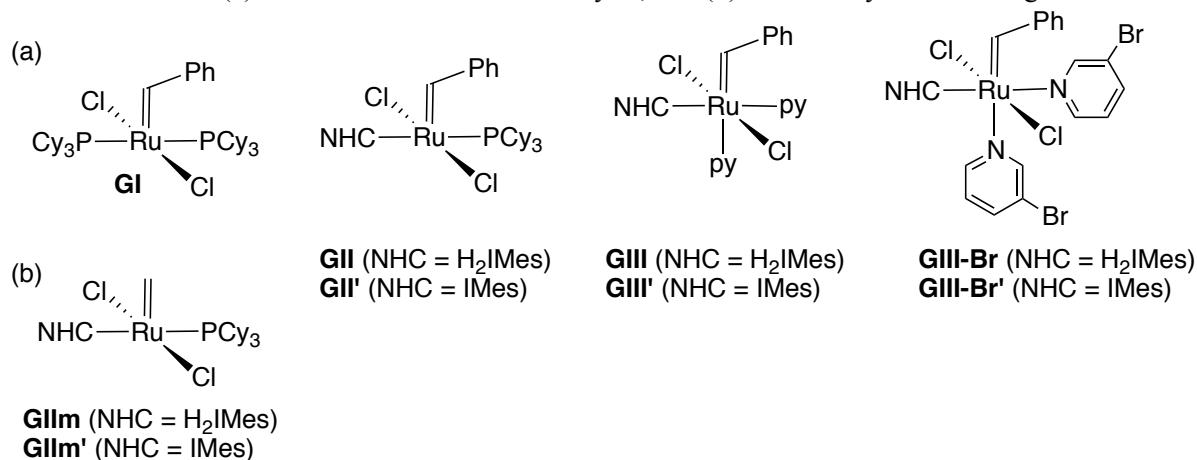
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Chapter 3. Decomposition of the Grubbs Catalysts by Amines: Benzyldiene Abstraction Pathways

3.1. Introduction

The excellent functional-group tolerance of ruthenium metathesis catalysts is widely accepted, but rarely examined. The perception of robustness is shaped largely by target-directed synthesis, which has led to spectacular advances with a broad array of functionalities.¹ In academic practice, however, catalyst deactivation is often masked by high catalyst loadings.² Even rather innocuous groups, like the carbonyl functionality in esters and ketones, can in fact be problematic where a 5–7-membered carbonyl chelate can be formed.^{2,3} Halides have likewise been shown to be problematic, depending on their placement relative to the olefin.⁴ The metathesis of directly-functionalized olefins is only beginning to be explored.²

Chart 3.1. (a) The Grubbs metathesis catalysts, and (b) their methyldiene resting states.



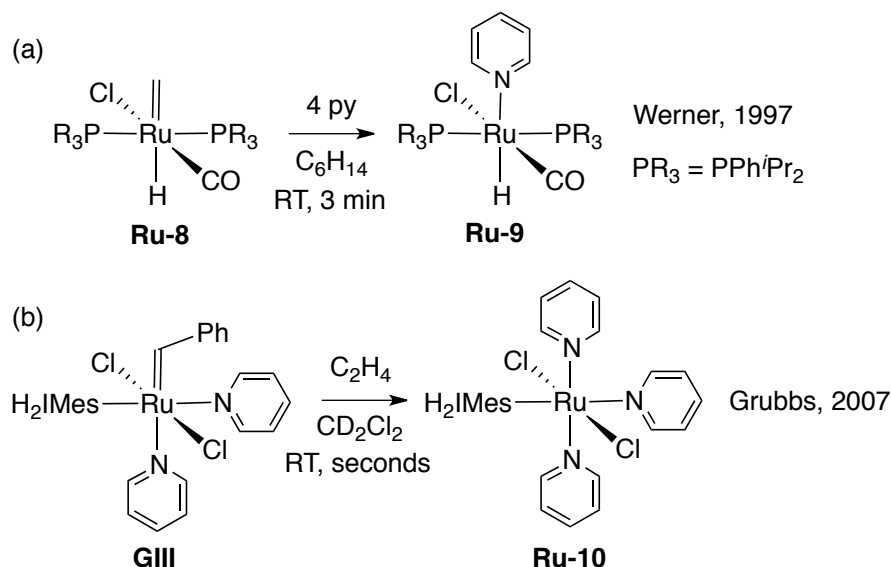
Among the groups known to enable decomposition of Grubbs-class ruthenium catalysts (Chart 3.1), only alcohols had been studied to an appreciable extent at the outset of this work.⁵⁻⁸ Explored in this Chapter is the tolerance of the Grubbs catalysts **GI** and **GII** toward amine functionalities. Amines and related Lewis bases have long been recognized⁹ as problematic in olefin metathesis, and protecting-group strategies are typically employed to allow efficient reaction.^{2,3} Reports from the pharmaceutical industry have linked poor RCM yields and undesired isomerization to the presence of morpholine¹⁰ and diazabicycloundec-7-ene (DBU)¹¹ impurities. In a groundbreaking 2007 review, Compain suggested that high metathesis yields are associated with the presence of steric or electronic factors that limit amine binding to the metal.³ The Cossy group has recently extended these ideas to metathesis of heteroaromatic substrates, particularly pyridine

derivatives. The poor CM yields of such substrates were improved by incorporating electron-withdrawing or bulky substituents adjacent to the nitrogen center.¹²

In striking contrast, the third-generation Grubbs catalysts (**GIII**, **GIII'**) are extraordinarily active in ROMP, despite the presence of pyridine ligands.¹³ The apparent conflict between these findings may be reconciled by considering the difference in the catalyst active site. ROMP reactions are propagated by alkylidene species, where RCM and CM reactions normally involve methylidene species. The greater vulnerability of the methylidene unit to amines was pointed out in early studies by Werner and co-workers.¹⁴ Immediate loss of the methylidene group was reported at RT on treating $\text{RuHCl}(\text{CO})(\text{P}^i\text{Pr}_2\text{Ph})_2(=\text{CH}_2)$ **Ru-8** with pyridine (py, 4 equiv; Scheme 3.1a). The hydride product $\text{RuHCl}(\text{CO})(\text{P}^i\text{Pr}_2\text{Ph})_2(\text{py})$ **Ru-9** was isolated in 95% yield, but the underlying mechanism was not further explored.

Related behaviour can be recognized in a report from the Sponsler group describing rapid decomposition of **GIII-Br** and related alkylidene derivatives by 1-alkenes. **GIII-Br** itself decomposed within seconds under ethylene at RT, presumably reflecting the incompatibility of the in situ-generated methylidene species with the displaced pyridine ligand.¹⁵ Hong and Grubbs reported similar behaviour for **GIII**, and identified one of the Ru products as tris-pyridine species **Ru-10** (Scheme 3.1b).¹⁶

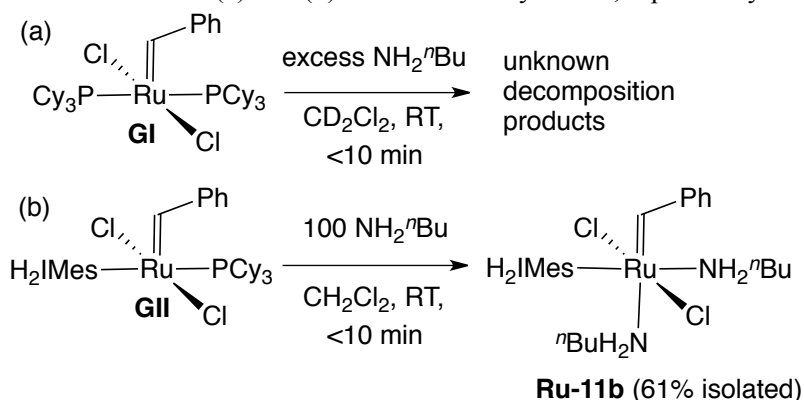
Scheme 3.1. (a) Loss of the methylidene functionality from $\text{RuHCl}(\text{CO})(\text{P}^i\text{Pr}_2\text{Ph})_2(=\text{CH}_2)$ on exposure to pyridine. (b) Rapid decomposition of **GIII** on exposure to ethylene.



Work from the Moore group notes that the first-generation Grubbs catalyst was decomposed

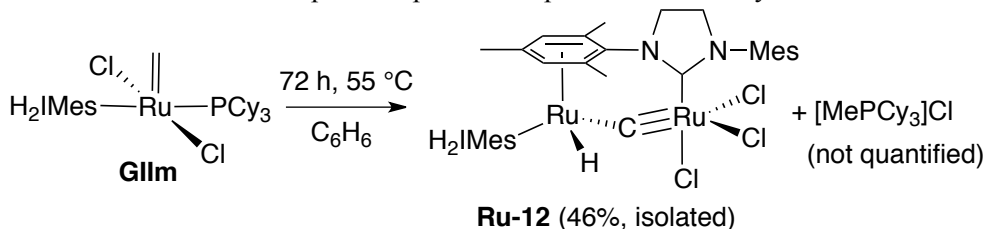
by a primary amine.¹⁷ Thus, loss of the benzyldiene moiety from **GI** was complete within 10 min at RT, on treating **GI** with excess $\text{NH}_2^{\text{n}}\text{Bu} **N1** (quantity not specified, Scheme 3.2) in CD_2Cl_2 . The products were not identified, though a bimolecular deactivation pathway was suggested. In contrast, the second-generation Grubbs catalyst **GII** retained its benzyldiene unit on treatment with **N1** (100 equiv), affording amine adduct **Ru-11b**. Importantly, **Ru-11b** was relatively efficient in ROMP, but resulted in very low conversions in RCM of diethyl diallylmalonate. This difference is consistent with the greater robustness toward free *n*-butylamine of the alkylidene intermediates, relative to their methylidene counterparts, proposed above.$

Scheme 3.2. Reactions of (a) **GI**. (b) **GII** with *n*-butylamine, reported by the Moore group.



Hong and Grubbs reported that the methylidene ligand is also thermally less robust than benzyldiene. Thus, loss of methylidene was observed on heating isolated **GIIIm** at 55 °C for 72 h.¹⁶ Products included the phosphonium salt $[\text{MePCy}_3]\text{Cl}$, formed in unspecified amounts, which was proposed to form by attack of PCy_3 at the $\text{Ru}=\text{CH}_2$ carbon. Also formed was dinuclear **Ru-12**, isolated in 46% yield based on Ru (Scheme 3.3).

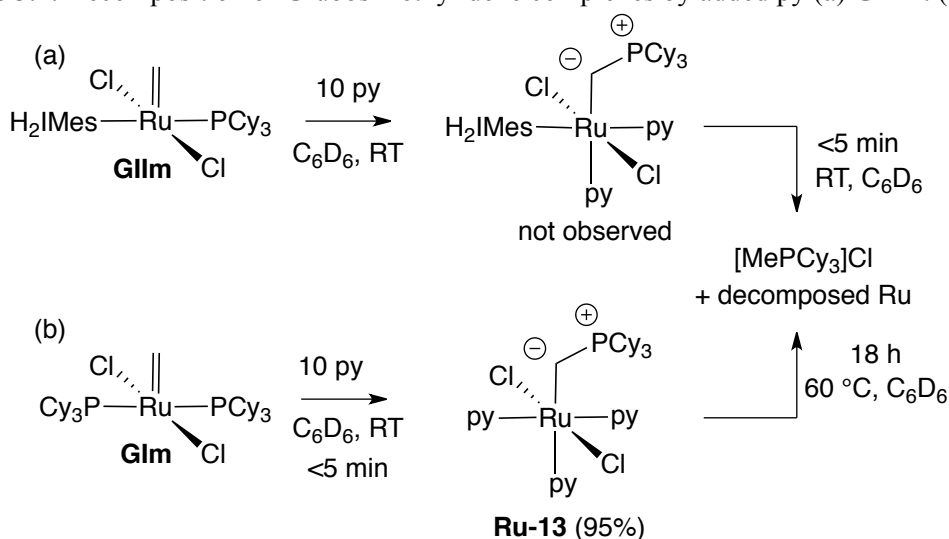
Scheme 3.3. Decomposition products reported on thermolysis of **GIIIm**.



In mechanistic studies of the methylidene complex **GIIIm**, carried out in parallel with this thesis work, the Fogg group described rapid decomposition of **GIIIm** in the presence of Lewis donors (Scheme 3.4a). Among these, amines, pyridine, and other nitrogen bases featured prominently.^{18,19} Decomposition was shown to involve donor-induced displacement of PCy_3 , nucleophilic attack of PCy_3 on the methylidene ligand to form zwitterionic σ -alkyl intermediate **Ru-13**, and release of

[MePCy₃]Cl via ensuing C-H activation. Liberation of the alkyl ligand is presumed to involve via C-H activation of the NHC ligand to furnish the proton required. A chloride ligand evidently supplies the counter-ion. The σ -alkyl intermediate formed from **GIm** was crystallographically characterized. Importantly, this species was the sole product at short reaction time, confirming that the multiplicity of products ultimately formed (including the Grubbs carbide **Ru-12**) arise from opportunistic reactions subsequent to the key deactivation event (Scheme 3.4b). A related study with ¹³C-labeled RuCl₂(PCy₃)(H₂IMes)(=CH¹³CH₂) confirmed that the [MePCy₃]Cl liberated during reaction with *n*-butylamine **N1** originated in the methylidene unit.²⁰

Scheme 3.4. Decomposition of Grubbs methylidene complexes by added py (a) **GIIIm**. (b) **GIm**.



Elucidation of the fate of the Ru=CHR moiety is crucial to understanding decomposition for olefin metathesis catalysts. Decomposition during catalysis may be mediated by the resting-state methylidene complex, as in the studies just described, by the benzyldiene precatalyst, or by metallacyclobutane intermediates. Observation of the latter is frustrated, for the dominant Grubbs- and Hoveyda-class catalysts, by facile formation of off-cycle species. In the Ru systems, they have so far only been observed in situ for the Piers catalyst.²¹⁻²³ Chapter 4 outlines indirect methods of intercepting the MCB species by use of the Hoveyda catalysts.

The work described in this Chapter focuses on the benzyldiene precatalysts, with the goal of gaining deeper insight into their reactions with amines. Preliminary experiments focus on the unstable system identified by Moore on treating **GI** with excess *n*-butylamine **N1**. The second-generation complexes **GII** and **GII'** were then examined, with a wider array of nitrogen bases.

3.2. Decomposition of the first-generation Grubbs catalyst **GI** by benzyldiene abstraction

3.2.1. Unexpected abstraction of the benzyldiene ligand from **GI** by *n*-butylamine

Initial experiments undertook a closer examination of the decomposition of benzyldiene **GI** by excess $\text{NH}_2^{\text{n}}\text{Bu}$ **N1**. A lower excess of amine was used than in the Moore study: thus, a 20 mM solution of **GI** in C_6H_6 was treated with excess **N1** (10 equiv vs. Ru). The purple solution changed colour to yellow within 1 h. GC-MS analysis of the crude mixture showed none of the stilbene product predicted to form via bimolecular deactivation. Instead, *N*-butylbenzylamine **7a** (m/z 163.1) and minor quantities of *N*-butyl-1-phenylmethanimine **7b** (m/z 161.1) were identified (Figure 3.1). Electron-ionization mass spectra of **7a** and **7b** matched an authentic sample (**7a**) or literature values (**7b**).²⁴

To quantify **7a** and **7b**, this experiment was repeated in C_6D_6 in the presence of 1,3,5-trimethoxybenzene (TMB) as an internal integration standard. ^1H NMR data collection began at 3 min, immediately after injection of butylamine. At this point, two benzyldiene doublets were observed (δ_{H} 20.58 (d, $^3J_{\text{HP}} = 13$ Hz), 20.07 (d, $^3J_{\text{HP}} = 14$ Hz)), each accounting for ca. 30% of the initial catalyst charge, and 40% loss of benzyldiene. Decomposition is complete at 25 min. A 1: 1 ratio of products was retained over the course of the reaction, suggesting an equilibrium (Figure 3.1b) between mono- and bis-amine species, $\text{RuCl}_2(\text{PCy}_3)(\text{NH}_2^{\text{n}}\text{Bu})_n(=\text{CHPh})$ ($n = 1, 2$). Consistent with the assignment of the signal at 20.07 ppm to mono-amine species **Ru-14a**, this is the sole signal observed on treating **GI** with 1 equiv **N1** (as discussed in a later section, and depicted in Scheme 3.6 below). The signal at 20.58 ppm is therefore assigned to bis-amine species **Ru-14b**, precedent for which was shown in Scheme 3.2, in the form of crystallographically-characterized $\text{RuCl}_2(\text{H}_2\text{IMes})(\text{NH}_2^{\text{n}}\text{Bu})_2(=\text{CHPh})$ **Ru-11b**. The mono-amine homologue **Ru-11a** was suggested to form on drying **Ru-11b** under vacuum, on the basis of microanalytical data that were inconsistent with the bis-amine species.¹⁷

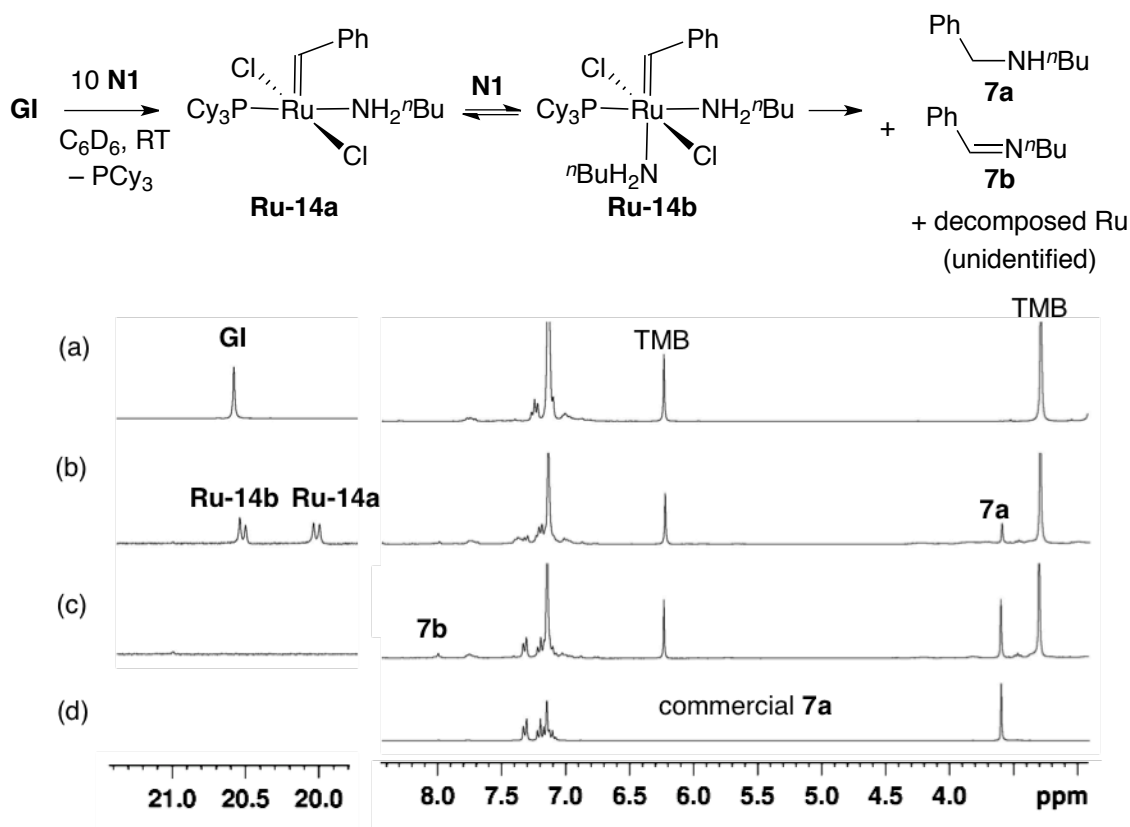


Figure 3.1. 1H NMR spectra (C_6D_6 , 300.1 MHz) of the reaction of **GI** with *n*-butylamine **N1**. (a) Spectrum before addition of **N1**; (b) 3 min after amine addition (40% decomposition); (c) 25 min after amine addition (complete decomposition); (d) commercial **7a** (Acros) for comparison.

The reaction profile is shown in Figure 3.2a. Loss of **GI** is first order in Ru (Figure 3.2b), notwithstanding Moore's original suggestion¹⁷ that decomposition occurs via bimolecular coupling of two Ru-benzylidene species. (A more detailed kinetic study was carried out with **GII**, as discussed in Section 3.3.2 below). For the **GI** experiment, no signals remained in the alkylidene region of the 1H NMR spectrum after 25 min. However, integration against an internal standard confirmed that 70% of the benzylidene moiety was converted into *N*-butylbenzylamine **7a**, which gives rise to a diagnostic methylene singlet at 3.62 ppm. Assignment as **7a** was further supported by $^{13}C\{^1H\}$ and DEPT-135 NMR analysis (δ_C 54.5, $PhCH_2N$; 49.5, $NCH_2C_3H_8$).

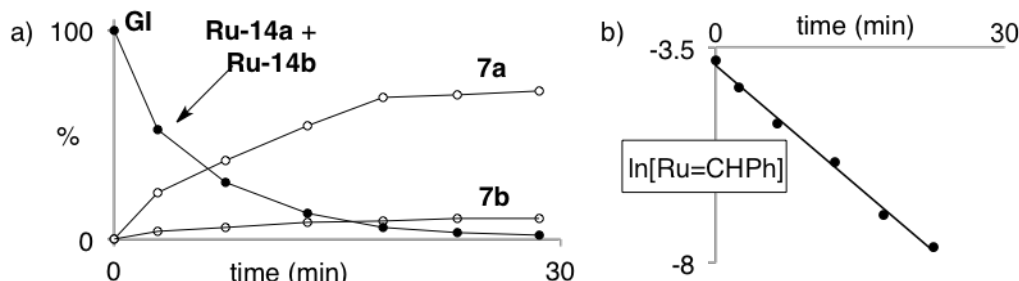
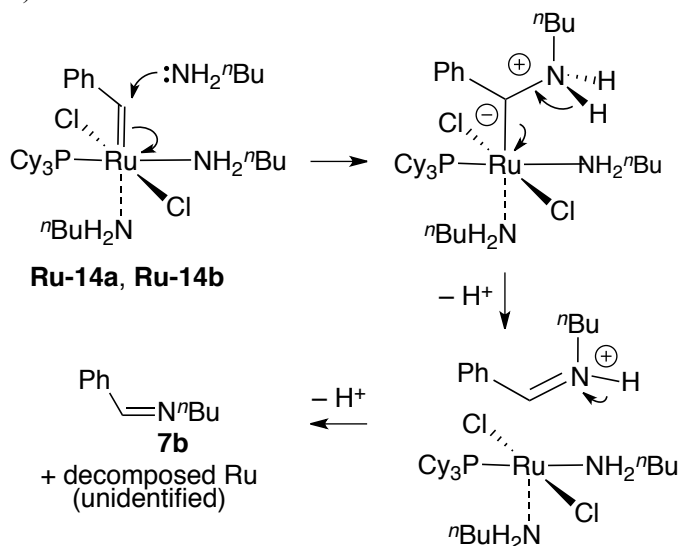


Figure 3.2. Reaction profile for decomposition of **GI** by **N1**. (a) Loss in alkylidene signal and formation of $\text{PhCH}_2\text{NH}^n\text{Bu}$ **7a** over 30 min. (b) Plot of $\ln[\text{Ru-14a} + \text{Ru-14b}]$ vs. time to 98% decomposition, % vs. TMB normalized to **GI** at t_0 (average of two trials, $\pm 2\%$).

A minor co-product, formed in ca. 10% yield based on starting **GI**, was assigned as imine derivative $\text{PhHC}=\text{N}^n\text{Bu}$ (**7b**) by GC-MS analysis (see Appendix 2, Figure A2.1a). The azomethine ($\text{CH}=\text{N}$) singlet for **7b** appeared at 8.04 ppm in C_6D_6 ; cf. the literature value of 8.27 ppm in CDCl_3 .²⁵ No change in the product distribution occurred over 4 h in solution, suggesting that **7a** and **7b** formed via competing pathways. A potential pathway is shown in Scheme 3.5. Importantly, however, *N*-butylbenzylamine **7a** accounts for the majority of decomposed **GI**. Formation of the $\text{N}-\text{CH}_2\text{Ph}$ bond in **7a** indicates abstraction of $\text{Ru}=\text{CHPh}$ by **N1**, behavior which had not previously been reported for nitrogen nucleophiles. The mechanism of benzyldiene abstraction to liberate **7a** is discussed in greater detail in Section 3.3.4 below.

Scheme 3.5. Proposed pathway for alkylidene abstraction from **GI** by *n*-butylamine **N1** to liberate the imine $\text{PhCH}=\text{N}^n\text{Bu}$ (**7b**).

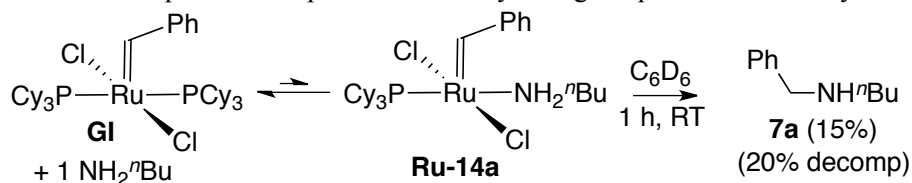


The accompanying inorganic chemistry was briefly examined. Two phosphine-containing products (δ_{P} 48.1, 36%; 46.6, 8%) were evident in the crude reaction mixture, in addition to free PCy_3 (δ_{P} 10.4, 56%). A mixture of two Ru-PCy_3 products was inferred. However, these species were not

successfully isolated. Removal of volatile components in vacuo, and washing with hexanes to remove free PCy₃, resulted in an ill-defined mixture (as judged by the emergence of multiple new ¹H and ³¹P NMR signals), suggesting decomposition on workup. While the **GI** chemistry was not probed further, similar behavior in the corresponding **GII** + **N1** reaction was traced to formation of [RuCl(NHC)(NH₂ⁿBu)₄]Cl: see Section 3.3.1. A mechanism is proposed in Section 3.3.4.

The corresponding reaction of **GI** with a single equivalent of **N1** resulted in 20% loss of benzyldiene over 1 h at RT (Scheme 3.6). Products included **7a** (15% yield) and mono-amine derivative **Ru-14a** (ca. 10%; δ_H 20.07 ppm). No further reaction occurred. Excess amine is evidently required for complete benzyldiene abstraction, likely due to retention of **N1** by Ru product(s).

Scheme 3.6. Incomplete decomposition of **GI** by a single equivalent of *n*-butylamine **N1**.

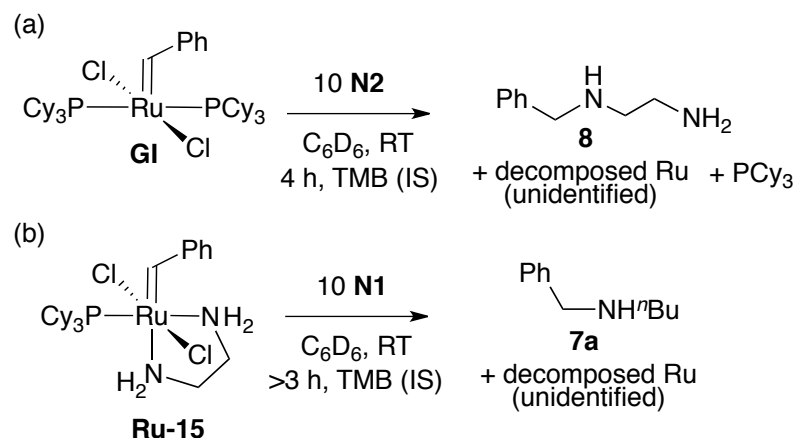


3.2.2. Benzyldiene abstraction from an ethylenediamine (en) derivative of **GI**

Similar behavior was observed for an en derivative, RuCl₂(PCy₃)(en)(=CHPh) **Ru-15**. Details of the synthesis of **Ru-15** are deferred to Chapter 5, which focuses chiefly on the synthesis and metathesis activity of new Ru metathesis catalysts bearing chelating amine ligands. Relevant to the present question, however, is the contrast between the stability of isolated **Ru-15** (which showed no decomposition for >3 days in solution at RT, and <10% after 6 h at 60 °C), and its rapid decomposition when generated in situ by treating **GI** with excess en **N2** (Scheme 3.7a). Under the latter conditions, no alkylidene signals were evident after 4 h at RT. While the expected benzyldiene abstraction product PhCH₂(NH)(CH₂)₂NH₂ **8** was not conclusively identified, broad singlets in the region 4.4–3.5 ppm would be consistent with the expected benzyl CH₂ and NH signals.* Consistent with this assignment, treatment of **Ru-15** in C₆D₆ with excess **N1** resulted in benzyldiene abstraction, forming **7a** (80% after 3 h at RT; Scheme 3.7b).

* GC-MS analysis data was not collected for this experiment.

Scheme 3.7. Abstraction of the benzyldiene ligand from **Ru-15**, and proposed products. (a) Decomposition of in situ-generated **Ru-15** by excess en **N2**. (b) Decomposition of **Ru-15** with excess *n*-butylamine **N1**.



Notable is the slower abstraction of benzyldiene from **Ru-15** by **N1**, relative to **GI** (>3 h, vs. 25 min; see Figure 3.2 above). This could reflect some degree of steric protection conferred by the coordinative saturation of **Ru-15**. More likely, however, may be the reduced electrophilicity of the benzyldiene carbon in **Ru-15** resulting from trans-coordination of an amine donor. In either case, this points toward a five-coordinate Ru complex as the more vulnerable species.

These experiments provide the first evidence that Ru benzyldiene complexes are vulnerable to direct nucleophilic attack on the Ru=CHPh carbon, a process that culminates in benzyldiene abstraction. This behavior had previously been demonstrated only for Ru-methyldiene complexes, which undergo methyldiene abstraction by free PCy₃. The greater crowding at the Ru=CHPh carbon, relative to Ru=CH₂, suggests that only sterically accessible nucleophiles should be able to trigger this pathway. Examined below is the relevance of this deactivation pathway to the important second-generation Grubbs catalysts **GII** and **GII'**, and its scope with respect to amine bulk.

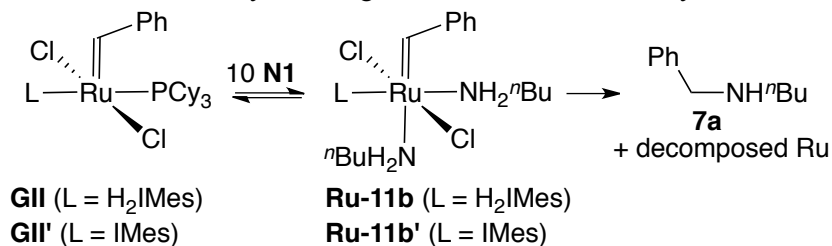
3.3. Reactions of **GII** with primary amines

3.3.1. Benzyldiene abstraction by *n*-butylamine: identification of products

In an NMR-tube experiment, **GII** was treated with a tenfold excess of NH₂^{*n*}Bu **N1** in C₆D₆ at RT. As expected, the Moore compound **Ru-11b** was the predominant product at 5 min (90% at 5 min, 19.56 ppm).¹⁷ Minor quantities of **GII** remained (8–9% vs. **Ru-11b** throughout), consistent with an equilibrium process. Instead of isolating **Ru-11b**, as in the Moore study, the reaction was left to stand for 12 h. A yellow precipitate deposited over this time, and loss of the benzyldiene signal was >95% complete, as judged by integration against an internal standard. PhCH₂NH^{*n*}Bu **7a** was identified as the major organic product (64% yield based on **GII**), as in the **GI** chemistry described in

the preceding sections.¹⁸ The yield of **7a** increased to 85% on adding a further 40 equiv **N1** (Figure 3.3c). We attribute the increase to liberation of bound **7a**.*

Scheme 3.8. Abstraction of the benzyldiene ligands from **GII** and **GII'** by excess *n*-butylamine **N1**.



Similarly, addition of a tenfold excess of **N1** to **GII'** caused emergence of a new benzyldiene singlet at 19.54 ppm (ca. 90%), accompanying minor amounts of **GII'** (8%). Loss of the benzyldiene signal was complete within 12 h at RT. The sample changed colour from pink to yellow, but remained fully soluble. Again, **7a** was the major organic decomposition product (86% yield). No evidence of $\text{PhCH=N}^i\text{Bu}$ **7b** was observed in either case by ¹H NMR or GC-MS analysis.

As with **GI** (Section 3.2), depletion of the amine adducts over time followed first-order kinetics (Figure 3.3b). Both **Ru-11b** and **Ru-11b'** proved significantly more robust than **GI** with respect to benzyldiene abstraction, requiring ca. 12 h for complete loss, vs. <30 min for **GI** under analogous conditions. The relative stability of the second-generation catalysts was in agreement with the prior Moore study (above),¹⁷ though the nature of the underlying chemistry was unchanged. The strong σ -donor NHC ligands might inductively reduce the electrophilicity of the **GII** and **GII'** benzyldienes relative to that of **GI**, though sterics cannot be ruled out as a contributing factor. Comparable rates of decomposition were evident for **GII'** and **GII** ($k_{\text{obs}} = 0.25$ and 0.22 h^{-1} , respectively) (Figure 3.3a). NHC unsaturation (IMes vs. H_2IMes) appeared to have negligible impact on the rate of benzyldiene abstraction by *n*-butylamine.

* When the reaction of **GII** with **N1** was performed in CDCl_3 , the imine **7b** (previously seen as a minor by-product in the reaction of **GI**; Figure 3.1) was generated instead, in 65% yield vs. initial **GII**. Key NMR values (CDCl_3): δ_{H} 8.27 ppm (PhHC=N); δ_{C} 161.2 ppm (PhHC=N), GC-MS m/z of $\text{M}^+ = 161.1$. The origin of this solvent effect was not examined.

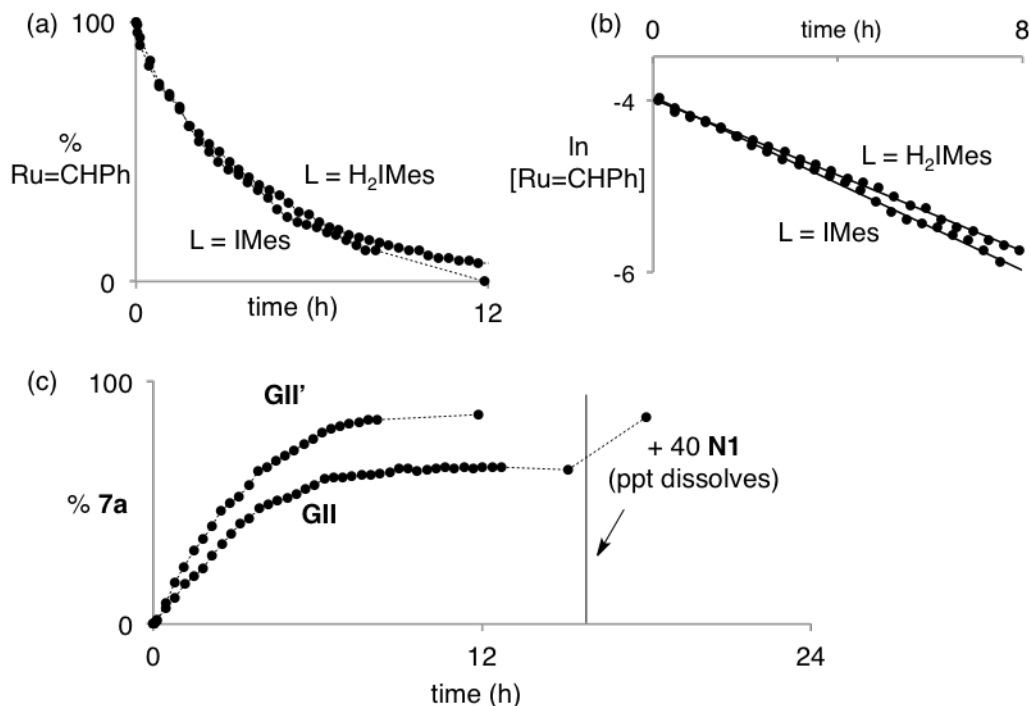
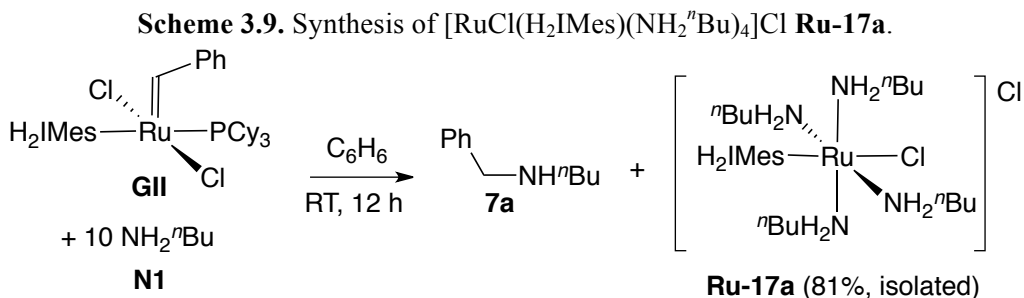


Figure 3.3. Decomposition of $\text{RuCl}_2(\text{L})(\text{PCy}_3)(=\text{CHPh})$ ($\text{L} = \text{H}_2\text{IMes}$, **GII**; IMes , **GII'**) by $\text{NH}_2^{\text{n}}\text{Bu}$ **N1**. (a) Loss of total $\text{Ru}=\text{CHPh}$ signals vs. internal standard. (b) Plot of $\ln[\text{Ru-11b} + \text{GII}]$ and $\ln[\text{Ru-11b}' + \text{GII}']$ vs. time to >95% decomposition. (c) Rate of formation of $\text{PhCH}_2\text{NH}^{\text{n}}\text{Bu}$ **7a** over the course of each reaction. % values vs. TMB internal standard normalized to **GII** or **GII'** at t_0 ($\pm 2\%$ in replicate runs for **GII** decomposition. Single-trial results for **GII'** decomposition and excess amine addition to **GII** in (c)).

Isolation of the organometallic products was not undertaken from **GII'**. Addition of a tenfold excess of **N1** in C_6D_6 resulted in emergence of multiple products, as judged from the emergence of more than a dozen ^1H NMR peaks in the region occupied by the methine and methylene signals (6.9–6.0 ppm, total 6 H vs. IS). That these species are phosphine-free is inferred from observation of solely free PCy_3 by $^{31}\text{P}\{^1\text{H}\}$ NMR analysis. The complexity of the ^1H NMR spectrum could reflect fluxionality or multiple decomposition products.

Greater success was obtained with the corresponding reaction with **GII**, from which (as noted above) a yellow precipitate deposited over 12 h. This reaction was repeated on 200 mg scale, and worked up after 24 h by removing volatiles under vacuum and extracting free **N1**, **7a**, and PCy_3 with hexanes. The yellow product, $[\text{RuCl}(\text{H}_2\text{IMes})(\text{NH}_2^{\text{n}}\text{Bu})_4]\text{Cl}$ **Ru-17a**, was filtered off and dried (81% yield, Scheme 3.9). The identical product was isolated from decomposition of **III**, as discussed in the published work of Chapter 4, which presents details of the structural assignment.



3.3.2. Benzyldiene abstraction from amine adducts of **GII** as compared with **GII**

Treating **GII** with a larger excess of $\text{NH}_2^{\text{n}}\text{Bu}$ **N1** (40 equiv) effected complete conversion into amine adduct **Ru-11b** within 3 min. Loss of benzyldiene was ca. 10% at this point, and was quantitative after ca. 8 h (Figure 3.4). The observed rate constant k_{obs} doubled, relative to the reaction with 10 equiv **N1** (Table 3.1). (The fact that it did not quadruple may indicate that the rate is saturated in amine). The rate dependence on amine concentration is consistent with recent work by Mr. William McClennan of this research group, which has demonstrated a first-order rate dependence on added donors (pyridine, dmsO, etc.) in decomposition of first- and second-generation methylidene complexes.

In contrast, addition of PCy_3 (10 equiv) inhibited decomposition of **GII**. Benzyldiene abstraction was incomplete even after 12 h (77%, vs. >95% in the absence of added PCy_3), and the observed rate constant halved (to $k_{\text{obs}} = 0.11 \text{ h}^{-1}$, vs. 0.22 h^{-1}). This inhibition is due to shifting of the equilibrium to favor **GII**, the steric bulk of which deters approach of amine to the benzyldiene carbon. From the perspective of catalysis, however, this protective effect of excess phosphine would be offset by inhibited initiation. Improved catalyst lifetime would thus not translate into increased productivity (higher metathesis yields).

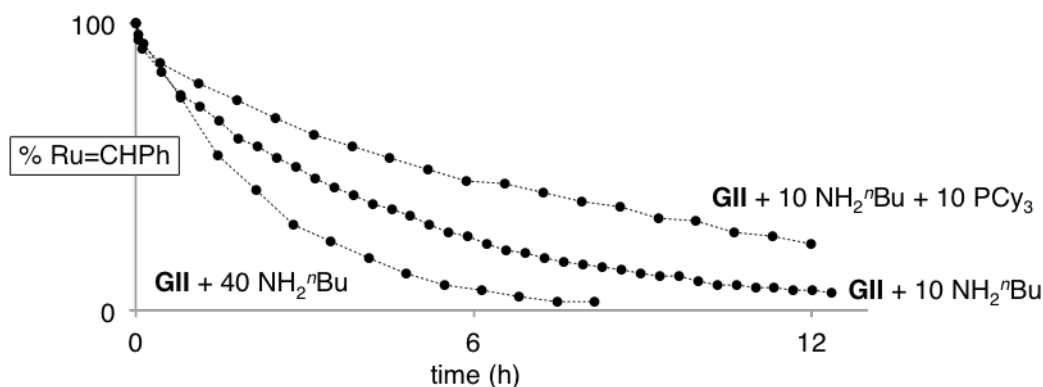


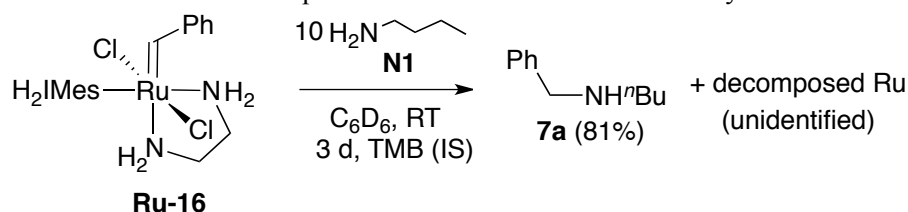
Figure 3.4. Benzyldiene abstraction from **GII** with excess **N1**: impact of added PCy_3 and **N1**. Values represent total $\text{Ru}=\text{CHPh}$ integration (vs. TMB, normalized to $\text{Ru}=\text{CHPh}$ at t_0).

Table 3.1. Summary of kinetic data for benzyldiene abstraction from **GII** by $\text{NH}_2^{\text{n}}\text{Bu}$ **N1**.

Added N1 (equiv vs. GII)	Added PCy_3 (equiv vs. GII)	decomp. at 12 h (%)	free 7a at 12 h (%)	Apparent rate constant (k_{obs} , h^{-1})
10	—	95	64 ^a	0.22
40	—	quant.	83	0.44
10	10	77	52	0.11

^a In situ yields increased to 85% following addition of a further 40-fold excess of **N1** to solubilize the precipitate.

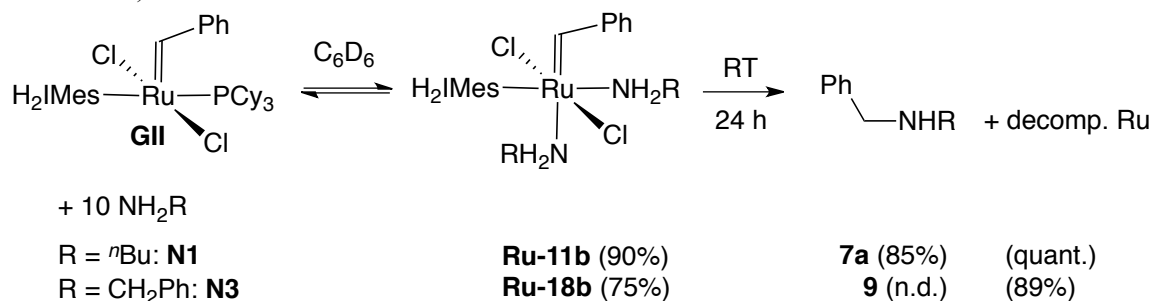
Similar reactions were explored with the en adduct **Ru-16** (synthesis of which is described in Chapter 5). As with the first-generation complex **Ru-15**, **Ru-16** was stable when isolated, but vulnerable to benzyldiene abstraction on treatment with *n*-butylamine **N1**. Thus, no decomposition was noted vs internal standard after heating isolated **Ru-16** to 60 °C for 24 h in C_6D_6 . On treating **Ru-16** with 10 equiv **N1** at RT, however, loss of the benzyldiene moiety was complete after 3 days (47% decomposition after 24 h; cf. >95% at 12 h for **GII**). *N*-butylbenzylamine **7a** (81%) was observed as the major organic product (Scheme 3.10). As noted for the **Ru-15** / **GI** comparison above, the slower decomposition of the en derivative reflects a greater stability for the coordinatively-saturated compound.

Scheme 3.10. Decomposition of **Ru-16** with excess *n*-butylamine **N1**.

3.3.3. Reactions of **GII** with larger primary amines

Having established the capacity of *n*-butylamine **N1** to abstract the benzyldiene ligand, the steric restrictions on this reaction were explored. Adding 10 equiv benzylamine **N3** to **GII** in C_6D_6 afforded free PCy_3 and a phosphine-free species characterized by a benzyldiene singlet at 19.57 ppm. The latter is assigned to bis-amine complex **Ru-18b** (Scheme 3.11), by analogy to bis-*n*-butylamine complex **Ru-11b**. The equilibrium yield of **Ru-18b** was lower than that seen for **N1** (ca. 75%, vs. 91%, exclusive of decomposition). This is consistent with the higher steric bulk and lower basicity of benzylamine (conjugate acid $pK_a = 16.9$ for **N3** in MeCN, vs. 18.3 for **N1**).²⁶ The reduced nucleophilicity of the amine nitrogen is also manifested in slower attack on the benzyldiene carbon. After 24 h at RT, $\text{Ru}=\text{CHPh}$ signals could still be observed (11%). Dibenzylamine **9** was observed by GC-MS analysis of a reaction aliquot. No imine product was observed. Quantification of **9** by ^1H NMR analysis was hampered by peak overlap with excess **N3**.

Scheme 3.11. Slow benzyldiene abstraction on reaction of **GII** with benzylamine **N3**. (N.D. = not determined).



The corresponding experiments with *sec*-butylamine ($\text{NH}_2^{\text{sec}}\text{Bu}$, **N4**) and *t*-butylamine (NH_2^tBu , **N5**) were aimed at examining the influence of steric bulk without significantly altering amine basicity (conjugate acid pK_a : 18.1–18.3 in MeCN).²⁶ Equilibrium conversion to a single new $[\text{Ru}]=\text{CHPh}$ species (Scheme 3.12) was observed on treatment of **GII** with 10 equiv **N4** or **N5** (Table 3.2). In each case, a mixture of free PCy_3 and **GII** was observed, but the equilibrium yield of the amine adduct decreased with increasing amine bulk (62% adduct for **N4**, 21% for **N5**; cf. 90% for **N1**, exclusive of decomposition). Equilibrium was achieved with **N4** and **N5** within 1 h at RT with no changes even after 24 h at 60 °C (Table 3.2). These data indicate that benzyldiene abstraction is inhibited by steric bulk α to the butylamine nitrogen. Indeed, incorporation of steric bulk α to the amine nitrogen completely suppresses benzyldiene abstraction, instead resulting in selective formation of mono-amine adducts.

Scheme 3.12. Adduct formation on reaction of **GII** with sterically less accessible primary amines, *sec*-butylamine **N4** and *t*-butylamine **N5**.

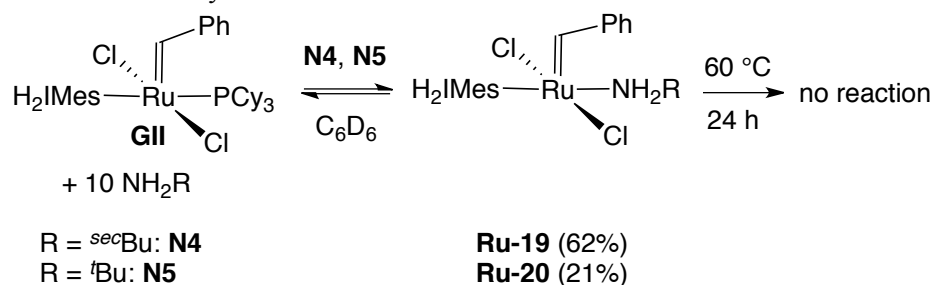
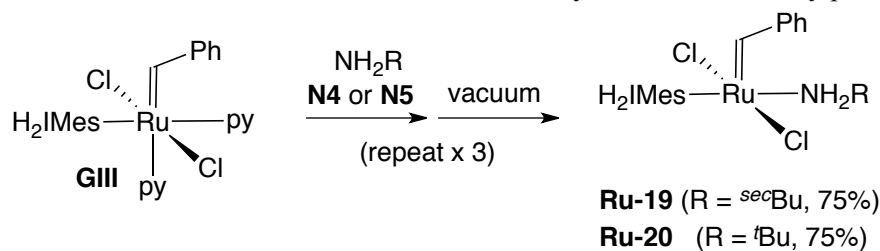


Table 3.2. Equilibrium yields and ^1H NMR data for new $[\text{Ru}]=\text{CHAr}$ species formed by reaction of **GII** with primary amines (10 equiv). Also shown is the proportion of the benzyldiene-abstraction product PhCH_2NHR observed.

Amine (NH_2R)	$\text{Ru}=\text{CHAr}$ δ_{H} ; (equilibrium yield, %)	time, temp	% decomp.
control	19.65	24 h, 60 °C	not observed
N1 , $\text{R} = ^n\text{Bu}$	19.56 (90) ^a	3 min, RT	6
		12 h, RT	>95
N3 , CH_2Ph	19.57 (75) ^a	15 min, RT	12
		24 h, RT	89
N4 , $^{\text{sec}}\text{Bu}$	19.58 (62)	24 h, 60 °C	not observed
N5 , ^tBu	19.63 (21) ^b	24 h, 60 °C	not observed

^a equilibrium for unstable mixtures determined from first available timepoint (3–15 min), exclusive of decomposition to show equilibrium position. ^b $[\text{Ru}]=\text{CHPh}$ signals not independently resolved. Ratio of **GII** / **Ru-20** estimated by $^{31}\text{P}\{^1\text{H}\}$ NMR (**GII** vs. free PCy_3).

Attempted isolation of the **Ru-19** or **Ru-20** adducts directly from **GII** was unsuccessful. Precipitation from hexanes – a strategy successfully employed for other amine adducts described in Chapter 5 – resulted only in recovery of the precursor **GII** after 24 h at RT. However, both species were successfully isolated in ca. 75% yield by repeatedly treating **GIII** with amine and removing excess pyridine in vacuo (Scheme 3.13). ^1H NMR analysis for each isolated complex was consistent with a mono-amine adduct: $\text{RuCl}_2(\text{H}_2\text{IMes})(\text{NH}_2\text{R})(=\text{CHPh})$ ($\text{R} = ^{\text{sec}}\text{Bu}$, ^tBu).

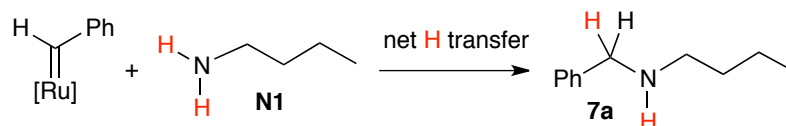
Scheme 3.13. Isolation of mono-amine derivatives of **GII** by reaction with bulky primary amines.

3.3.4. Proposed mechanism for benzyldiene abstraction by primary amines

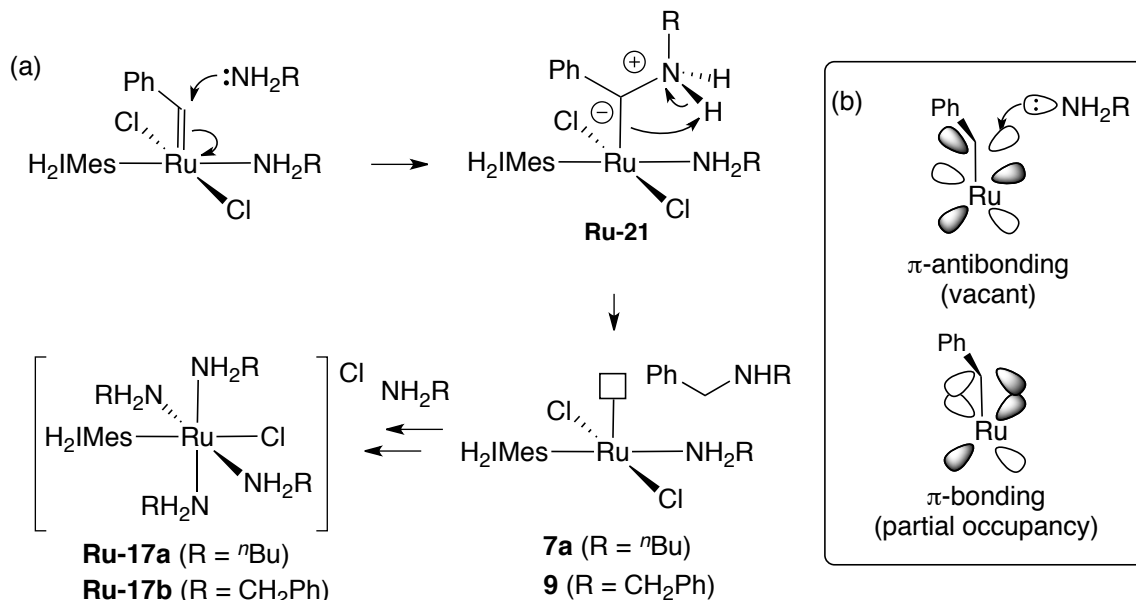
Several inferences may be drawn from the studies described above. Benzyldiene abstraction follows first-order kinetics with respect to precatalyst, ruling out the possibility of bimolecular coupling of Ru entities. The high stability of isolated **Ru-15** and **Ru-16** in the absence of excess amine suggests that benzyldiene abstraction does not occur via an inner-sphere process. Further, the much slower rate at which excess **N1** decomposes **Ru-15**, relative to **GI**, suggests that attack occurs preferentially on a five-coordinate, rather than a six-coordinate species.

Finally, and perhaps most obviously, formation of the products PhCH_2NHR ($\text{R} = {}^n\text{Bu}$, CH_2Ph) requires net transfer of a proton from amine to alkylidene (Scheme 3.14). This does not appear to involve C-H activation. The possibility that this proton originates in the benzyldiene unit (by analogy to the “Grubbs carbide” **Ru-12** of Scheme 3.3) is ruled out based on the high in situ yield of **7a** (85%). Activation of a mesityl methyl group is likewise excluded, based on the structure of **Ru-17a** (81% isolated yield), which exhibits an intact H_2IMes ligand. More likely, N-H bond activation supplies the required proton, as discussed below.

Scheme 3.14. Benzyldiene abstraction requires net transfer of one H (red) from amine: illustrated with $\text{NH}_2{}^n\text{Bu}$.



A possible mechanism is given in Scheme 3.15. Initial nucleophilic attack is proposed to occur from a five-coordinate amine adduct, as discussed above. Precedent for formation of a σ -alkyl intermediate (**Ru-21**) is given by prior studies from Hofmann²⁷ and by Diver.²⁸ Intermediate **Ru-21** is further supported by isolation of the related complex **Ru-13** (Scheme 3.4, above) in related studies within the Fogg research group. Ru σ -alkyl species are highly reactive and readily promote E-H activation to liberate the alkyl ligand.^{19,28-30} A concerted 1,2-proton shift, conceptually analogous to a Stevens rearrangement,³¹ would provide the necessary H-transfer step (Scheme 3.15). Following release of the organic product, coordinative saturation and migration of the chloride ion to the outer coordination sphere occurs, forming a Ru product analogous to **Ru-17a**. Similar behavior has been established for related Ru(II) nitrile complexes.³²

Scheme 3.15. (a) Proposed mechanism for abstraction of the benzyldiene ligand by primary amines (**N1**, **N3**) and (b) proposed molecular orbital (MO) interaction for the initial nucleophilic attack.^a^a The electrophilic nature of the Ru=CHPh bond has been described in computational work by Jensen.³⁴

3.4. Reactions of **GII** with secondary amines and larger N-donors

Finally, we examined the reactions of **GII** with a range of nitrogen nucleophiles of varying basicity: morpholine **N6**, pyrrolidine **N7**, pyridine **N8**, DBU **N9** (DBU = 1,8-diazabicycloundec-7-ene), and triethylamine **N10** (conjugate acid *pK_a* in MeCN: 12.6–24.1).²⁶ No reaction was observed between NEt₃ and **GII**, even after 24 h at 60 °C. In all other cases, stable adducts were formed. Equilibrium yields ranged from 55% to 94% within 1 h at RT, and no loss of the benzyldiene signals was observed over 24 h at 60 °C (Table 3.3, Scheme 3.16).

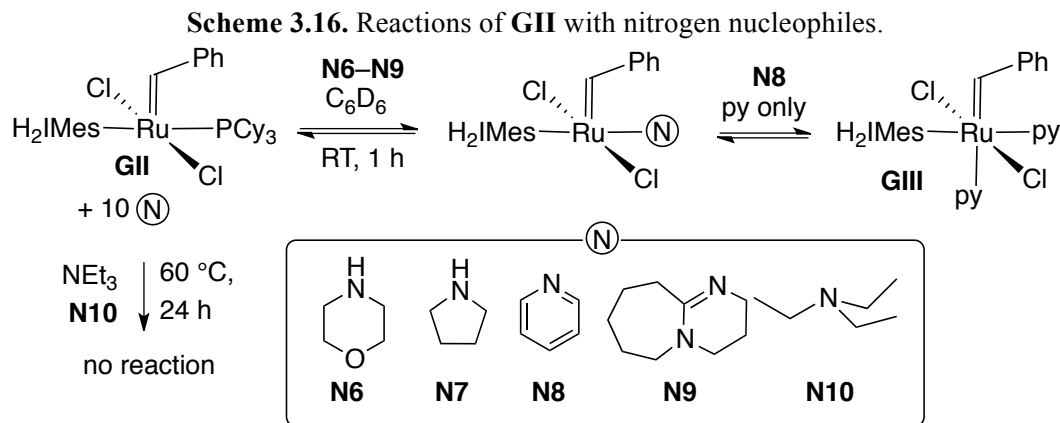
Table 3.3. Equilibrium yields and chemical shift of the benzyldiene proton for **GII**-amine adducts (10 equiv amine).^a

N-donor	equilibrium yield, %)	δ _H
none	—	19.65
morpholine N6	65	19.73
pyrrolidine N7	94	19.67
pyridine N8	55	19.83
DBU N9	75	19.93
triethylamine N10	0	—

^aAll values quantified vs. TMB internal standard after 1 h at RT (reproducible ±2.5%, mass balance **GII**). No changes were observed after heating to 60 °C for 24 h in any case.

The bis-pyridine adduct, **GIII**, has been previously reported.³³ The derivatives of morpholine, pyrrolidine, and DBU¹⁸ were isolated in 60–80% yield by selective precipitation from hexanes. NMR data for the isolated compounds were identical to those observed in situ. ¹H NMR

characterization and microanalysis support assignment as the mono-amine complexes. Characterization of these complexes is described in Chapter 5, which addresses synthesis and characterization of related Grubbs amine adducts.



3.5. Conclusions and future work

Low yields for nitrogen-containing metathesis reactions are generally attributed to Lewis behavior: that is, coordination of nitrogen to Ru. This is insufficient, however, to account for the detrimental impact of such species on metathesis. A negative impact on turnover frequency is expected if the amine ligands are less labile than PCy_3 , but should not affect turnover number. This Chapter presents a closer examination of the underlying organometallic chemistry of ruthenium alkylidenes with amines, and provides the first evidence that these species can decompose via facile alkylidene-abstraction pathways.

Benzyldiene abstraction by sterically accessible primary amines is established as general for **GI**, and for the second-generation catalysts **GII** and **GII'**. Kinetic analysis revealed a first-order dependence on Ru-benzyldiene concentration, ruling out an earlier-proposed bimolecular decomposition pathway. For **GII**, addition of PCy_3 inhibited decomposition, implying that benzyldiene abstraction occurs from NH_2^tBu adducts formed in situ, rather than **GII** itself. Accordingly, increasing the concentration of amine increased the rate of decomposition. Five-coordinate amine adducts are most vulnerable to benzyldiene abstraction.

Key to these findings was identification of the fate of the benzyldiene ligand. The benzyl derivatives PhCH_2NHR ($\text{R} = ^t\text{Bu}, \text{CH}_2\text{Ph}$) were assigned by NMR and mass spectrometric analysis. For the reaction of **GII** with **N1**, the Ru coproduct was also successfully isolated in high yield (>80%), and identified as $[\text{RuCl}(\text{H}_2\text{IMes})(\text{NH}_2^t\text{Bu})_4]\text{Cl}$ **Ru-17a**. The intact NHC ligand present **Ru-17a** is important evidence that benzyldiene abstraction does not occur via C–H activation of the

H₂IMes ligand. Instead, H-transfer from bound amine to Ru=CHAr is proposed, following initial formation of a σ -alkyl intermediate.

While benzyldiene abstraction for **GII** was observed with benzylamine (**N3**), it was inhibited for larger nucleophiles (NH₂^{sec}Bu, NH₂^tBu, pyrrolidine, morpholine, pyridine, DBU). The benzyldiene functionality thus appears to be sterically protected against nucleophilic abstraction, although it remains vulnerable to sterically unencumbered nucleophiles (**N1**, **N3**). The relevance of this decomposition pathway during catalysis is explored in greater detail in Chapter 4.

The rate dependence of alkylidene abstraction on Ru=CHPh concentration was determined, as described above. The rate dependence on amine concentration is of potentially greater interest. Due to the protective influence of PCy₃ and relative vulnerability of five-coordinate amines adducts, this question was not easily assessed using **GI**, **GII**, or **GII'**. Phosphine-free, coordinatively saturated en adduct **Ru-16** might prove a more convenient model for assessing amine rate dependence. A kinetic study (as shown in Figure 3.3) at a range of amine concentrations (e.g. 1–10 equiv. NH₂ⁿBu vs. Ru) might prove more convenient for this purpose. Longer-term recommendations for future experimental work are discussed in Chapter 6.

3.6. References

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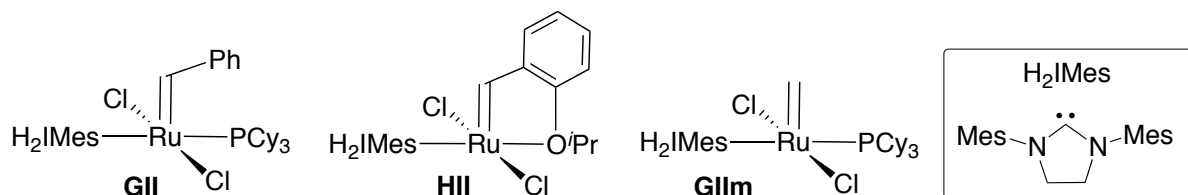
Chapter 4. The Impact of Nitrogen Bases on the Stability and Metathesis Performance of the Hoveyda Catalyst: Alkylidene and Proton Abstraction Pathways

Sections 4.1–4.3 reprinted with permission from: Ireland, B. J., Dobigny, B. T., Fogg, D. E. *ACS Catalysis*, **2015**, 5, 4690–4698. Copyright 2015 American Chemical Society.*

4.1. Introduction

Olefin metathesis offers exceptional power and efficiency in the assembly of carbon-carbon bonds.¹ The development of readily-handled, highly active ruthenium catalysts (preeminently the second-generation Grubbs and Hoveyda catalysts **GII** and **III**; Chart 4.1)^{2,3} led to widespread uptake of these methodologies in organic synthesis. Notwithstanding the importance of metathesis in the synthesis of alkaloids and other nitrogen heterocycles,⁴ however, compounds bearing sterically accessible nitrogen sites challenge the functional-group tolerance of these catalysts.^{5–7}

Chart 4.1. Metathesis catalysts discussed, and the resting-state methylidene complex for **GII**.



Reports from pharma highlight the destructive effect on metathesis of even traces of morpholine, DBU (1,8-diazabicyclo[5.4.0]-undec-7-ene), and other nitrogen bases.^{8–10} Likewise, metathesis of amine-bearing substrates has long been known to require either *N*-protection,[†] or an adjacent substituent to block access to and/or withdraw electron density from the nitrogen site.^{5–7} The Cossy group recently extended the latter strategy to metathesis of *N*-heteroaromatic compounds.¹³ For protected amines, a survey of recent examples^{14–22} illustrates moderate to excellent metathesis yields. Reaction is relatively slow even at high catalyst loadings, however, suggesting competing catalyst deactivation.

A clear understanding of the processes by which catalysts decompose is key to designing solutions.^{23–25} The deleterious effect of sterically accessible amine and pyridine donors on metathesis

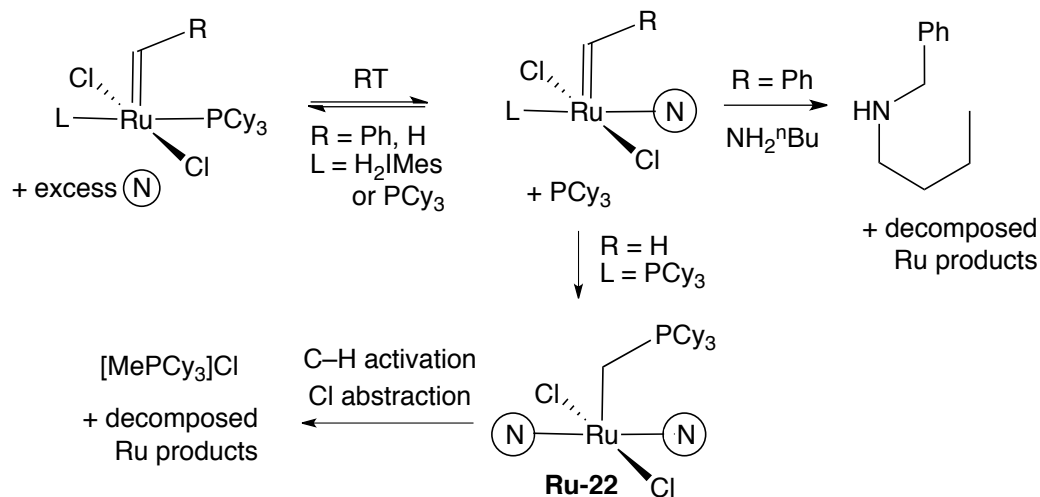
* Compound numbers have been modified for consistency throughout the thesis. For a Table of Compound Numbers and Structures, see p. VII. For Experimental, see Chapter 2, Section 2.3.1.

† For an early report noting the importance of protecting groups in RCM of amine-containing substrates, see Ref. 11. For an excellent overview of effective and undesirable protecting-group strategies, and the inhibiting effect of carbonyl chelation, see Ref. 7. For later updates, see Refs. 5,6. Robinson and co-workers have reported the efficacy of simple ammonium salts, where solubility permits.¹²

is widely presumed to be due to their excellent Lewis basicity,^{6,7,13} owing in large part to studies of the Grubbs catalysts.²⁶⁻²⁹ Particularly damaging, even toward the robust precatalyst **GII**, are sterically accessible primary amines. We recently demonstrated that *n*-butylamine abstracts the benzylidene ligand from **GII** over several hours at room temperature (Scheme 4.1, top).^{27,28*} In contrast, secondary amines,²⁷ DBU,²⁷ and pyridine³⁰ form stable adducts with **GII**.

Much more vulnerable is the resting-state methyldiene complex **GIIIm**. Amines greatly accelerate decomposition of this species.^{27,28} Such donors cause complete loss of the methyldiene ligand over hours at RT, a process that requires days for **GIIIm** at 55 °C in the absence of amine.²⁹ In both cases, decomposition occurs via dissociation of the PCy₃ ligand, which then abstracts the methyldiene ligand. Consistent with the general pathway depicted in Scheme 4.1 (bottom), we recently intercepted and crystallographically characterized the σ -alkyl species **Ru-22** for the first-generation Grubbs catalyst RuCl₂(PCy₃)₂(=CHPh) **GI**.³¹

Scheme 4.1. Amine-induced deactivation of the Grubbs catalysts.



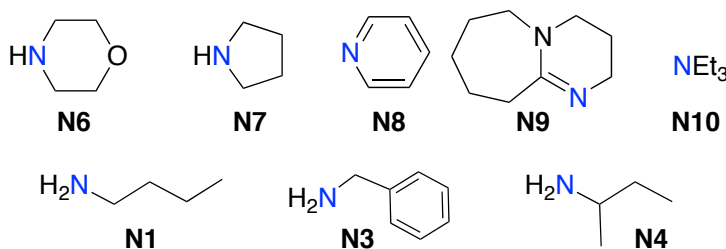
While free PCy₃ plays a central role in this decomposition chemistry, a related pathway can be envisaged for phosphine-free catalysts: that is, attack on the methyldiene ligand by nitrogen nucleophiles, in place of PCy₃. Despite the growing importance of **III** and its congeners, the decomposition behavior of such phosphine-free catalysts has seen little attention.[†] In the present

* Moore and co-workers reported that the first-generation Grubbs catalyst is immediately decomposed to non-alkylidene products by excess NH₂ⁿBu. They also isolated the first amine adduct of **GII** (61% yield) via use of low temperatures and short reaction times.²⁶

† In a rare study of the decomposition of **III**, Bessalova and co-workers reported that the catalyst is completely decomposed by ethylene after 24 h at 55 °C (C₆D₆). Organic products included propylene, 2-butene, and minor quantities of ArCH=CHCH₃ (Ar = *o*-C₆H₄-OⁱPr).³² Hong and Grubbs noted that the Ru products are unidentified hydrides.²⁹ The Piers group reported that decomposition of ruthenocyclobutane RuCl₂(H₂IMes)(κ^2 -C₃H₆) on warming above -25 °C in CD₂Cl₂ afforded propylene as the major decomposition product.³³

study, we examined the reactions of nitrogen bases with **HII** in the presence and absence of metathesis substrates. The bases selected for study (Chart 4.2) include examples highlighted in the literature as particularly deleterious, with the addition of others (pyrrolidine **N7**, NEt_3 **N10**) designed to gauge the effect of amine bulk and basicity. Here we report that Bronsted basicity – specifically, proton abstraction from the metallacyclobutane intermediate – is the primary contributor to deactivation of **HII** during metathesis. Lewis basicity is found to play a significant role only for the smallest, most accessible primary amines.

Chart 4.2. Nitrogen bases studied, with binding site shown in blue.



Prior to examining the impact of these additives on **HII** during catalysis, we established the reaction chemistry in the absence of substrate. These experiments are important to dissect out the respective roles of the metallacyclobutane or other intermediates, relative to **HII** itself. They carry further weight given that **HII** functions as not only the pre-catalyst, but also a key resting state during metathesis.³⁴ Despite the presence of the oxygen donor in the styrenyl ether ligand, the chemistry of **HII** itself was found to parallel that previously communicated²⁷ for reaction of **GII** with a subset of these donors.

4.2. Adduct formation on reaction of **HII** with N-donors

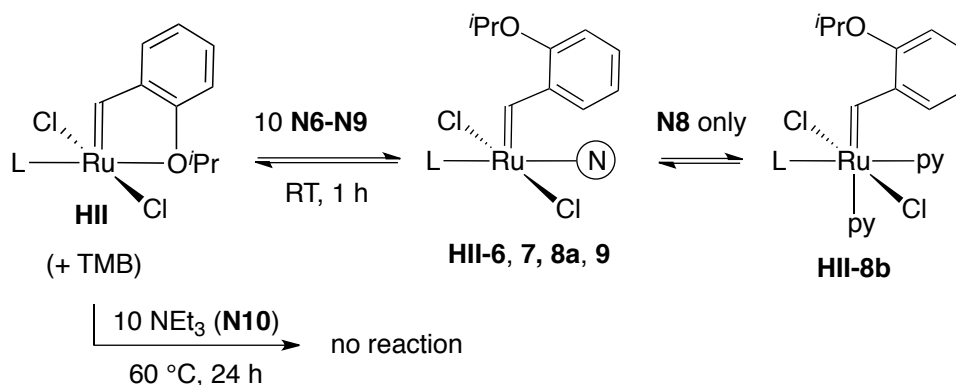
In a series of NMR experiments, **HII** was treated with a tenfold excess of **N1**, **N3-N4**, and **N6-N10** in C_6D_6 , in the presence of an internal integration standard (TMB, trimethoxybenzene) to enable quantification of non-alkylidene Ru products. As shown in Scheme 4.2 and described below, stable adducts were observed for the secondary amines, pyridine, and DBU (**N6 to N9**), while no reaction was evident for NEt_3 **N10**, even at 60 °C.

For the adducts of **N6 to N9**, a new singlet for the alkylidene proton was observed in the region 20.0–20.7 ppm (Table 4.1). Diagnostic for release of the chelated ether oxygen is the downfield location of this signal relative to that for **HII** at 16.72 ppm.* Release of the chelate is

* Precedent for a downfield shift in the $[\text{Ru}]=\text{CHAr}$ signal following adduct formation is found in the data reported for the PCy_3 adduct of **HII**, $\text{RuCl}_2(\text{H}_2\text{IMes})(\text{PCy}_3)(=\text{CHAr})$ (where Ar is the non-chelated aryl group)

further supported by the upfield location of the $CHMe_2$ septet, for which the midpoint appears between 4.2-4.0 ppm, near that of the free styrenyl ether (4.15 ppm). In comparison, a midpoint of 4.48 ppm is found for this signal in **III** itself. A through-space interaction between the isopropoxy $CHMe_2$ methine and the alkylidene proton was confirmed by NOE experiments with the pyrrolidine adduct **III-7**. Control experiment showed no such NOE effect for **III** itself, in which the position of the isopropoxy group is locked by chelation.

Scheme 4.2. Reaction of **III** with di- or trisubstituted *N*-donors.^a



^aL = H₂IMes. For primary amines (**N1**, **N3**, **N4**), see below.

Table 4.1. Key ¹H NMR data and equilibrium yields for *N*-adducts of **III** and **GII**.^a

<i>N</i> -donor	III adducts δ_H (equilibrium yield, %)	GII adducts ^{27,*} δ_H (equilibrium yield, %)
none	16.72	19.65
morpholine (N6)	20.39 (71)	19.73 (65)
pyrrolidine (N7)	20.25 (100)	19.67 (94)
pyridine (N8)	19.97 (100)	19.83 (55)
DBU (N9)	20.71 (74)	19.93 (75)
triethylamine (N10)	no reaction	no reaction
NH ₂ ^{<i>n</i>} Bu (N1)	19.81 (95), ^b 18.58 (5)	19.56 (90) ^{b,d}
NH ₂ CH ₂ Ph (N3)	19.74 (78), ^b 18.84 (22)	19.57 (75)
NH ₂ ^{<i>sec</i>} Bu (N4)	20.00 (100) ^c	19.58 (62)

^aChemical shift of [Ru]=CHAr (C₆D₆, 500 MHz). Equilibrium yields in brackets, exclusive of decomposition. ^bAssigned as bis(amine) adduct; see text. ^cValue at -20 °C in C₇D₈ (br s at RT). ^dCf. value of 18.96 reported²⁶ for **Ru-11b** at -30 °C in CD₂Cl₂.

The resulting adducts were thermally stable at 60 °C, showing no detectable decomposition after heating for 24 h. A dynamic equilibrium between the adducts and **III** is operative, as indicated

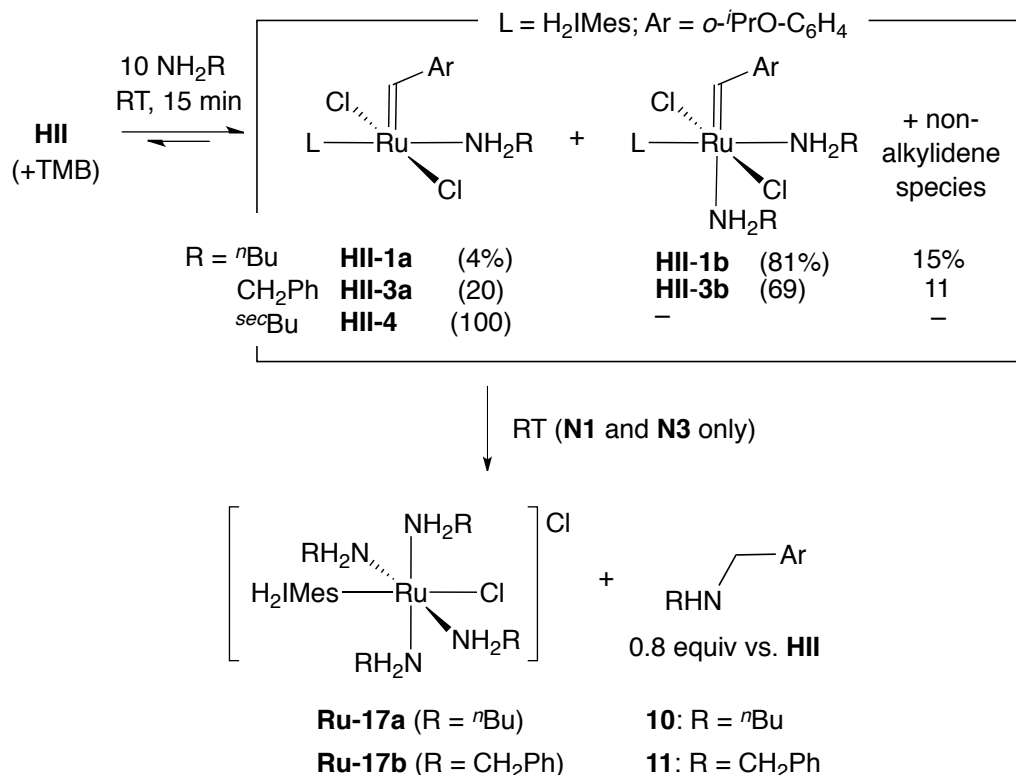
o-^{*i*}PrO-C₆H₄). This signal appears at 19.88 ppm (CDCl₃).³⁵ In comparison, a value of 16.56 ppm was reported for **III** itself in CDCl₃ solvent.³⁶

* Data for **N3**, **N4** with **GII** added post-publication, for completeness.

by ^1H EXSY experiments with **HII-7**, which exhibited a correlation cross-peak between the alkylidene signals for **HII** and **HII-7** (see Appendix 1) Partial reversion to **HII** was induced on exposure to vacuum, consistent with an equilibrium reaction.*

In comparison, treating **HII** with **N1** (Scheme 4.3) resulted in immediate formation of mono- and bis-amine adducts: no **HII** was visible, but 9% loss of alkylidene was evident at the time of the first NMR measurement (4 min), increasing to 15% at 15 min. The dominant product ($[\text{Ru}]=\text{CHAr}$ δ_{H} 19.81 ppm) is assigned as bis-amine adduct **HII-1b**, by analogy to the structure crystallographically established for **Ru-11b**.²⁶ Mono-amine derivative **HII-1a** was present in minor amounts (δ_{H} 18.58 ppm, <5%). The analogous mono-amine complex was not observed for **GII**, but reportedly formed via loss of amine on drying **Ru-11b** under vacuum.^{26,27}

Scheme 4.3. Reaction of **HII** with primary amines.



Ensuing benzyldiene abstraction by **N1** was slightly faster than in the **GII** system.²⁷ Loss of alkylidene was complete after 12 h at RT (vs. 95% for **GII**), and the diagnostic methylene singlet for

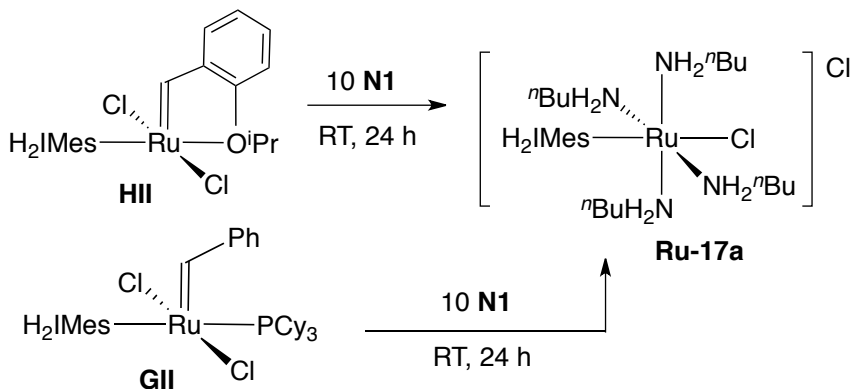
* Subsequent to publication, isolation of the **HII**–pyrrolidine adduct was attempted by precipitation from hexanes to circumvent exposure to vacuum. ^1H NMR analysis indicated a 2:1 mixture of **HII-7** and **HII**. ^1H NMR signals for the pyrrolidine subunit were not independently resolved; however, the aliphatic signals between 3.9–0.3 ppm were consistent with one pyrrolidine per Ru. On diluting the NMR twofold, the product ratio changed to 1 : 1 within 30 min, indicating a concentration-dependent equilibrium.

the amine product $\text{NH}(^n\text{Bu})(\text{CH}_2\text{Ar})$ **10** ($\text{Ar} = \text{C}_6\text{H}_4\text{-}o\text{-O}^i\text{Pr}$) was evident at 3.93 ppm (0.8 equiv vs. starting **III**).^{*}

The corresponding reactions with benzylamine **N3** proceeded similarly, affording mono- and bis-amine derivatives **III-3a** and **III-3b** (Scheme 4.3; Table 4.1). Decomposition was much slower, however, presumably reflecting the greater bulk and lower basicity[†] of the amine. Thus, after 96 h, the alkylidene signal for the **III-3b** adduct was still observable at 19.74 ppm (ca. 6%; cf. zero remaining **III-3a** after 12 h). A similar proportion of the amine derivative $\text{NH}(\text{CH}_2\text{Ph})(\text{CH}_2\text{Ar})$ **11** was observed.

In situ quantification of the ruthenium co-product is hampered by the excess amine present. We isolated the *n*-butylamine derivative **Ru-17a** from both **III** and **GII**, by addition of 10 equiv. *n*-butylamine at RT in benzene (Scheme 4.4). The yellow product precipitated over 24 h, and was purified by extracting with hexanes (81% isolated yield for **GII**; or 69% for the smaller-scale reaction with **III**). This cationic complex is unstable in solution in the absence of excess amine, presumably because of competing coordination of the chloride counter-ion and displacement of bound NH_2^iBu . Similar behavior, including a cascade of ensuing reactions associated with solvent-induced chlorination, was previously reported for nitrile derivatives of Ru(II).³⁸ The structure shown is supported by combustion analysis, and by NMR analysis in the presence of a small amount of added amine (1% v/v).[‡]

Scheme 4.4. Isolation of **Ru-17a** from the reaction of **III** or **GII** with *n*-butylamine.^a



^aAmine co-products $\text{NH}(^n\text{Bu})(\text{CH}_2\text{Ar})$ **10** or $\text{NH}(^n\text{Bu})(\text{CH}_2\text{Ph})$ **7a** not shown.

^{*} The identity of the benzylamine derivative is supported by GC-MS analysis of a reaction aliquot, and by comparison of the ¹H NMR spectrum with that of an authentic sample prepared by reductive amination of the parent aldehyde. See Appendix 2 for NMR and MS data.

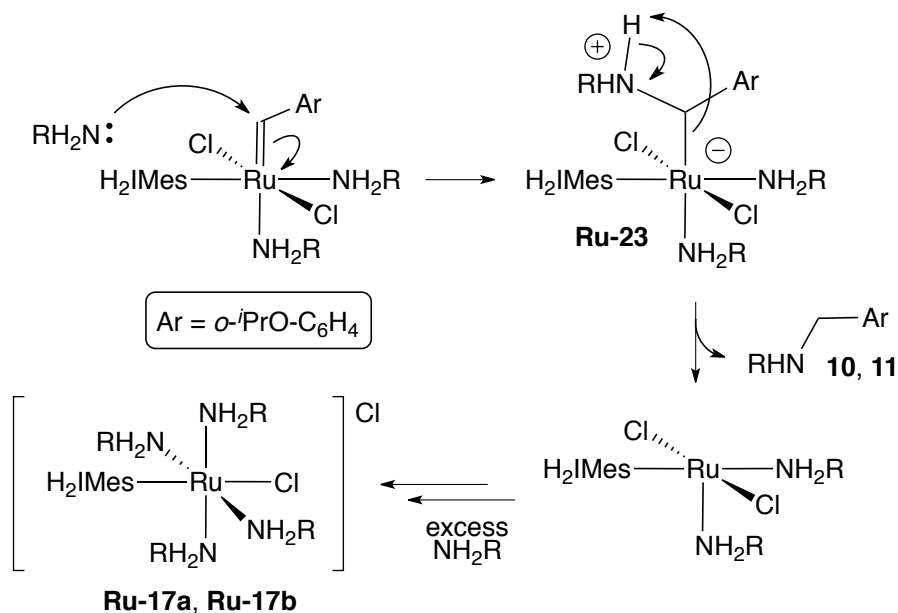
[†] Reported pK_a values for the conjugate acids in acetonitrile: pyridine: 12.6; morpholine: 16.6; benzylamine: 16.9; *n*-butylamine: 18.3; triethylamine: 18.5; pyrrolidine: 19.6; DBU: 24.1.³⁷

[‡] The structure depicted for **Ru-17a**, in which the chloride ligand has migrated to a site trans to the H₂IMes ligand, is proposed on the basis of the high symmetry evident by ¹H NMR analysis. Consistent with the presence of four equivalent butylamine ligands, one singlet is seen for the H₂IMes backbone protons, and for the mesityl CH protons, integrating 4:4:8 relative to the multiplet for the *n*-butylamine NCH₂ protons.

Notably, no benzyldiene abstraction occurred in the corresponding reaction of **III** with *sec*-butylamine **N4**. Instead, mono-amine adduct **III-4** was formed as the sole product, and this species resisted decomposition even after heating for 24 h at 60 °C. We infer that disubstitution at the carbon α to the nitrogen atom is sufficient to block approach to the benzyldiene ligand.

Consistent with this steric sensitivity is a mechanism involving benzyldiene abstraction via nucleophilic attack at the [Ru]=CHAr carbon (Scheme 4.5).^{*} Precedent for the σ -alkyl moiety in intermediate **Ru-23** (Scheme 4.5) is provided by structurally characterized **Ru-22** (Scheme 4.1) in the Grubbs system.³¹ Elimination of the alkyl ligand – whether by a concerted pathway, as shown, or via a Ru-hydride intermediate – would liberate the secondary amine **10**.

Scheme 4.5. Proposed mechanism for benzyldiene abstraction by sterically-accessible primary amines.



The overall pattern of decomposition by primary amines outlined above indicates a sharp decline in aggressiveness in the order $\text{NH}_2^{\text{sec}}\text{Bu} \gg \text{NH}_2\text{CH}_2\text{Ph}$, while attack by α -substituted $\text{NH}_2^{\text{sec}}\text{Bu}$ is completely inhibited. **III** is thus relatively tolerant toward amines or related nucleophiles for which benzyldiene abstraction is curbed by bulk or limited basicity. Because ligation of these Lewis donors is readily reversible, their negative impact on the precatalyst (that is, **III** itself) is better

^{*} Nucleophilic attack of phosphines on Ru-benzyldiene species has likewise been reported, although the occurrence is relatively rare, presumably owing to steric restrictions. Exceptions include Hofmann's $\text{RuCl}_2(\text{tBu}_2\text{PCH}_2\text{P}^t\text{Bu}_2)(=\text{CHPh})$ system, in which the ring strain of the four-membered κ^2 -PP chelate is relieved by attack at the benzyldiene carbon.³⁹ In a second example, reaction of **GI** with CO triggered migration of a PCy_3 ligand to the alkylidene carbon: the presence of the π -acceptor CO ligands renders the alkylidene carbon more electrophilic, while also reducing steric congestion at the metal.⁴⁰

described as deactivation than decomposition. Very different results are found in the presence of olefin, as described in the next section.

4.3. Base-induced decomposition of **HII** and its active species during metathesis

We next examined the impact of base on the longevity and productivity of **HII** during metathesis. As a probe reaction, we chose the self-metathesis of styrene by **HII** (1 mol%) at 60 °C in benzene. The homodimerization of styrene to form stilbene is known to proceed in high yield, but at relatively slow rates even using 3-5 mol% Ru.⁴¹⁻⁴³ It thus provides a convenient model for assessing the detrimental effect of base.

In control reactions without added base, yields of stilbene reached ca. 80% after 2 h, and 94% after 24 h. In the presence of **N1**, **N6** to **N10**, the maximum yield decreased in all cases (Figure 4.1). The impact of just one equivalent of amine per **HII** is offset by adduct formation. With 10 equiv **N1**, **N6-N10**, however, metathesis activity is dramatically reduced, and a general trend toward lower CM yields with increasing Bronsted basicity is evident.³⁷ A minor anomaly with $\text{NH}_2^{\text{n}}\text{Bu}$ **N1** is attributed to the capacity of this sterically accessible primary amine to abstract the alkylidene ligand from **HII**, as described above.

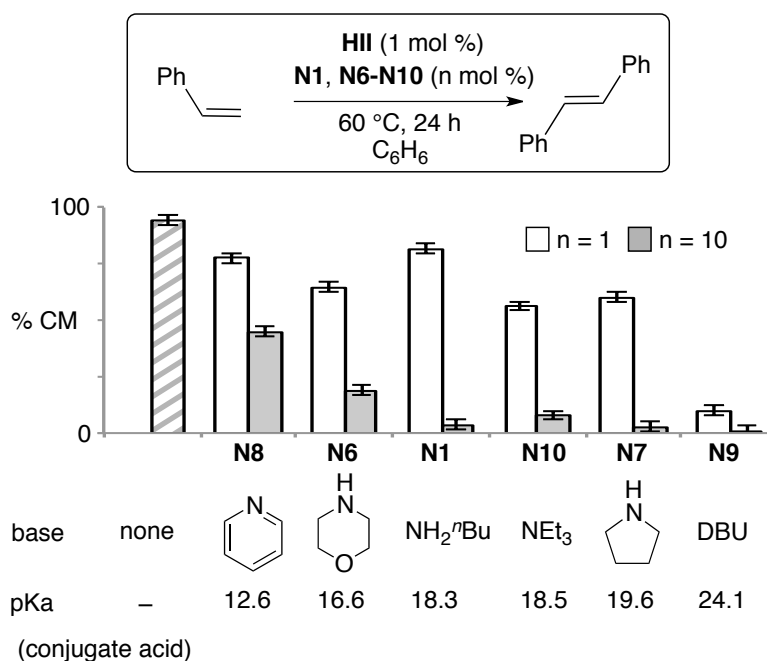


Figure 4.1. Impact of *N*-base on metathesis yields.^{37*}

* The pK_{a} of the conjugate acid for MeCN is given as a qualitative measure of basicity, rather than reported pK_{b} values in benzene, because the pK_{a} values have been directly measured in MeCN, and are more broadly comparable.³⁷

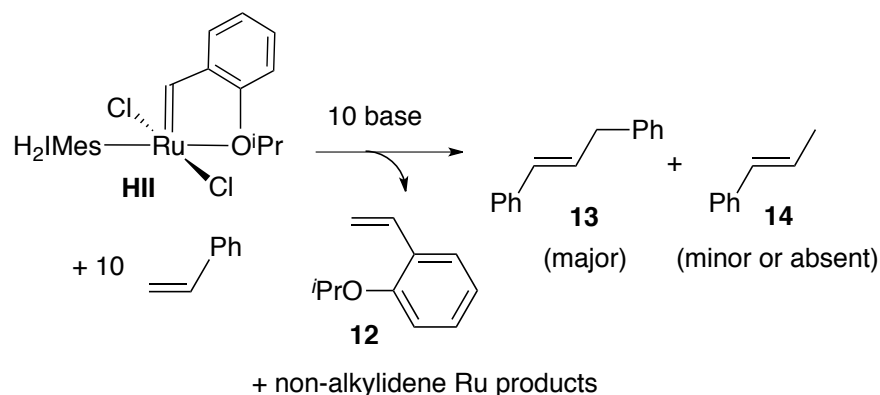
The negligible proportion of stilbene (<5%) formed with the stronger bases attests to the efficiency of decomposition. Perhaps most unexpected is the low CM yield observed in the presence of a tenfold excess of NEt_3 **N10**. This is particularly important given the steric protection presumed for tertiary amine centers, as noted in the Introduction. A role for proton abstraction in catalyst deactivation is proposed below. *N*-binding (i.e. sequestration of amine by binding to the metal, as in Scheme 4.1) is presumed to compete with this pathway.

To gain insight into the mechanism by which bases decompose the active catalyst, NMR experiments were carried out under the conditions above, but using 10 equiv each of styrene and amine. In this portion of the study, we focused on the three most deleterious bases, pyrrolidine **N7**, DBU **N9**, and NEt_3 **N10**. We omitted primary amine **N1** in order to highlight decomposition that originates in the active species, as opposed to the precatalyst.* For DBU and NEt_3 , loss of all alkylidene species was complete within 30 min at 60 °C (Table 4.2); cf. 18 h for pyrrolidine **N7**.

Unexpectedly, experiments directed at assessing temperature effects indicated that decomposition by NEt_3 **N10** is fast even at RT, with complete loss of alkylidene by 1 h. In comparison, ca. 90% loss is found with DBU **N9** after 10 h at RT. In all cases, the sole or principal organic decomposition product is (*E*)- $\text{PhCH=CHCH}_2\text{Ph}$ **13**, irrespective of temperature. The identity of **13** was confirmed by MS and NMR analysis. The olefinic signals offer characteristic NMR values, in terms of both chemical shift and multiplicity: a doublet at 6.31 ppm ($^3J_{\text{HH}} = 16$ Hz) for the PhHC proton, and a doublet of triplets at 6.19 ppm ($^3J_{\text{HH}} = 16$ Hz, $^3J_{\text{HH}} = 7$ Hz) for the $=\text{CHCH}_2\text{Ph}$ proton, in excellent agreement with literature values,⁴⁴ and with DEPT-135 and COSY data. Trans-selectivity is indicated by the magnitude of the $^3J_{\text{HH}}$ coupling constant (16 Hz). A minor co-product, observed in the control reaction without base, and in the presence of NEt_3 , is the related species (*E*)- PhCH=CHCH_3 **14**.† The origin of these products, and the mechanistic implications thereof, are discussed below.

* The reaction with **N1** was subsequently examined: see Section 4.4.6.

† Not seen was ArCH=CHPh , which would arise from a metallacyclobutane intermediate bearing the aryl and phenyl groups on adjacent carbons. This kinetically disfavoured “head to head” cycloaddition is further inhibited by competing decomposition.

Table 4.2. Decomposition rates and products on reaction of **HII** with styrene and base.^a

base	T (°C)	time (h)	% loss of [Ru]=CHR	% 13	% 14
none	60	24	91	–	17
pyrrolidine N7	60	10	90	72	–
		18	quant	81	–
DBU N9	60	0.5	quant	88	–
NEt ₃ N10	60	1	quant	70	13
DBU N9	21	18	quant	90	–
NEt ₃ N10	21	0.5	quant	74	9

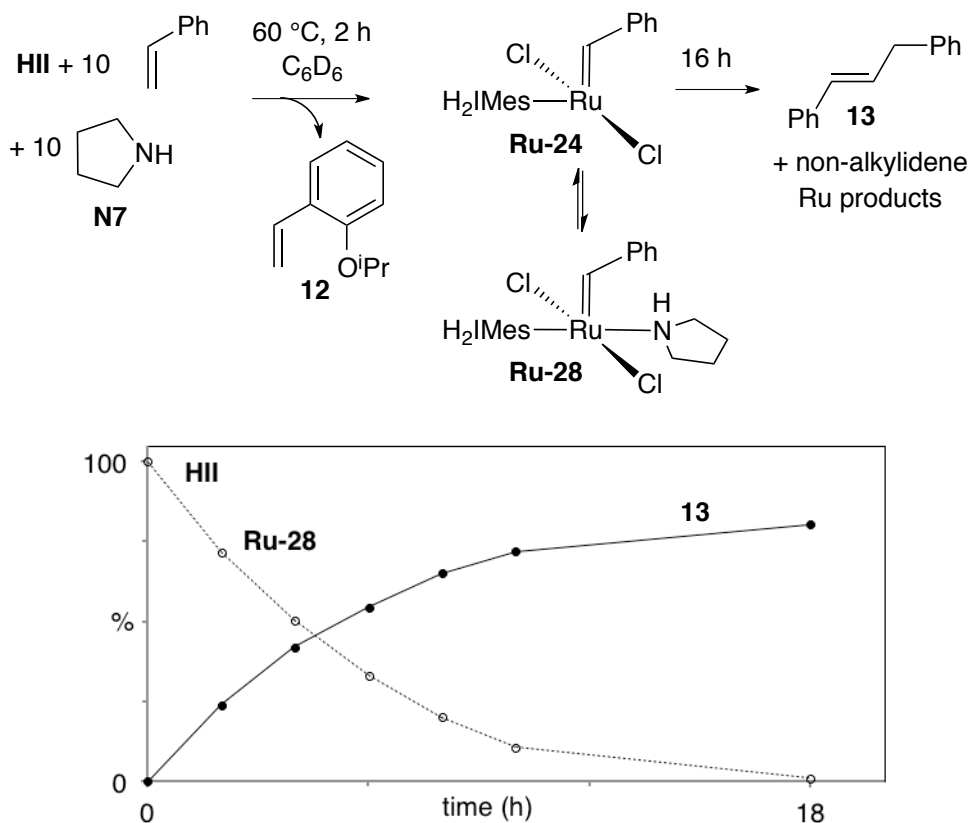
^a Conditions: 200 mM styrene, C₆D₆, J. Young tube. ¹H NMR integration vs. TMB; ±2.5% in replicate runs. Yields of PhCH=CHCH₂Ph and PhCH=CHCH₃ are based on starting **HII**. Yields of stilbene vs. starting styrene <4% except control (ca. 70%).

These reactions proceed via initial cross metathesis of **HII** with styrene, liberating isopropoxystyrene **12** in near-quantitative amounts (95% based on starting **HII**).^{*} Complete, efficient uptake of the entire **HII** charge is indicated, notwithstanding the relatively small proportion of substrate present. This point is worth emphasis, as it contradicts the widespread view that **HII** initiates slowly: it is fully consistent, however, with the rapid turnon established for this catalyst in recent ¹³C-labeling studies.³⁴

^{*} Isopropoxystyrene **12** is readily identified from the well-isolated signals for its geminal protons. Each gives rise to a characteristic doublet of doublets, one at 5.74 ppm (³J_{HH}(trans) = 18 Hz, ²J_{HH} = 2 Hz); the other at 5.21 ppm (³J_{HH}(cis) = 11 Hz, ²J_{HH} = 2 Hz).

In the slower reaction with pyrrolidine **N7**, we were able to observe the known adduct **Ru-28**²⁷ (70% yield at 2 h, based on starting **HII**). This complex is formed by trapping of the four-coordinate benzyldiene intermediate **Ru-24** (Scheme 4.6). While **Ru-28** disappears relatively slowly, it does not successfully engage in metathesis. Decomposition accounts for the failure to observe **Ru-28** and **HII-7** in the expected equilibrium ratio. Instead, the organic product of catalyst decomposition, PhCH=CHCH₂Ph **13**, accounts for 80-90% of the “missing” **HII** at any time (see conversion plot of Scheme 4.6).

Scheme 4.6. Reaction of **HII** with styrene and pyrrolidine, and rate plot for loss of alkylidene.

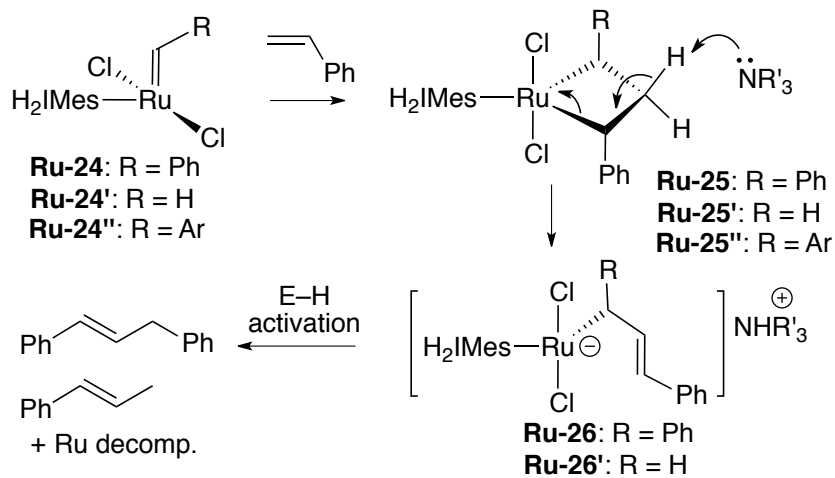


The three-carbon backbone present in **13** is an important marker implicating attack of base on the metallacyclobutane intermediate (e.g. **Ru-25**, Scheme 4.7). Proton abstraction from the C β site is proposed to generate an anionic σ -alkyl complex such as **Ru-26**, the basicity of which enables E–H bond activation (as earlier established for σ -alkyl complex **Ru-22**; p. 67), and liberation of **13**.^{*} Key to this pathway is poor steric protection of the kite-shaped³³ metallacyclobutane ring, which permits

^{*} Such σ -alkyl species are highly reactive, and readily participate in E–H activation processes that liberate the alkyl ligand.^{31,40,45,46} Note added post-publication: Recent findings suggest the potential alternative involvement of an H2IMes o-methyl proton. For experiments aimed at corroborating the site of initial deprotonation, see Ch. 6.

approach of amine. Notably absent is the *o*-isopropoxyphenyl analog of **13** (i.e. PhCH=CHCH₂Ar). We infer that the increased bulk of the aryl substituent in **Ru-25''** impedes approach of base to C β , and hence inhibits deprotonation of this species.

Scheme 4.7. Proposed mechanism for base-induced decomposition of the metallacyclobutane.



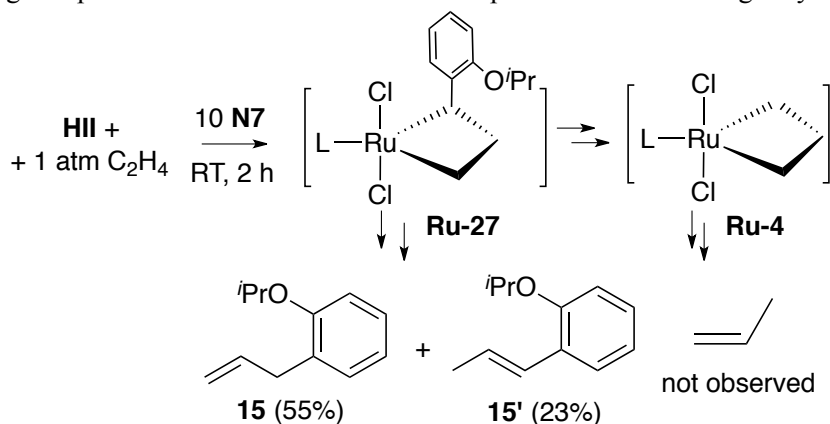
Interestingly, on replacing pyrrolidine **N7** with the bulkier, less basic amine NEt₃ **N10**, 10–15% PhCH=CHMe **14** is observed, depending on temperature. Formation of **14** indicates that metathesis proceeds to the monosubstituted metallacyclobutane (MCB) **Ru-25'**, a reflection of the inability of NEt₃ **N10** to trap out the four-coordinate intermediate (see **Ru-24**, etc.) via adduct formation. More extensive metathesis is inhibited by decomposition. The rapidity of decomposition even at RT, indicates that the transition state for β -elimination (i.e. transformation of **Ru-25** to **Ru-26**) is rather low in energy. The barrier appears to decline as MCB substitution decreases, as indicated by the very rapid degradation of **III** in the presence of ethylene and base at RT; see below.

In the absence of base, catalyst decomposition during styrene metathesis was much slower, with 9% **III** still present after 24 h at 60 °C. Stilbene was observed in ca. 70% yield. Of note, small amounts of PhCH=CHCH₃ **14** and propylene (0.2 equiv vs. starting **III**) were also evident, indicating decomposition via the monosubstituted MCB intermediate. MCB deprotonation can thus occur even without assistance by base. The Sasol group earlier reported evidence for β -hydride transfer from MCB intermediates as a key deactivation pathway for **GIIm** in the presence of ethylene.⁴⁷ Bespalova and co-workers subsequently invoked such a pathway to account for decomposition of **III** and formation of propylene under ethylene.³²

Decomposition was much faster under ethylene atmosphere, even at RT. Exposing **III** to ethylene in the presence of pyrrolidine **N7** (Scheme 4.8) resulted in >90% loss of all alkylidene signals within 2 h. This should be compared with just 8% loss at 2 h under these conditions in the

absence of base. Major products were $\text{ArCH}_2\text{CH}=\text{CH}_2$ **15** and its β -methylstyrene isomer **15'** $\text{ArCH}=\text{CHMe}$, formed in nearly 80% total yield relative to starting **III**. Both originate in MCB **Ru-27**, consistent with the pathway shown for the analogous intermediate **Ru-25** in Scheme 4.7. Somewhat unexpectedly, no propylene was observed, in contrast to the pyrrolidine-free control reaction. This is certainly due in part to the efficiency of decomposition, which hampers the ensuing formation of the unsubstituted MCB **Ru-4**. We do not rule out, however, the possibility that the balance of decomposition (20%) occurs via this pathway, and that the propylene gas is lost in the headspace.

Scheme 4.8. Organic products from base-induced decomposition of **III** during ethylene metathesis.



Accelerated catalyst decomposition during metathesis of ethylene, as compared with styrene, is consistent with the greater accessibility of the monosubstituted metallacyclobutane ring in **Ru-27**, relative to disubstituted **Ru-25**. This heightened vulnerability to base in the presence of ethylene is of particular interest from the perspective of “ethenolysis” reactions used to generate α -olefins from internal olefins, a subject of considerable interest in multiple contexts, including metathesis of renewable feedstocks.⁴⁸ More generally, it underscores the importance of efficiently sweeping ethylene out of metathesis reactions where amines or other Brønsted bases are present, as a means of minimizing catalyst decomposition. Decomposition via base-induced deprotonation of the unsubstituted MCB is thus expected to be particularly problematic during industrial processes involving **III** and related catalysts, where mass transfer limitations apply; during synthetic reactions with limited headspace; and during NMR-tube or other sealed-tube experiments.

The foregoing represents the first study of the effect of additives on decomposition of the important Hoveyda catalyst **III**. The precatalyst itself proved tolerant toward all but the most sterically accessible, unbranched primary amines. While the ether ligand is readily displaced by *N*-donors, in most cases this merely generates stable adducts, which exist in equilibrium with **III**.

Sterically unencumbered amines, however, attack the precatalyst and abstract the benzyldiene moiety as $\text{NHR}(\text{CH}_2\text{Ar})$ ($\text{R} = ^t\text{Bu}, \text{CH}_2\text{Ph}$).

In the presence of substrate, the impact of base is much more dramatic. Metathesis yields are highly sensitive to the basicity of the amine, and even 1 equivalent of DBU **N9** causes almost complete loss of activity. In all cases, however, metathesis is sharply reduced by a stoichiometric excess of amine. Closer examination of the reactions with pyrrolidine **N7**, NEt_3 **N10**, and DBU **N9** revealed attack on the key metallacyclobutane (MCB) intermediate, and indicated that decomposition was complete within ca. two cycles of metathesis. The organic products of decomposition were consistent with deprotonation of the metallacyclobutane by the Bronsted base to form a Ru-alkyl intermediate, the basicity of which enables E-H bond activation (as earlier established for π -alkyl complex **Ru-22**; p. 67), and liberation of **13**. The rapid deactivation by NEt_3 **N10** is particularly noteworthy, given the steric protection widely presumed for tertiary nitrogen centers.

Also of note is the dramatically higher vulnerability of the MCB intermediate formed in the presence of ethylene, which was rapidly decomposed in the presence of base even at ambient temperatures. These data suggest that, where basic substrates or contaminants are present, catalyst productivity will be highly sensitive to removal of ethylene, the usual co-product of metathesis.

4.4. Subsequent advances

4.4.1. C–H activation of the N-heterocyclic carbene during metallacyclobutane decomposition

As noted in Section 4.3, the organic products $\text{PhHC}=\text{CHCH}_2\text{R}$ ($\text{R} = \text{Ph}$, **13**; H , **14**) are generated by base-induced decomposition of **III** during metathesis. The Ru product(s) could not be identified in situ due to overlap of the ^1H NMR signals with those of excess base. Even a single equivalent of the strong Bronsted base DBU **N9**, however, almost completely quenched metathesis (Figure 4.1, above). Subsequent to publication of the work described in Sections 4.1–4.3, this reaction was revisited to gain insight into the nature of the ruthenium products.

Accordingly, a green solution of **III** (C_6D_6 ; TMB present as internal standard) was treated with DBU **N9** and styrene (1 and 10 equiv, respectively). A colour change to red was evident after 30 min at 60 °C, and no $\text{Ru}=\text{CHR}$ signals remained in the ^1H NMR spectrum. Both $\text{PhHC}=\text{CHCH}_2\text{Ph}$ (**13**, 70%) and $\text{PhHC}=\text{CHCH}_3$ (**14**, 21%) were present (Figure 4.2). This contrasts with the observation of **13** as the sole organic product in the presence of 10 equiv DBU (see above), conditions under which decomposition out-competes metathesis. Formation of **13** can thus be taken as a marker for decomposition early in catalysis, when the disubstituted MCB **Ru-25** is the dominant metallacyclobutane (Scheme 4.9).

Scheme 4.9. Origin of the three-carbon marker compounds **13** and **14**. (a) early in catalysis. (b) later in catalysis.

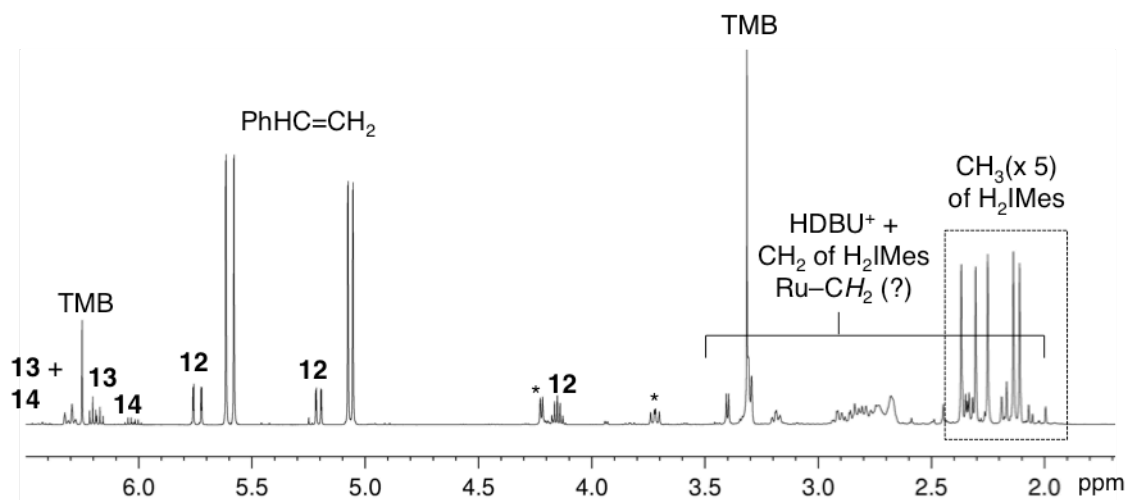
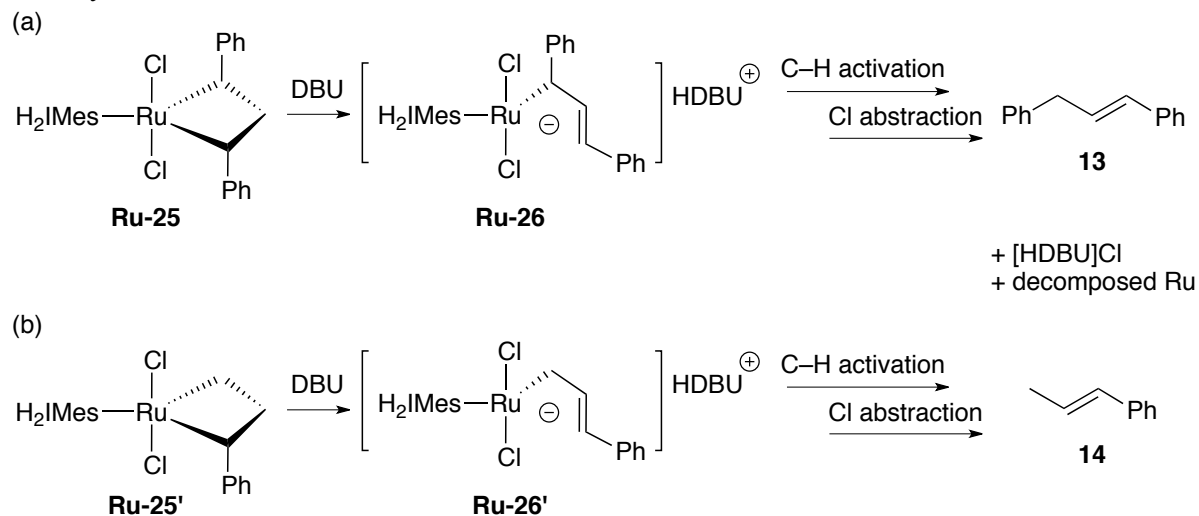


Figure 4.2. ^1H NMR spectra (C_6D_6 , 500.1 MHz) of **HII** + 1 DBU + 10 styrene after 0.5 h at 60 $^\circ\text{C}$. Peaks denoted (*) are not assigned.

A single dominant Ru-NHC product was present, as indicated by the observation of five major signals due to the mesityl methyl groups, in the region 2.4–2.1 ppm (Figure 4.2). Integration of these indicates an in situ yield of 80% based on **HII**. As either three or six methyl groups are expected for an intact H_2IMes ligand, depending on symmetry, we suspected C–H activation of an *o*-methyl group. Precedents for such activation have been reported for **GII**²⁹ and other complexes of ruthenium, rhodium, and iridium (Chart 4.3).^{49–54} The diastereotopic methylene protons for the Ru– CH_2 moiety in these complexes typically appear between 3.8 and 2.2 ppm (Table 4.3). Several signals between 3.8 and 2.2 ppm are indeed evident in the spectrum of Figure 4.2, but owing to signal overlap, these cannot be conclusively assigned as Ru– CH_2 . (HMQC experiments could be highly

useful in confirming this assignment: see Future Work). Signals for $[\text{HDBU}]^+$ are also observed: the counter-ion is not identified, but (following decomposition of **Ru-26**) is presumed to be chloride.

Chart 4.3. Exemplary Group 8–9 complexes with C–H activated NHC ligands.

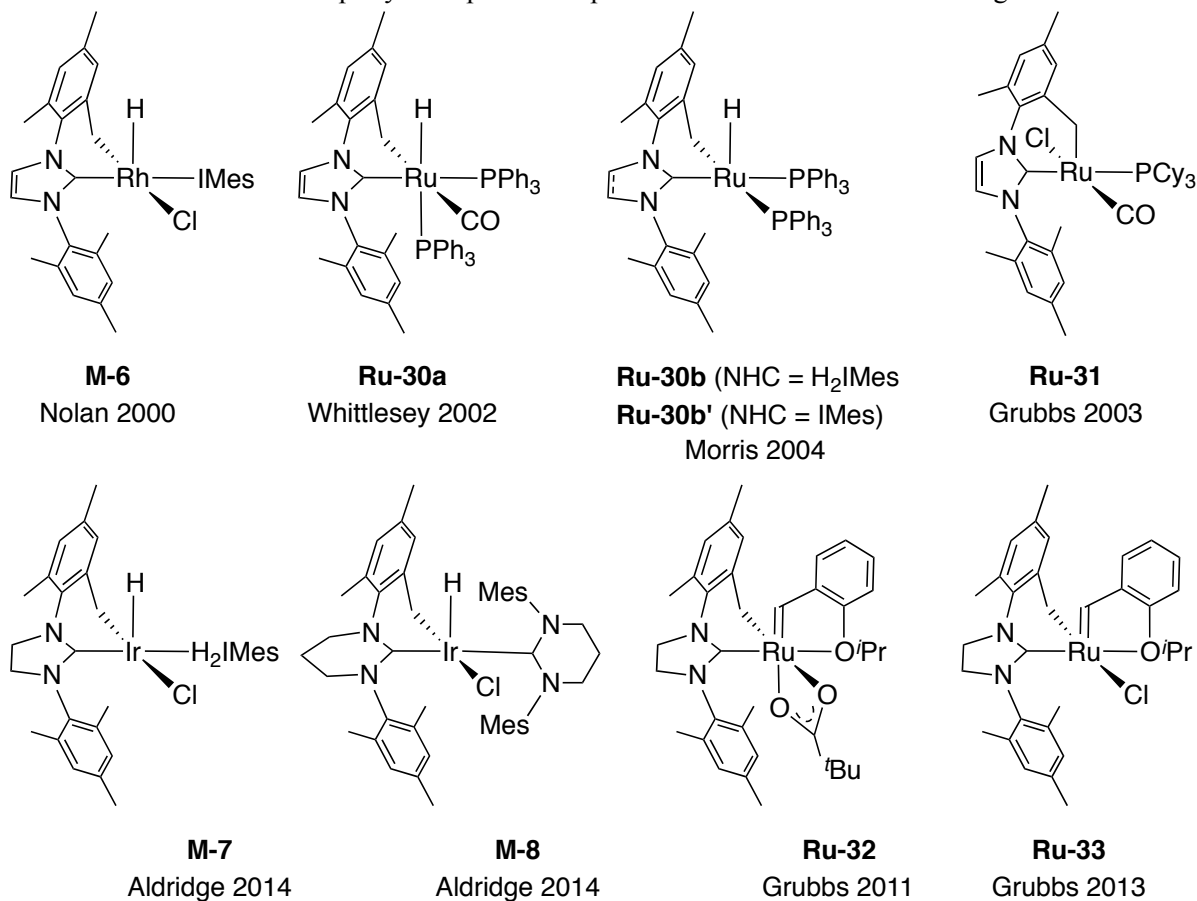
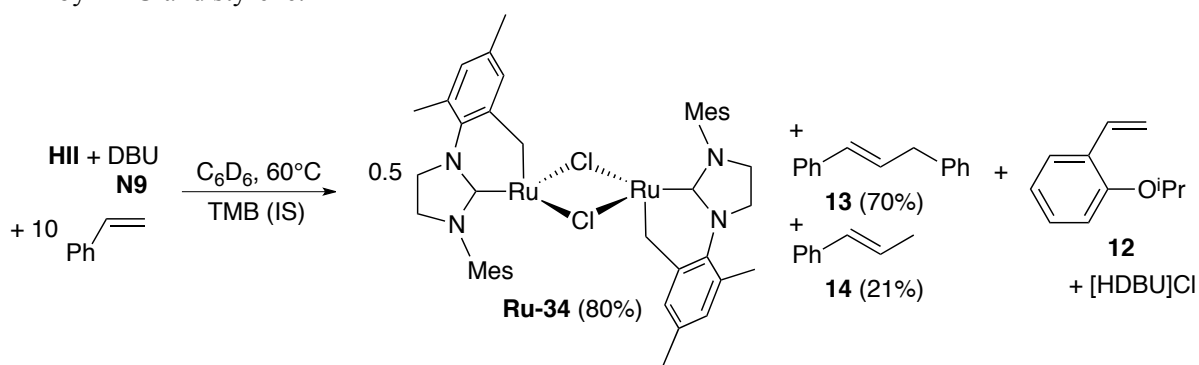


Table 4.3. NMR data for the complexes of Chart 4.3.

structure	δ_{H} RuCH ₂ Ar	δ_{C} RuCH ₂ Ar	solvent	ref
M-6	2.41 (s)	NR	THF-d ₈	49
Ru-30a	2.76 (dd, 11 Hz, 10 Hz) 1.35 (dd, 12 Hz, 11 Hz)	12.1 (d, 8 Hz)	C ₇ D ₈	50
Ru-30b	3.38 (m), 2.25 (m)	NR	C ₆ D ₆	51
Ru-30b'	3.80 (m), 2.20 (m)	NR	C ₆ D ₆	51
Ru-31	3.44 (d, 9 Hz), 3.30 (d, 11 Hz)	7.4 (d, 4 Hz)	C ₆ D ₆	53
M-7	2.41 (br)	NR	C ₆ D ₆	54
M-8	2.30 (d, 12 Hz), 2.19 (d, 12 Hz)	-13.2 (d, 10 Hz)	C ₆ D ₆	54
Ru-32	3.2 (m), 2.17 (d, 10 Hz)	NR	C ₆ D ₆	52
Ru-33	3.15 (d, 7 Hz), 2.18 (d, 7 Hz)	NR	CD ₂ Cl ₂	55

We propose that the proton required for release of $\text{PhHC=CHCH}_2\text{R}$ ($\text{R} = \text{Ph}, \text{H}$) from the σ -alkyl intermediate **Ru-26** / **Ru-26'** originates in C–H activation of a mesityl group. Given the anticipated abstraction of chloride from the resulting Ru species by $[\text{HDBU}]^+$, the C–H activated product would plausibly dimerize to afford **Ru-34** in the absence of excess, ligating DBU (Scheme 4.10). Precedents for such edge-bridged dimers are found in work by (inter alia) Grubbs,²⁹ Johnson,⁵⁶ Crudden,^{57,58} and Danopoulos.⁵⁹ The ethylene adduct of **Ru-34** was identified by Grubbs and Hong via single-crystal XRD, though no NMR data was reported.²⁹

Scheme 4.10. Organic products and proposed C–H activated complex **Ru-34** from decomposition of **HII** by DBU and styrene.^a



^a in situ yields reported vs. TMB internal standard, normalized to decomposition of **HII**.

4.4.2. Can **GII** decompose via deprotonation of the metallacyclobutane?

The RCM studies in Chapter 3 demonstrated that during metathesis by **GII**, *N*-donors trigger methylenide abstraction by PCy_3 as the primary decomposition pathway.^{27,31} As the metallacyclobutane species formed by **GII** and **HII** in catalysis are identical, we postulated that MCB deprotonation should also be observable for **GII**. We therefore expanded the scope of the published experiments to examine the impact of added *N*-base on CM by **GII**. We find that MCB deprotonation may be induced for **GII** in the presence of a sufficiently strong Bronsted base (DBU), or for the monosubstituted metallacyclobutane formed under ethylene.

4.4.3. Impact of *N*-donors on CM yield: **GII** vs. **HII**

Given the observed formation of $[\text{MePCy}_3]\text{Cl}$ from **GII** during metathesis in the presence of amines, and the added susceptibility of its MCB intermediate to deprotonation, **GII** is expected to show heightened sensitivity to base, relative to **HII**. The metathesis productivity of **GII** in the presence of base should therefore be poorer than that of **HII**.

Self-metathesis of styrene using 1 mol% **GII** was examined to provide a comparison with existing **HII** experiments (Figure 4.1). Maximum yields were assessed after 24 h at 60 °C in C₆H₆. No increase in stilbene yields were observed after 24 h, and this time period was therefore set as a convenient point at which to assess maximum metathesis yields. In the presence of base, yields for **GII** were indeed lower than those of **HII**, by 15–50% in almost all cases (Figure 4.3). The sole exception was DBU, for which <10% CM was observed for both **GII** and **HII**, and no significant difference was observed. We earlier demonstrated that DBU is exceptional in not triggering [MePCy₃]Cl formation from **GII** during RCM studies, and proposed that this base induces deactivation via the MCB intermediate.²⁷

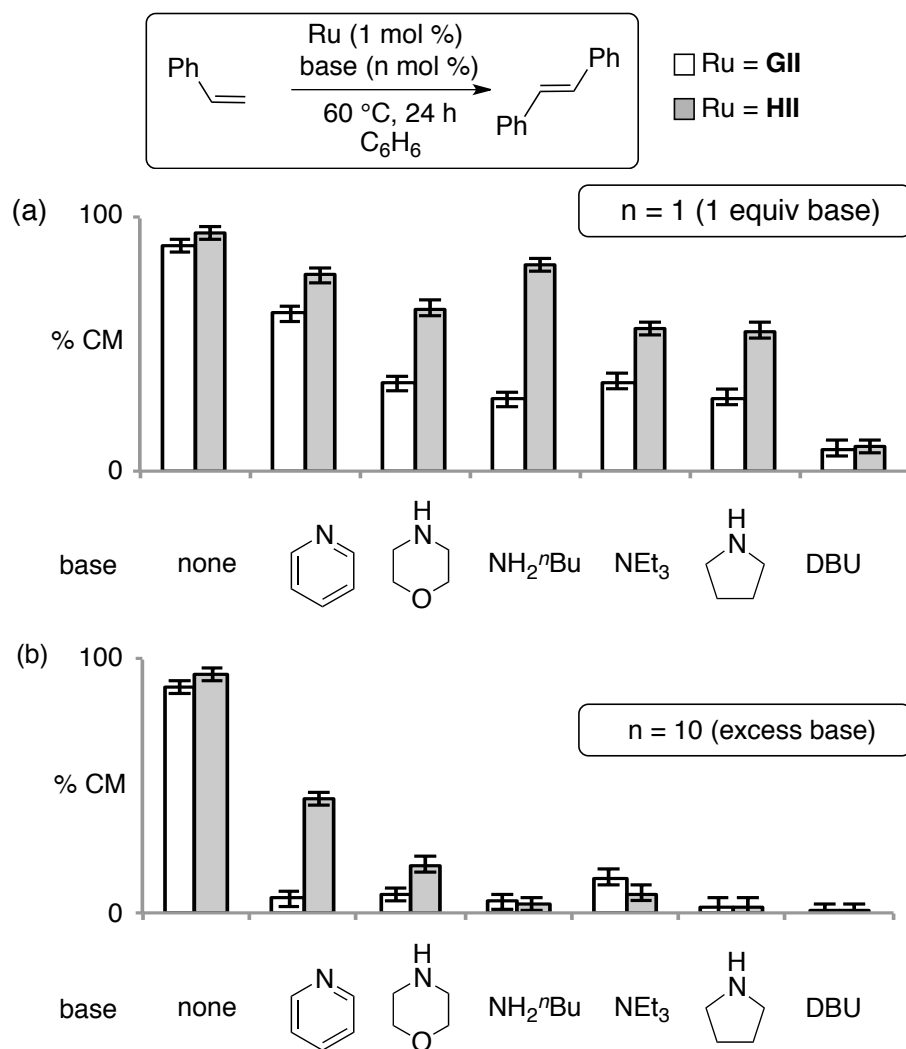


Figure 4.3. Impact of (a) one equivalent and (b) ten equivalents of base on metathesis yields. Grey bars indicate yields for **HII** shown in Section 4.3 above; reproduced here for comparison.

In the absence of added base, **GII** afforded 88% stilbene after 24 h. On addition of even 1 equiv *N*-donor (Figure 4.3), yields dropped to $\leq 36\%$ for all donors except pyridine (62% in situ yield). We attribute the relatively low impact of 1 equiv py to the competing formation of di- or tri-pyridine complexes (e.g. **GIII**, $\text{RuCl}_2(\text{H}_2\text{IMes})(\text{py})_3$ **Ru-10**).²⁹ Consistent with this, yields of stilbene decreased to ca. 5% on addition of 10 py (Figure 4.3b). Interestingly, while NEt_3 **N10** did not bind to **GII** (Table 4.1), 1 equiv NEt_3 decreased CM yields considerably more for **GII**, relative to **HII** (to 36% and 56%, respectively).

4.4.4. The role of amine basicity in determining the decomposition pathway for **GII**

We recently reported that amines decompose **GII** during metathesis by triggering abstraction of the methyldiene ligand by PCy_3 .²⁷ Formation of $[\text{MePCy}_3]\text{Cl}$ accounted for 73–97% of the original catalyst charge for most of the *N*-donors studied (NH_2^tBu **N1**, morpholine **N6**, pyrrolidine **N7**). DBU **N9** was an anomaly, as noted above, and attack on the MCB was proposed. To test this hypothesis, a series of NMR-tube experiments was performed to probe the capacity of **GII** to undergo deprotonation of the MCB during metathesis. Our original decomposition studies with **GII** examined the impact of base during RCM macrolactonization.²⁷ Here we focus on styrene self-metathesis. To assess the impact of amine basicity, we carried out these reactions with pyrrolidine **N7**, as well as DBU **N9**. Formation of the organic products (**13**, **14**), would constitute evidence for MCB deprotonation.

In a J. Young NMR tube, a pink solution of **GII** and TMB was prepared, and ^1H NMR data collected to determine the initial Ru : TMB ratio. Addition of styrene and DBU **N9** (10 and 1 mol%, respectively) caused a colour change to green. After 1 h at 60 °C, the solution had turned brown. Just 5% alkylidene was still present, comprising **GII** and its DBU adduct. Also present were the MCB decomposition products $\text{PhHC}=\text{CHCH}_2\text{Ph}$ **13** and $\text{PhHC}=\text{CHCH}_3$ **14** (63% and 13%, respectively, based on starting **GII**). $^{31}\text{P}\{^1\text{H}\}$ NMR analysis revealed free PCy_3 (93%), unreacted **GII** (3%) and $[\text{MePCy}_3]\text{Cl}$ (4%). The corresponding reaction in the absence of base resulted in only 12% decomposition (53% **GII**m, 35% **GII**), of which ca. 10% was $[\text{MePCy}_3]\text{Cl}$.

Results for decomposition of **GII** during self-metathesis of styrene are summarized in Table 4.4. In the absence of base, $>90\%$ $[\text{MePCy}_3]\text{Cl}$ and ca. 4% **14** were present after 6 h. In the presence of pyrrolidine **N7**, a smaller amount of $[\text{MePCy}_3]\text{Cl}$ was formed (67%), accompanied by free PCy_3 (32%) and trace quantities of **GII**. Smaller amounts of **13** (20%) and **14** (8%) were evident. The proportion of $[\text{MePCy}_3]\text{Cl}$ agrees well with that observed in the earlier RCM studies²⁷ (73%). In comparison, however, the stronger base DBU **N9** induced decomposition predominantly through MCB decomposition. As expected from the RCM study, only traces of the phosphonium salt were

observed (4%). Instead, 63% **13** was observed, and 13% **14**, confirming attack on the MCB. Clearly, a very strong Bronsted base, in conjunction with sterically inhibited Lewis basicity, can switch the dominant decomposition pathway for **GII** from PCy₃-induced methylidene abstraction to MCB deprotonation.

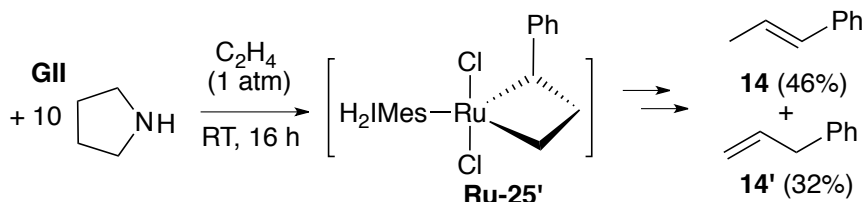
Table 4.4. Decomposition Rates and Products Formed on Treating **GII** with Styrene and Base.

base	time (h)	% loss of [Ru]=CHR	% [MePCy ₃]Cl	% 13	% 14
none	1	12	10	—	—
	6	57	53	—	4
pyrrolidine	6	96	68	20	8
DBU	1	95	4	63	13

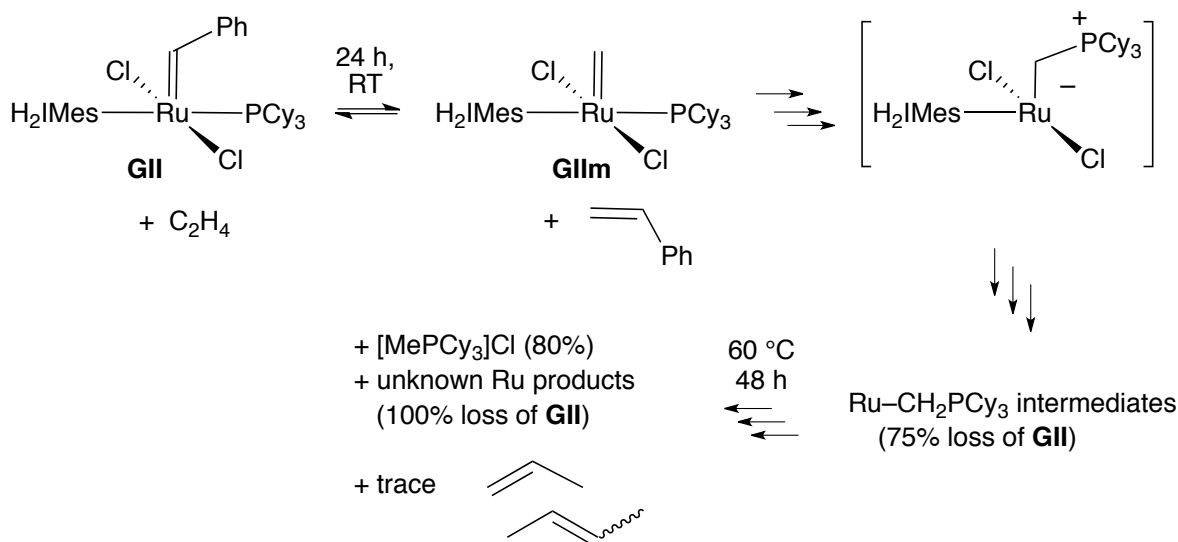
Conditions: 200 mM styrene, C₆D₆, J. Young tube. Results shown are single trials. Yields of **13** and **14** are based on starting **GII** vs. internal standard. Yields of [MePCy₃]Cl estimated based on % of total ³¹P NMR integration.

4.4.5. Metallacyclobutane deprotonation with **GII** – ethenolysis

As noted at the end of Section 4.3, the metallacyclobutanes generated from **HII** under ethylene are particularly vulnerable to deprotonation. A further experiment was carried out to determine whether the same is true for **GII**. On treating **GII** with C₂H₄ and pyrrolidine **N7** at RT (Scheme 4.11), loss of the alkylidene signals occurred, but much more slowly than for **HII**: ca. 25% loss after 2 h, vs. 90% for **HII**. The diagnostic benzylidene singlets for pyrrolidine adduct **Ru-28** and **GII** were detected at 19.67 and 19.63 ppm (59% and 16%, respectively). After 16 h, however, no alkylidene signals remained. Nearly 80% of the initial **GII** charge is accounted for by the three-carbon markers for MCB decomposition, PhHC=CHCH₃ **14** and PhCH₂CH=CH₂ **14'** (46% and 32%, respectively). Of note, ³¹P{¹H} NMR analysis revealed solely PCy₃. The absence of [MePCy₃]Cl indicates preferential attack of **N7** on the MCB.

Scheme 4.11. Observed products for base-induced decomposition of **GII** via metallacyclobutane intermediate **Ru-25'**.

A control experiment was carried out to confirm that the MCB products **14** / **14'** are not formed in the absence of base. In this reaction, ca. 25% **GII** remained even after 24 h (as compared with complete decomposition at 16 h in the **N7** experiment above). Neither **14** nor **14'** was observed. Interestingly, the ³¹P{¹H} NMR spectrum at 24 h revealed an ill-defined mixture of species, with many small peaks between 47 and 30 ppm. These may correspond to Ru-alkyl intermediates generated by decomposition of a σ-alkyl intermediate (Scheme 4.12), itself formed by nucleophilic attack of free PCy₃ on the methyldiene carbon.^{28,29,31} On heating this mixture at 60 °C for 48 h, [MePCy₃]Cl accounted for >80% of total ³¹P{¹H} NMR integration. Also present in the crude reaction were trace propene and butene, identified by ¹H NMR analysis. Such products were likewise observed by the Sasol group, and attributed to β-elimination of the MCB intermediates.⁴⁷

Scheme 4.12. Observed products for ethenolysis of **GII**.

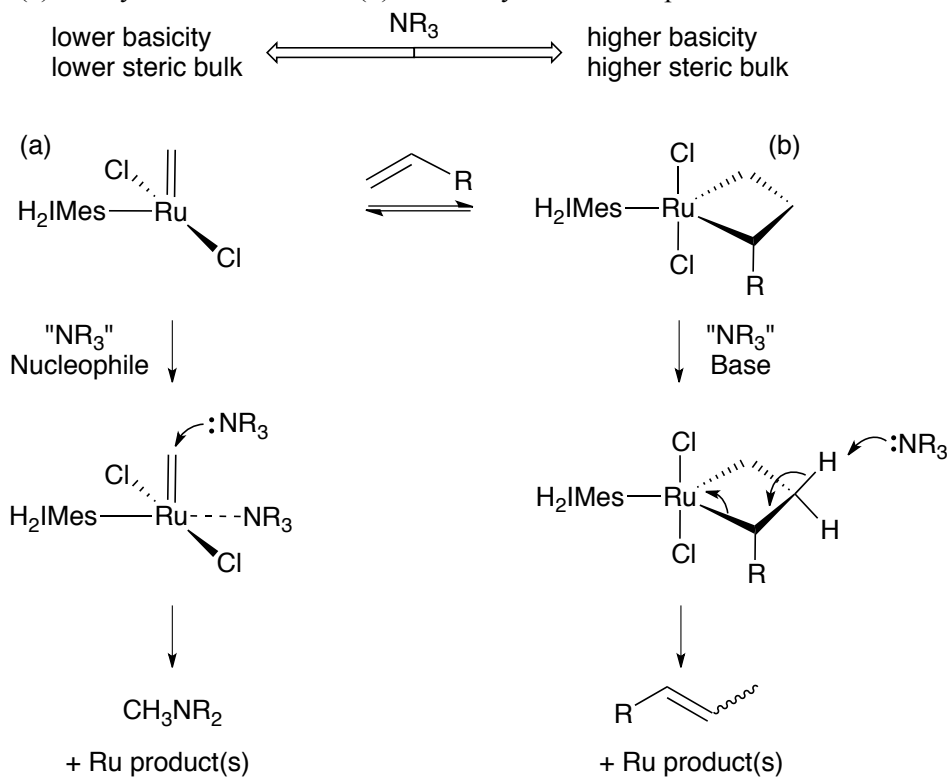
4.4.6. Alkylidene abstraction from **III** during catalysis

The studies above focused on strong Bronsted bases, which favor MCB deprotonation. Here we examine the decomposition of the active species generated by **III** with weaker bases. We speculated that slower MCB deprotonation might enable direct abstraction of the methyldiene unit by

amine, by analogy to the pathways for **GII** described in detail in Chapter 3. That is, we considered a continuum of behavior, controlled by bulk and basicity / nucleophilicity (Scheme 4.13).

As shown in Chapter 3 (for **GII**) and Section 4.2 (for **III**), bulky nucleophiles are unable to abstract the alkylidene. The methylidene intermediates are expected to be more vulnerable. Amines can indeed abstract the methylidene ligand of the resting-state species **GII_m** (albeit in a minor pathway), as recently established by Justin Lummiss of this research group. Unequivocal evidence for such attack was provided by the reaction of isotopically-labeled **GII_m*** with excess $\text{NH}_2^{\text{n}}\text{Bu}$ **N1**, which afforded ca. 30% $\text{H}_3\text{C}^*\text{NH}^{\text{n}}\text{Bu}$, accompanying 70% of the $[\text{H}_3\text{C}^*\text{PCy}_3]\text{Cl}$ product.²⁸ We questioned whether, in PCy_3 -free catalyst systems, methylidene abstraction may be preferred over metallacyclobutane deprotonation.

Scheme 4.13. The influence of amine bulk and basicity on the preferred decomposition pathway in metathesis. (a) Methylidene abstraction. (b) Metallacyclobutane deprotonation.



To gauge whether alkylidene abstraction competes with MCB deprotonation for **III**, we examined styrene self-metathesis in the presence of morpholine and *n*-butylamine. These experiments provide a useful counterpoint to the experiments of Section 4.3, in which **III** was treated with styrene in the presence of pyrrolidine, DBU, or triethylamine. Morpholine was chosen for its dramatically reduced Bronsted basicity (but similar steric bulk) relative to pyrrolidine. In contrast, *n*-

butylamine was studied as an example of an amine with minimal steric bulk, but comparable Bronsted basicity vs. triethylamine.*

Addition of styrene and morpholine **N6** (10 equiv each) to **HII** at 60 °C afforded the known²⁷ morpholine adduct $\text{RuCl}_2(\text{H}_2\text{IMes})(\text{HNC}_4\text{H}_8\text{O})(=\text{CHPh})$ **Ru-29** (δ_{H} 19.73 ppm, 69% vs. initial **HII**) as the sole alkylidene species after 30 min. Styrenyl ether $\text{ArHC}=\text{CH}_2$ **12** was formed in equilibrium amounts (93%). After 6 h, no alkylidene signals remained, but the three-carbon markers $\text{PhHC}=\text{CHCH}_2\text{R}$ accounted for only ca. 30% of the initial **HII** charge (**13**, 26%; **14**, 3%). *N*-methylmorpholine **16** was detected in the crude reaction mixture (53%). The identity of **16** is supported by GC-MS and $^{13}\text{C}\{^1\text{H}\}$ NMR analysis of the crude reaction mixture (see Appendix 2). The ^1H signals for NCH_3 (2.00 ppm, s, 3H) and NCH_2 (3.58 ppm, dd, $^3J_{\text{HH}} = 4 \text{ Hz}, 5 \text{ Hz}, 4\text{H}$) of **16** appear at distinct locations from the signals for excess **N6** and unknown Ru product(s) (Figure 4.4).

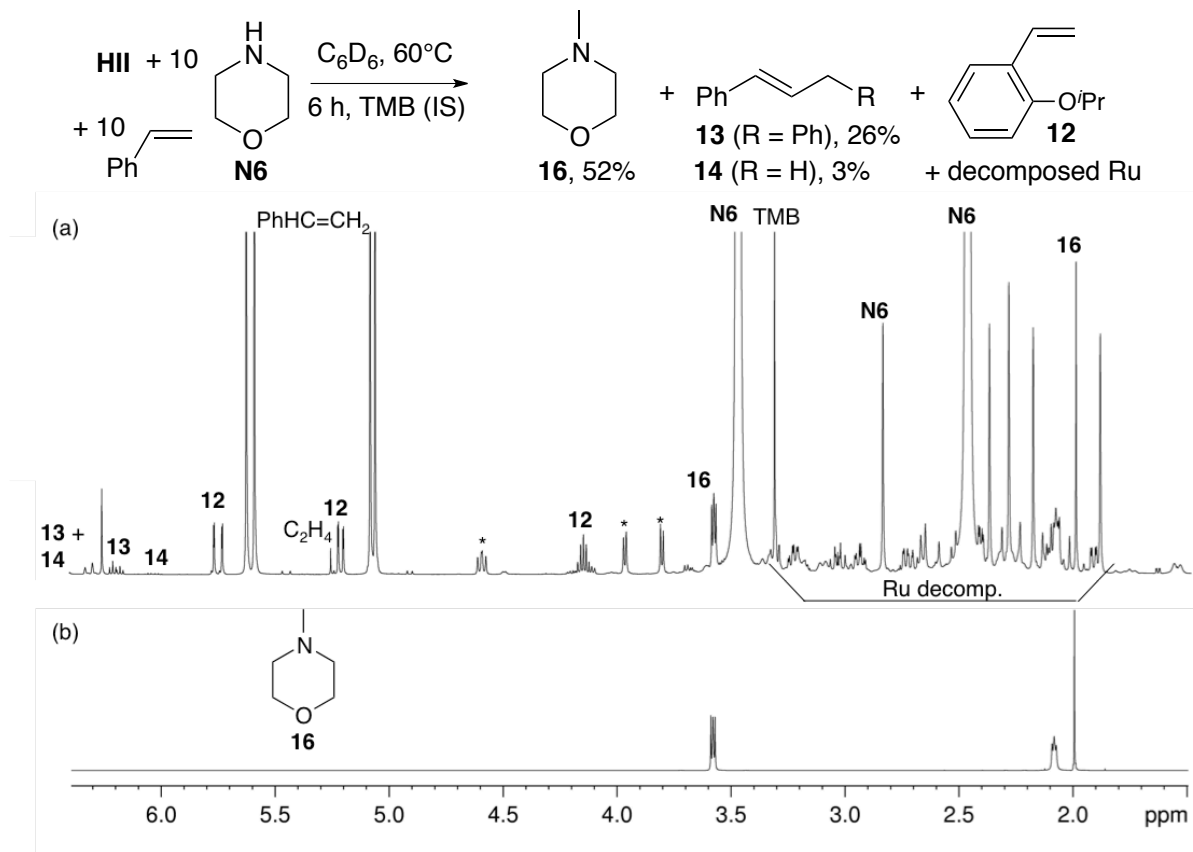
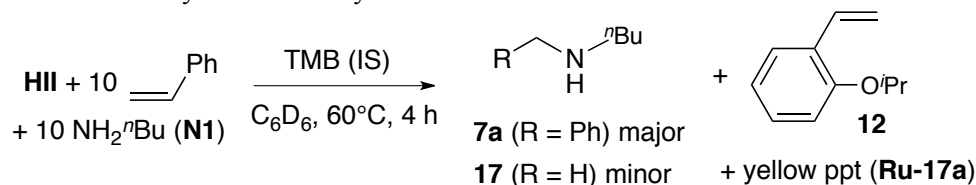


Figure 4.4. ^1H NMR spectra (C₆D₆, 500.1 MHz) for the reaction of (a) **HII** + 10 morpholine **N6** + 10 styrene, after 6 h at 60 °C. Expansion shows olefinic signals for $\text{PhHC}=\text{CHCH}_2\text{Ph}$ (minor product) and $\text{PhHC}=\text{CHCH}_3$ (trace quantities) (b) commercial *N*-methylmorpholine **16**. Peaks denoted (*) not assigned.

* Reported pK_{a} values for the conjugate acids in acetonitrile: morpholine: 16.6; *n*-butylamine: 18.3; triethylamine: 18.5; pyrrolidine: 19.6; DBU: 24.1.³⁷

In a J. Young NMR tube, **III** in C₆D₆ was treated with excess **N1** and styrene (10 equiv each). After 1 h at 60 °C, a sole Ru=CHR species was observed at 19.56 ppm (ca. 30% vs. internal standard, 70% decomposition), consistent with formation of butylamine adduct **Ru-11b**.²⁶ Complete loss of Ru=CHR was observed after 4 h at 60 °C (97% loss at 2 h) with formation of a pale yellow precipitate, proposed to be **Ru-17a** (Chapters 3.3, 4.2). *N*-butylbenzylamine **7a** was identified as the dominant organic product via a diagnostic ¹H NMR methylene signal at 3.62 ppm (ca. 70% vs. initial **III**) and its identity was confirmed by GC-MS analysis. A singlet was also observed at 2.26 ppm in the ¹H NMR spectrum, consistent with formation of MeNH^{*n*}Bu **17** (ca. 15% vs. initial **III**, Scheme 4.14). ¹H NMR signals for the *n*-butyl fragment of **17** were obscured by excess **N1**. The identity of **17** could not be corroborated by GC-MS analysis, as its GC signal overlapped with those for **N1** and C₆D₆ (bp 83 °C, 79 °C, 79 °C, respectively). *N*-methylbutylamine **17** is tentatively assigned as a minor product of this reaction. Its formation could be confirmed by an isotopic labeling study (see Future Work).

Scheme 4.14. Observed major and proposed minor products for decomposition of **III** in the presence of excess *n*-butylamine and styrene.



No *o*-^{*i*}PrO-C₆H₄-NH^{*n*}Bu **10** was observed by ¹H NMR or GC-MS analysis. Instead, *o*-isopropoxystyrene **12** (85% vs. initial **III**) was identified in the crude reaction mixture by ¹H NMR and GC-MS analysis, indicating that decomposition of **III** is slow relative to initiation. Ethylene (1% vs. styrene) and stilbene (ca. 18% vs. styrene)* were observed in the crude reaction mixture. Selective abstraction of Ru=CHPh but not Ru=CH(*o*-^{*i*}PrO-C₆H₄) was unexpected given the instability of **III** toward **N1** demonstrated in Section 4.1. The absence of **10** suggests rapid catalyst initiation, and decomposition prior to re-uptake of the styrenyl ether.

Also striking is the absence of MCB deprotonation products **13** and **14**. This is partially attributable to the efficiency of benzyldiene abstraction prior to forming phenyl-disubstituted MCB **Ru-25** (Scheme 4.7, above). Formation of stilbene and C₂H₄; however, indicate that a portion of the catalyst charge proceeds beyond initial formation of **Ru-11b**. Given the similarity in basicity between NH₂^{*n*}Bu **N1** (*p*K_a conjugate acid = 18.3) and NEt₃ **N10** (*p*K_a conjugate acid = 18.5),³⁷ for which MCB

* Maximum yield estimated by consumption of styrene, notwithstanding formation of PhCH₂NH^{*n*}Bu. Stilbene not directly quantified due to peak overlap with *o*-isopropoxystyrene. The identity of stilbene was confirmed by GC-MS (ca. 10% vs. styrene by total ion count, not calibrated).

deprotonation is the major decomposition pathway (Chapter 4.3), the complete absence of **13** and **14** is surprising. It is, however, noteworthy that a portion of the initial **III** charge (15%, assuming **17**, otherwise 30%) could not be assigned, and minor amounts of MCB deprotonation (e.g. propene or butene formation) cannot be conclusively ruled out.

4.5. Conclusions and future work

The foregoing describes new mechanistic insights into the amine-induced decomposition of **III** during metathesis. These studies are therefore complementary to those focusing on the amine-induced decomposition of PCy₃-stabilized **GII**, outlined in Chapter 3. Bulky bases (NEt₃, pyrrolidine, DBU) trigger deprotonation of the metallacyclobutane intermediate. Markers for this pathway are RHC=CHCH₂R' species; formation of which accounted for 80–90% of the total loss in Ru alkylidene, irrespective of temperature (RT and 60 °C). The monosubstituted metallacyclobutane formed under C₂H₄ was particularly vulnerable to attack. For amines that are less bulky (*n*-butylamine) or less basic (morpholine), alkylidene abstraction competes with MCB deprotonation. Markers for the abstraction pathway were PhCH₂NH^{*n*}Bu or *N*-methyldmorpholine, respectively.

Prior studies by our research group had implicated methylidene abstraction by PCy₃ as the dominant deactivation pathway for **GII** during catalysis, for all but DBU.^{27,29} We speculated that the MCB might be involved in the latter case. Re-examination of the **GII**–DBU chemistry in light of the newly-uncovered MCB deprotonation pathway indicates that where the Bronsted base is both strongly basic and sterically bulky, MCB deprotonation dominates over methylidene abstraction, even in the presence of PCy₃. Importantly, deprotonation of the MCB dominates in the presence of ethylene, even for the weaker Bronsted base pyrrolidine. These findings illustrate that, though methylidene abstraction by PCy₃ is often dominant, the underlying MCB chemistry of **GII** ultimately parallels that of **III**. Moreover, they shed a new and unexpected light on the critical importance of ethylene removal to catalyst longevity.

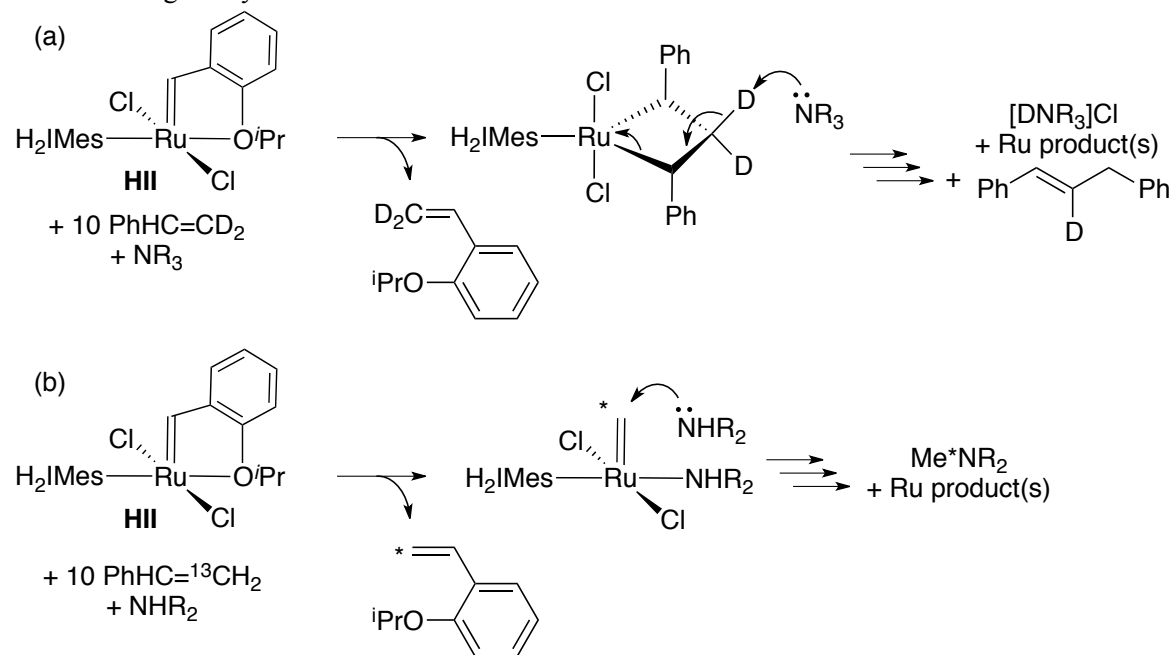
Long-term opportunities uncovered by this chemistry are discussed in the final Chapter. Short-term issues requiring confirmation are provided here. Isolation of the C-H-activated Ru product **Ru-34** proposed in Section 4.4.1 is of keen interest. ¹H-¹³C HMQC NMR analysis would aid in confirming the presence of the Ru–CH₂R functional group, given the diagnostic value of the ¹³C chemical shift for this entity, upfield of the NHC methyl groups.^{31,50,53,54} To confirm the structure of **Ru-34**, larger-scale synthesis (ca. 200 mg) should be carried out. Ideally, **Ru-34** could be isolated from the crude reaction mixture by addition of a non-polar solvent (i.e. hexanes) following loss of the alkylidene. Failing this, volatiles may be removed under vacuum and liquid organic products extracted using a non-polar solvent. Recrystallization would then be necessary to isolate the desired

Ru product from *E*-stilbene and (proposed) [HDBU]Cl. The appropriate solvent system would need to be determined experimentally, though toluene/hexanes may prove to be a suitable starting point.

Also of interest is the fate of the abstracted β -MCB proton, at present presumed to be an ammonium salt. Reaction of **HII** and a strong base (e.g. DBU) with β -D labeled substrate (Scheme 4.15a) could aid in confirming retention of the proton by base. Extraction from the reaction mixture would further support this hypothesis. Alternately, direct involvement of C-H activation in the mesityl substituent of the H2IMes ligand might be confirmed using a CD₃-labelled ligand (discussed in greater detail in Chapter 6).

Finally, formation of methyldene abstraction products (MeNR₂), particularly in the *n*-butylamine study in Section 4.4.6 could not always be easily assessed due to signal overlap by ¹H NMR methods. In such cases, isotopic labeling may again prove useful. A β -¹³C labeled substrate would be expected to produce labeled **GIIIm*** in situ. Ultimately, methyldene abstraction would form (¹³CH₃)NR₂ (Scheme 4.15b), which could be detected via ¹³C{¹H} NMR analysis, as previously demonstrated for isolated **GIIIm***.²⁸

Scheme 4.15. Proposed isotopic labeling studies for (a) determining the fate of β -MCB H during metallacyclobutane decomposition. (b) confirming the identity of methyldene abstraction products formed during catalysis.



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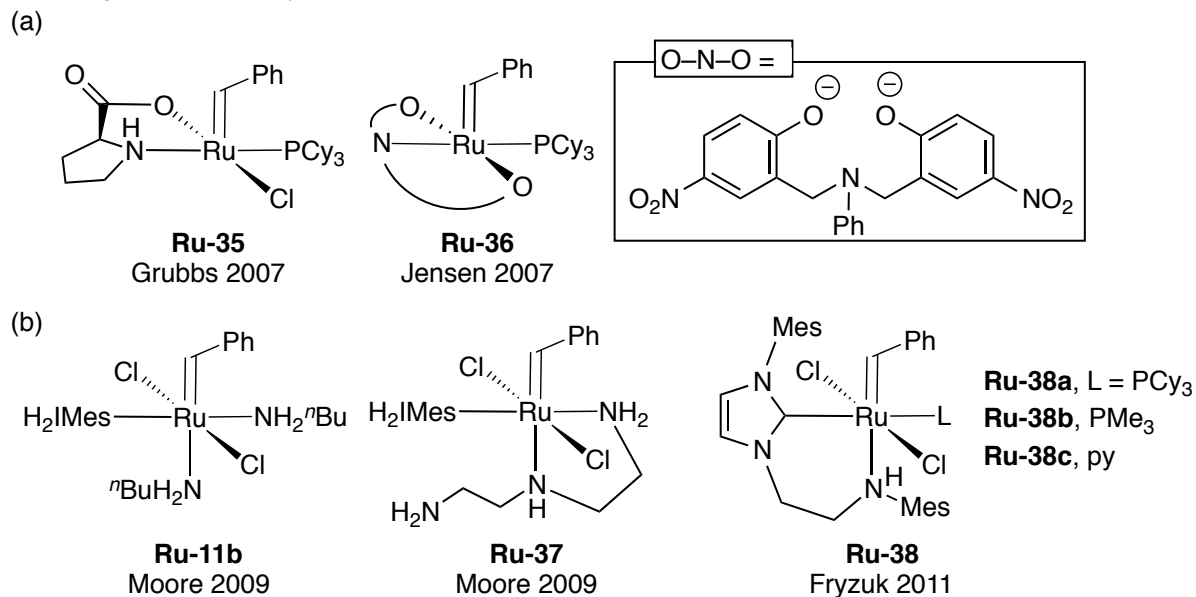
Chapter 5. Amines as Ligands in Olefin Metathesis

5.1. Nitrogen ligands in olefin metathesis – design opportunities

Chapters 3 and 4 described deactivation of the Grubbs and Hoveyda metathesis catalysts by amines, and demonstrated that deactivation could be inhibited by tuning amine bulk and Bronsted basicity. The present Chapter explores the potential of suitably modified amines in catalyst design. Prior attempts to incorporate nitrogen ligands into Ru catalysts have focused largely on pyridine derivatives or chelating Schiff base (imine) donors. Pyridine derivatives such as **GIII**,¹ while excellent initiators for ROMP,² show poor activity in CM and RCM reactions, for the reasons discussed in prior Chapters.^{3,4} Schiff base catalysts are generally less active, requiring high reaction temperatures (70–90 °C),^{5,6} with the exception of **HII** variants in which an imine replaces the ether donor, and is therefore lost during catalysis.⁷ A detailed analysis of the limitations of such catalysts has been presented.⁸

In comparison, catalysts bearing amine ligands are relatively few. Derivatives of **GI** bearing bidentate O,N-ester or tridentate O,N,O-phenoxy ligands were reported by the Grubbs and Jensen groups in 2007 (**Ru-35**,⁹ **Ru-36**;¹⁰ Chart 5.1a). Metathesis activity was low in both cases, with incomplete RCM of diethyl diallylmalonate (DDM) using 1 mol% Ru.

Chart 5.1. Grubbs-class metathesis catalysts bearing neutral amine ligands. (a) First-generation; (b) Second-generation catalysts.

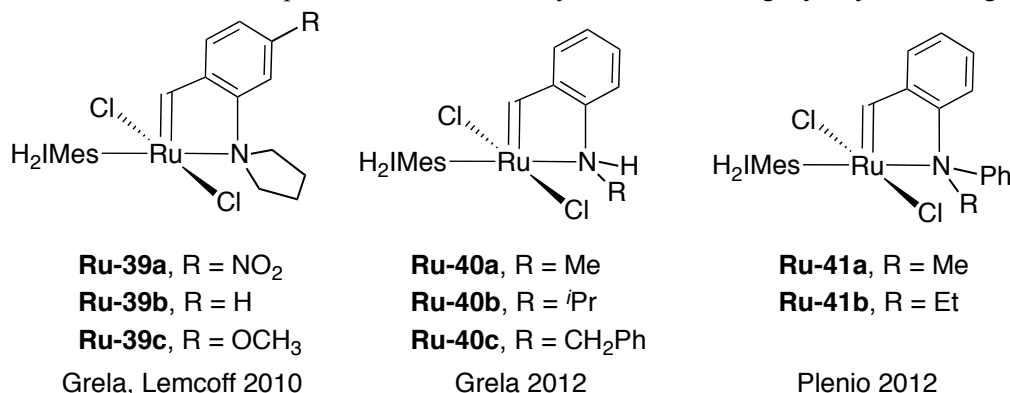


Of the second-generation NHC derivatives, Moore's *n*-butylamine complex **Ru-11b**¹¹ was described in Chapter 3, which uncovers the basis of its feeble RCM performance (<10% RCM of

DDM after 30 min at 23 °C, using 2 mol% Ru). The related diethylenetriamine complex **Ru-37** suffers from the same limitations. In subsequent work, Fryzuk¹² described complexes **Ru-38**, bearing chelating NHC–amine ligands. However, metathesis activity (in both RCM and ROMP reactions) was significantly lower than the benchmark catalysts **GII** and **GII'**. The origin of the poor metathesis performance was not examined.

Hoveyda-class complexes in which the aryloxy donor is replaced by a neutral arylamine donor have also been explored (Chart 5.2).¹³ The pyrrolidine derivatives **Ru-39** proved inactive in olefin metathesis at RT, unless an electron-withdrawing group was used to temper amine donor ability (see **Ru-39a**). For **Ru-39b** and **Ru-39c**, turnover numbers (TONs) for DDM were below 80 even after 1–3 days at 55 °C. Even nitro-functionalized **Ru-39a** was only marginally active at 24 °C, requiring 27 h to achieve a TON of 93 at a catalyst loading of 1 mol%. Grela subsequently reported high RCM and CM yields for **Ru-40a/b** with a variety of substrates, but catalyst loadings ranged from 1–5 mol%, reaction times were typically up to 8 h, and high temperatures were again required (80 °C).¹⁴ An *N*-benzyl substituent improved activity relative to *N*-Me or *N*-*i*Pr (see **Ru-40c**). However, Plenio reported dramatically higher productivity for aniline-derivative amine donors (**Ru-41**).¹⁵ While only terminal olefins were studied, at temperatures of ca. 50 °C, high RCM yields were reported even at low catalyst loadings (0.0025–0.01 mol%). RCM yields were comparable to, and in some cases exceeded, values for benchmark catalyst **III**.

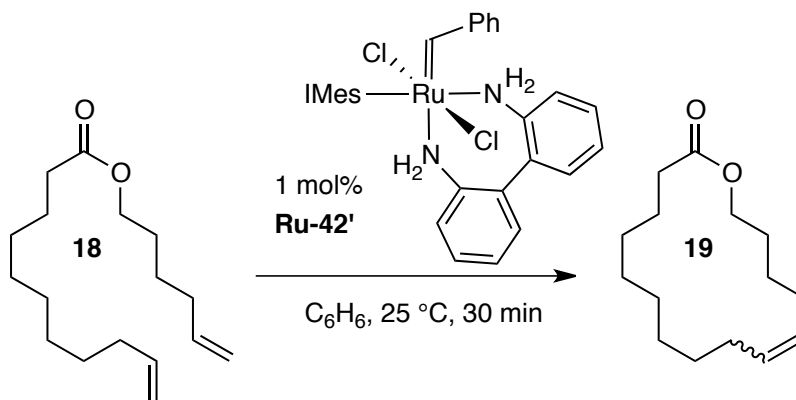
Chart 5.2. Literature examples of metathesis catalysts with chelating styrenyl-amine ligands.



Collectively, these studies indicate a general trend toward higher metathesis yields where the nitrogen donor is sterically bulky, or electron-withdrawing groups diminish amine basicity. It should be noted that in these styrenyl-amine complexes, the nitrogen donor is an aniline derivative, which attenuates its basicity, relative to alkylamines. In a recent review, Compain noted that arylamines were among the more successful amine-containing metathesis substrates.¹⁶ We considered that use of bulky, less Bronsted basic anilines is key to inhibiting catalyst deactivation.

An early clue as to the validity of this proposition emerged from a study by Mr. Stephan Audörsch, an exchange student with this research group.¹⁷ This study focused on incorporation of biphenyldiamine ligand **N11** onto **GII'**. Complex **Ru-42'** proved highly active for RCM, even at RT. Particularly notable was its near-quantitative macrolactonization of **18** within 30 min at RT using 1 mol% Ru (Scheme 5.1). In comparison, **GII'** requires hours at 40 °C to achieve comparable yields.¹⁸

Scheme 5.1. Prior RCM studies with **Ru-42'**.¹⁷



The first part of this Chapter describes the synthesis of **GII** derivatives containing selected amines. The pyrrolidine, morpholine, and ethylenediamine adducts were prepared not for the sake of catalysis, but to gain insight into species generated in situ during the decomposition (Chapters 3 and 4). Inspired by the promising preliminary behavior of **Ru-42'** (Scheme 5.1),¹⁷ we then examined the H₂IMes analogue **Ru-42**. Its preparation, characterization, performance in catalysis, and a preliminary examination of its decomposition chemistry are described. The second part of this Chapter summarizes work originally aimed at installation of *N*-anionic ligands. Motivation for this work is described in greater detail in Section 5.5.

5.2. Synthesis of Ru benzylidenes with amine ligands

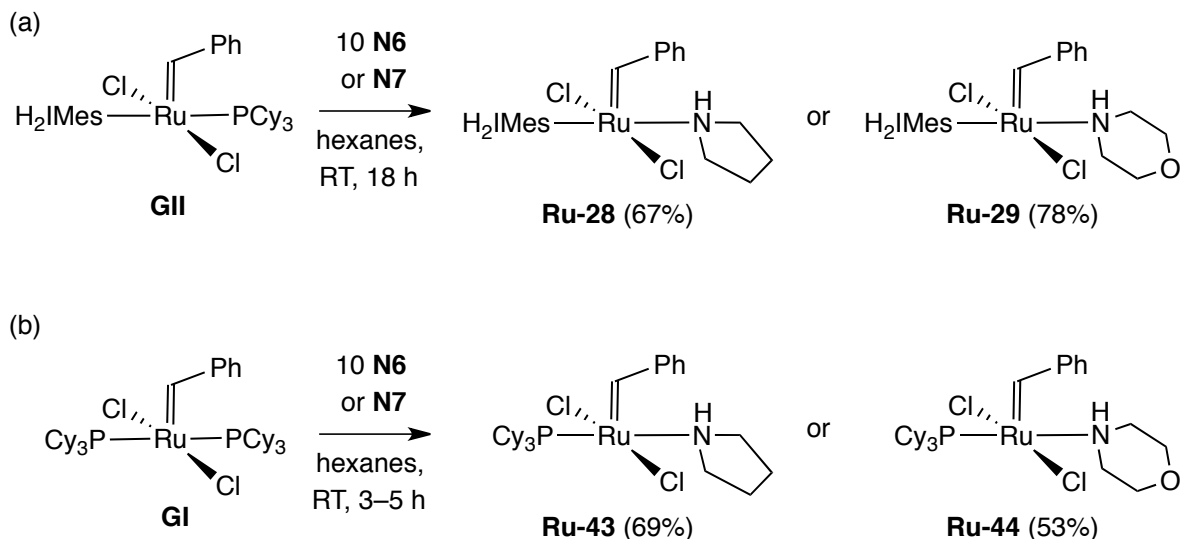
5.2.1. Synthesis and characterization of Grubbs benzylidenes with monodentate amine ligands

Adducts of monodentate amines exist in equilibrium with **GII** (Chapter 3, Section 3.4). The Moore compound **Ru-11b** was isolated by precipitation, following addition of cold pentane to a CH₂Cl₂ solution containing 100 equiv NH₂ⁿBu.¹¹ As a strategy for isolation of other amine adducts, we exploited the higher solubility of **GII** in hexanes.

Addition of excess morpholine (**N6**) or pyrrolidine (**N7**) to a suspension of **GII** in hexanes at RT resulted in a colour change from pink to green over ca. 12 h. Stirring was continued for a further 6 h, after which the **GII** adducts were isolated in >65% yield by filtration and washing with hexanes (see Scheme 5.2a; Table 5.1). NMR data for isolated **Ru-28** and **Ru-29** were identical to those for the

in situ-generated species described in Chapter 3, Section 3.4. NMR integration and microanalysis was consistent with formulation as mono-amine adducts. Each complex exhibited a single infrared $\nu(\text{N-H})$ stretching band at 3200–3250 cm^{-1} , and one singlet for the alkylidene proton at ca. 19.7 ppm, with a corresponding $^{13}\text{C}\{^1\text{H}\}$ NMR singlet at ca. 303 ppm. The NH signal for bound amine appears at ca. 3.2 ppm. The different environments above and below the basal plane of the square pyramid result in the appearance of four singlets for the H_2IMes methyl groups (2.81–1.97 ppm; 18 H), and two multiplets for the inequivalent NHC backbone protons (3.57–3.21 ppm; 4 H). Rotation about the Ru-C_{NHC} bond is evidently slow on the NMR timescale. For both complexes, the $\beta\text{-CH}_2$ protons are diastereotopic: their assignment is supported by the HMQC correlation with a $^{13}\text{C}\{^1\text{H}\}$ NMR singlet near the location for the free amine (see Table 5.1). Both complexes were thermally stable once isolated, with no evidence of decomposition on heating for 24 h at 60 °C in C_6D_6 in the presence of TMB as an internal integration standard.

Scheme 5.2. Synthesis of morpholine (**N6**) or pyrrolidine (**N7**) adducts of (a) **GII** and (b) **GI**.



At the outset of this study, the Grubbs *N,O*-proline complex **Ru-35** (Chart 5.1)⁹ was the sole example of a first-generation Grubbs benzylidene bearing a primary or secondary amine that had been successfully isolated. Indeed, Moore's prior report¹¹ indicated that **GI** is decomposed by amines, although by what means was unknown until we established the benzylidene-abstraction pathway¹⁹ (Chapter 3). To test the general utility of hexanes precipitation with a (presumably) more challenging target, the **GI** adducts of morpholine (**N6**) and pyrrolidine (**N7**) were prepared. Treatment of purple suspensions of **GI** in hexanes by excess **N6** or **N7** resulted in deposition of a pale green solid within 5 h. After filtration, no additional material deposited from the supernatant over a subsequent 12 h.

The desired **GI** adducts were isolated in >50% yield. The yield of pyrrolidine adduct **Ru-43** was comparable to that of its second-generation analogue **Ru-28**: ca. 68%. A lower yield of first-generation morpholine adduct **Ru-44** was observed (53% vs. 78% for **Ru-29**), but is attributed to an additional reprecipitation step in purification (to remove minor quantities of **GI**). Retention of a single PCy₃ ligand in each first-generation adduct was indicated by observation of a ³¹P{¹H} singlet at ca. 43 ppm and the multiplicity of the Ru=CHPh proton at ca. 20.1 ppm (d, 12 Hz, s by ¹H{³¹P}). Spectroscopic characterization for **Ru-43** and **Ru-44** gave similar results to those described above for **Ru-28** and **Ru-29**, with the obvious exception of phosphine in place of H₂IMes. ¹H NMR and microanalyses were consistent with mono-amine adducts in each case. The thermal stability of **Ru-43** and **Ru-44** was not examined in detail, though no evidence of decomposition was noted over the course of NMR data collection (ca. 24 h, RT) in either case. Selected spectroscopic data are summarized in Table 5.1.

Table 5.1. NMR and IR data for derivatives of **GI** and **GII** bearing monodentate amines (morpholine, **N6**; pyrrolidine, **N7**).

		Ru-28	Ru-29	Ru-43	Ru-44
¹ H NMR (δ _H)	Ru=CHPh	19.67 (s)	19.74 (s)	20.16 (d, 12 Hz)	20.13 (d, 12 Hz)
	Ru(NH)	3.31 ^a	3.14	3.89	3.53
	β-CH ₂ of amine	1.10, 0.72	3.19, 2.58	1.30 ^a , 0.83	2.80, 2.31
¹³ C{ ¹ H} NMR (δ _C)	Ru=CHPh	302.1	304.2	304.1	303.4
	RuC _{NHC}	222.9	221.9	—	—
	β-CH ₂ of amine ^b	24.8	67.4	25.2	67.8
³¹ P{ ¹ H} NMR (δ _P)	PCy ₃	—	—	42.9	43.8
IR (cm ⁻¹)	ν N-H	3242	3213	3254	3217

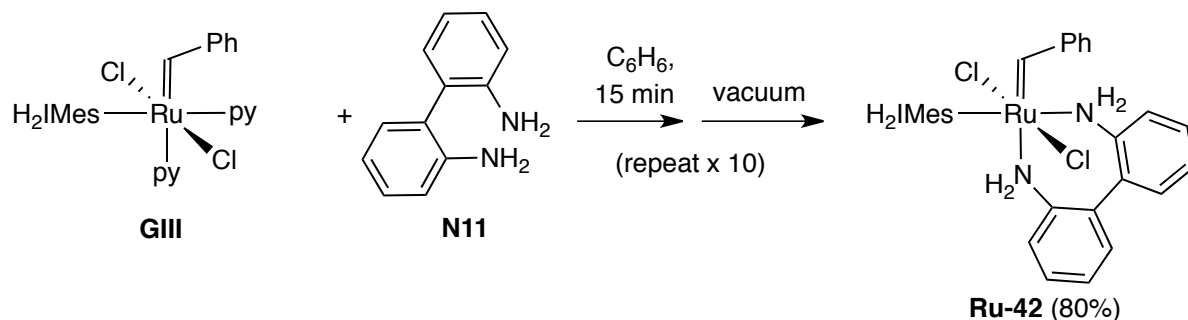
^a The signal overlaps with a methylene group of H₂IMes or PCy₃. Its location is confirmed by COSY correlation to NCH₂; the midpoint is specified. ^b Cf. 68.3 ppm for morpholine **N6**; 25.9 ppm for pyrrolidine **N7**.

5.2.2. Synthesis and characterization of benzyldiene complexes with chelating diamines.

Motivated by promising preliminary studies on **Ru-42'** (Scheme 5.1), RuCl₂(H₂IMes)(κ²-(H₂NC₆H₄)₂)(=CHPh) **Ru-42** was targeted for synthesis. Isolation of **Ru-42** was achieved by modification of the previously-developed synthesis of IMes analogue **Ru-42'**.^{17*} One equivalent of **N11** was added to a C₆H₆ solution of **GIII** (H₂IMes). After 15 min, volatiles were removed (including free pyridine) and the mixture was re-dissolved in fresh C₆H₆. After three iterations of dissolution and

* Synthesis was also attempted from a suspension of **GII** and excess **N11** in hexanes (under conditions shown in Scheme 5.2). Persistent contamination by **N11** was noted even following reprecipitation from CH₂Cl₂ / hexanes or toluene / hexanes. NMR data for the **N11**-contaminated product was identical to that of **Ru-42** later isolated from **GIII**.

drying under vacuum, ^1H NMR analysis (C_6D_6) of the crude reaction mixture indicated **GIII** (ca. 30%) with a new alkylidene at 18.99 ppm ($\text{Ru}=\text{CHPh}$). No change was observed on standing for 1 h, indicating that iterative exposure to vacuum, rather than extended reaction time, was required to complete conversion of **GIII**. After a subsequent seven iterations of dissolution (15 min) and drying in vacuo, >99% conversion of **GIII** to the new alkylidene was observed. $\text{RuCl}_2(\text{H}_2\text{IMes})(\kappa^2\text{-(H}_2\text{NC}_6\text{H}_4)_2)(=\text{CHPh})$, **Ru-42** was isolated in 80% yield following reprecipitation from CH_2Cl_2 / hexanes (Scheme 5.3).

Scheme 5.3. Isolation of **Ru-42** from **GIII**.

N–H signals for the isolated species were observed as a broad singlet at RT (ca. 4.5 ppm, C_6D_6 or CDCl_3). Four unique N–H environments were observed at $-20\text{ }^\circ\text{C}$ in CDCl_3 . Assignment of N–H signals was confirmed based on exchange with D_2O (Figure 5.1c). Resolution of the four *NH* unique chemical environments for **N11** only at low temperature was previously noted for **Ru-42'**,¹⁷ though the nature of the chemical exchange process at RT was not identified in the prior report.

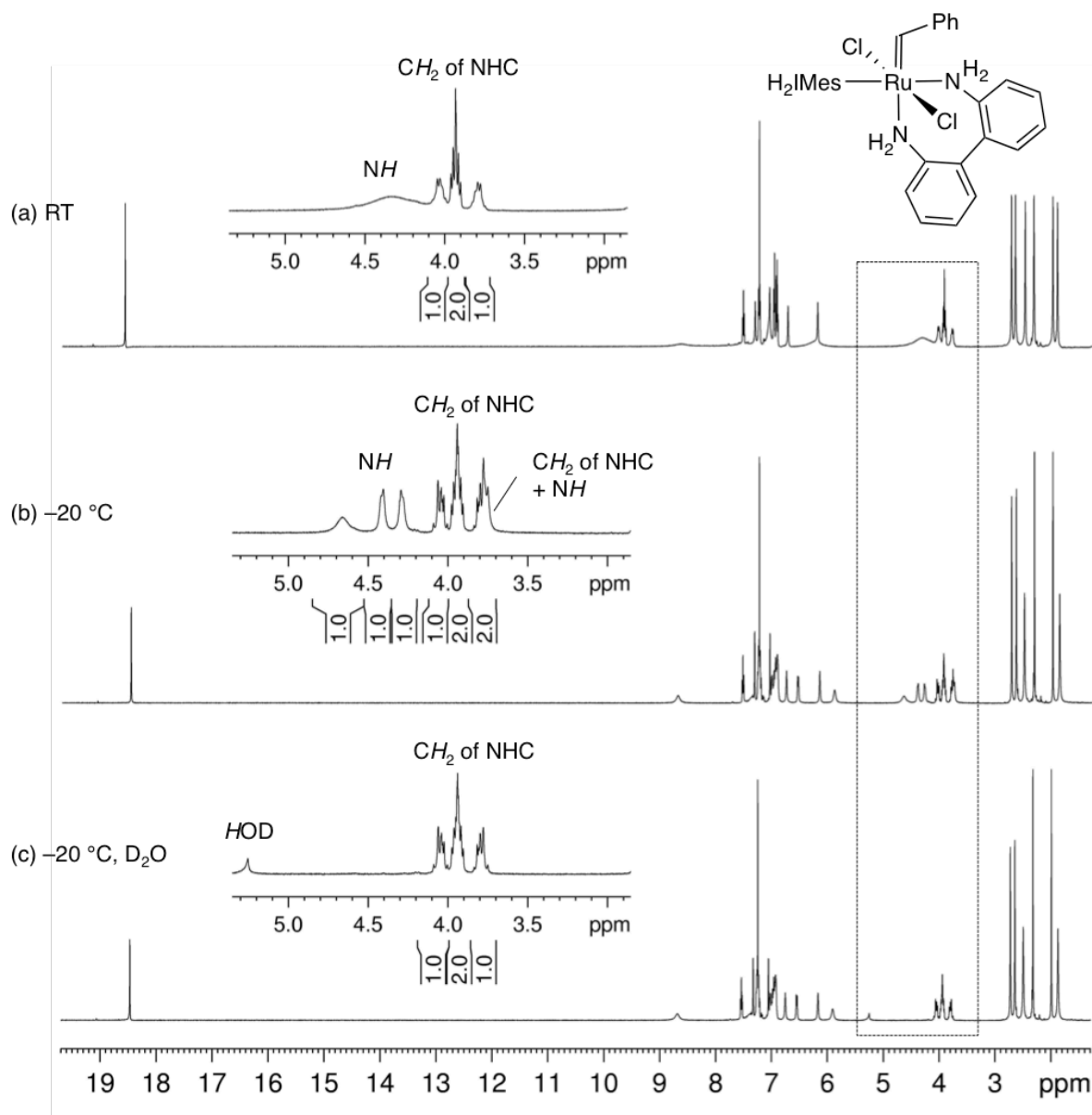


Figure 5.1. ^1H NMR spectra (CDCl₃, 500.1 MHz) of $\text{RuCl}_2(\text{H}_2\text{IMes})(\kappa^2\text{-(H}_2\text{NC}_6\text{H}_4)_2\text{)=CHPh} **Ru-42**. (a) at RT. (b) at -20°C . (c) at -20°C with 1 drop D₂O. Expansions show region containing N-H signals (5.0–3.5 ppm).$

For **Ru-42**, chemical exchange between all four NH environments was observed in a ^1H EXSY experiment at -20°C (Figure 5.2). Also evident was exchange between two well-resolved CH signals for the biphenyl moiety at 6.58 (d, 9 Hz, 1H) and 5.93 (br s, 1H) indicating that the *N,N* chelate ligand in **Ru-42** is sufficiently labile to permit exchange of the non-equivalent nitrogen atoms, even at low temperature. Assignment of the key signals as biphenyl CH *ortho* to NH₂ was supported by the doublet multiplicity of the signal at 6.58 and the upfield location relative to the

remainder of the biphenyl subunit.* Alternative assignment as the aromatic *CH* of Mes or Ph was ruled out by ^1H COSY NMR, which allowed identification of Mes and Ph signals (see Experimental, Chapter 2 for details). ^1H EXSY analysis of **Ru-42'** likewise indicated chemical exchange between inequivalent biphenyl *CH* positions at $-20\text{ }^\circ\text{C}$.

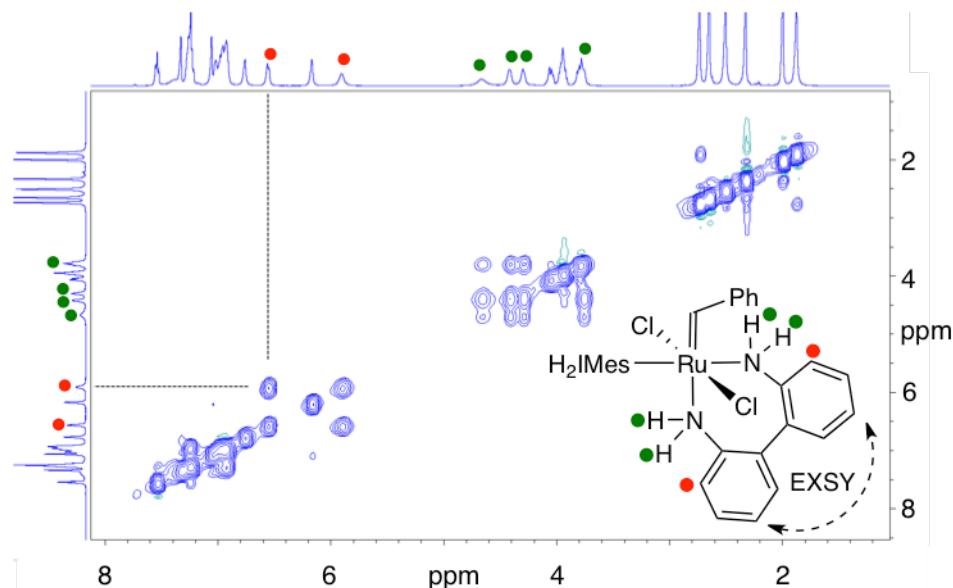
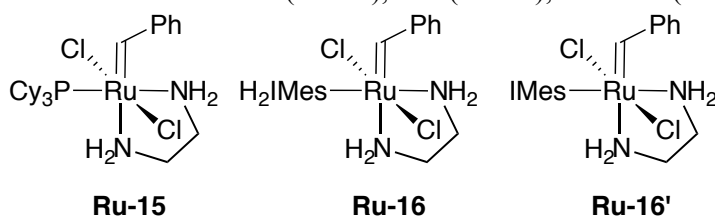


Figure 5.2. ^1H EXSY (500.1 MHz, CDCl_3 , $-20\text{ }^\circ\text{C}$, $t_8 = 0.25\text{ s}$) of $\text{RuCl}_2(\text{H}_2\text{IMes})(\kappa^2\text{-(H}_2\text{NC}_6\text{H}_4)_2\text{)(=CHPh)}$ **Ru-42** showing chemical exchange of NH_2 (green) and *o*-CH of biphenyl (red) subunits.

Ethylenediamine adducts of **GI** and **GII** (Chart 5.3, below) were originally developed to assay their susceptibility to abstraction by primary amines, as described in Chapter 3. Their characterization data are described here to allow comparison with **Ru-42**. Complexes **Ru-15** and **Ru-16'** were prepared prior to development of the route of Section 5.2.1 above. They were obtained by slowly adding en **N2** (1 equiv) to rapidly-stirred benzene solutions of **GI** or **GIII'**, stirring for 30 min, and then removing the volatiles and washing with hexanes. The PCy_3 complex **Ru-15** was obtained in 79% yield, and **Ru-16'** in 88% yield. The **GII** adduct **Ru-16** was subsequently prepared (also in 88% yield) by treating a hexanes suspension of **GII** with en **N2**, as described for the pyrrolidine and morpholine complexes **Ru-28** and **Ru-29** above.

* In comparison, *o*-CH signals for aniline are found at 6.64 ppm in CDCl_3 , ca. 0.5 ppm upfield of *m*-CH. All other aromatic signals for **Ru-42** were located downfield of the proposed *o*-CH amine signals (see Figure 5.2), except one singlet at 6.19, assigned to the Mes subunit by COSY correlation to CH_3 of Mes.

Chart 5.3. En adducts of **GI (Ru-15)**, **GII (Ru-16)**, and **GII' (Ru-16')**.

Retention of one phosphine ligand in the **GI** adduct **Ru-15** was indicated by the doublet multiplicity of the benzylidene proton at 20.29 ppm (d, $^3J_{\text{HP}} = 11$ Hz). This signal collapses to a singlet in the $^1\text{H}\{^{31}\text{P}\}$ spectrum. An alkylidene singlet was observed for **Ru-16** and **Ru-16'**; as expected, no $^{31}\text{P}\{^1\text{H}\}$ NMR signals was detected. In each case, microanalysis supported the proposed structure. Two unique chemical environments were consistently evident for the *NH* moieties, assignment of which was confirmed by exchange with D_2O). These broad ^1H NMR signals (each of which integrates to 2H) are centered at 3.5–2.6 ppm and 2.0–1.7 ppm. Similarly, two downfield *NH* signals were reported for literature complex **Ru-37** (Chart 5.1) at ca. 3.8 ppm in CD_2Cl_2 with the remaining three *NH* protons between 2.9 and 1.1 ppm (not distinguished from CH_2 signals).¹¹ However, it remains unclear which signals are due to the group *cis*, vs. *trans*, to the alkylidene ligand.

Table 5.2. NMR and IR characterization data for second-generation benzylidenes with N,N chelates.

N,N chelate “L” donor		N2^a			N11^b	
		PCy ₃ Ru-15	H ₂ IMes Ru-16	IMes Ru-16'	H ₂ IMes Ru-42	IMes ^d Ru-42'
^1H NMR (δ_{H})	Ru=CHPh	20.29 (d, 11 Hz)	19.09 (s)	19.40 (s)	18.49 (s)	18.77 (s)
	CH ₍₂₎ of NHC	–	3.30	6.69	4.17–3.67	7.11–6.89
	Ru(NH)	3.54, 1.96	2.64, 1.59	2.85, 1.67	4.69, 4.44, 4.32, 3.80	4.87, 4.63, 4.51, 3.82
$^{13}\text{C}\{^1\text{H}\}$ NMR (δ_{C})	Ru=CHPh	317.8	312.0	312.8	307.5	308.7
	RuC _{NHC}	–	221.9	189.1	215.7	181.6
$^{31}\text{P}\{^1\text{H}\}$ NMR (δ_{P})	Ru-PCy ₃	35.3	–	–	–	–
IR (cm ^{–1})	ν N-H	3377, 3300 , 3234 ^c	3368, 3346, 3299, 3274	3368, 3329, 3298, 3239	3346, 3324, 3258 ^c	3358, 3342, 3320, 3254

^a NMR data reported for C_6D_6 . ^b NMR data reported for CDCl_3 at -20 °C (NH signals not resolved at RT, see discussion). ^c The highest wavenumber N–H stretch (3377 or 3346) is more intense, perhaps indicating two incompletely-resolved signals for this compound. ^d This compound was originally prepared by S. Audörsch.¹⁷

For each en adduct, two methylene carbon signals were assigned by HMQC and DEPT analysis. These are located at 42–41 ppm in C_6D_6 (cf. 44.9 for free en in CDCl_3). In contrast to **Ru-42** and **Ru-42'**, no chemical exchange for NH_2 or NCH_2 positions was inferred from EXSY experiments with **Ru-16** and **Ru-16'**, even at RT. The implied decrease in lability for the en ligand, relative to biarylamine **N11**, can be expected to limit catalyst initiation.

5.3. Olefin metathesis studies with biphenylamine catalysts

Of keen interest is the metathesis activity of the biphenylamine derivatives, given the low Bronsted basicity of this amine, and its relatively high bulk. High lability for **N11** was inferred from EXSY experiments, as discussed above. Reactions were therefore performed at RT. The activity of **Ru-42** was benchmarked against the most widely-used commercial catalysts, **GII** and **III**.²⁰ Its total productivity in RCM is usefully compared with that of **GIII**, to assess the extent to which deactivation is curbed by switching from pyridine to biphenyldiamine.

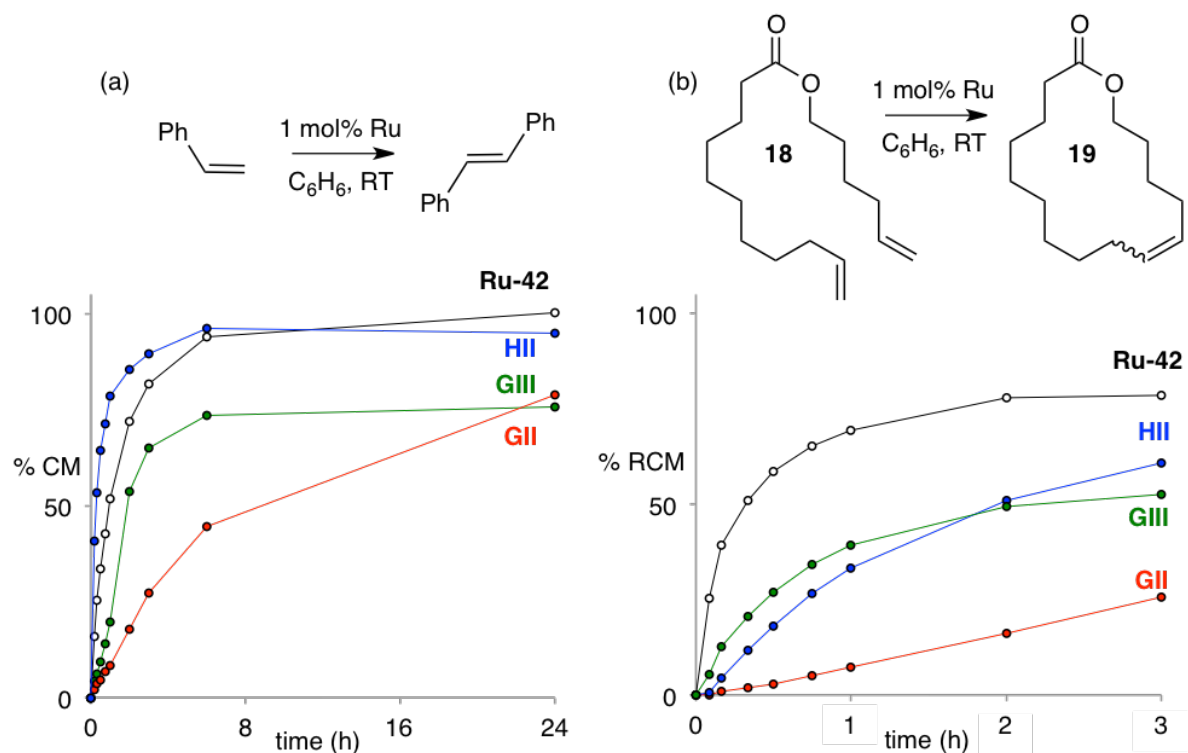


Figure 5.3. Metathesis of (a) styrene; (b) pro-lactone **18** by **Ru-42** relative to benchmark catalysts **GII**, **GIII**, and **HII**. Conditions: initial olefin concentration 100 mM (styrene) or 5 mM (**18**); RT, C₆H₆; $\pm 2.5\%$ in replicate experiments.*

* Carolyn Higman of this research group recently repeated the RCM **18** using freshly-prepared **Ru-42**, and observed >99% conversion of the diene within 1 h at RT under the conditions of Figure 5.3b. The discrepancy may arise from substrate contamination in the present experiments.

The metathesis activity of **Ru-42** was assessed against these comparator catalysts in homodimerization of styrene and macrocyclization of **18** at RT (Figure 5.3). Metathesis yields were consistently higher for **Ru-42** than **GIII**, suggesting that replacing pyridine with the biaryllamine **N11** indeed limited catalyst deactivation. **Ru-42** likewise out-performed **GII**: in this case, the greater lability of the biaryllamine ligand certainly contributes. Of interest is the possibility that deactivation is also slower: this question is probed below.

Perhaps most intriguing, however, is the comparison of **Ru-42** with **HII**. In CM of styrene, **HII** initially out-performs **Ru-42** by a small margin. For RCM of prolactone **18**, the reverse is observed. This may reflect the different concentrations used in the two reactions: 100 mM for CM, but 5 mM for macrocyclization (as required to maximize equilibrium yields of the 16-membered lactone **4**, over oligomeric rings and chains).¹⁸ Because **HII** initiates via interchange-associative pathways,^{21,22} it reacts considerably faster in the CM reaction than in RCM. In contrast, six-coordinate **Ru-42** is constrained to initiate via the dissociative pathway, and its reactions will therefore be independent of substrate concentration. The high performance of **Ru-42** is striking given the fact that **HII** and **GII** are the dominant catalysts used in metathesis today.

Comparable reactivity was likewise found for **Ru-42** in RCM of DDM **20** at a catalyst loading of 1 mol %. Thus, RCM was quantitative in 30 min at RT (Figure 5.4a), as compared with reported timescales of 20–30 min for **GII** and **HII** at 30 °C, also at 1 mol% Ru.³ On twentyfold reduction of the catalyst loading to 0.05 mol% Ru, however, RCM was seen to plateau at ca. 60% RCM (ca. 1,200 turnovers per Ru) for **Ru-42**. Parallel studies by Gwendolyn Bailey of this research group indicated that at 0.005 mol% Ru (a further tenfold reduction), both **GII** and **HII** achieve >90% RCM (ca. 19,000 turnovers per Ru) over 6 h in C₆H₆ at RT. The decomposition chemistry of complex **Ru-42** is discussed in further detail in Section 5.4 below.

A further comparison was undertaken with IMes analogue **Ru-42'**. In RCM of DDM and CM of styrene, **Ru-42** was significantly more active than **Ru-42'** (Figure 5.4). Puzzlingly, however, the trend in macrocyclization of **18** is the opposite: RCM was reportedly complete within 30 min for **Ru-42'** under the conditions of Figure 5.3b,¹⁷ but reached only 80% in 2 h for **Ru-42**.^{*} The inconsistency may originate in differential susceptibilities to decomposition. A preliminary assessment of the decomposition chemistry induced by biaryllamine **N11** was therefore undertaken.

^{*} On repeating the RCM reaction of **18** using catalysts **Ru-42** and **Ru-42'**, Carolyn Higman (see previous footnote) observed 76% conversion with **Ru-42** after 5 min, vs. 58% with **Ru-42'**. Both reactions reached >90% conversion within 45 min, >99% within 3 h. Initial data (above) suggesting unexpectedly lower catalyst activity for **Ru-42** relative to **Ru-42'** are now suspected to be an artifact of experimental error.

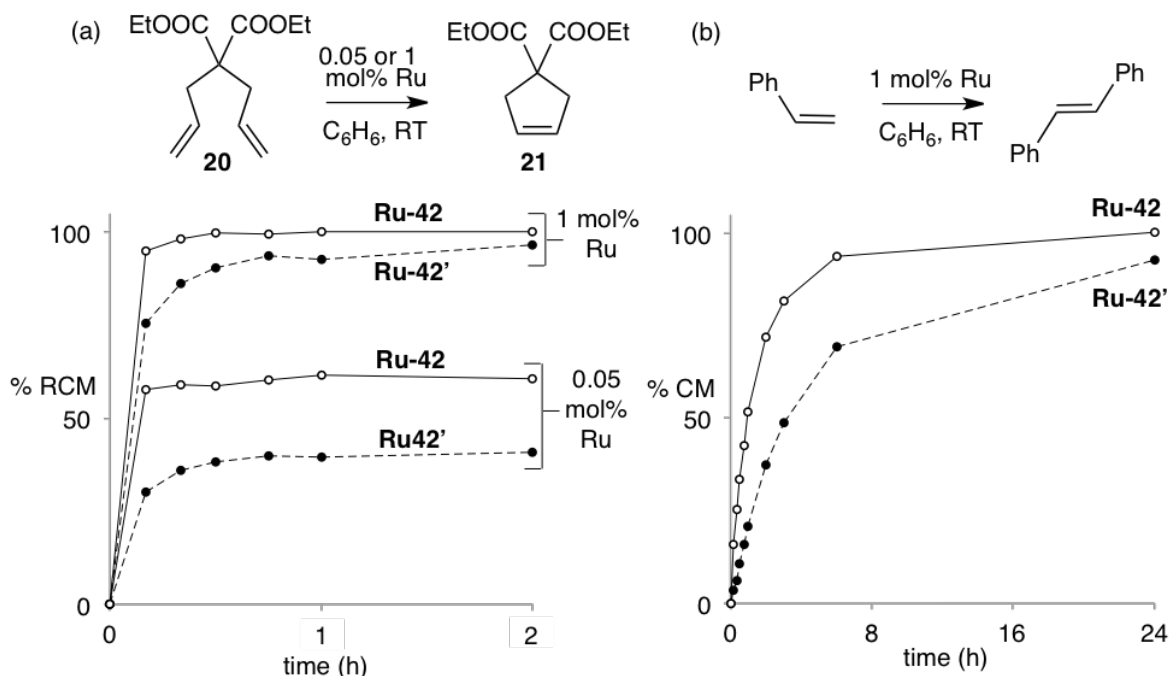


Figure 5.4. Metathesis of (a) DDM **20**; (b) styrene by **Ru-42** and **Ru-42'**. Conditions: initial olefin concentration 100 mM, RT, C_6H_6 ; $\pm 2.5\%$ in replicate experiments.

5.4. Decomposition studies of biphenyldiamine derivatives

5.4.1. Impact of aniline derivatives on cross metathesis yield

The impact of added biphenyldiamine **N11** on catalyst productivity was examined using the methodology set out in Chapter 4. Thus, styrene metathesis was carried out with **H11** at 60 °C, in the absence and presence of **N11** (10 equiv). To dissect out the importance of amine basicity and bulk (Chart 5.4), a systematic comparison of **N11** with *o*-phenylaniline **N12** and aniline **N13** was undertaken (Figure 5.5). The basicity of **N11** is presumed to be comparable with that of aniline.

Chart 5.4. Biphenyldiamine **N11** and its comparator amines. Note: cf. pK_a 16.6–24.1²³ for other bases studied in Chapter 4.

	N11	N12	N13	N8
pK_a (conjugate acid)				
in MeCN:	NR	NR	10.8	12.6
in H_2O :	NR	3.82	4.60	5.22

The effect of **N11** was much smaller than that of the amines previously studied, with 80% stilbene at 24 h, vs. 94% for the control reaction (Figure 5.5). The impact of aniline **N13** proved comparable to that of pyridine **N8** (the least detrimental base in Chapter 4), despite its dramatically reduced Bronsted basicity. This suggests that MCB deprotonation is not a significant contributor to catalyst deactivation for either aniline or py. Importantly, *o*-phenylaniline **N12** had almost no impact on CM yield (ca. 90% at 24 h; cf. 94% for **HII** without amine). The Bronsted basicity of *o*-phenylaniline is lower than that of aniline.²⁴ Given the minimal difference in the impact of aniline vs. pyridine, steric bulk, rather than Bronsted basicity, can be identified as the dominant factor in deactivation by these amines.

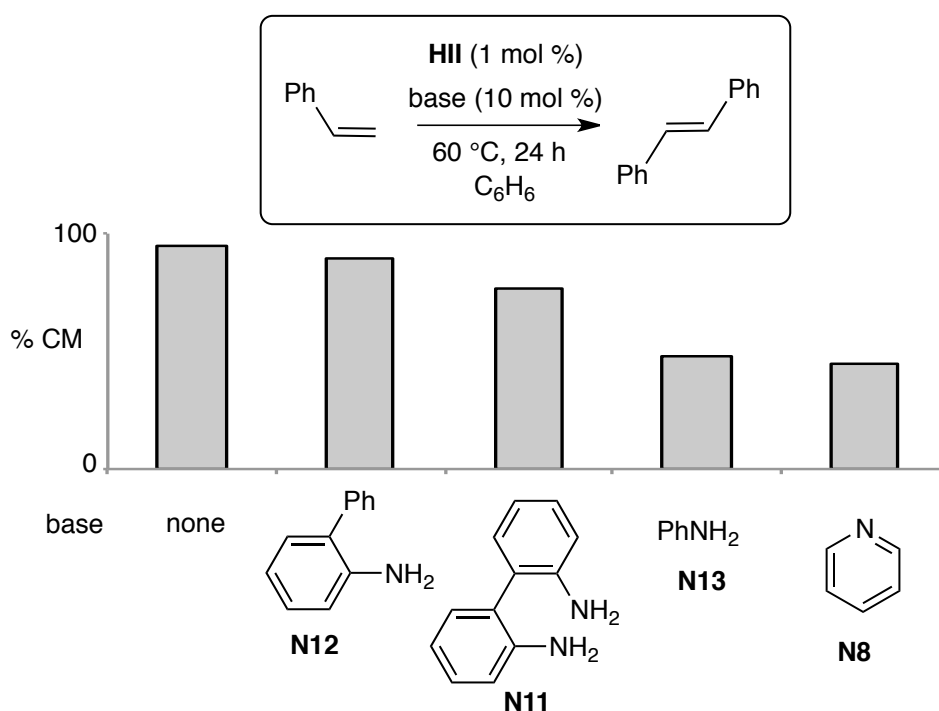


Figure 5.5. Impact of aniline derivatives (**N11**, **N12**, **N13**) on CM yield for homodimerization of styrene by **HII**. (Results for control and py reactions reproduced from Chapter 4 for comparison.)

5.4.2. Thermolysis of biphenylamine derivatives

The thermal stability of **Ru-42** and **Ru-42'** was assessed by monitoring the loss of the benzylidene signal vs. TMB at 60 °C in C₆D₆ (Figure 5.6). For **Ru-42'**, decomposition reached 70% after 24 h, and 90% after 96 h. The fate of the benzylidene moiety was traced to stilbene formation (85%). Decomposition of **Ru-42** was significantly slower (55% after 96 h), and stilbene again accounted for >90% of the “missing” Ru=CHPh. GC-MS analysis confirmed the presence of *E*-stilbene, as well as free **N11** and TMB. The ruthenium product was identified as biphenylamine

derivative **Ru-45** or **Ru-45'**, as inferred from observation of four NH doublets at 4.8–3.4 ppm (ca. 90%). Characterization of **Ru-45** is described in greater detail in the following section.

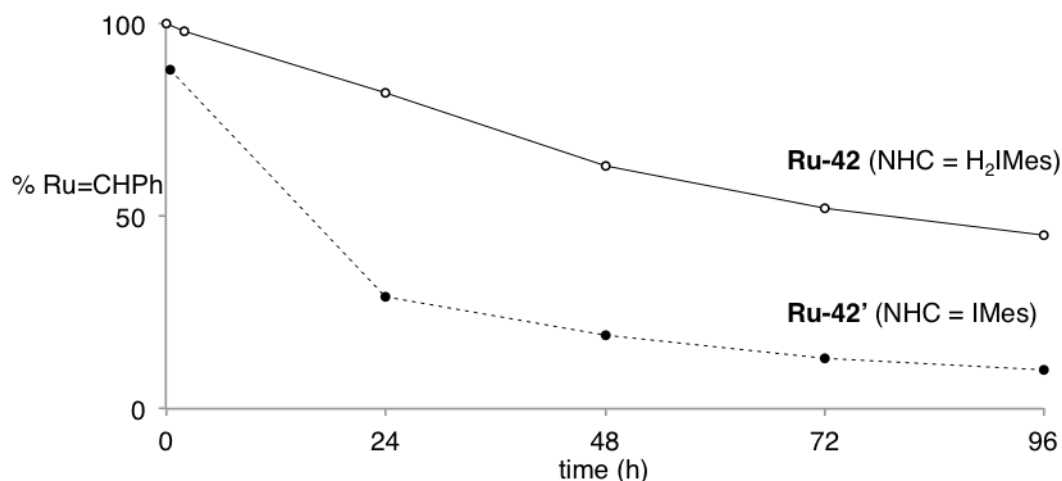
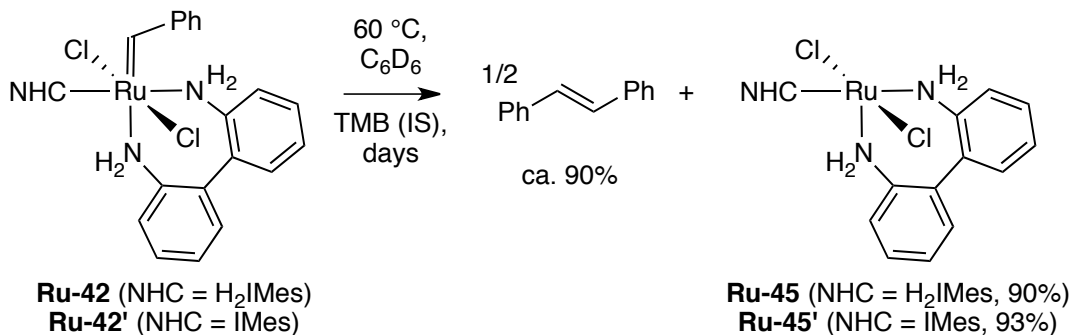
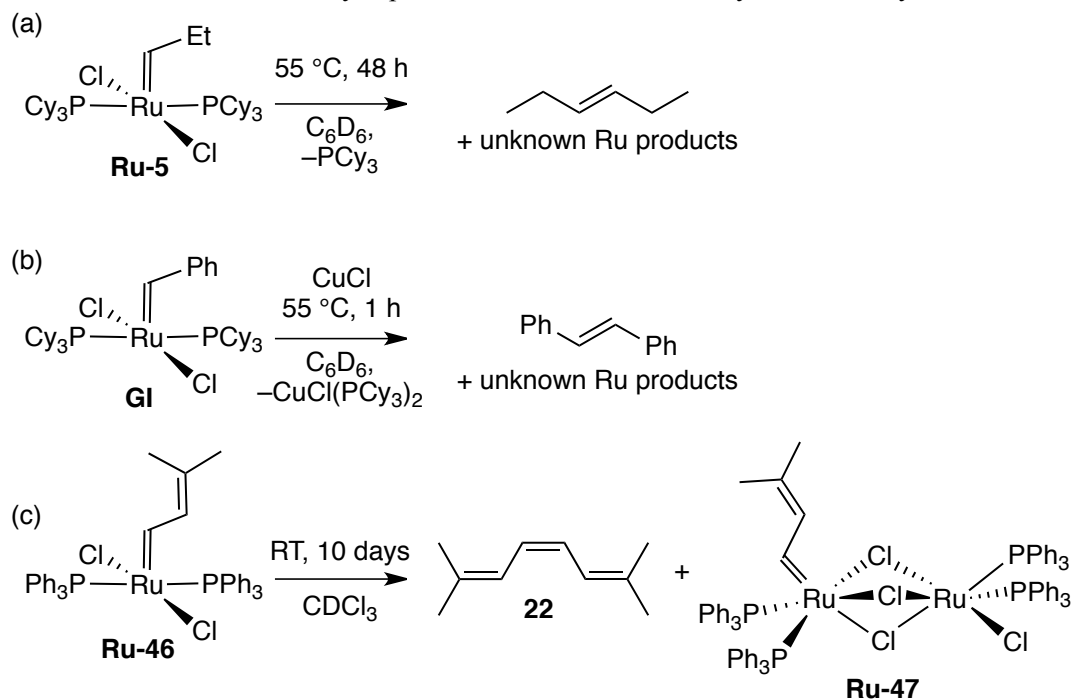
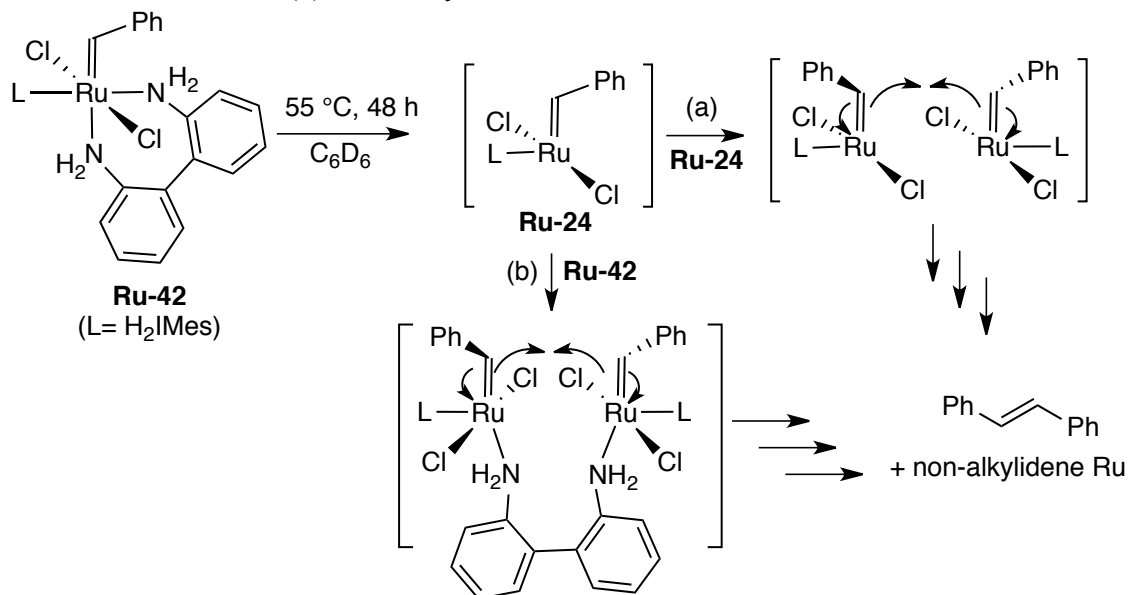


Figure 5.6. Reaction profile for thermolysis of **Ru-42** and **Ru-42'** (C₆D₆, 60 °C). Product yields (above) are normalized to decomposed Ru=CHPh against TMB internal standard at 96 h.

Precedent for stilbene formation is given by prior thermolysis studies carried out by the Grubbs^{25,26} and Fogg²⁷⁻²⁹ groups. Thermal decomposition of RuCl₂(PCy₃)₂(=CHCH₂CH₃) **Ru-5** was observed to ultimately form *E*-3-hexene (Scheme 5.4a).²⁵ Decomposition was proposed to originate in the four-coordinate propylidene following PCy₃ dissociation, as decomposition was slower in the presence of excess phosphine. (It should be noted that added PCy₃ does not retard decomposition of **GIIm** or related catalysts, where PCy₃ is directly involved in the decomposition process).³⁰ The corresponding decomposition of **GI** was slow, with a half-life of 8 days at 55 °C, but accelerated greatly in the presence of phosphine scavenger CuCl (t_{1/2} 10 min) (Scheme 5.4b).^{25,26} Similarly, thermolysis for vinylidene **Ru-46**, results in formation of a triene **22** and the face-bridged dimer **Ru-47** (Scheme 5.4a).^{27,29} Further details of this mechanism have not since been elucidated.

Scheme 5.4. Previously-reported “bimolecular” thermolysis of Ru alkylidenes.

The lability of **N11**, which is designed to give access to four-coordinate, metathetically active $\text{RuCl}_2(\text{NHC})(=\text{CHPh})$, presumably also promotes decomposition. Of interest is the possibility that **N11** can also enable bimolecular deactivation (Scheme 5.5b).

Scheme 5.5. Proposed bimolecular decomposition pathways of **Ru-42/Ru-42'** (a) without involvement from **N11**. (b) induced by **N11**.

The thermal instability of IMes analogue **Ru-42'** relative to H₂IMes complex **Ru-42** contrasts with the behavior of the Grubbs methylenes **GIIIm** and **GIIIm'**. In the latter case, the IMes analogue **GIIIm'** is more thermally robust.³⁰ The mechanism of thermolysis necessarily differs for the Grubbs methylenes (which decompose via PCy₃-induced methylene abstraction),⁴ but both are proposed to occur following initial formation of a four-coordinate alkylidene species. Very recent work from our group has proposed that phosphine dissociation from **GIIIm** and **GIIIm'** is inhibited by Ru→PCy₃ backbonding, which is stronger for the IMes derivative **GIIIm'**.³⁰ The thermal instability of **Ru-42'** suggests that in the absence of such an interaction, the IMes analogue initiates more quickly.

A preliminary assessment of the decomposition of **Ru-42** during catalysis is described below. Further experimental work aimed at mechanistic clarification is proposed in Section 5.7 and Chapter 6 (Conclusions and Future Work).

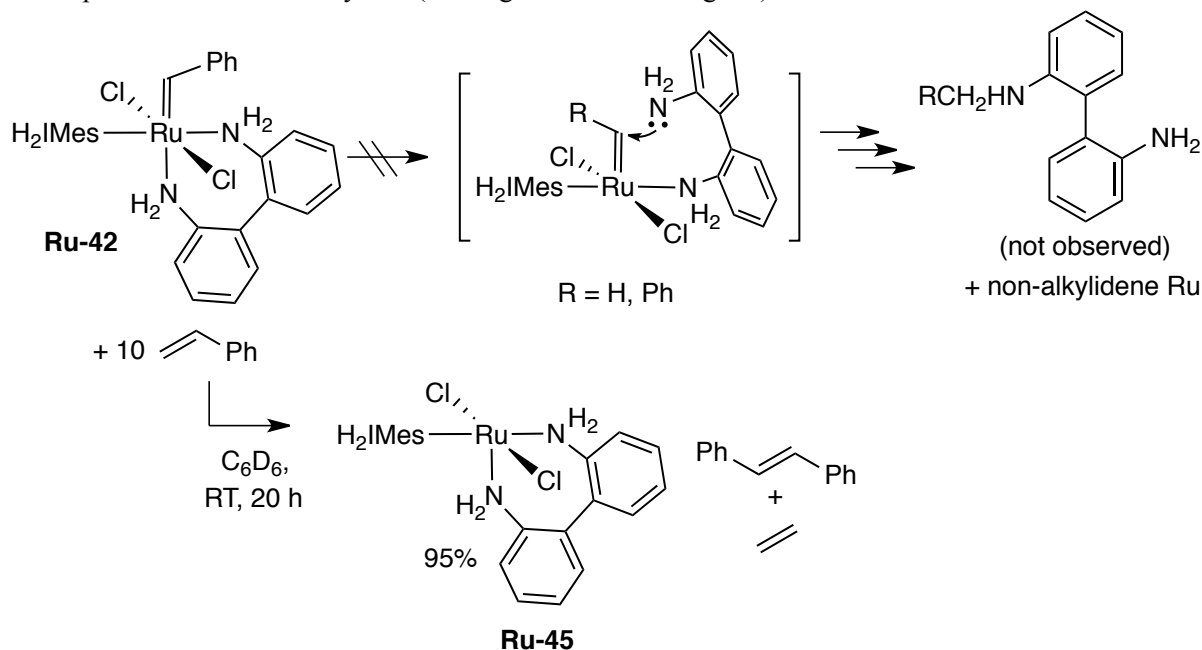
5.4.3. Decomposition of **Ru-42** during catalysis

Two metathesis experiments were carried out to assess whether **Ru-42** is protected against the decomposition pathways established in Chapters 3 and 4 (i.e. metallacyclobutane deprotonation and alkylidene abstraction). Thus, a solution of **Ru-42** (20 mM in C₆D₆) was treated with 10 equiv styrene at RT in a sealed NMR tube; TMB was also present as an internal standard. In the presence of styrene, **Ru-42** decomposed more rapidly than benchmark catalyst **III**, consistent with its performance in RCM and CM reactions (Section 5.3). Loss of the alkylidene signals reached 25%, as compared with 4% for **III** after 2 h at RT. At this point, 63% conversion of styrene to stilbene was apparent by ¹H NMR analysis. Importantly, given the vulnerability of the unsubstituted metallacyclobutane, >2 mol C₂H₄ vs. Ru remained in solution (s, 5.25 ppm) under sealed-vessel conditions. After 20 h at RT, the yield of stilbene had increased slightly, to 70%, and decomposition of **Ru-42** was near-complete (Table 5.3). Despite the apparent instability of **Ru-42**, no evidence of MCB deprotonation was apparent: that is, no PhHC=CHCH₂R (R = Ph, H) or propene was observed by NMR or GC-FID analysis. No evidence of an expected “alkylidene abstraction” product (Scheme 5.6) was observed, and its formation is ruled out by observation of a product assigned as **Ru-45** (Scheme 5.6) in 95% yield, which bears an intact **N11** ligand.

Table 5.3. Comparison of styrene CM yields and decomposition for **Ru-42** vs. **H11**.

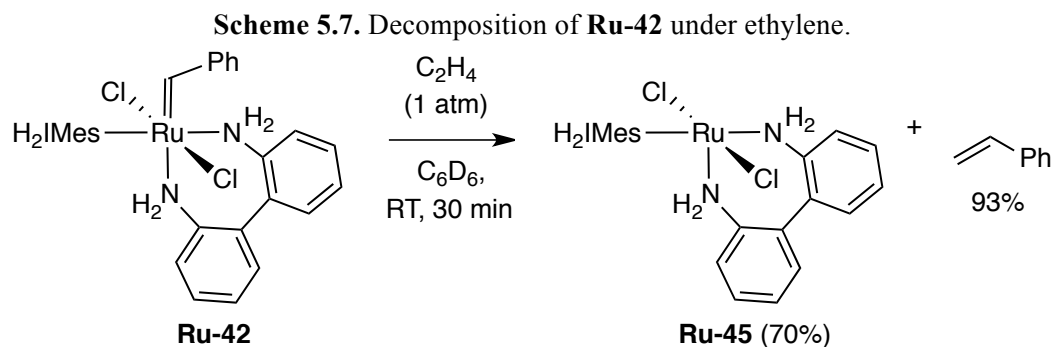
	time	% CM	loss of [Ru]=CHR
Ru-42	2 h	63	25%
	20 h	70	99%
III	2 h	68	4%
	24 h	71	52%

Scheme 5.6. Expected “alkylidene abstraction” amine product(s) and proposed Ru product from decomposition of **Ru-42** + styrene (bearing an intact **N11** ligand).



The proposed structure of **Ru-45** is supported by the observation of four *NH* doublets at chemical shifts that accord well with those for the *NH* signals for **Ru-42** (4.8–3.4 ppm, vs. 4.7–3.8 ppm; Table 5.2). Connectivity of the *NH* signals was confirmed by ¹H COSY NMR analysis. The methylene protons of the H₂IMes ligand partially overlapped with one *NH* signal at 3.63–3.35, and corresponded to the expected 4H (m, 5H total w *NH*). The aliphatic region 3.0–1.5 (18 H) was poorly resolved at RT, but at 60 °C, simplified to three singlets (2.67, 2.47, and 2.01 ppm, 6H each). Chemical exchange was observed between singlets at 2.67 and 2.47 by ¹H EXSY (assigned as *o*-CH₃ of Mes). Collectively, this data was consistent with a single Ru product bearing intact biphenyldiamine **N11** and H₂IMes ligands; proposed to correspond to RuCl₂(H₂IMes)(κ²-(H₂NC₆H₄)₂) **Ru-45**. Assignment of *NH* protons was confirmed by exchange with added D₂O. Isolation of **Ru-45** was not attempted.

The reaction of **Ru-42** under C_2H_4 was also examined, to determine whether the trapped ethylene in the experiment above was responsible for deactivation. A solution of **Ru-42** in C_6D_6 with TMB as internal standard was freeze-pump-thaw degassed, thawed, and exposed to 1 atm C_2H_4 at RT. The solution immediately changed colour from green to yellow and complete loss of $Ru=CHPh$ was confirmed after 30 min at RT. Analysis of an aliquot revealed styrene (93%) and **Ru-45** (70%) (Scheme 5.7). Again, significant alkylidene abstraction and MCB deprotonation could be ruled out, although trace propene was detected (5% vs initial **Ru-42**).^{*}



Having identified as **Ru-45** the major Ru product formed from **Ru-42** in the presence of metathesis substrates, the (incomplete) thermolysis study described in Section 5.4.2 was revisited to confirm that **Ru-45** is detected. This species indeed accounted for the bulk of the decomposed Ru (50% in situ yield at 55% decomposition). Given the stability of **Ru-42** in the absence of substrate (days at 60 °C vs. minutes to hours at RT with C_2H_4 or styrene), decomposition of the benzylidene **Ru-42** itself is implausible. However, an analogous “bimolecular” process involving at least one $Ru=CH_2$ might occur more rapidly. This might offer an explanation for the loss in catalyst activity observed for **Ru-42** (Section 5.3). Because decomposition products (styrene or ethylene) are indistinguishable from expected metathesis products, however, the mechanism of decomposition for **Ru-42** during catalysis is not conclusively confirmed. Possible strategies to clarify the mechanism are proposed in the final Chapter (Conclusions and Future Work).

5.5. Toward *N*-Anionic ligands in metathesis catalysts

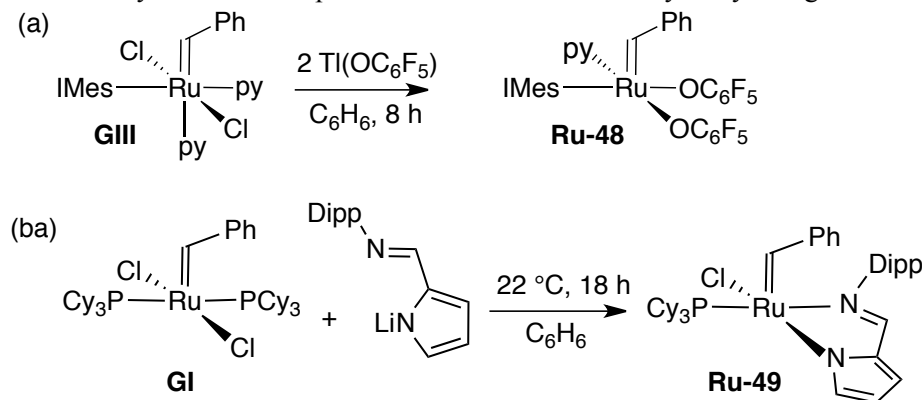
5.5.1. Motivation

A decade ago, the Fogg group reported unprecedentedly high turnover numbers in RCM following the replacement of a chloride ligand of **GIII** with a perhaloaryloxide ligand.^{32,33} However, these catalysts were limited by poor initiation efficiency.³⁴ This behavior was attributed to the

^{*} 1H NMR (C_6D_6) signals were observed at locations in good agreement with literature values:³¹ 5.71 (m, 0.05H), 4.98 (d, 17 Hz, 0.05H), 4.92 (d, 10 Hz, 0.05H), 1.55 (d, 7 Hz, 0.15H) ppm.

inductive effect of the oxygen donor, vs. the chloride ligands present in the parent catalysts (Pauling electronegativity 3.5 vs. 3.0). A compounding factor was the inductive effect of the halide substituents on the aryloxide ligand, used to inhibit isomerization to a piano-stool structure³⁵ (**Ru-48**; see also Section 5.6 below). More recently, Jensen and co-workers explored related arylthiolate ligands.³⁶ Amide derivatives are largely unexplored: a rare example, **Ru-49**, was developed in the Fogg group (Scheme 5.8b).³⁷ This section explores routes to anilido derivatives.

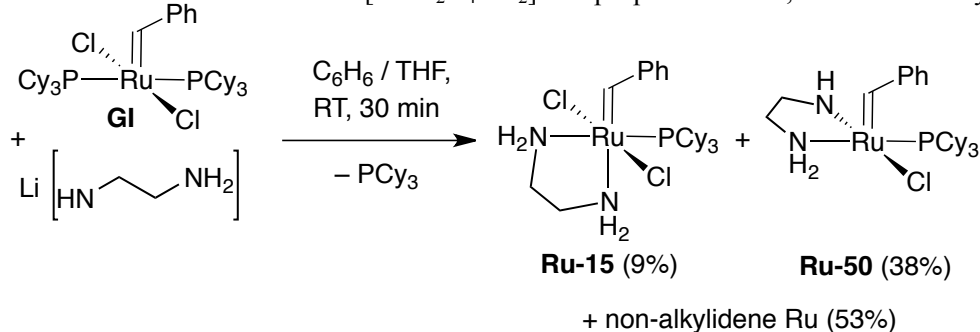
Scheme 5.8. Synthesis of Ru-pseudohalide metathesis catalysts by halogen exchange.



5.5.2. Attempted syntheses of *N*-anionic alkylidenes by halogen exchange

In order to probe the general utility of the synthesis described above for **Ru-49** (Scheme 5.8b), **GI** was treated with the Li salt of ethylenediamine. A solution of $[\text{Li}[\text{NHC}_2\text{H}_4\text{NH}_2]]_n$ in THF was added slowly to a stirred solution of **GI** in C_6H_6 . A colour change from purple to red-brown was noted over 30 min at RT. $^{31}\text{P}\{^1\text{H}\}$ NMR analysis indicated predominantly free PCy_3 (10.4 ppm, 70%) though formation of a new species was observed (49.6 ppm, 18%) with minor quantities of unreacted **GI** (36.9 ppm, 7%). Present in minor amounts was the previously-isolated adduct **Ru-15** (35.4 ppm, 4%), presumably from incomplete lithiation of **N2** in a prior step or reaction with trace H_2O in the reaction medium. No changes were observed by $^{31}\text{P}\{^1\text{H}\}$ NMR analysis of a reaction aliquot after 3 h at RT. Volatiles were removed under vacuum and the mixture was re-dissolved in C_6D_6 for analysis. Minor quantities of **GI** and **Ru-15** notwithstanding, a single Ru-alkylidene was observed at 15.84 ppm (d, $^3J_{\text{HP}} = 11 \text{ Hz}$, s by $^1\text{H}\{^{31}\text{P}\}$ NMR). A ^1H - ^{31}P HMQC experiment correlated the benzylidene doublet at 15.84 ppm with a $^{31}\text{P}\{^1\text{H}\}$ singlet at 49.6 ppm. No changes were detected by ^1H or $^{31}\text{P}\{^1\text{H}\}$ NMR after 4 h at RT, consistent with a persistent new alkylidene.

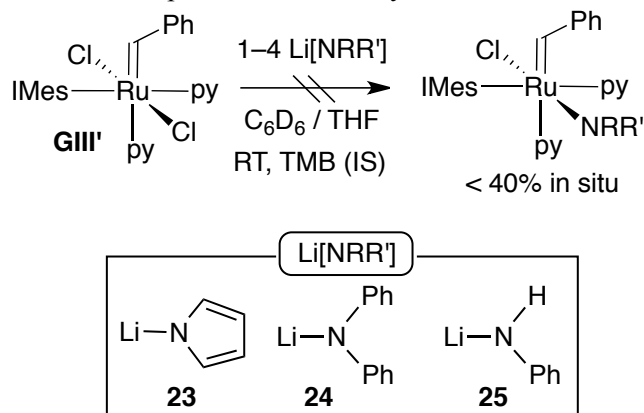
Given the prominence of free PCy_3 , 53% decomposition to non-alkylidene products was inferred (38% new alkylidene; 47% combined yield including **Ru-15**). Formation of a new, persistent, Ru benzylidene species (potentially desired product **Ru-50**) was encouraging, though in situ yields were prohibitively low, and isolation at increased scale was not attempted.

Scheme 5.9. Reaction of **GI** with Li[NHC₂H₄NH₂] and proposed **Ru-50**, formed in low yield.^a

^a In situ yields exclusive of 7% **GI**, corrected for expected 1 equiv free PCy₃ per **Ru-49** or **Ru-50**.

Synthesis of second-generation complexes bearing *N*-anionic ligands was also attempted. Second-generation (NHC) analogues of **Ru-49** or **Ru-50** would lack a labile L donor or vacant coordination site proximal to Ru=CHPh; thus, inefficiently bind olefin substrates. Reactions with a series of non-chelating *N*-anion precursors (**23** to **25**) was instead examined. The experiments described in this section were performed prior to development of clean, high-yielding syntheses of H₂IMes complexes,³⁸ and therefore focus on the IMes NHC. The pyridine adduct **GIH'** was selected rather than **GIH** itself, to maximize potential for further derivatization (e.g. installation of **N11**). Precursor **GIH'** was presumed to be compatible with anion exchange, given previously-successful syntheses of aryloxide complexes such as **Ru-48** (Scheme 5.8a)

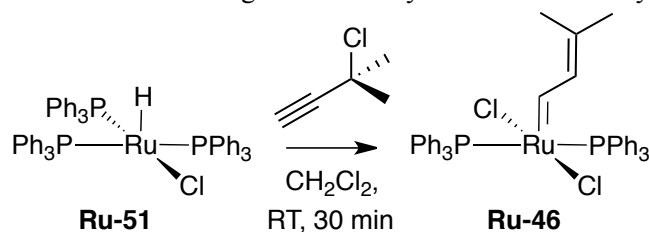
Solutions of **GIH'** with a TMB (internal integration standard) were prepared in C₆D₆ and treated with THF stock solutions of various Li[NRR'] salts (Table 5.4). The Li salt of pyrrole was included as a non-chelating analogue of the *N*-anionic ligand of **Ru-49** (Scheme 5.8b, above). Salts of Li[NPhR] (R = H, Ph) were easily prepared, and included to examine halogen exchange with *N*-anions of varying steric bulk. In each case >40% decomposition was observed within 30 min at RT on treatment with 1.1 equivalent of Li salt. For Li[NC₄H₄] **23**, an incomplete reaction was observed with formation of minor quantities of a persistent alkylidene at 19.31 ppm in the ¹H NMR spectrum. The in situ yield did not improve on standing, and was limited to ca. 35% following addition of excess **23** to induce complete reaction of **GIH'**. For Li[NPh₂], a transient alkylidene at 19.59 ppm was observed but decomposed on standing. For Li[NHPh], partial decomposition of **GIH'** was observed over 30 min with no observable alkylidene product. No further reaction was observed by 3 h, but full decomposition of **GIH'** was induced by addition stoichiometric excess Li[NHPh]. The mechanism of decomposition was not determined.

Table 5.4. Decomposition of **GIII'** by N-anionic salts **23** to **25**.

Lithium Salt	equiv added	time (h)	% GIII'	% new Ru=CHPh	% decomp
none	—	1	>99%	—	—
Li[NC ₄ H ₄] 23	1.1	0.5	51	9 (δ_{H} 19.31)	40
		3	48	9	42
		0.5 ^a	—	35	65
Li[NPh ₂] 24	1.1	0.5	11	29 (δ_{H} 19.59)	60
		1	8	—	92
		0.5 ^a	0	—	quant.
Li[NHPh] 25	1.1	0.5	38	—	62
		3	34	—	66
		0.5 ^a	0	—	quant.

Conditions: [Ru] = 15 mM, [Li[NRR']] = 17 mM or 60 mM, C₆D₆ w ca. 3% THF, RT. % values quantified against TMB internal standard, normalized to **GIII'** at *t*₀. ^a 3 equiv add'l Li[NRR'] salt added after 3 h at RT w 1 equiv Li[NRR'].

Attempts to install an amido ligand on **GI** or **GIII'** by reaction with lithium anilide, pyrrolide, diphenylamide, or the salt of ethylenediamine, were unsuccessful. New Ru=CHPh products consistent with halogen exchange were observed in several cases, but were unstable in solution and/or formed in low in situ yields (<40%). We therefore explored the alternative strategy depicted in Scheme 5.10, in which RuHCl(PPh₃)₃ **Ru-51** serves as a synthetic precursor to alkylidene **Ru-46**²⁹

Scheme 5.10. Prior work demonstrating ruthenium hydride **Ru-51** as a synthon for Ru=CHR

Section 5.6 examines whether monodentate anilido ligands are, like the Ru aryloxides,³⁹⁻⁴⁴ susceptible to binding via the π -system of the ring.³⁹ The coordination chemistry of NPh₂[−] with

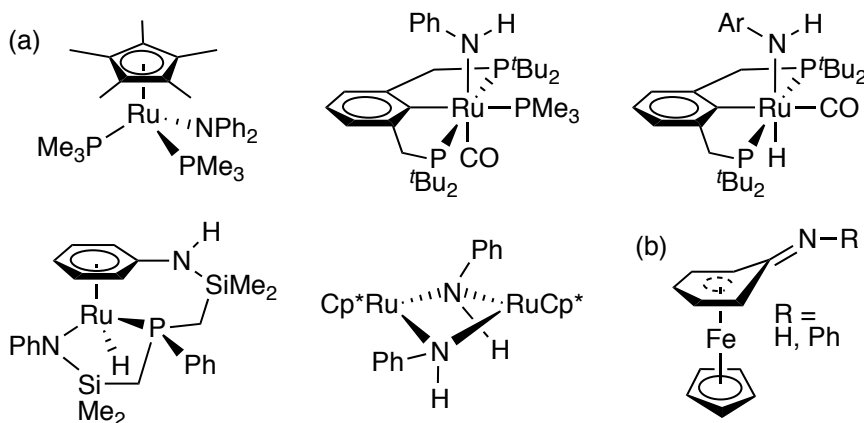
ruthenium was explored both out of fundamental interest, and to determine the practical stability of the Ru- σ -arylamide moiety.

5.6. Exploring the variable hapticity of the arylamide ligands

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Examples of amido complexes of the late transition metals have expanded greatly in recent years, driven largely by interest in their catalytic properties.^{45–47} Arylamido ligands are of particular interest for their potential steric and electronic tunability. In the dominant anilido derivatives, the anionic nitrogen may be monodentate or bridging (Chart 5.5a),^{45–47} but the η^5 -cyclohexadienylimine structure (Chart 5.5b) is also known.^{48,49} Analogous bent-seat piano-stool complexes are well documented in Ru-aryloxide chemistry.^{39–44}

Chart 5.5. (a) Selected Ru(σ -NRAr) Derivatives.^{50–54} (b) η^5 -Cyclohexadienylimine Complexes of Iron.^{48,49}



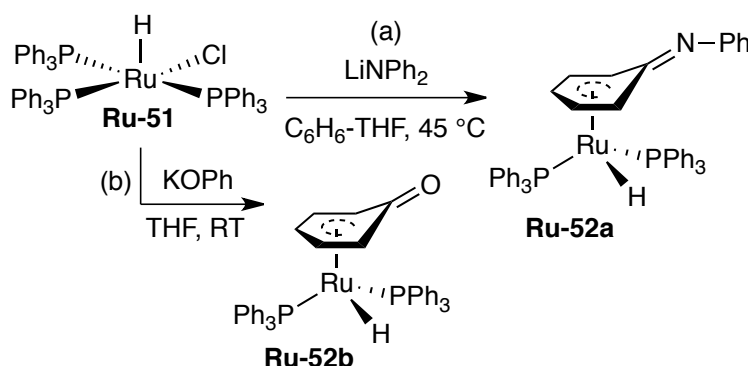
The potential for reversible isomerization between such σ - and π -bound structures is of interest in catalysis, as it may affect the lifetime and productivity of coordinatively unsaturated σ -NRAr complexes. We earlier suggested that Ru(π -OAr) structures may be expected for monodentate aryloxides wherever the ancillary ligands are sufficiently labile to give access to the required three coordination sites.³⁹ Subsequent work demonstrated that binaphtholate complexes of ruthenium can adapt between the extremes of η^1, η^1 - and η^3, η^3 -binding, depending on the number of other ligands

* Compound numbers have been modified for consistency throughout the thesis. For a Table of Compound Numbers and Structures, see p. VII. For Experimental, see Chapter 2, Section 2.4.4. Table 5.5 was originally published in the supporting information of this article, and has been incorporated into the main text for convenience.

present.⁵⁵⁻⁵⁷ Here we report a study of the $\text{RuHX}'(\text{PPh}_3)_n$ system, a well-developed model that enables examination of these effects without the difficulties associated with identification of metal complexes formed during catalysis. We provide evidence that the arylamide ligand can likewise adapt its hapticity, and that it may do so even more readily than phenoxide. For either ligand class, however, incorporation of a single π -acid carbonyl ligand proves sufficient to bias selectivity toward the σ - EAr_n coordination mode ($\text{E} = \text{O}, \text{N}$).

Addition of $\text{Li}[\text{NPh}_2]$ as a solution in THF to a purple suspension of $\text{RuHCl}(\text{PPh}_3)_3$ **Ru-51** in benzene caused a color change to orange within 15 min at 45 °C. Formation of $\text{RuH}[(\eta^5\text{-C}_6\text{H}_5)\text{NPh}](\text{PPh}_3)_2$ **Ru-52a** (Scheme 5.11a) was complete within 1 h, as judged by $^{31}\text{P}\{^1\text{H}\}$ NMR analysis. The sole species observed in the crude reaction mixture were free PPh_3 and **Ru-52a** (molar ratio 1/1). Pale orange $\text{RuH}[(\eta^5\text{-C}_6\text{H}_5)\text{NPh}](\text{PPh}_3)_2$ was isolated in 73% yield after workup. X-ray quality crystals deposited from toluene–hexanes at -30 °C.

Scheme 5.11. Piano-Stool products Formed by Reaction of $\text{RuHCl}(\text{PPh}_3)_3$ with Diphenylamide or Phenoxide.³⁹



Crystallographic analysis of **Ru-52a** (Figure 5.7) reveals that the amide ligand is bound to the metal via an η^5 -cyclohexadienyl ring. Loss of aromaticity is evident from the non-planar structure of the ring, C11 being bent by 24° out of the plane. Partial imine character is suggested by the short N-C11 bond distance of 1.313(6) Å; cf. a value of 1.406(6) Å for the unperturbed NPh moiety, and $\text{N}=\text{C}$ bond lengths of ca. 1.26-1.27 Å for related aniline-derived ketimines.⁵⁸⁻⁶⁰ The $120.9(4)^\circ$ angle for the C11-N-C21 bond is consistent with formulation as an imine.

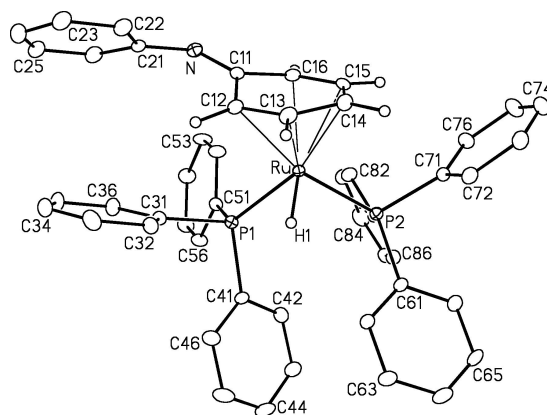


Figure 5.7. Perspective view of **Ru-52a**. Non-hydrogen atoms are represented by Gaussian ellipsoids at the 20% probability level. The hydride ligand is shown with an arbitrarily small thermal ellipsoid. Key metrics: C21-N: 1.406(6) Å; C11-N: 1.313(6) Å; C21-N-C11: 120.9(4)°.

NMR analysis of **Ru-52a** confirms the distorted piano-stool structure. Diagnostic ^1H NMR markers for the η^5 -bound ring are depicted in Figure 5.8. Five NC_6H_5 signals are shifted dramatically upfield from the aromatic region: they appear at ca. 4.0–5.3 ppm, vs. the region of 6.6–7.7 ppm occupied by the remaining phenyl protons. A hydride triplet appears at -11.94 (t, $^2J_{\text{PH}} = 33$ Hz). The quaternary imine carbon appears at 152.5 ppm; cf. a value of 175.6 ppm reported for $\text{Cy}=\text{NPh}$ in CDCl_3 .⁶¹ Similar structural and ^1H NMR data were reported for the $\eta^5\text{-C}_6\text{H}_5\text{O}$ moiety in known $\text{RuH}[(\eta^5\text{-C}_6\text{H}_5\text{O})(\text{PPh}_3)_2]$ **Ru-52b** (Scheme 5.11b).^{40,41}

To assess the impact of a π -acid ligand on the preferred coordination mode of the anionic donor, we explored the corresponding reaction of $\text{RuHCl}(\text{CO})(\text{PPh}_3)_3$ with LiNPh_2 . A color change from white to red occurred over 15 min at 23 °C in THF, with full conversion to $\text{RuH}(\sigma\text{-NPh}_2)(\text{CO})(\text{PPh}_3)_2$ **Ru-53** (Scheme 5.12) after 1 h. $^{31}\text{P}\{^1\text{H}\}$ NMR analysis of crude **Ru-53** revealed a singlet at 41.7 ppm, accompanying that for equimolar free PPh_3 . Additional Ru species present in minor amounts include known⁶² $\text{RuH}_2(\text{CO})(\text{PPh}_3)_3$ and unidentified hydride co-products that give rise to signals between -3 and -8.5 ppm. Clean **Ru-53** was isolated in 76% yield after washing with hexanes.

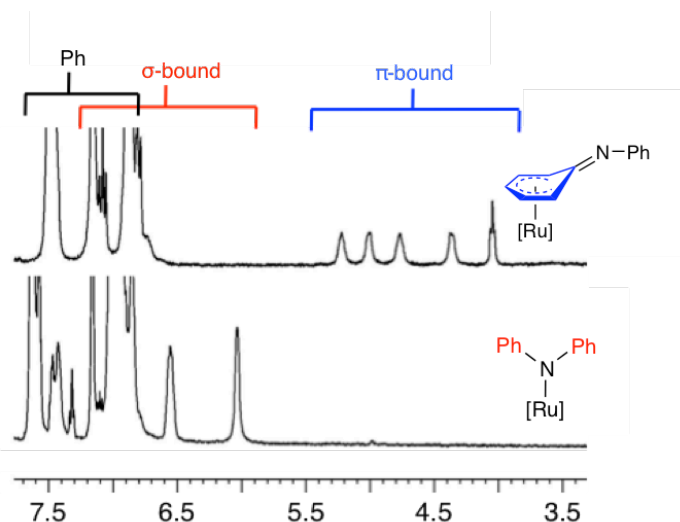
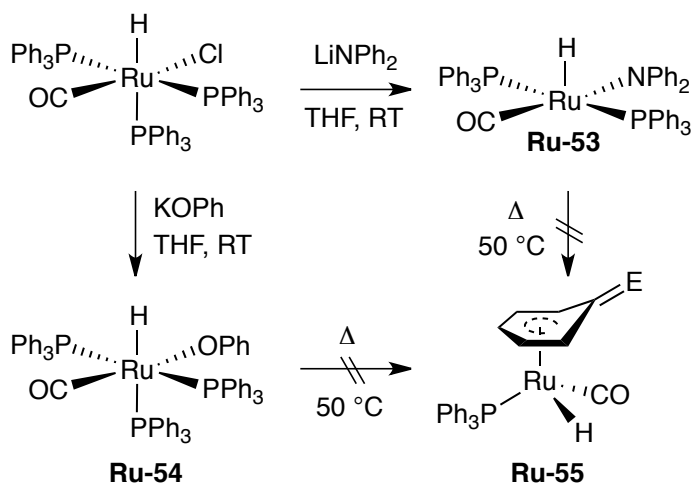


Figure 5.8. Diagnostic ^1H NMR locations (C_6D_6 solvent) for the π - and σ -bound $\text{N}(\text{C}_6\text{H}_5)_2$ ligand in **Ru-52a** and **Ru-53**.*

The hydride signal for **Ru-53**, a triplet at -17.19 ppm ($^2J_{\text{PH}} = 22$ Hz), is ca. 5 ppm upfield of that for **Ru-52a**. These data imply a square pyramidal structure with an apical hydride and two mutually trans phosphine ligands. σ -Coordination of the diphenylamide ligand is confirmed by the downfield location of all phenyl signals in the ^1H NMR spectrum (6.0–7.7 ppm; Figure 5.8).

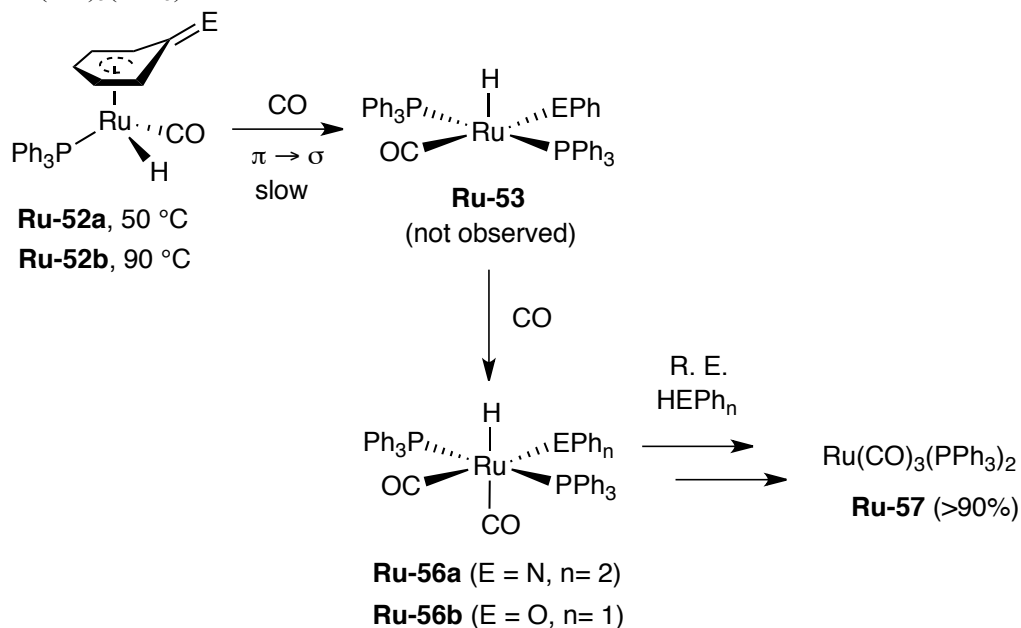
Scheme 5.12. σ -Arylamide and σ -Aryloxide Complexes Accessible from $\text{RuHCl}(\text{CO})(\text{PPh}_3)_3$.



* Subsequent to publication, the rotational symmetry of the π -aryl subunit was examined in greater detail. Signals corresponding to *ortho* and *meta* C_6H_5 signals can be assigned at low temperature, as the doublet (5 Hz) and apparent triplet (5 Hz) multiplicities, respectively, are resolved below 20°C . At 80°C , sets of *ortho* and *meta* signals each converged into a broad singlet. A well-defined triplet (5 Hz) corresponding to *para* CH of $\eta^5\text{-C}_6\text{H}_5$ was observed at all temperatures (-20 and 80°C). Rotation of the arene occurs even at 0°C , evidenced by chemical exchange in the ^1H EXSY NMR spectrum. For VT NMR spectra, see Appendix 1.

The σ -bound amide ligand in **Ru-53** does not convert into a the π -structure **Ru-55** over 24 h at 50 °C (C_6D_6 ; <3% loss vs. internal standard). We attribute this stability to the presence of the π -acid CO ligand, which inhibits phosphine loss. Treating piano-stool complex **Ru-52a** with CO, however, triggers release of $HNPh_2$ and formation of $Ru(CO)_3(PPh_3)_2$ **Ru-57**,⁶³ most plausibly via reductive elimination of $HNPh_2$ from $RuH(\sigma-NPh_2)(CO)_2(PPh_3)_2$ **Ru-56a** (Scheme 5.13). Formation of **Ru-57** reaches 92% in 2 h at 50 °C. The potential intermediacy of **Ru-53** was verified by exposing **Ru-53** to CO: this effected complete conversion into **Ru-57** and $HNPh_2$ within 2 h at 50 °C. Room-temperature experiments indicated that the reductive elimination step was considerably faster for **Ru-53** than for **Ru-52a**. For **Ru-53**, evolution of $HNPh_2$ reached 90% within 20 min vs. 65% for **Ru-52a** at 24 h. Initial $\pi \rightarrow \sigma$ isomerization of phenylamide thus appears to be the principal barrier to carbonylation of **Ru-52a**. (The higher proportion of $HNPh_2$ than **Ru-57** (Table 5.5) also indicates that reductive elimination occurs prior to formation of **Ru-57**.) Attempts to independently prepare **Ru-56a** by treating $RuHCl(CO)_2(PPh_3)_2$ with $LiNPh_2$ yielded ca. 1/1 **Ru-53** and **Ru-57**: while the observed CO disproportionation is unexpected, this finding confirms the instability of **Ru-56a** toward reductive elimination.

Scheme 5.13. Proposed reductive elimination pathway in carbonylation of **Ru-52a**, **Ru-52b** to form $HEPh_n Ru(CO)_3(PPh_3)_2$



The generality of this arylamide behavior is demonstrated by the accessibility of a σ -aryloxide complex related to **Ru-53** via addition of $KOPh$ to $RuHCl(CO)(PPh_3)_3$. The reaction was

complete within 2 h at RT in THF, and clean $\text{RuH}(\sigma\text{-OPh})(\text{CO})(\text{PPh}_3)_3$ **Ru-54** was obtained as a white powder in 91% yield (Scheme 5.12). Retention of all three phosphine ligands in **Ru-54** – a function of the reduced bulk of the OPh ligand, relative to the NPh_2 ligand in **Ru-53** – is indicated by the multiplicity and location of the hydride signal, which appears as a doublet of triplets at -6.63 ppm ($^2J_{\text{HP}} = 112$ and 24 Hz). Other spectroscopic data are consistent with the proposed structure. Thus, the room-temperature $^{31}\text{P}\{^1\text{H}\}$ NMR spectrum revealed two broad singlets at 38.1 and 16.3 ppm (ratio 2:1; C_6D_6), which resolve into an A_2B pattern ($^2J_{\text{PP}} = 17$ Hz) at 263 K in C_7D_8 .

As with the arylamide derivatives, aryloxide **Ru-54** resisted $\sigma \rightarrow \pi$ isomerization at 50°C , but thermolysis of piano-stool complex **Ru-52b** under CO (90°C , 6 h; Scheme 5.13) liberated **Ru-57** and phenol (Scheme 5.13; 93% after 6 h). No reaction was observed over 24 h at 50°C , suggesting a higher barrier to $\pi \rightarrow \sigma$ isomerization of phenoxide than diphenylamide.

Table 5.5. Carbonylation and Reductive Elimination Products from Arylamide and Alkoxy-Containing Ru Hydrides.*

Ru Hydride	T ($^\circ\text{C}$)	time (h)	loss of [Ru]H (%) ^a	$\text{Ru}(\text{CO})_3(\text{PPh}_3)_2$ (%) ^b	EPh_{1-2} product	% EPh_{1-2} ^a
$\text{RuH}[(\eta^5\text{-C}_6\text{H}_5)\text{NPh}](\text{PPh}_3)_2$	RT	24	71	36	HNPh_2	65
		40	quant	58		90
	50	2	quant	92		80
$\text{RuH}(\eta^1\text{-NPh}_2)(\text{CO})(\text{PPh}_3)_2$	RT	0.3	quant	52	HNPh_2	90
	50	2	quant	<99%		– [†]
$\text{RuH}[(\eta^5\text{-C}_6\text{H}_5)\text{O}](\text{PPh}_3)_2$	RT	24	<3 %	–	HOPh	–
	50	24	<3 %	–		–
	90	6	quant	93		90

Conditions: $[\text{Ru}] = 12$ mM, 1 atm CO, C_6D_6 or C_7D_8 solvent. ^a Quantified by ^1H NMR integration against TMB internal standard, normalized to initial $[\text{Ru}]_0$. ^b % of total species present by $^{31}\text{P}\{^1\text{H}\}$ NMR.

The foregoing demonstrates that monodentate arylamide and aryloxide ligands exhibit qualitatively similar tendencies in terms of the parameters that favor σ -binding via the heteroatom, vs. π -coordination via a dearomatized ring. For either ligand class, piano-stool structures are favored where three binding sites are available. When the lability of the PPh_3 ligands is restricted, even by introduction of a single CO ligand, σ -arylamide or -aryloxide derivatives are formed. In the presence of additional ligands, however, the piano-stool complexes can slip to lower-hapticity structures. Exposure to CO is shown to induce $\pi \rightarrow \sigma$ interconversion and reductive elimination of diphenylamine or phenol. Of note is the lower barrier of this transformation for the amido complex, which may

* Table 5.5, originally published as Table S1 in the supporting information, is incorporated here for reference.

[†] The breadth of the NH signal hampered accurate integration.

indicate that the arylamide ligand adjusts its hapticity to accommodate incoming ligands more readily than does aryloxide. This potential advantage may be offset, for hydride derivatives, by relatively facile reductive elimination. Whether non-hydride derivatives also readily eject the arylamide ligand is presently under study.

5.7. Conclusions and future work

This Chapter describes the incorporation of *N*-donor ligands into new metathesis catalysts. One strategy focused on neutral, bidentate arylamines. These were investigated as labile replacements for the PCy₃ ligand in the second-generation Grubbs catalysts, or non-lethal replacements for the pyridine ligand in **GII**, which could potentially increase initiation rates, and resistance to decomposition. A second strategy focused on *N*-anionic ligands. Synthesis by anion exchange was unsuccessful, prompting development of related hydride complexes.

Several new Grubbs amine adducts were successfully isolated. Solely the biphenyldiamine **N11** adduct of **GII** (**Ru-42**) was expected to effectively participate in metathesis reactions based on prior studies with **Ru-42'**. Isolated **Ru-42** was obtained in good yield, and preliminary metathesis studies indicate a dramatic increase in activity at RT relative to **GII**. Catalyst stability was improved relative to the analogous compound **GIII**. At low catalyst loadings, catalyst decomposition competed with productive catalysis. Complex **Ru-42** was unstable under C₂H₄ or in the presence of styrene, resulting in total loss of Ru=CHPh within minutes (C₂H₄) or hours (styrene) at RT. The mechanism of decomposition did not appear to follow the established alkylidene abstraction or metallacyclobutane decomposition pathways outlined in prior Chapters. A short-term experimental recommendation is discussed below. Implications and possible future directions are discussed in Chapter 6.

An unresolved ambiguity was noted above regarding the nature of decomposition for **Ru-42** during catalysis. To support the claim that alkylidene abstraction does not occur, the proposed structure of product **Ru-45** should be confirmed by isolation and full characterization. To minimize the number of reaction components, thereby simplifying workup, thermolysis of **Ru-42** (>92 h at 60 °C in C₆H₆) on a larger scale (ca. 200 mg) is recommended as an initial strategy. Isolation might be achieved by reprecipitation to remove the stilbene co-product. Toluene/hexanes or CH₂Cl₂/hexanes may prove to be a suitable solvent system for initial attempts.

Treating **GI** or **GIII'** with Li[NRR'] led to loss of the benzyldiene signal by ¹H NMR analysis. Attempts to install the amide ligands onto Ru hydrides instead, for subsequent transformation into alkylidene derivatives, revealed π -coordination of the NPh₂[−] anion via a dearomatized phenyl ring, rather than formation of a σ -arylamido complex. The analogous reaction

of $\text{RuHCl}(\text{CO})(\text{PPh}_3)_3$ resulted in a σ -arylamide structure due to the restricted lability of PPh_3 . Attempts to induce $\pi \rightarrow \sigma$ isomerization under CO resulted in reductive elimination of HNPh_2 and formation of $\text{Ru}(\text{CO})_3(\text{PPh}_3)_2$. This work reveals two key synthetic challenges. First, the coordination behavior of the arylamide anion exhibited similar coordination behavior to aryloxides; therefore, σ/π isomerization must be considered in a synthetic strategy involving N-phenyl derivatives. Second, in the presence of Ru-H, the arylamide anion exhibited a greater tendency to undergo reductive elimination, relative to the corresponding aryloxide. This susceptibility severely limits the utility of these ruthenium hydride derivatives as an entry point to Ru metathesis catalysts containing an amide ligand.

5.8. References

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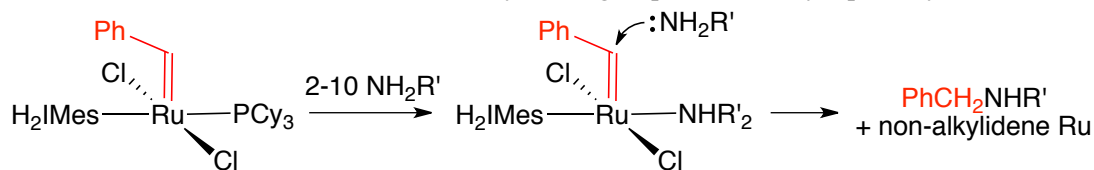
Chapter 6. Conclusions and Future Work

6.1. Conclusions

Functional group tolerance is a significant challenge in the industrial implementation of any transition-metal catalyzed process. In the context of olefin metathesis, the deleterious effect of amines is a major challenge, the mechanistic basis of which was almost wholly unexamined at the outset of this thesis work. A specific goal was therefore to explore the organometallic chemistry by which amines trigger decomposition of the Grubbs and Hoveyda metathesis catalysts, especially during catalysis. The present work complements recent findings from the Fogg group which revealed that amines trigger decomposition of the Grubbs methyldiene complexes via a two-step pathway, involving displacement of PCy_3 , and subsequent abstraction of the methyldiene moiety by nucleophilic attack of the phosphine.^{1,2}

Uncovered herein is a related, but previously unsuspected pathway, in which unencumbered primary amines are shown to trigger abstraction of the benzylidene ligand (Scheme 6.1). Specifically, $\text{PhCH}_2\text{NR}'_2$ products were observed, indicating transfer of the $\text{Ru}=\text{CHR}$ subunit to an amine. This is important in revealing that these critical decomposition pathways are not limited to the resting-state species, but can also destroy the precatalyst before it enters the active cycle for metathesis.

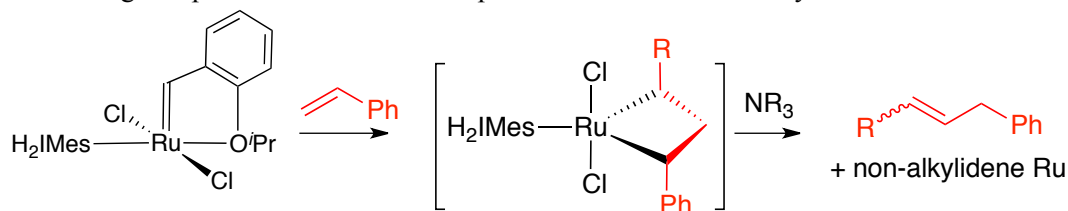
Scheme 6.1. Abstraction of the benzylidene group from **GII** by a primary amine.



Further, this work provides the first insights into the decomposition of phosphine-free metathesis catalysts by amines. This is of particular interest given the expanding use of phosphine-free **III** in olefin metathesis reactions. Decomposition of **III** appears to involve both the alkylidene and the metallacyclobutane species formed during olefin metathesis. A combination of quantitative ^1H NMR and GC-MS analysis was used to identify the organic products of decomposition, which accounted for 70–95% of the starting catalyst charge. The favored decomposition pathway was shown to be greatly influenced by the Bronsted basicity of the amine, and the combined steric bulk of the amine and substrate. Weaker Bronsted bases or smaller amines favoured alkylidene abstraction. Highly basic or bulky amines favoured deprotonation of the metallacyclobutane complex, as judged from the extrusion of “three-carbon markers” originating in the metallacyclobutane ring (Scheme

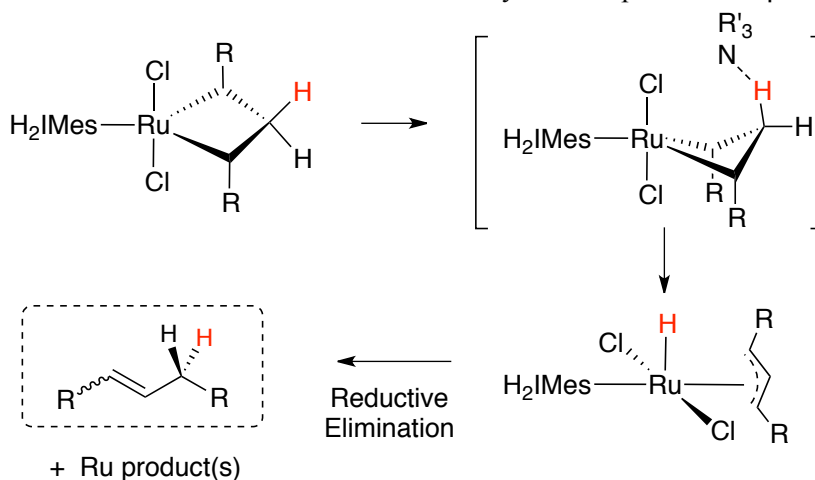
6.2). Such products were especially prominent for monosubstituted metallacyclobutanes (and by inference, from their unsubstituted counterparts). The monosubstituted MCB formed under ethylene was found to be particularly vulnerable to decomposition by amines. This finding offers a new perspective on the established detrimental effect of C_2H_4 in metathesis, and carries particular weight given the ubiquity of ethylene as a co-product of most RCM or CM reactions.

Scheme 6.2. Organic products attributed to deprotonation of the metallacyclobutane intermediate.



Of keen interest is the precise mechanistic pathway by which the three-carbon markers are liberated. This could involve first deprotonation at the β -CH₂ site (Scheme 6.2a), followed by C-H activation of a mesityl group to enable elimination. Alternatively, C-H activation could precede loss of the β -CH₂ proton. Finally, amine could potentially contribute to β -CH₂ transfer pathways previously proposed from the observation of propene evolution (Scheme 6.3).⁵ Experiments aimed at establishing whether the Mes C-H functions as the proton source are discussed in Future Work below.

Scheme 6.3. Potential involvement of amine in catalyst decomposition via β -CH₂ transfer.



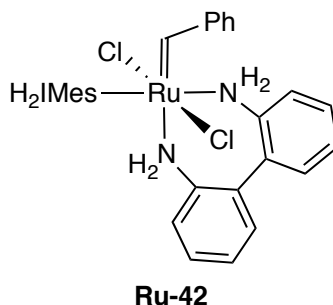
It should be noted that, despite the capacity of free PCy₃ to trigger methyldene abstraction from the Grubbs methyldene in the presence of amines (see above),^{1,2} MCB deprotonation was dominant for DBU. Strong Bronsted basicity clearly promotes this pathway. Interestingly, substrate

bulk is also relevant. Thus, deprotonation likewise reached nearly 80% of the total catalyst charge on treating **GII** with ethylene and pyrrolidine (conjugate acid pKa 19.6).

With the exception of NEt₃, all amines examined (as well as the imine nitrogen of DBU) were observed to coordinate to Ru. New amine adducts of **GI**, **GII**, and **GII'**, wherein the PCy₃ ligand had been replaced by various *N*-donors, were successfully isolated. This was achieved either by selective precipitation or using **GIII** / **GIII'** as a synthetic intermediate. Adducts were isolated modest to good yields (ca. 50-90%) and fully characterized by NMR and IR spectroscopy and elemental analyses.

The second part of this thesis describes progress toward implementing amine and related amido ligands into the catalyst scaffold – a largely unexplored opportunity. The **GII** adduct of biphenyldiamine was targeted, with the hypothesis that the low Bronsted basicity and moderate steric bulk of the amine would limit the decomposition pathways outlined in Scheme 6.1. The complex gave high RCM and CM yields at RT using 1.0 mol%, thus out-performing **GII** and **GIII**. The nature of deactivation pathways for **Ru-42** has not yet been explored.

Chart 6.1. Structure of biphenyldiamine adduct **Ru-42**.



Amido “pseudohalide” catalysts were briefly explored. Installation of amido anions by halogen exchange of **GI** or **GIII'** with various Li-amido salts was unsuccessful. This prompted an investigation of Ru-hydrides as an alternative synthetic approach. As with prior aryloxide ligands, the hapticity of the “NPh₂[−]” anion was found to be variable. Coordination via the phenyl π -system was observed when sufficient coordination sites were available. The σ -NPh₂ coordination geometry could be obtained by blocking coordination sites with CO, though attempts to interconvert σ and π coordination modes resulted in decomposition via reductive elimination of HNPh₂. Development of amido pseudohalide metathesis catalysts might be achieved instead using neutral amine adducts as a synthetic precursor (see Section 6.2.4 below).

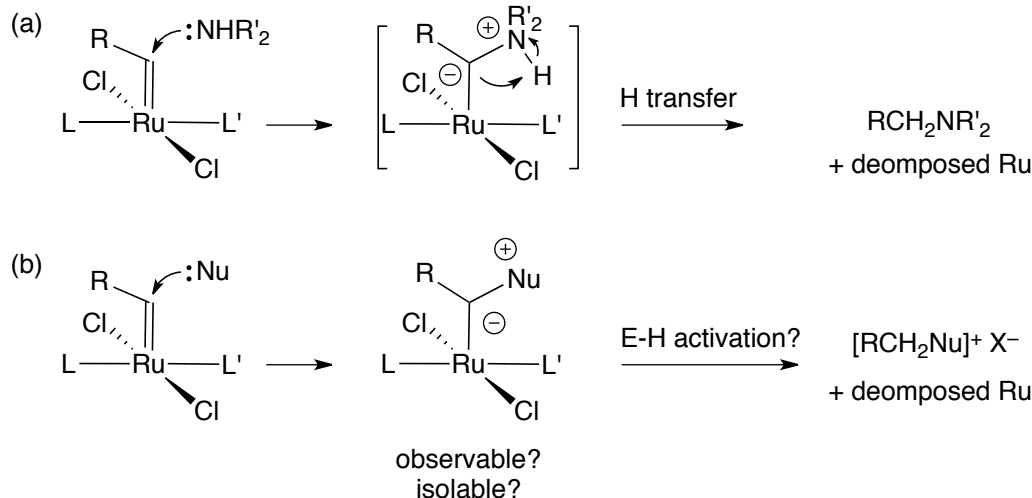
6.2. Future Work

6.2.1. Scope and Relevance of Catalyst Decomposition Pathways

Extension of the mechanistic studies described above to pyridine derivatives would be of great interest, given the importance of **GIII** and related py-derivatives in ROMP.³ Further, the broader relevance of alkylidene abstraction and MCB deprotonation pathways to other Bronsted bases or nucleophiles is of great interest. The experimental methods employed in this work should be easily adapted to a range of other potential poisons (alkoxides, thiols, etc.).

Mechanistic clarification in the context for alkylidene abstraction could also be obtained with a broader range of nucleophiles. Examples observed in Chapters 3 and 4 focused on primary or secondary amines. It is unclear if the NH proton transfer step (Scheme 6.4a) proposed in Chapter 3 has a crucial mechanistic role in alkylidene abstraction, or is merely an artifact of the high basicity of a Ru σ -alkyl intermediate. An analogous process involving an aprotic nucleophile is plausible, though not observed in this work (i.e. for NEt_3 or DBU) since benzylidene catalysts are sterically shielded against attack and MCB deprotonation dominates for these additives in the presence of substrate. Less bulky, aprotic nucleophiles (e.g. thiolate anions) might provide insight (Scheme 6.4b).

Scheme 6.4. Alkylidene abstraction involving (a) a protic nucleophile, as discussed in Chapter 3. (b) an aprotic nucleophile.

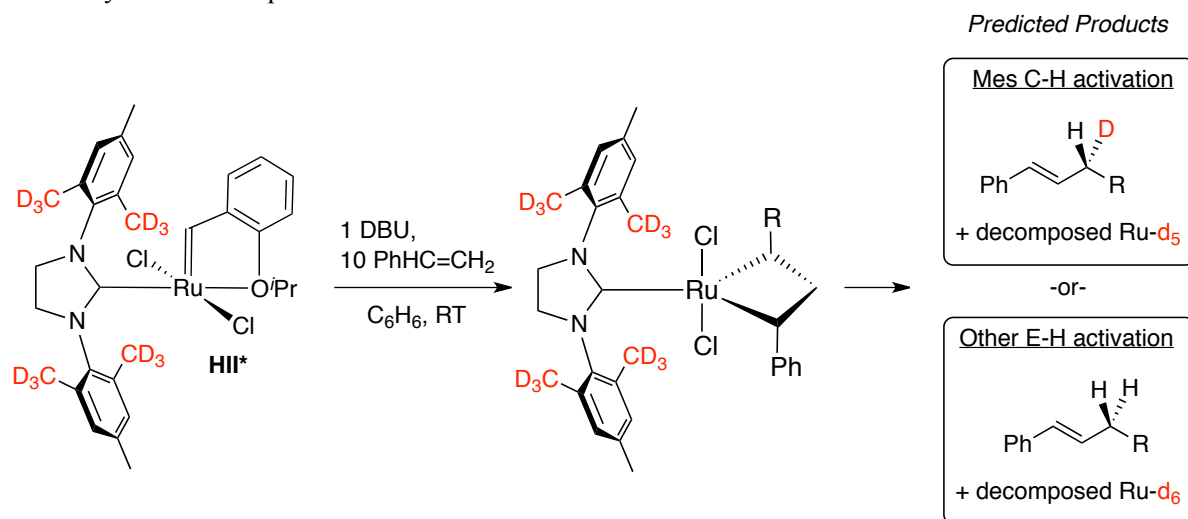


Colleagues within the Fogg lab have recently isolated Ru σ -alkyl complexes arising from nucleophilic attack by PCy_3 on $\text{Ru}=\text{CH}_2$.² Similar σ -alkyl intermediates for other nucleophiles might be observed or even isolated over the course of the work suggested above, providing opportunity to further study the chemistry of these reactive species.

Clarification of the role of E-H activation might yield further insight into the nature of the decomposition pathways discussed above. Activation of the mesityl-methyl group of the H_2IMes ligand may occur during amine-induced metallacyclobutane deprotonation (see Chapter 4, Section

4.4.1). Evidence for C-H activation as a key step in MCB decomposition may be obtained by repeating decomposition experiments using deuterium-labeled precatalyst, as depicted in Scheme 6.5, below. Such studies are indeed currently underway within the Fogg group.

Scheme 6.5. Proposed deuterium labeling studies to discern whether C-H activation occurs during metallacyclobutane deprotonation.^{a,b}



^aDegree of D-labeling in Ru product(s) refers to *o*-Mes methyl subunit. ^bR = H, Ph.

Mechanistic studies described in Chapters 3 and 4 were performed at relatively high concentrations and high catalyst loading with simple substrates, to permit unambiguous characterization and quantitation of decomposition products by NMR methods. Having established the nature of diagnostic products for alkylidene abstraction and metallacyclobutane deprotonation, extension to other substrates such as macrocycles (relevant to pharmaceutical synthesis) could expand the scope and relevance of these findings. Use of lower (more realistic) catalyst loadings is feasible using mass spectrometry to detect the products.

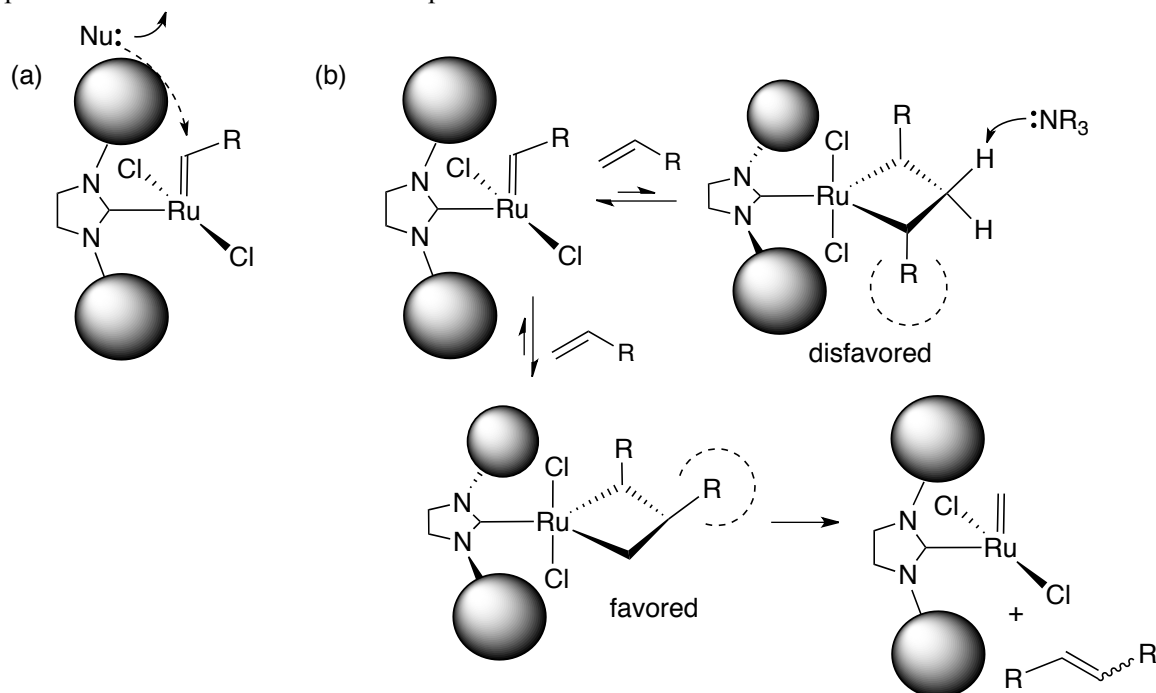
6.2.2. Catalyst modifications to mitigate amine-induced decomposition

Potential improvements to catalyst design emerge from the mechanistic studies described in Chapters 3 and 4. One obvious approach lies in increasing steric restrictions on access to the MCB carbons. Incorporation of steric bulk above and below the basal plane of the catalyst would retard metathesis, but may slow decomposition to a greater extent, improving total catalyst productivity. Similarly, alkylidene abstraction occurs via “outer sphere” attack pathway. Therefore, blocking the approach of the nucleophile would therefore also be expected to limit alkylidene abstraction (Scheme 6.6a). Finally, deprotonation of disubstituted MCBs in Chapter 4 was observed to occur selectively from the (α,γ) disubstituted structure associated with degenerate metathesis. Increased steric bulk, as

discussed above, could promote formation of less vulnerable (α,β) MCB intermediates, associated with productive metathesis (Scheme 6.6b).

For proof-of-concept testing, adamantyl-substituted NHCs may serve as a suitable model.⁴ Though normally employed in the context of stereoselective olefin metathesis, such species might prove to be more robust in the presence of amine poisons by comparison to **GII**.

Scheme 6.6. Proposed addition of steric bulk above and below the basal plane of **GII**. (a) Potentially improved stability to nucleophilic attack (alkylidene abstraction). (b) Improved selectivity for productive metathesis over MCB deprotonation.

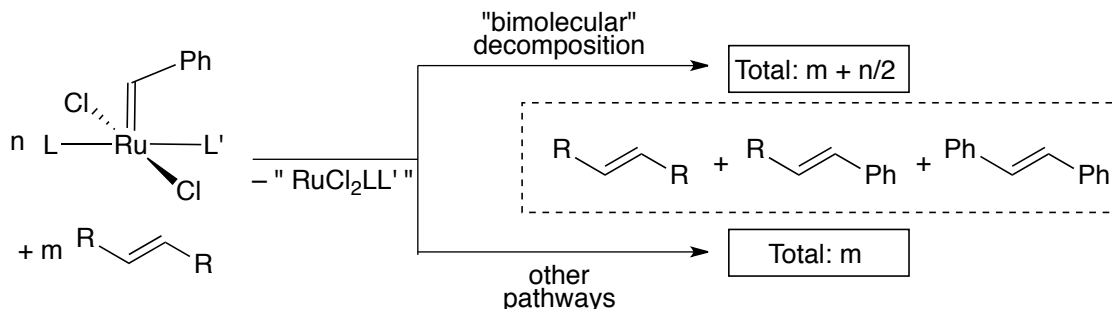


6.2.3. Experimental evidence for bimolecular deactivation during catalysis

The decomposition behavior of biaryl adduct **Ru-42** was not explained by alkylidene abstraction or metallacyclobutane deprotonation. Bimolecular deactivation was suspected based on thermolysis behavior of the isolated precatalysts. If such a pathway is operative during catalysis, empirical evidence could be provided by the quantity, rather than identity of olefinic products. Bimolecular deactivation leads to net increase in the total amount of olefinic products during a reaction (albeit by only 0.5 equivalent vs. Ru; Scheme 6.7). Accurate quantitation could not be achieved in initial studies, primarily due to loss of ethylene as an olefin co-product. Modification of the experimental design to decrease the reaction headspace or form non-volatile products would

permit accurate quantitation. If identified during catalysis, the bimolecular deactivation pathway may be relevant more broadly to catalysts with high-lability ligands (e.g. **GIII**).

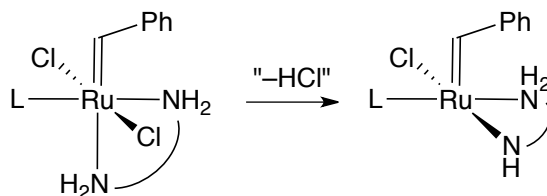
Scheme 6.7. Method for detection of “bimolecular” decomposition during catalysis.



6.2.4. Amine adducts as a synthetic route to amido complexes

Several amine adducts were developed over the course of mechanistic studies described in Chapters 3 and 4. Though generally not useful as catalysts in their own right, these species may prove valuable in an alternative synthetic route to amido metathesis catalysts described in the later portion of Chapter 5. The approach shown in Scheme 6.8 would circumvent both the need to directly expose the $\text{Ru}=\text{CHPh}$ precursor to amido salts, and the alternative approach involving synthesis of an amido/hydride Ru complex. (The latter being vulnerable to reductive elimination of N-H). Given the observed variable hapticity for the NPh_2^- anion, described in Chapter 5, non-aromatic amines are recommended to mitigate the risk of deactivation by π -coordination.

Scheme 6.8. Deprotonation / halide abstraction as a synthetic route to amido “pseudohalide” catalysts.



6.3. References

- (1) Lummiss, J. A. M.; Ireland, B. J.; Sommers, J. M.; Fogg, D. E. *ChemCatChem* **2014**, 6, 459–463.
- (2) Lummiss, J. A. M.; McClennan, W. L.; McDonald, R.; Fogg, D. E. *Organometallics* **2014**, 33, 6738–6741.
- (3) Knall, A.-C.; Slugovc, C., Olefin metathesis polymerization. In *Olefin Metathesis-Theory and Practice*, Grela, K., Ed. Wiley: Hoboken, NJ, 2014; pp 269–284.
- (4) Dinger, M. B.; Nieczypor, P.; Mol, J. C. *Organometallics* **2003**, 22, 5291–5296.
- (5) van Rensburg, W. J.; Steynberg, P. J.; Meyer, W. H.; Kirk, M. M.; Forman, G. S. *J. Am. Chem. Soc.* **2004**, 126, 14332–14333.

Appendix 1. NMR Spectra for New Compounds

A1.1. ^1H and $^{13}\text{C}\{^1\text{H}\}$ NMR spectra for new compounds in Chapter 3.

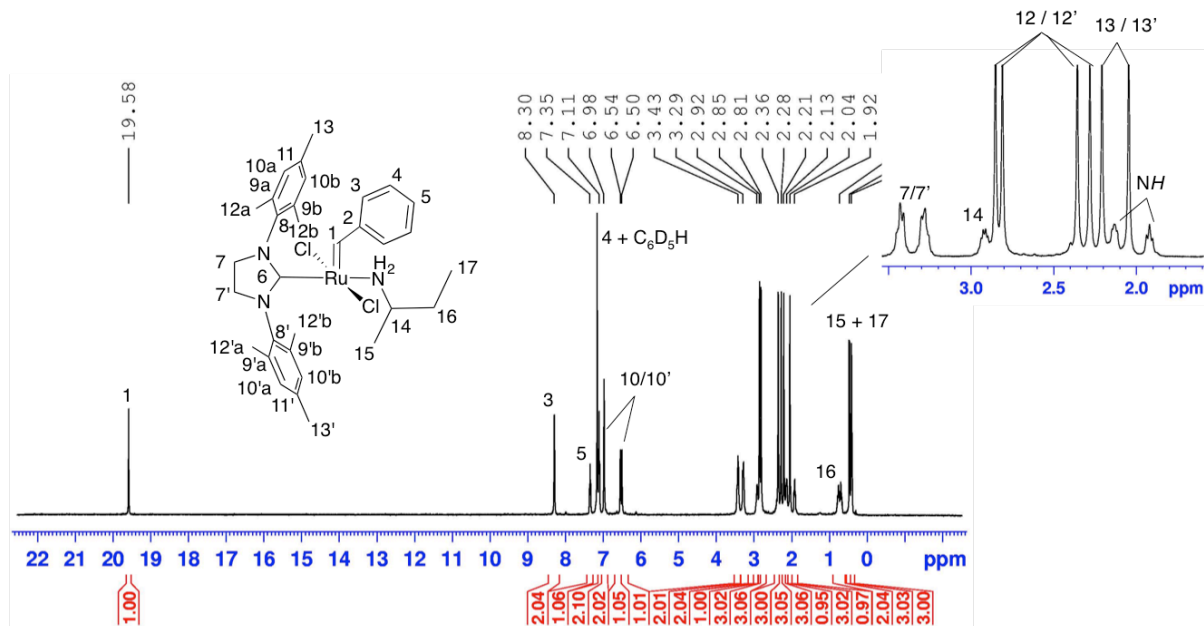


Figure A1.1. ^1H NMR spectrum (C_6D_6 , 500.1 MHz) for $\text{RuCl}_2(\text{H}_2\text{IMes})(\text{NH}_2^{\text{sec}}\text{Bu})(=\text{CHPh})$ **Ru-19**.

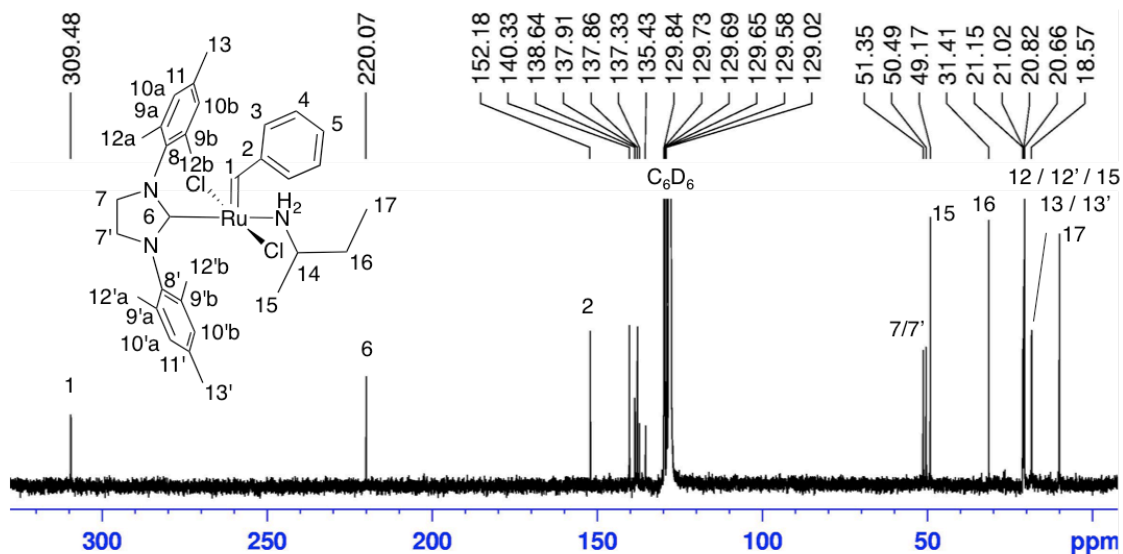


Figure A1.2. $^{13}\text{C}\{^1\text{H}\}$ NMR spectrum (C_6D_6 , 75.53 MHz) for $\text{RuCl}_2(\text{H}_2\text{IMes})(\text{NH}_2^{\text{sec}}\text{Bu})(=\text{CHPh})$ **Ru-19**.

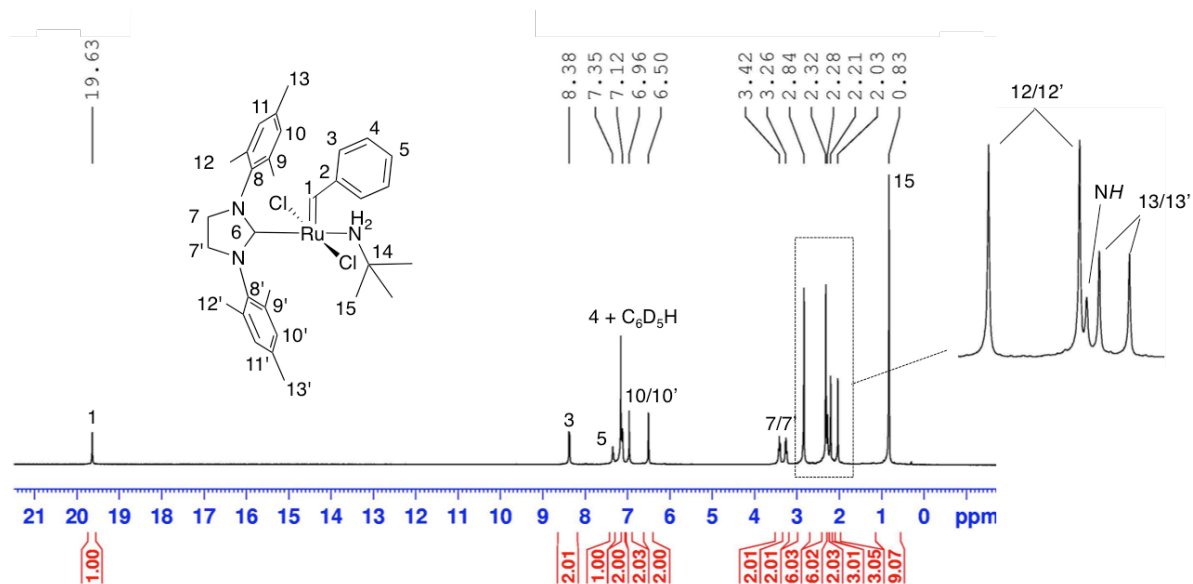


Figure A1.3. ^1H NMR spectrum (C_6D_6 , 500.1 MHz) for $\text{RuCl}_2(\text{H}_2\text{IMes})(\text{NH}_2^t\text{Bu})(=\text{CHPh})$ **Ru-20**.

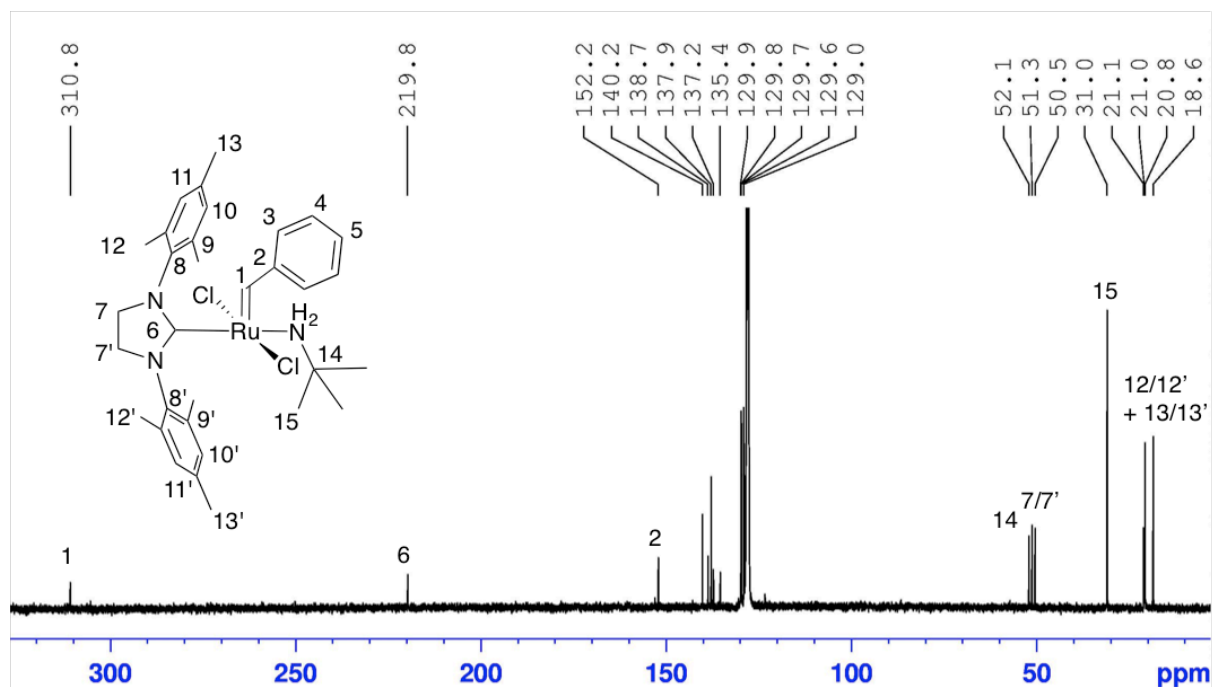


Figure A1.4. $^{13}\text{C}\{^1\text{H}\}$ NMR spectrum (C_6D_6 , 75.53 MHz) for $\text{RuCl}_2(\text{H}_2\text{IMes})(\text{NH}_2^t\text{Bu})(=\text{CHPh})$ **Ru-20**.

A1.2. ^1H and $^{13}\text{C}\{^1\text{H}\}$ NMR spectra for new compounds in Chapter 4

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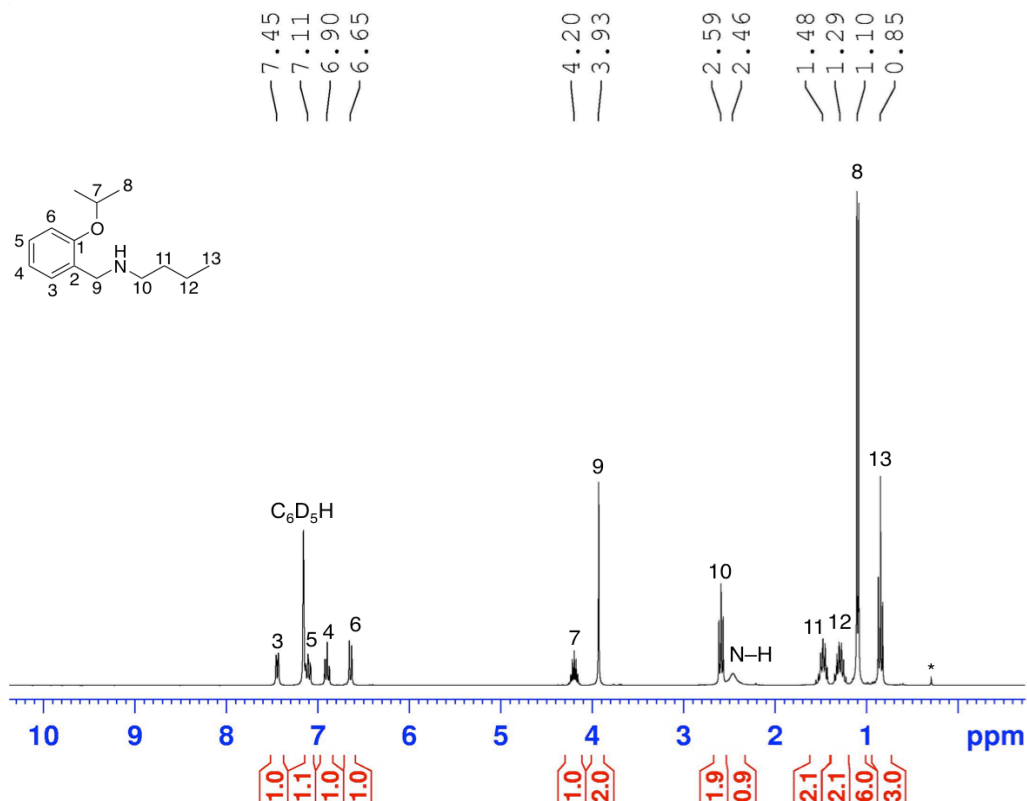


Figure A1.5. ^1H NMR spectrum (C_6D_6 , 300.1 MHz) for $\text{NH}(\text{}^n\text{Bu})(\text{CH}_2\text{Ar})$ (**10**; $\text{Ar} = \text{C}_6\text{H}_4\text{-}o\text{-O}^i\text{Pr}$).

* Compound numbers have been modified for consistency throughout the thesis. For a Table of Compound Numbers and Structures, see p. VI.

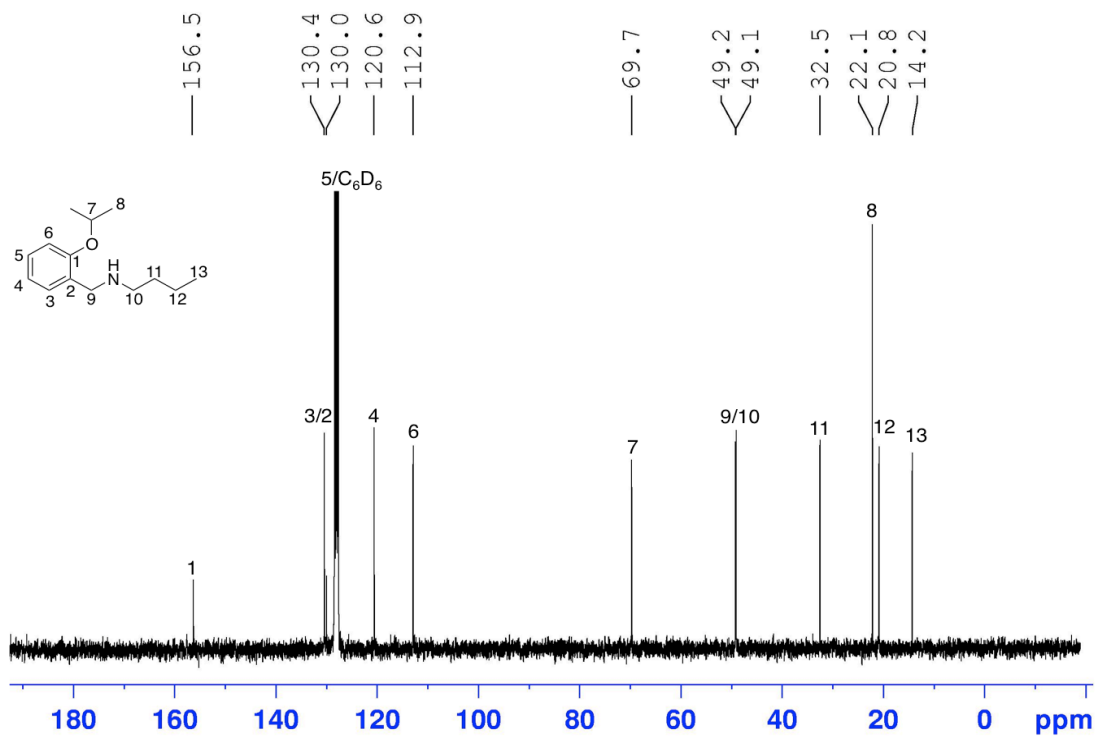


Figure A1.6. $^{13}\text{C}\{^1\text{H}\}$ NMR spectrum (C_6D_6 , 75.4 MHz) for $\text{NH}(^i\text{Bu})(\text{CH}_2\text{Ar})$ (**10**; Ar = C_6H_4 -*o*- O^iPr).

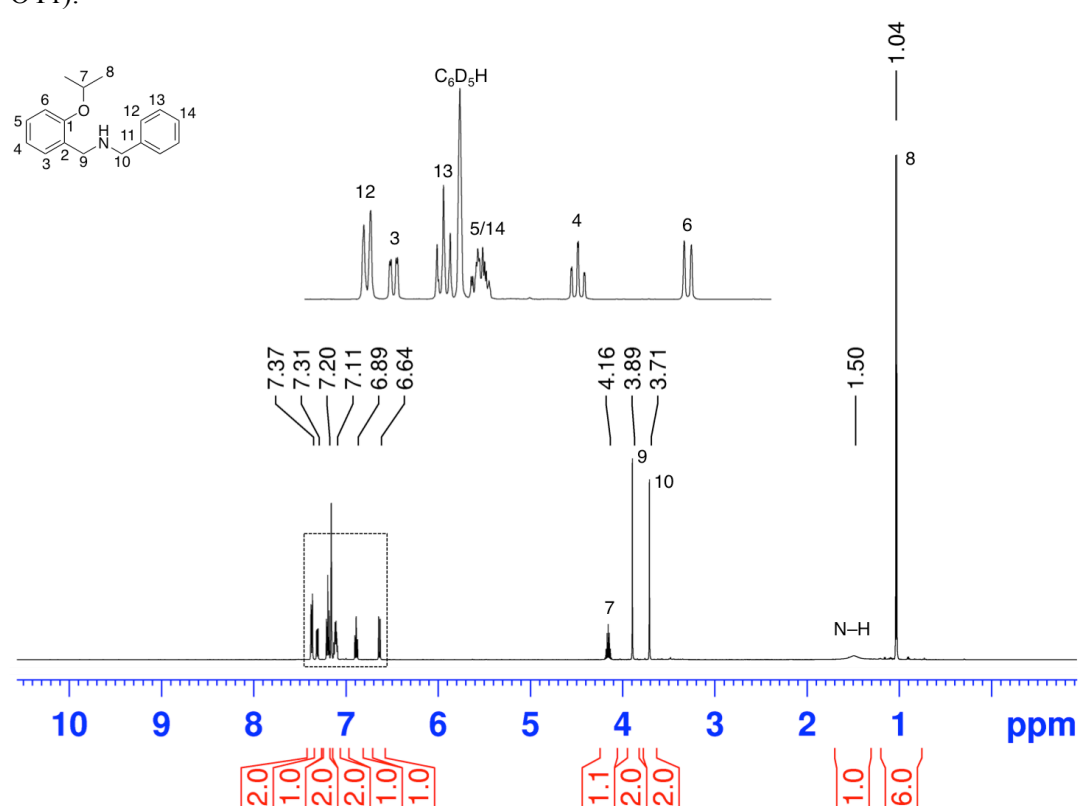
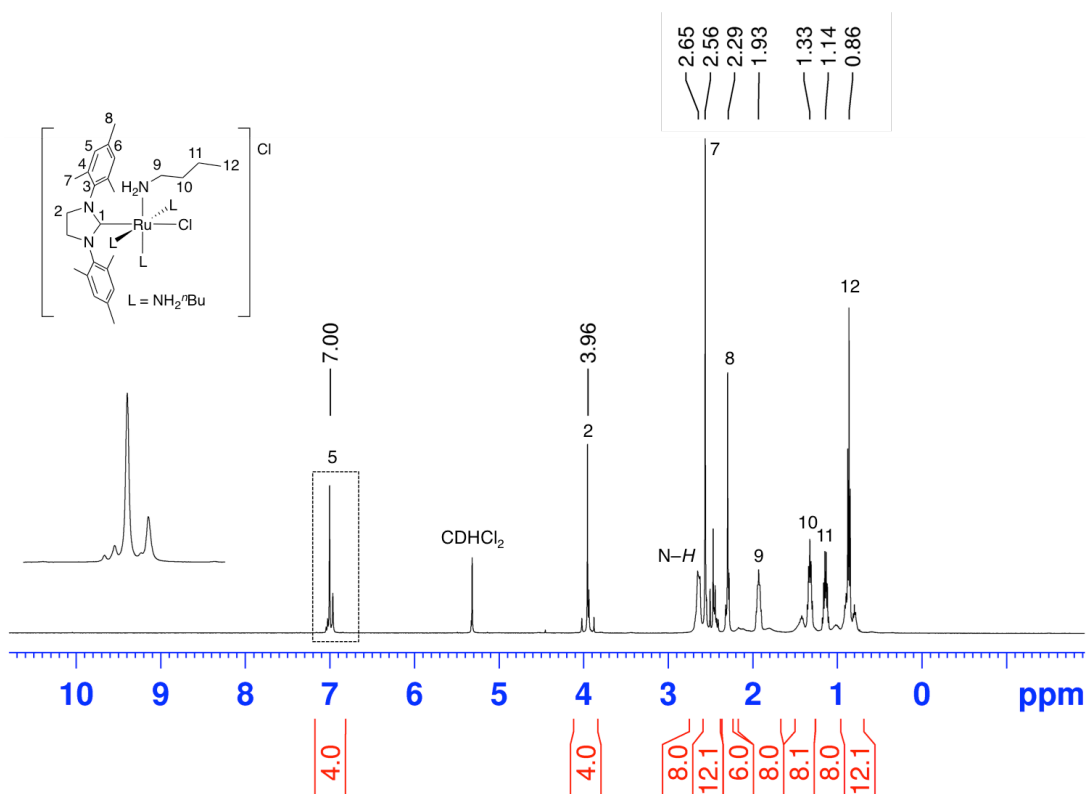
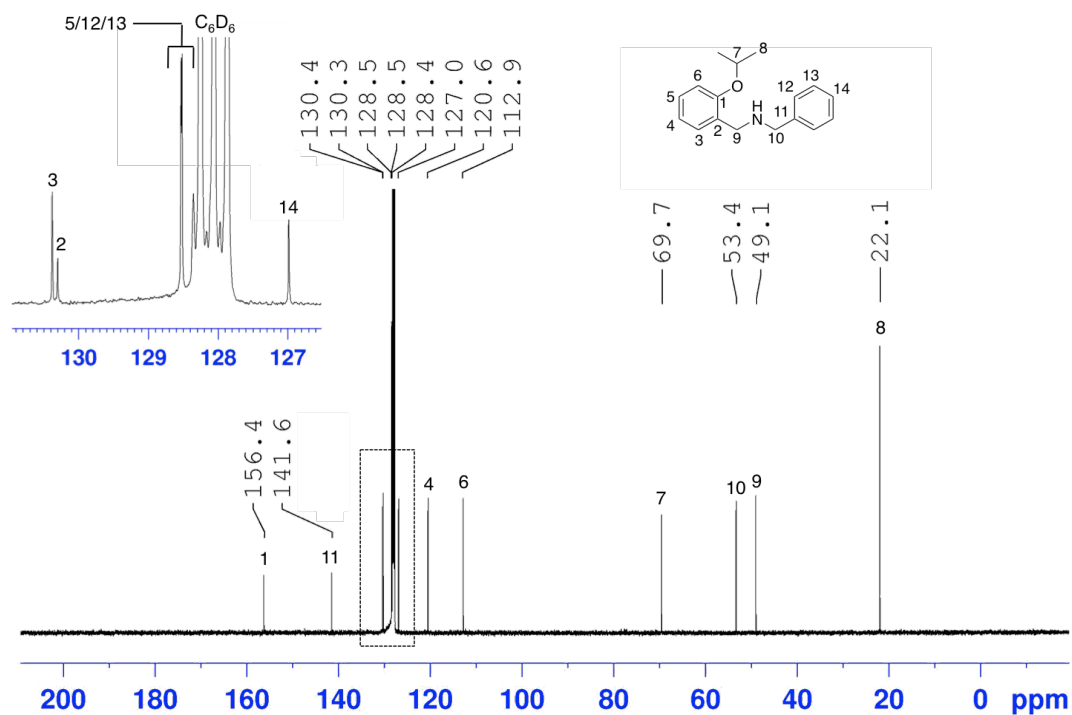


Figure A1.7. ^1H NMR spectrum (C_6D_6 , 300.3 MHz) for $\text{NH}(\text{CH}_2\text{Ph})(\text{CH}_2\text{Ar})$ (**11**; Ar = C_6H_4 -*o*- O^iPr).



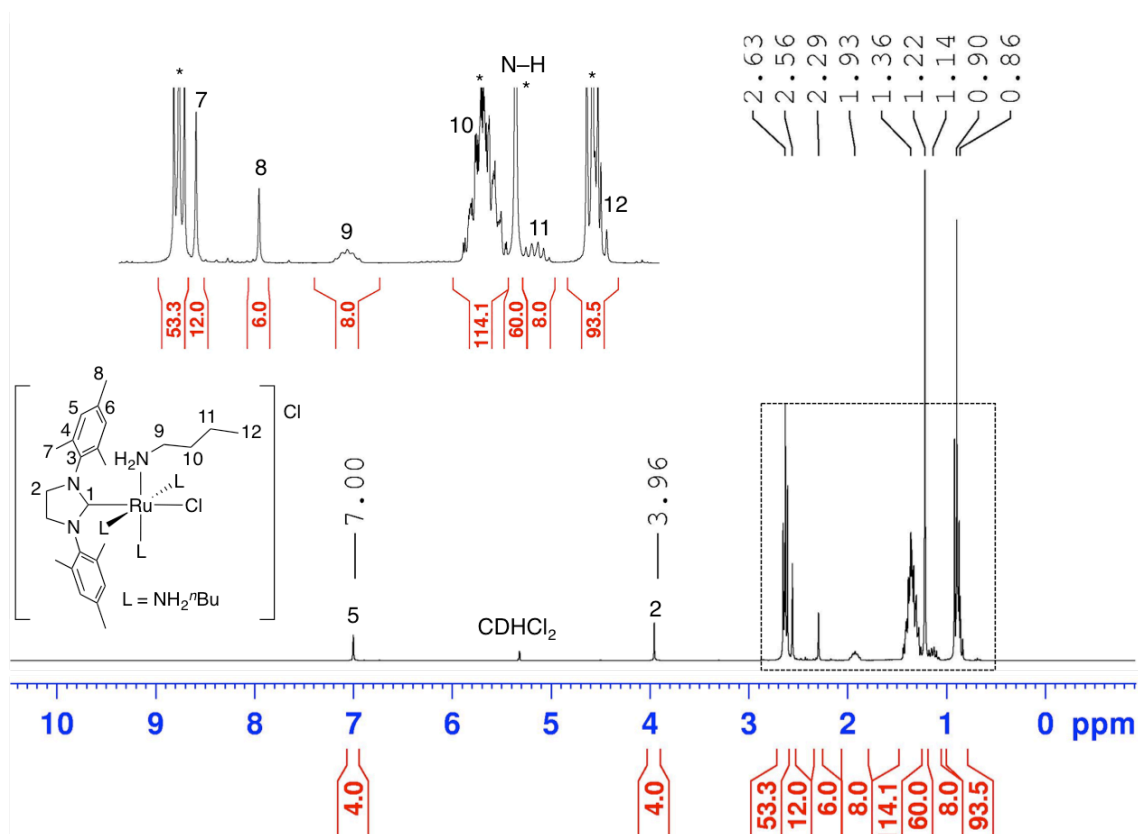


Figure A1.10. ^1H NMR spectrum (CD_2Cl_2 , 500.1 MHz) for isolated **Ru-17a** in the presence of added NH_2^nBu (1% v/v). Signals for excess NH_2^nBu are labeled (*).

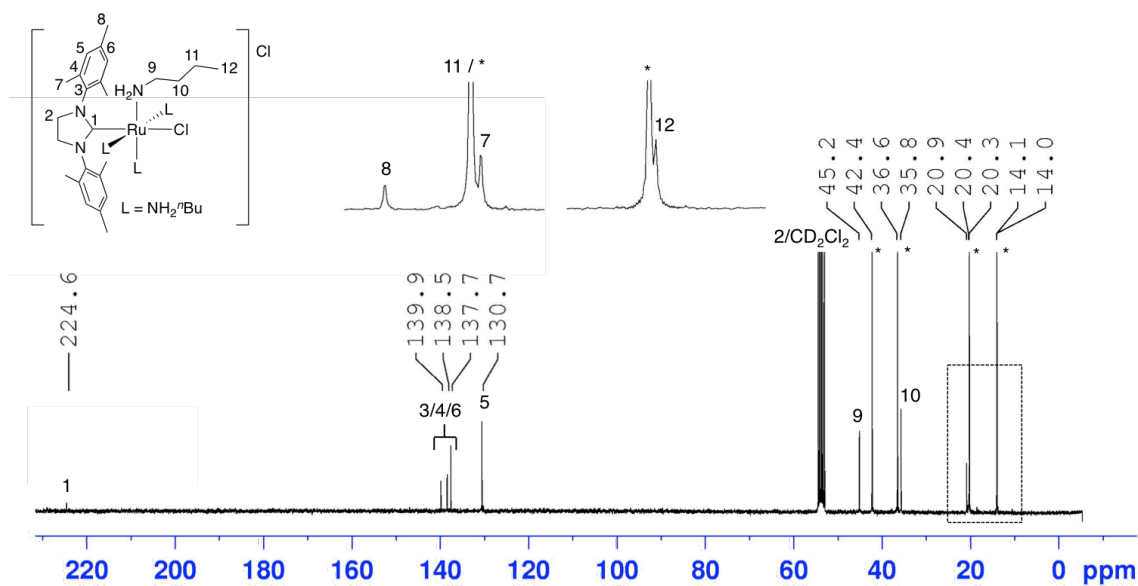


Figure A1.11. $^{13}\text{C}\{^1\text{H}\}$ NMR spectrum (CD_2Cl_2 , 125.8 MHz) for isolated **Ru-17a** in the presence of added NH_2^nBu (1% v/v). Signals for excess NH_2^nBu are labeled (*).

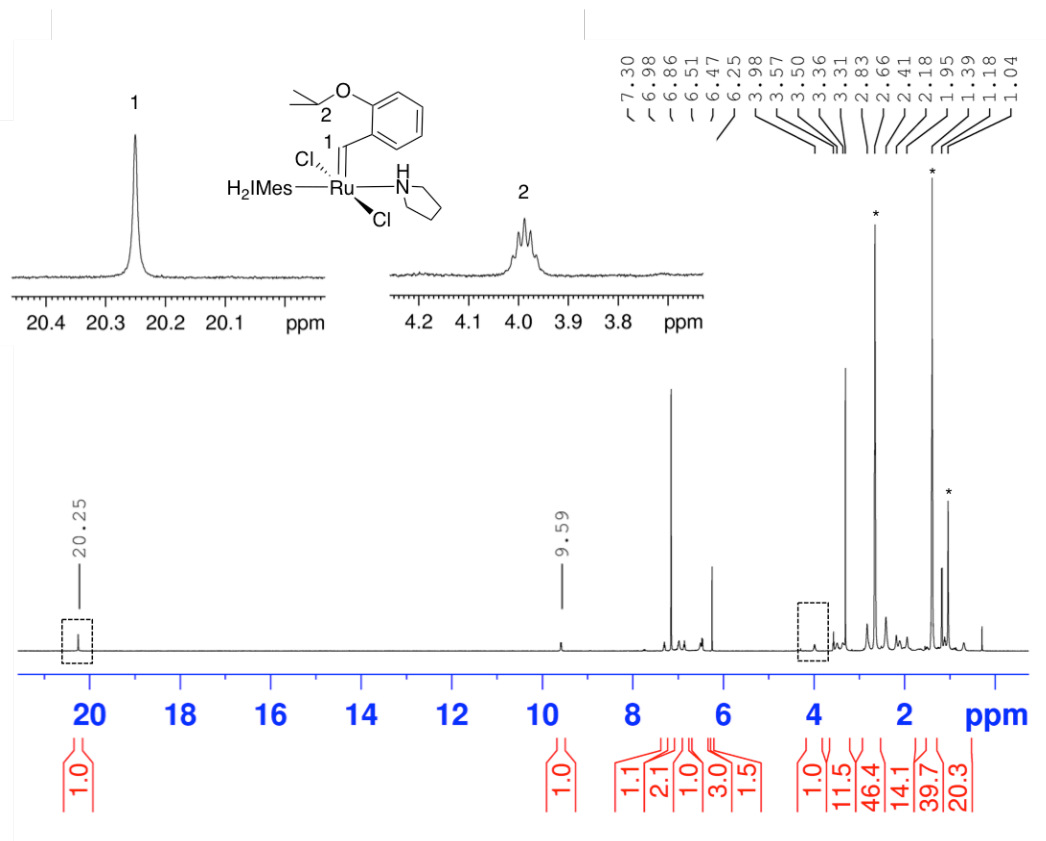


Figure A1.12. In situ ^1H NMR spectrum (C_6D_6 , 500.1 MHz) for $\text{RuCl}_2(\text{H}_2\text{IMes})(\text{NHC}_4\text{H}_8)_2(=\text{CHAr})$, **III-7**. Signals for excess pyrrolidine N7 are labelled (*).

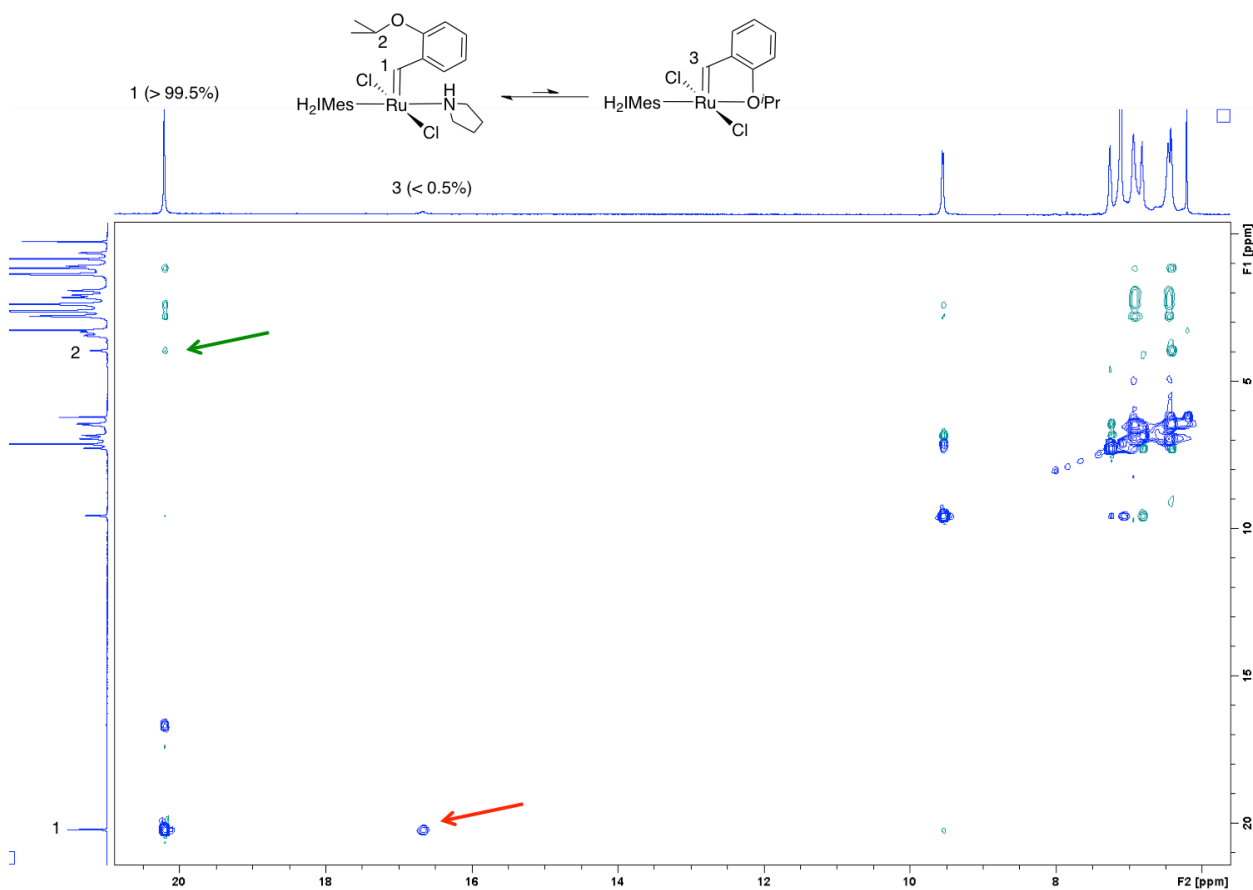


Figure A1.13. ^1H NOESY/EXSY spectrum (C_6D_6 , 500.1 MHz) showing chemical exchange between **III** and **III-7**. Green arrow: NOE cross-peak for $[\text{Ru}]=\text{CHAr}$ and OCHMe_2 . Red arrow: cross-peak for chemical exchange between **III-7** and **III**.

A1.3. ^1H and $^{13}\text{C}\{^1\text{H}\}$ NMR spectra for new compounds in Chapter 5

A1.3.1. NMR spectra for new compounds, in Chapter 5, pyrrolidine N7 and morpholine N6 adducts of GII.

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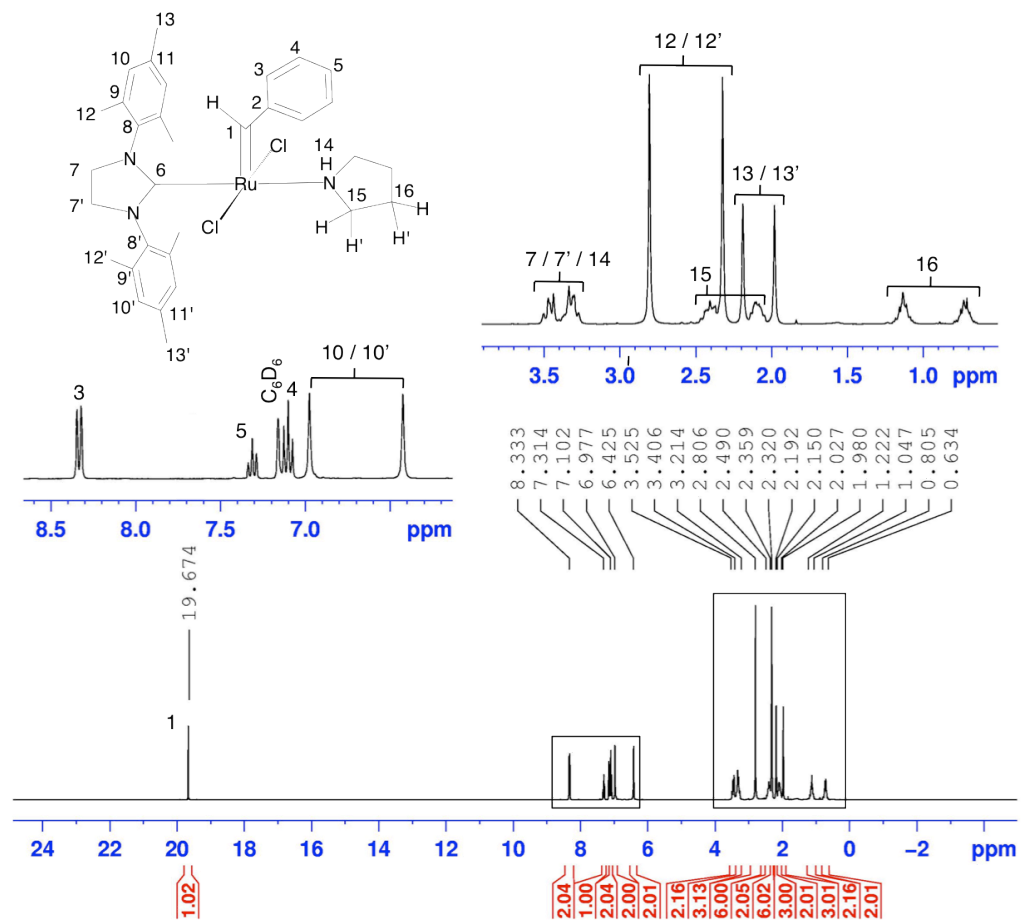
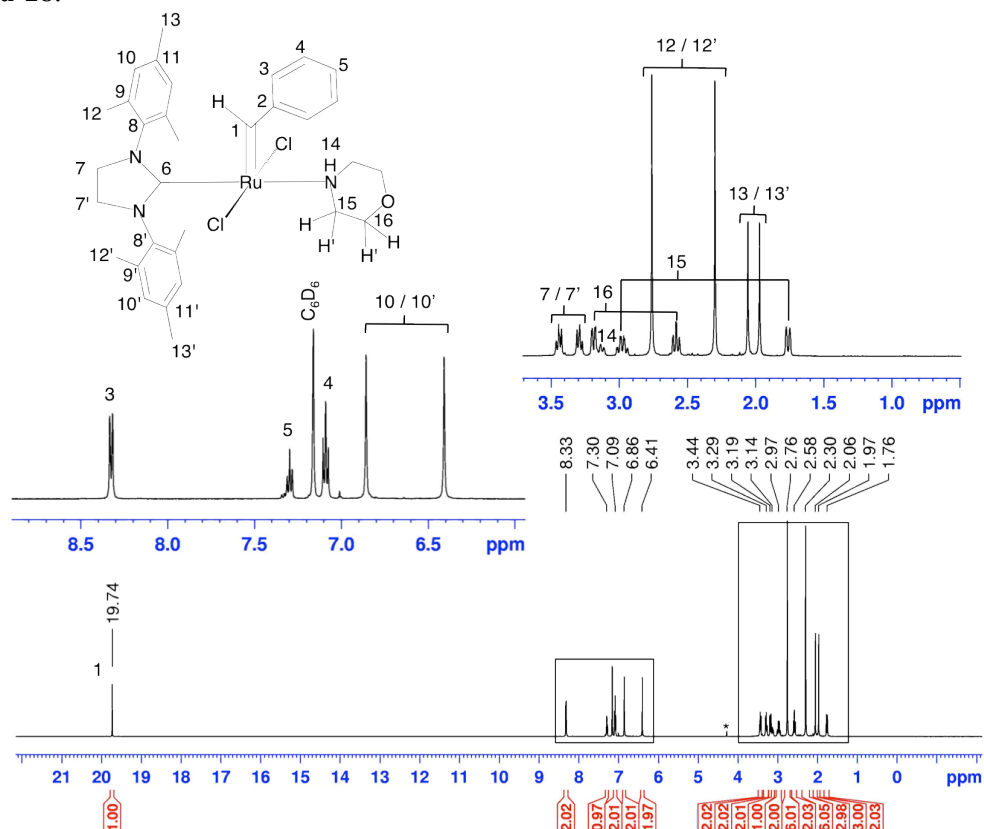
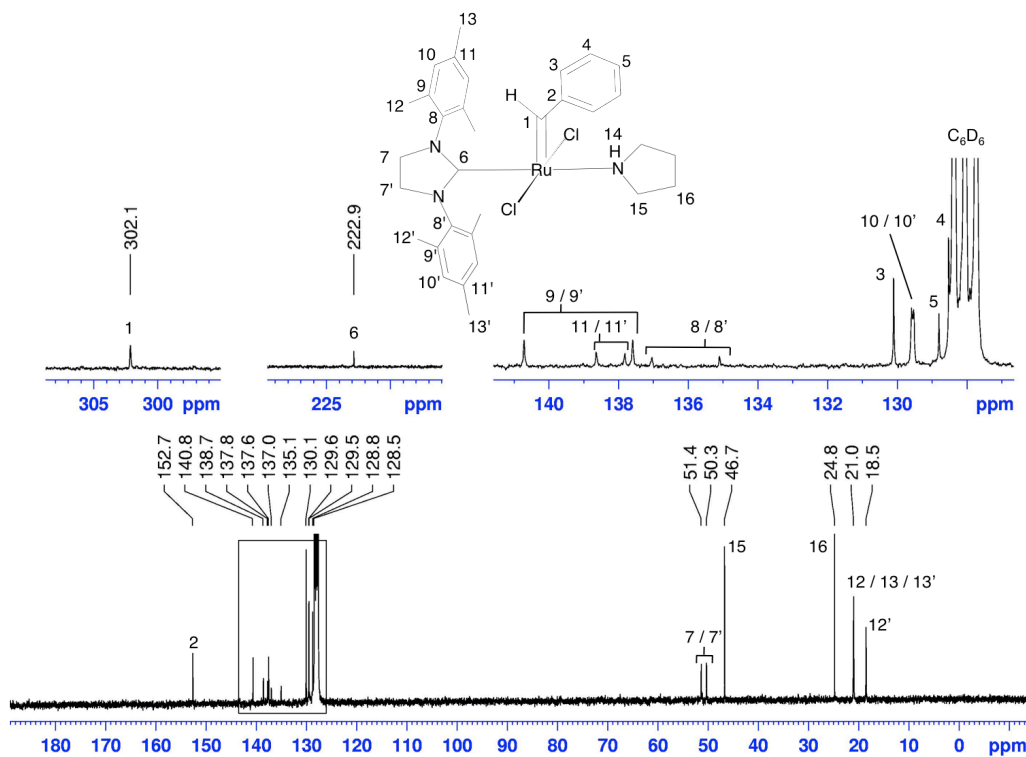


Figure A1.14. ^1H spectrum (C_6D_6 , 300.3 MHz) for $\text{RuCl}_2(\text{H}_2\text{IMes})(\text{HNC}_4\text{H}_8)(=\text{CHPh})$ **Ru-28**.

* Compound numbers and figure caption syntax have been modified for consistency throughout the thesis. For a Table of Compound Numbers and Structures, see p. VI.



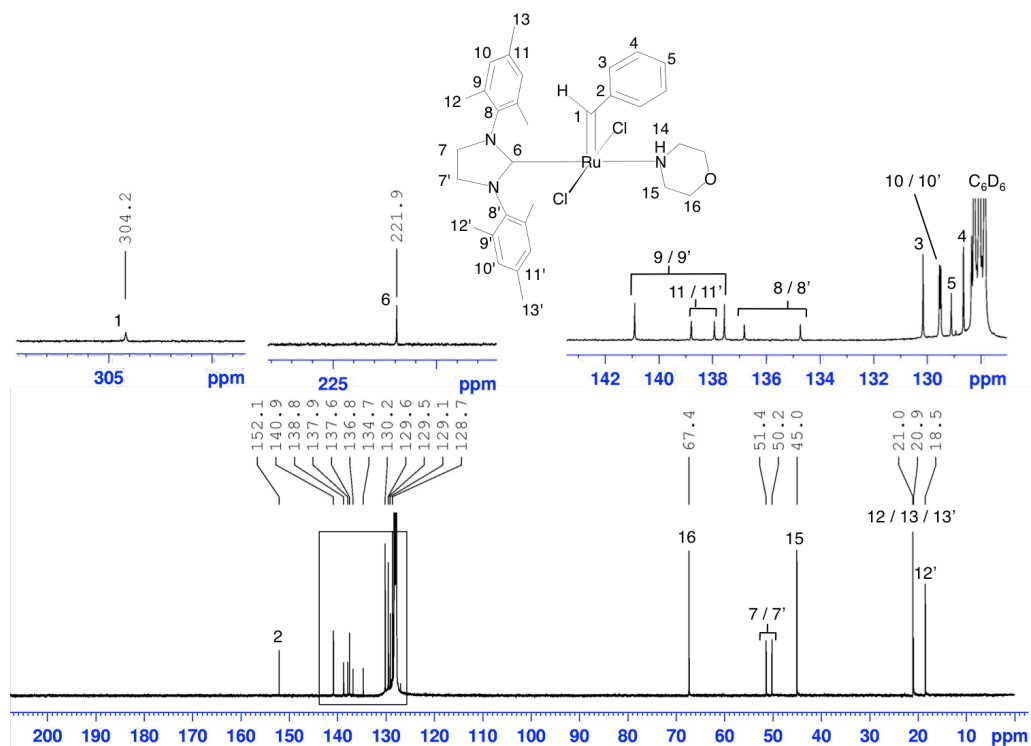


Figure A1.17. $^{13}\text{C}\{^1\text{H}\}$ NMR spectrum (C_6D_6 , 75.5 MHz) for $\text{RuCl}_2(\text{H}_2\text{IMes})(\text{HNC}_4\text{H}_8\text{O})(=\text{CHPh})$ **Ru-29**.

A1.3.2. NMR spectra for other new compounds, in Chapter 5, Section 5.2.

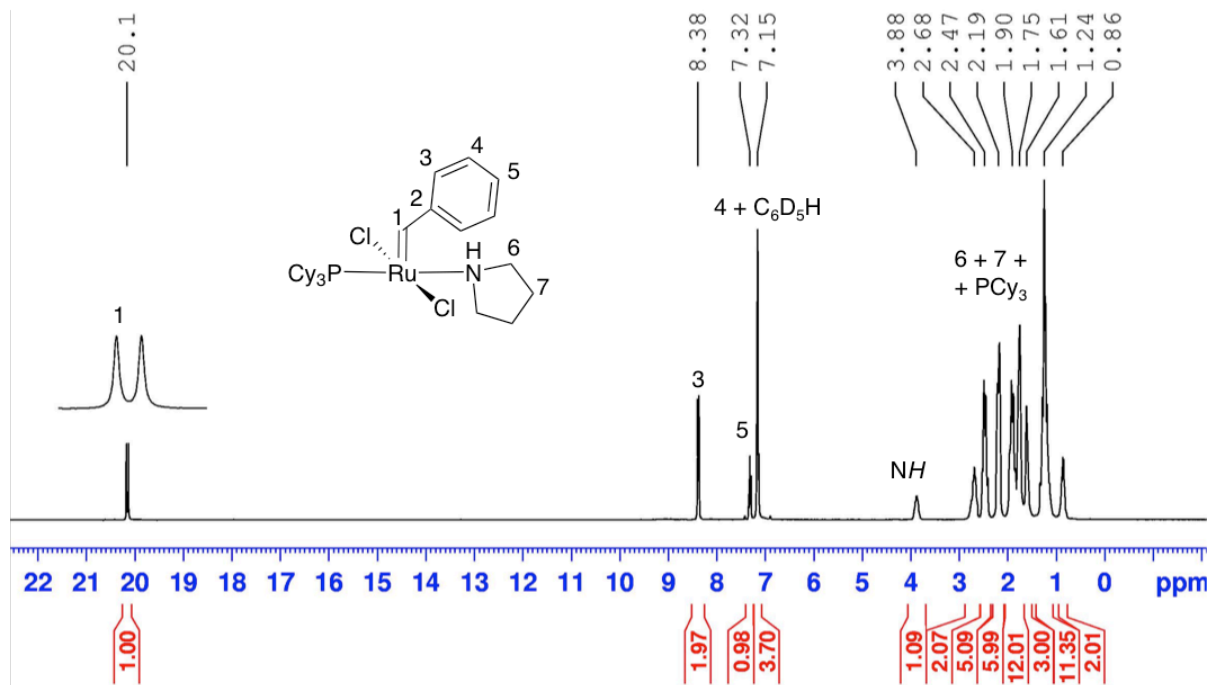


Figure A1.18. ^1H NMR spectrum (C_6D_6 , 300.3 MHz) for $\text{RuCl}_2(\text{PCy}_3)(\text{NHC}_4\text{H}_8)(=\text{CHPh})$ **Ru-43**.

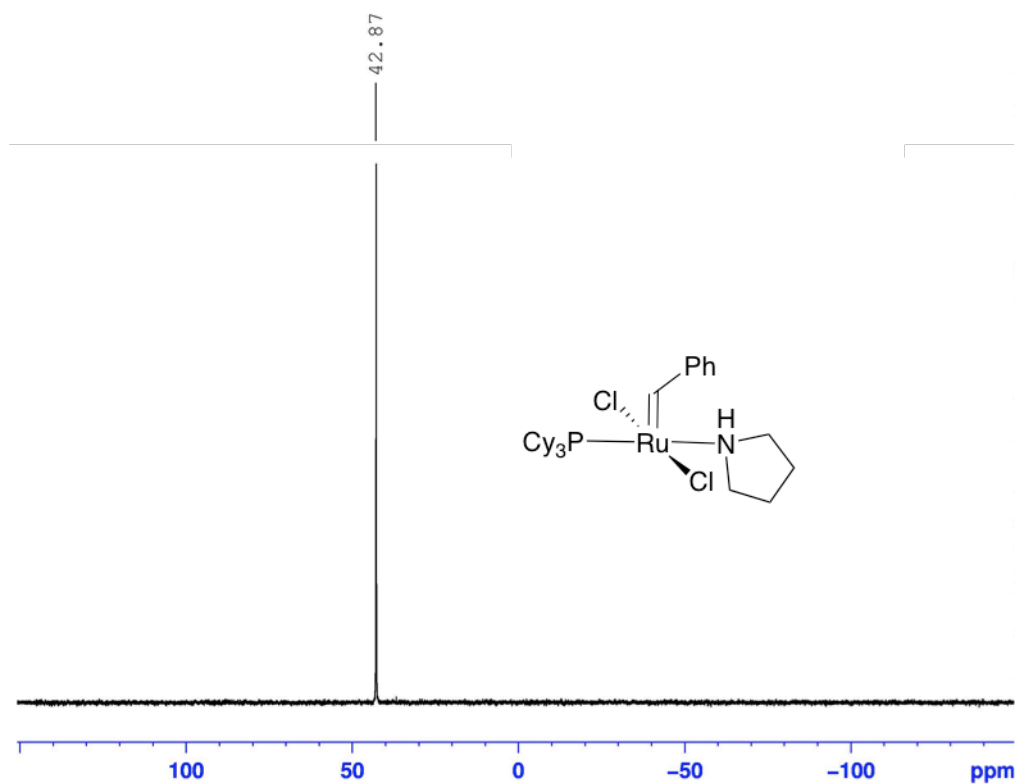


Figure A1.19. $^{31}\text{P}\{^1\text{H}\}$ NMR spectrum (C_6D_6 , 121.5 MHz) for $\text{RuCl}_2(\text{PCy}_3)(\text{NHC}_4\text{H}_8)(=\text{CHPh})$ **Ru-43**.

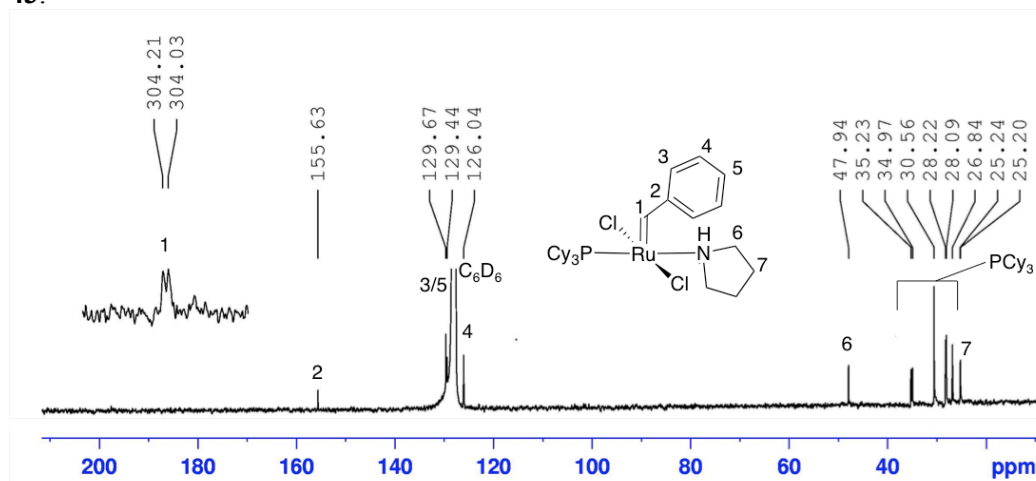


Figure A1.20. $^{13}\text{C}\{^1\text{H}\}$ NMR spectrum (C_6D_6 , 75.5 MHz) for $\text{RuCl}_2(\text{PCy}_3)(\text{NHC}_4\text{H}_8)(=\text{CHPh})$ **Ru-43**. Inset: $[\text{Ru}]=\text{CHPh}$.

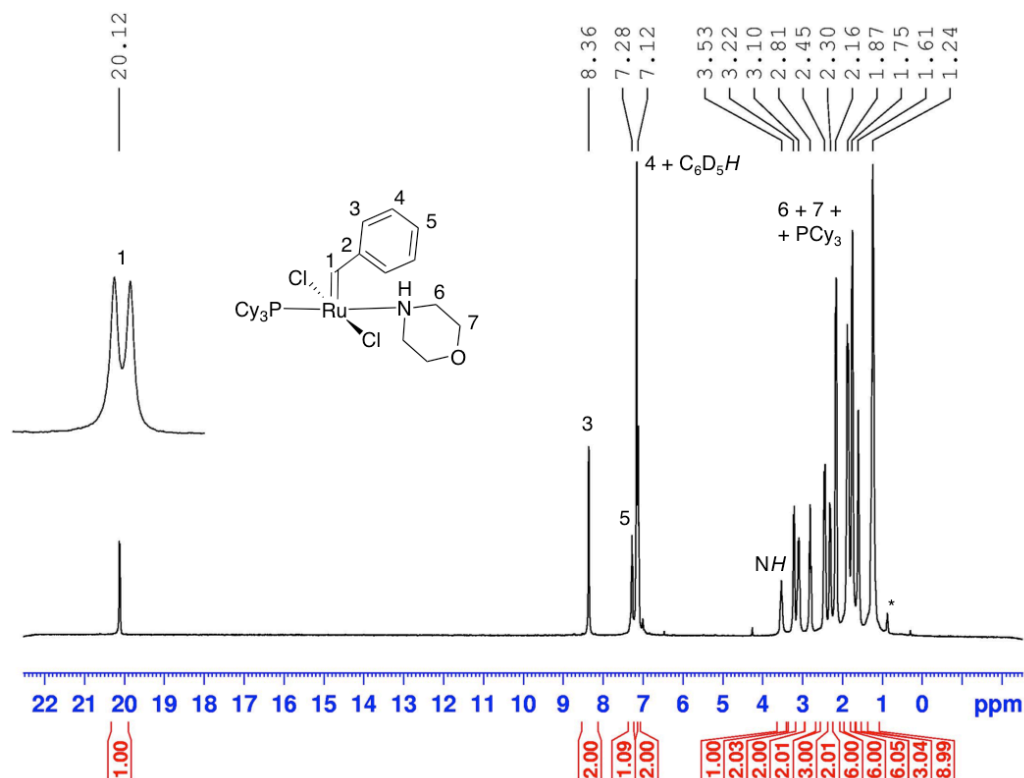


Figure A1.21. ¹H NMR spectrum (C₆D₆, 500.1 MHz) for RuCl₂(PCy₃)(NHC₄H₈O)(=CHPh) **Ru-44**.
* hexanes (impurity in sample).

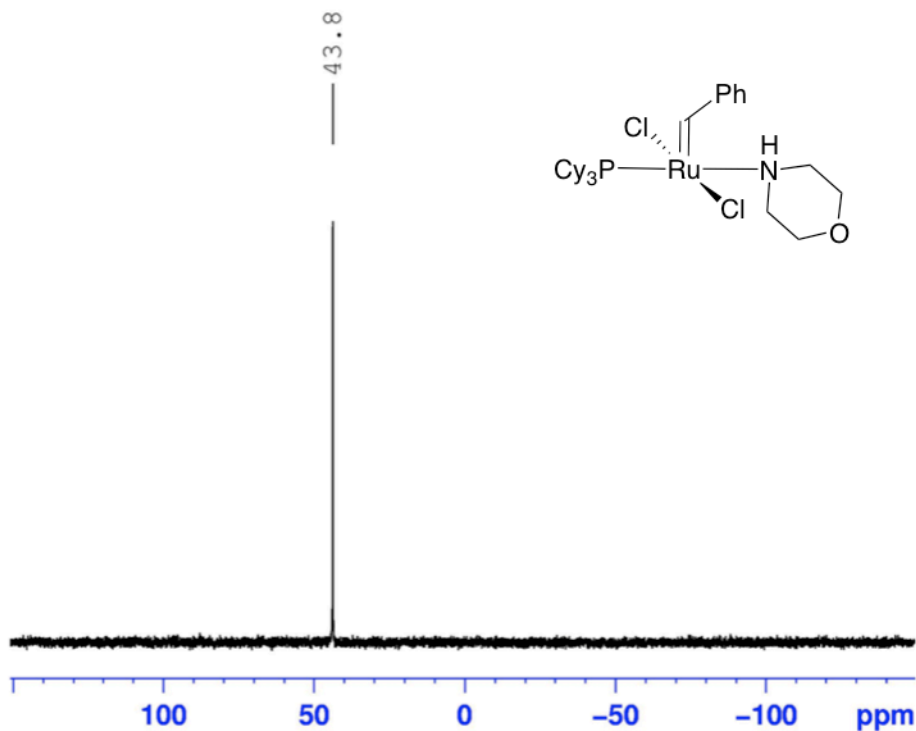


Figure A1.22. ³¹P{¹H} NMR spectrum (C₆D₆, 121.5 MHz) for RuCl₂(PCy₃)(NHC₄H₈O)(=CHPh) **Ru-44**.

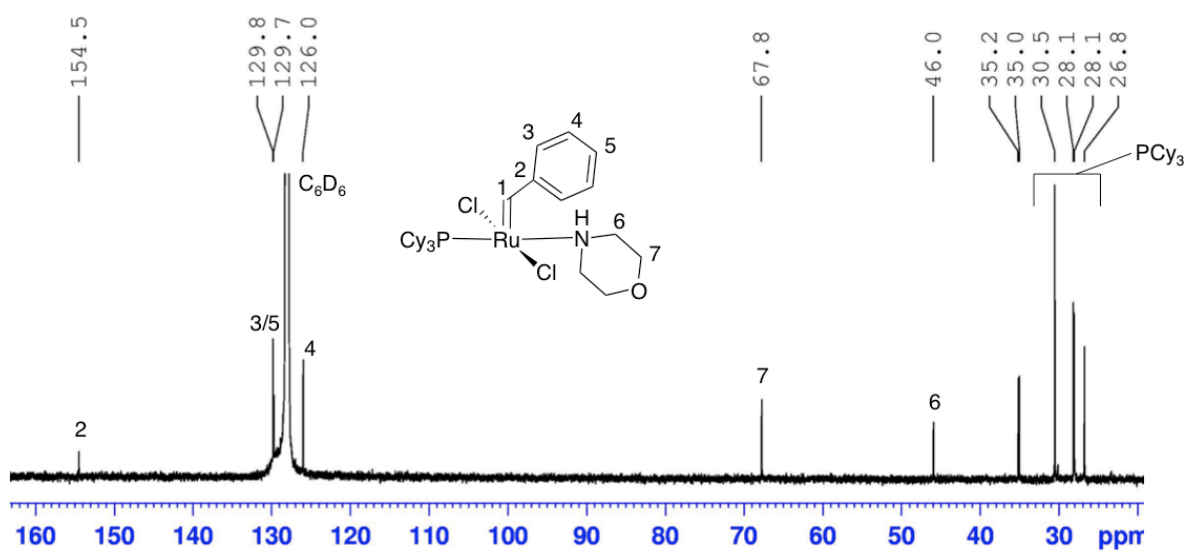


Figure A1.23. ¹³C{¹H} NMR spectrum (C₆D₆, 128.5 MHz) for RuCl₂(PCy₃)(NHC₄H₈O)(=CHPh) **Ru-44**.

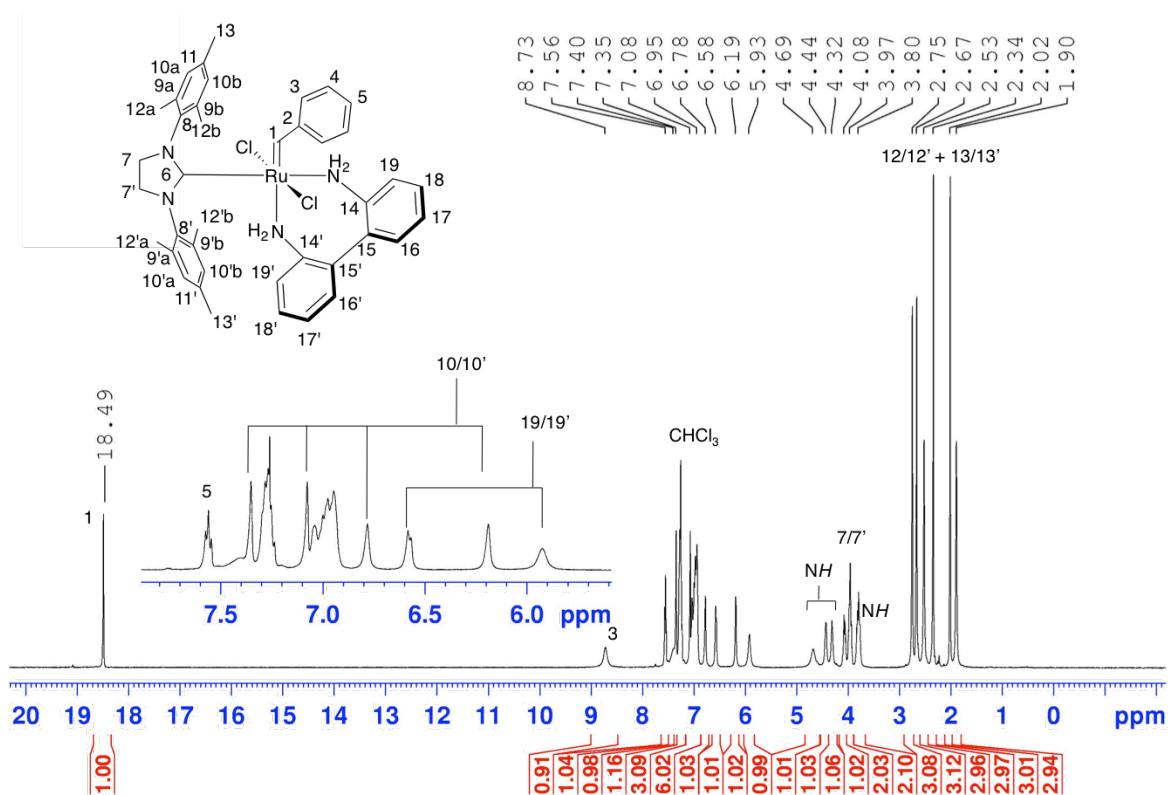
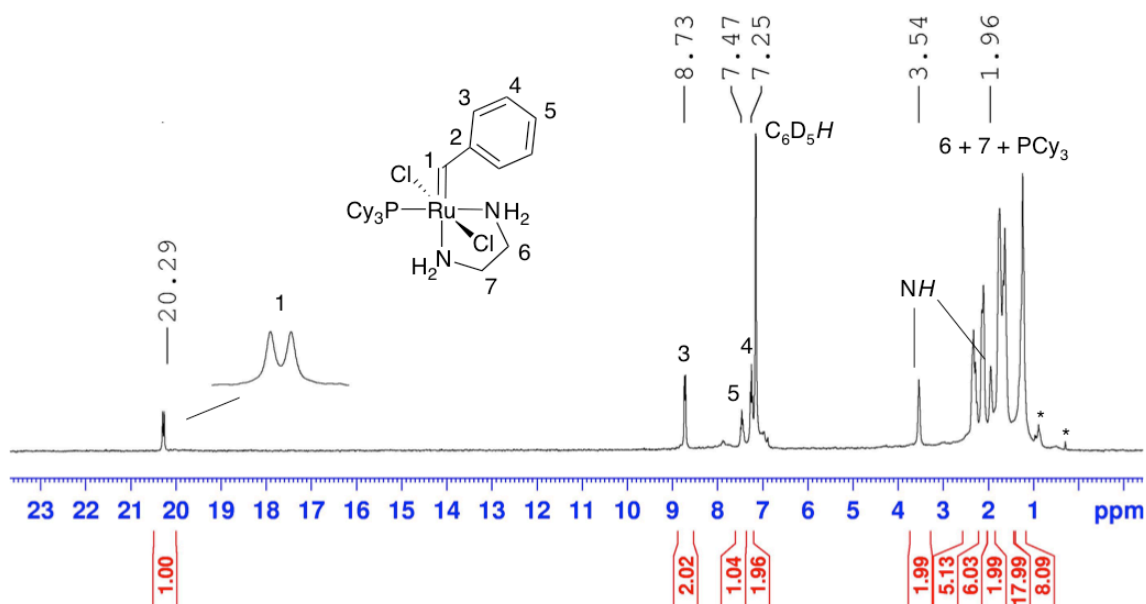
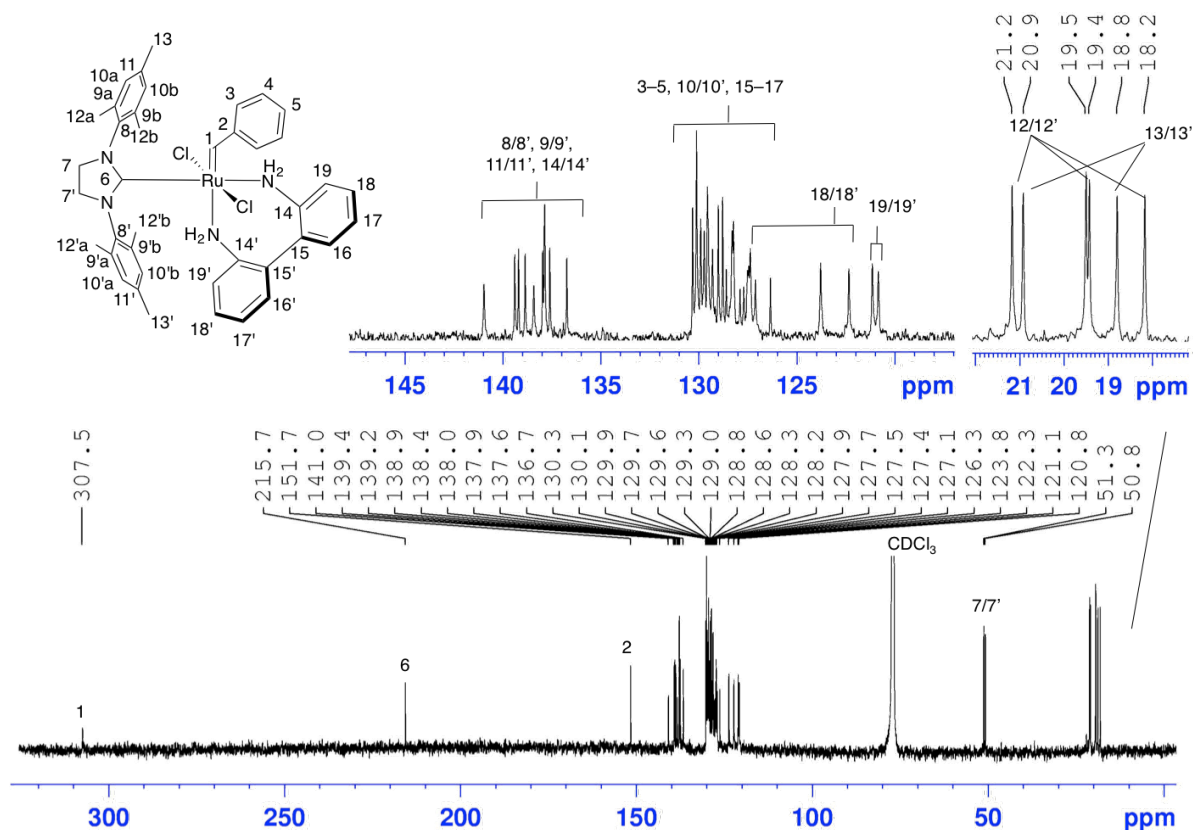


Figure A1.24. ¹H NMR spectrum (CDCl₃, 500.1 MHz, -20 °C) for RuCl₂((H₂IMes)(biphenyl-2,2'-diamine)(=CHPh) **Ru-42**.



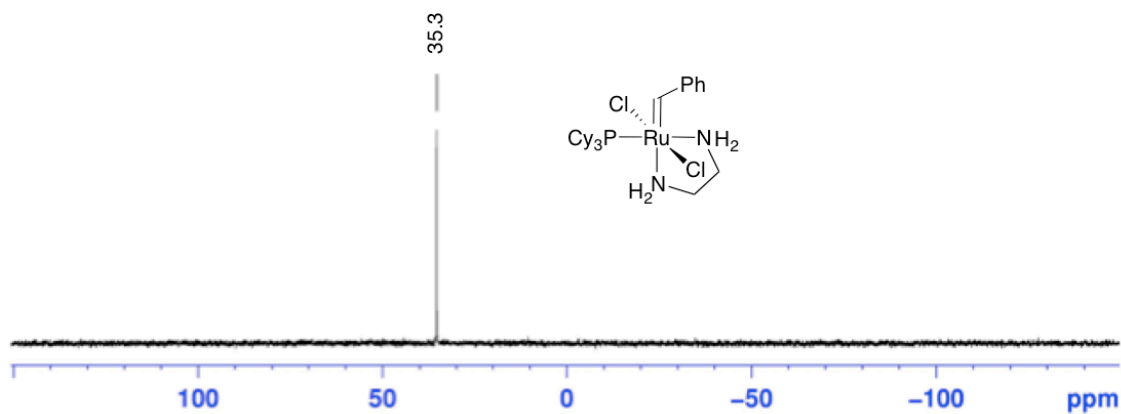


Figure A1.27. $^{31}\text{P}\{^1\text{H}\}$ NMR spectrum (C_6D_6 , 121.5 MHz) for $\text{RuCl}_2(\text{PCy}_3)(\text{en})(=\text{CHPh})$ **Ru-15**.

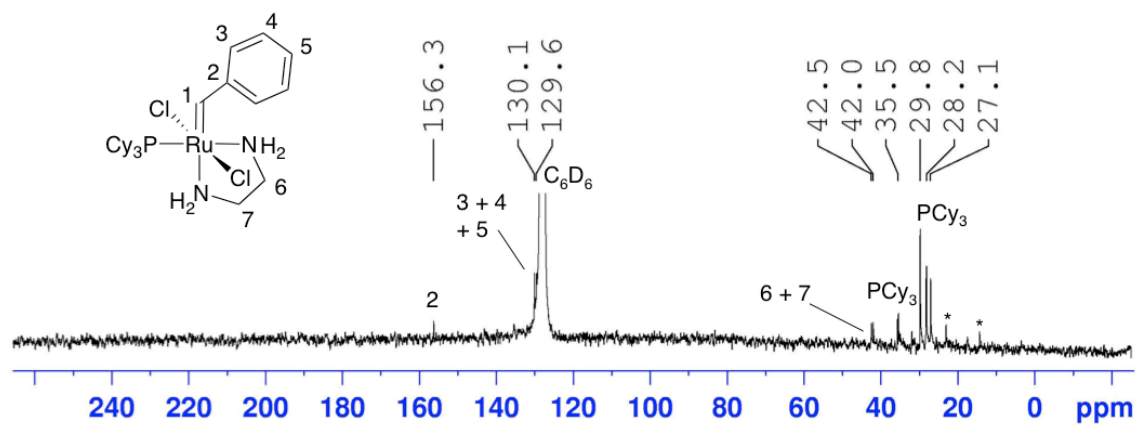


Figure A1.28. $^{13}\text{C}\{^1\text{H}\}$ NMR spectrum (C_6D_6 , 75.5 MHz, * hexanes) for $\text{RuCl}_2(\text{PCy}_3)(\text{en})(=\text{CHPh})$ **Ru-15**. * hexanes (impurity)

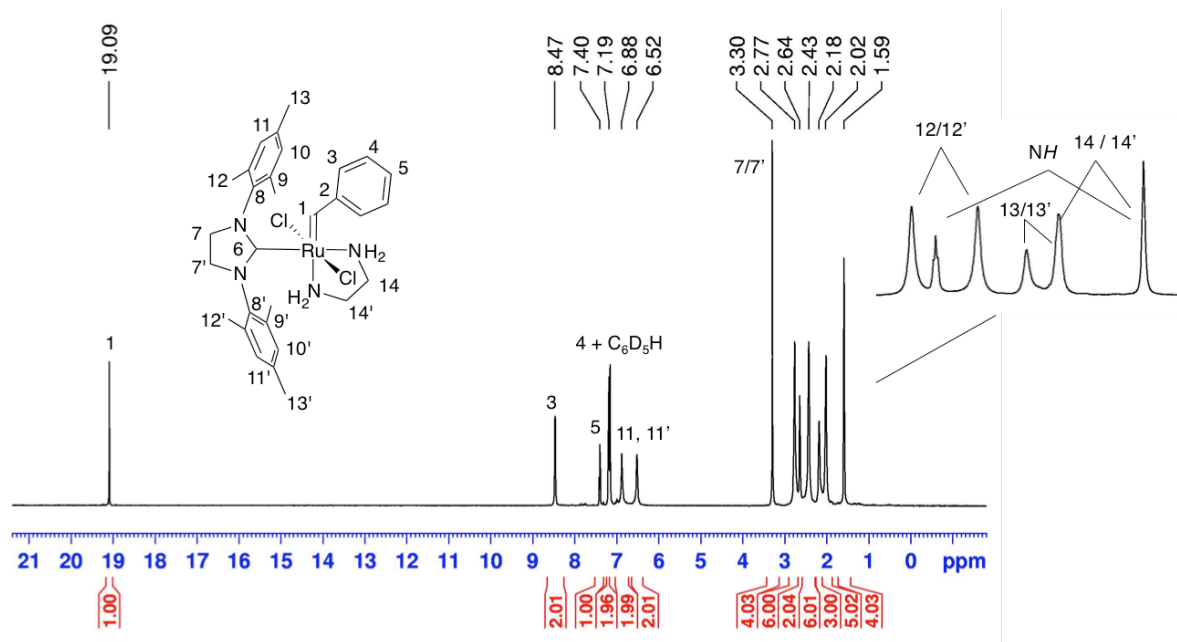


Figure A1.29. ¹H NMR spectrum (C₆D₆, 500.1 MHz) for RuCl₂(H₂IMes)(en)(=CHPh) **Ru-16**.

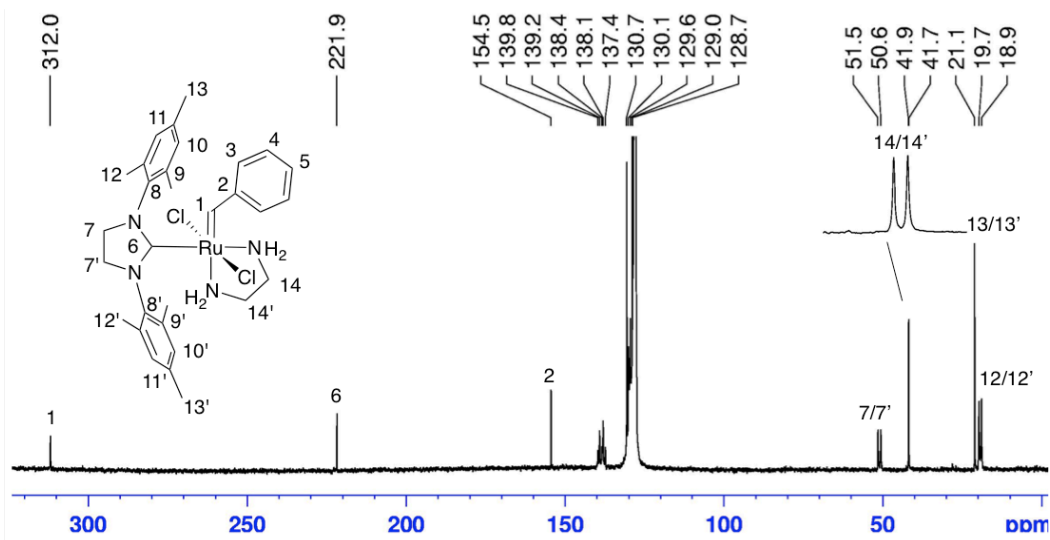


Figure A1.30. ¹³C{¹H} NMR spectrum (C₆D₆, 125.8 MHz) for RuCl₂(H₂IMes)(en)(=CHPh) **Ru-16**.

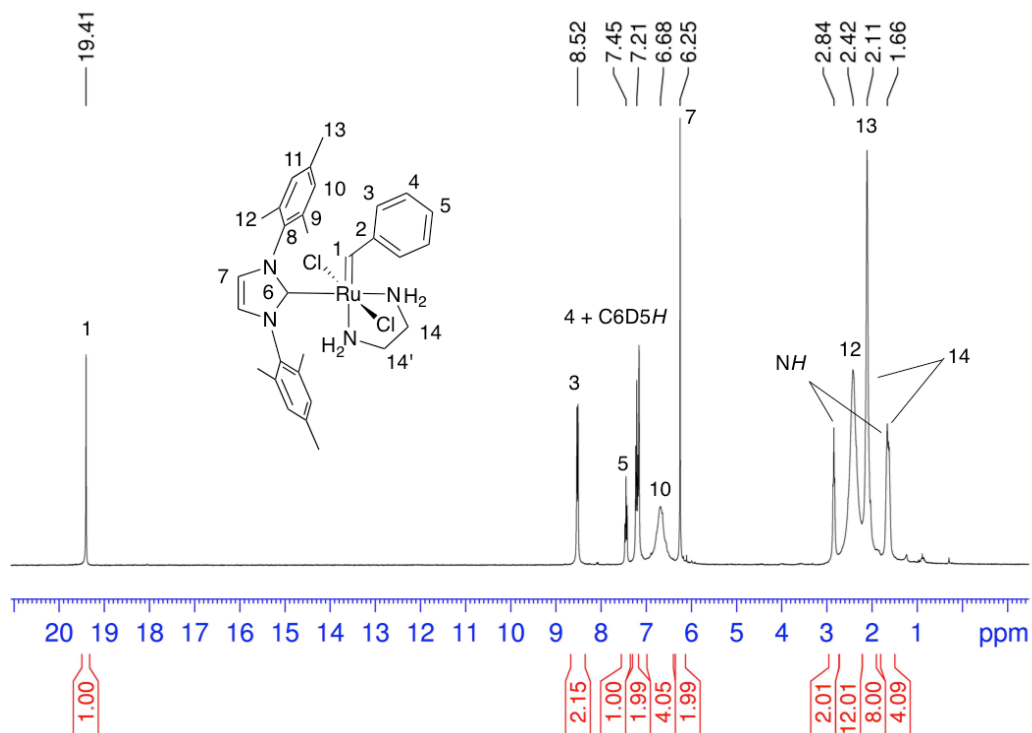


Figure A1.31. ¹H NMR spectrum (C₆D₆, 300.3 MHz) for RuCl₂(IMes)(en)(=CHPh) **Ru-16'**.

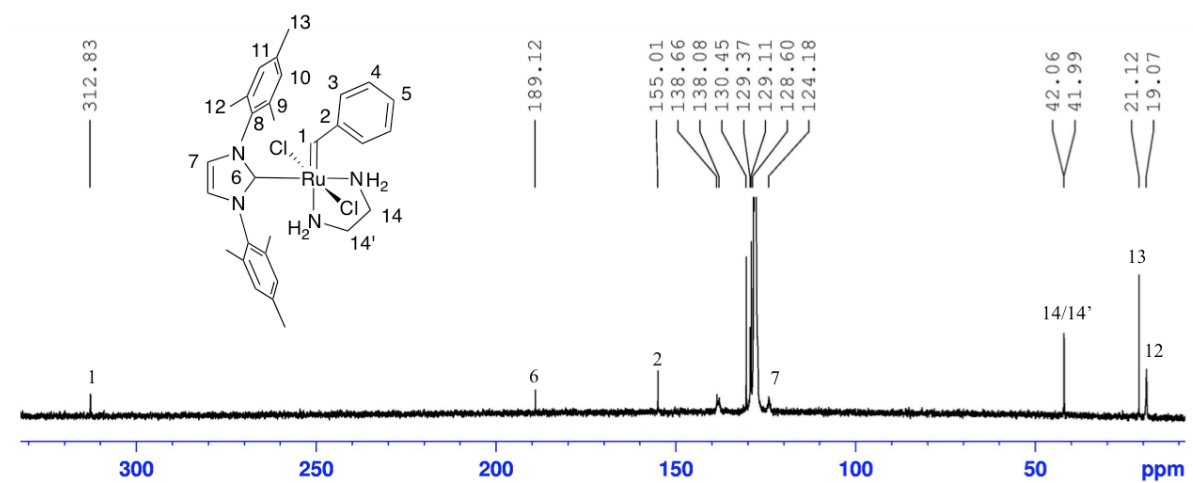


Figure A1.32. ¹³C{¹H} NMR spectrum (C₆D₆, 75.5 MHz) for RuCl₂(IMes)(en)(=CHPh) **Ru-16'**.

A1.3.3. NMR spectra for new compounds, in Chapter 5, Section 5.3.

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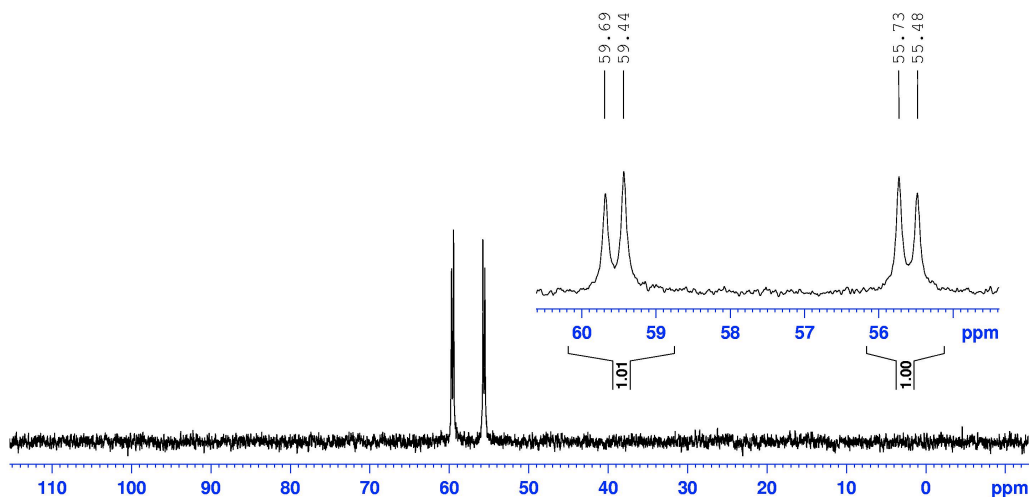


Figure A1.33 $^{31}\text{P}\{^1\text{H}\}$ NMR spectrum (C_6D_6 , 121.6 MHz) for $\text{RuH}[(\eta^5\text{-C}_6\text{H}_5)\text{NPh}](\text{PPh}_3)_2$ **Ru-52a**.

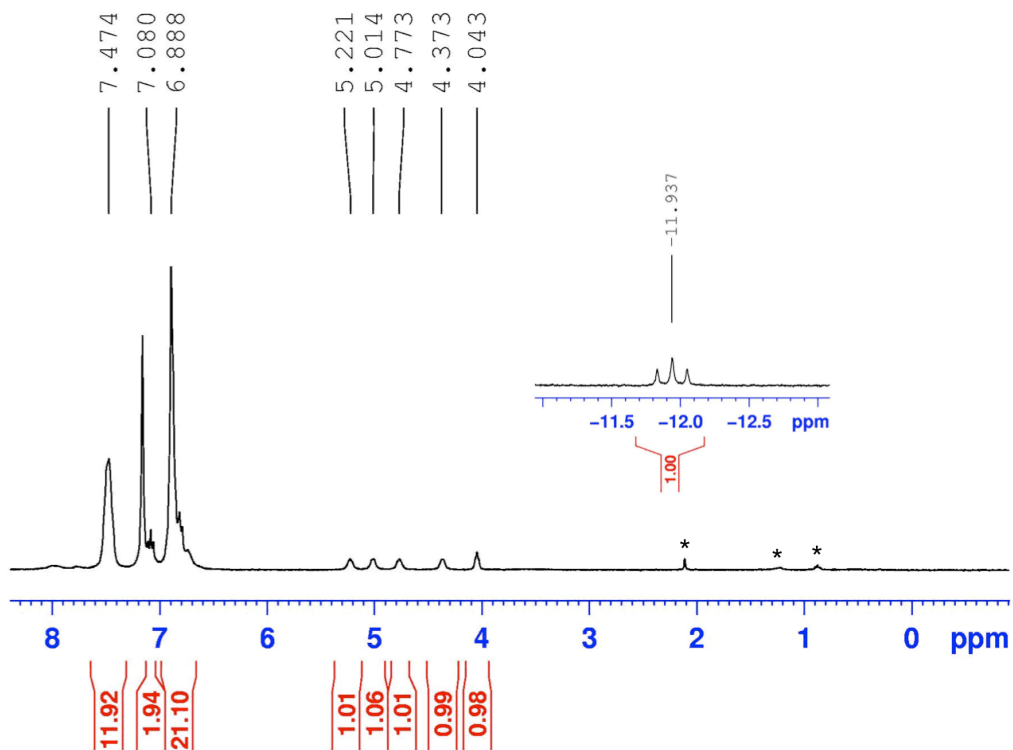


Figure A1.34 ^1H NMR spectrum (C_6D_6 , 300.3 MHz) for $\text{RuH}[(\eta^5\text{-C}_6\text{H}_5)\text{NPh}](\text{PPh}_3)_2$ **Ru-52a**. Inset shows hydride signal; * denotes residual toluene and pentane.

* Compound numbers and figure caption syntax have been modified for consistency throughout the thesis. For a Table of Compound Numbers and Structures, see p. VI.

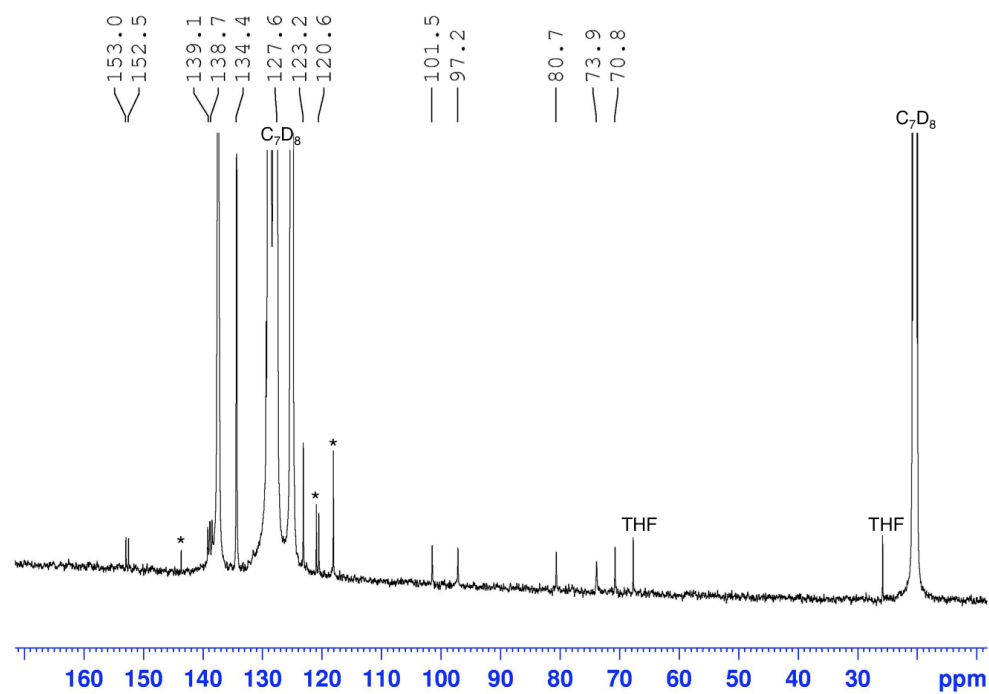


Figure A1.35. $^{13}\text{C}\{^1\text{H}\}$ NMR spectrum (C_7D_8 + 1% THF for solubility; 75.5 MHz); for $\text{RuH}[(\eta^5\text{-C}_6\text{H}_5)\text{NPh}](\text{PPh}_3)_2$ **Ru-52a**. * denotes HNPh_2 impurity. See Figure A1.36 for HNPh_2 -free spectrum.

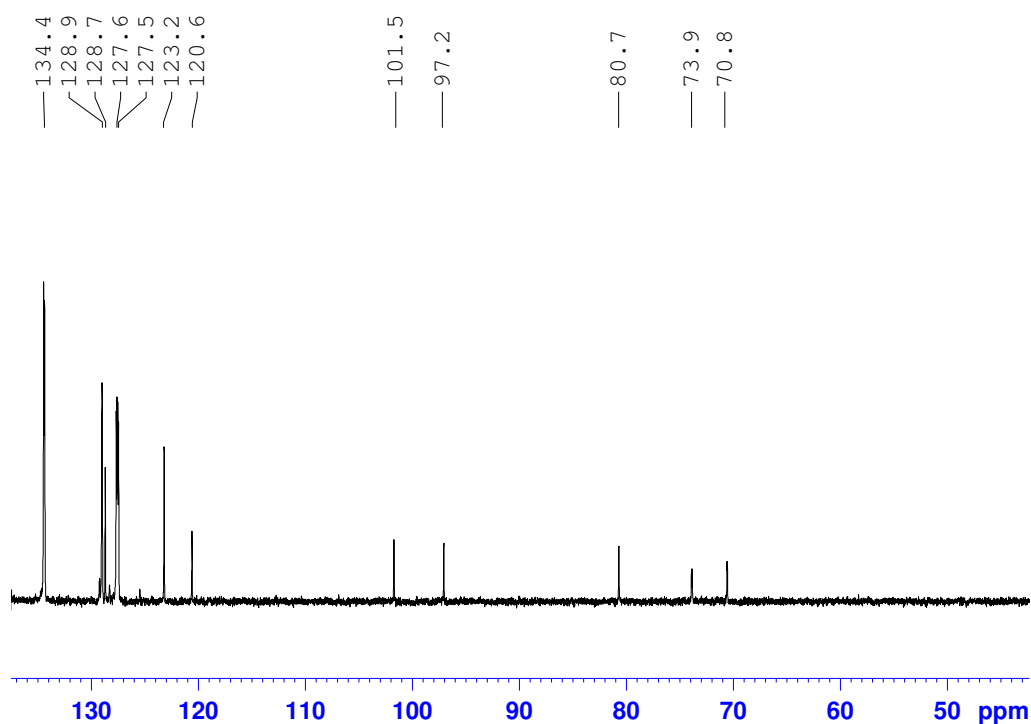


Figure A1.36. ^{13}C DEPT-135 NMR (C_7D_8 , 75.5 MHz) spectrum for $\text{RuH}[(\eta^5\text{-C}_6\text{H}_5)\text{NPh}](\text{PPh}_3)_2$ **Ru-52a**.

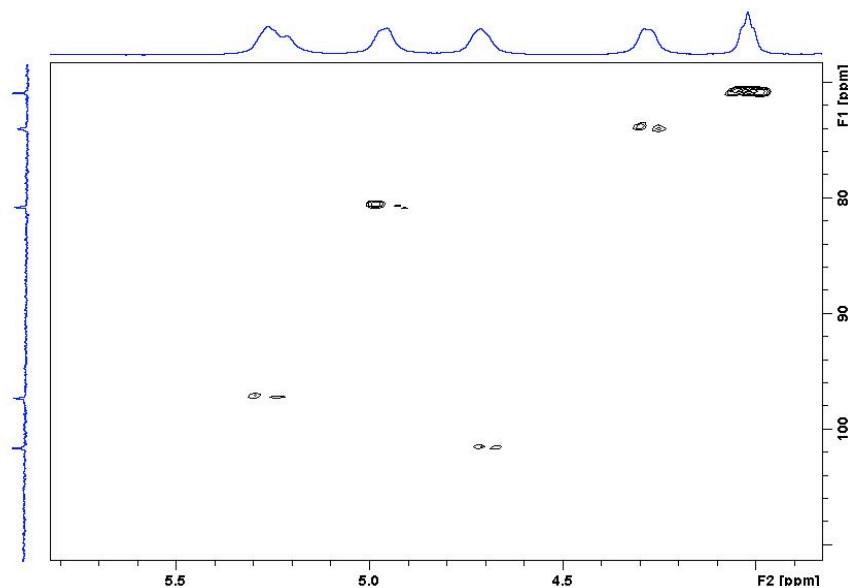


Figure A1.37. ^1H - ^{13}C HMQC spectrum for $\text{RuH}[(\eta^5\text{-C}_6\text{H}_5)\text{NPh}](\text{PPh}_3)_2$ **Ru-52a**, showing correlations in the $\eta^5\text{-C}_6\text{H}_5$ region (C_7D_8).

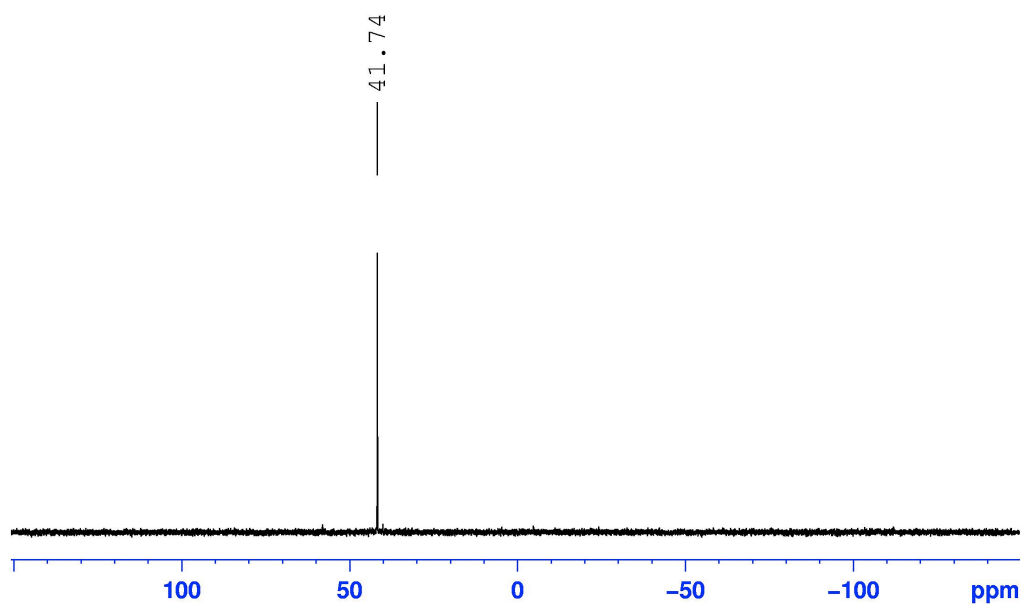


Figure A1.38. $^{31}\text{P}\{^1\text{H}\}$ NMR spectrum (C_6D_6 , 121.6 MHz). for $\text{RuH}(\sigma\text{-NPh}_2)(\text{CO})(\text{PPh}_3)_2$ **Ru-53**.

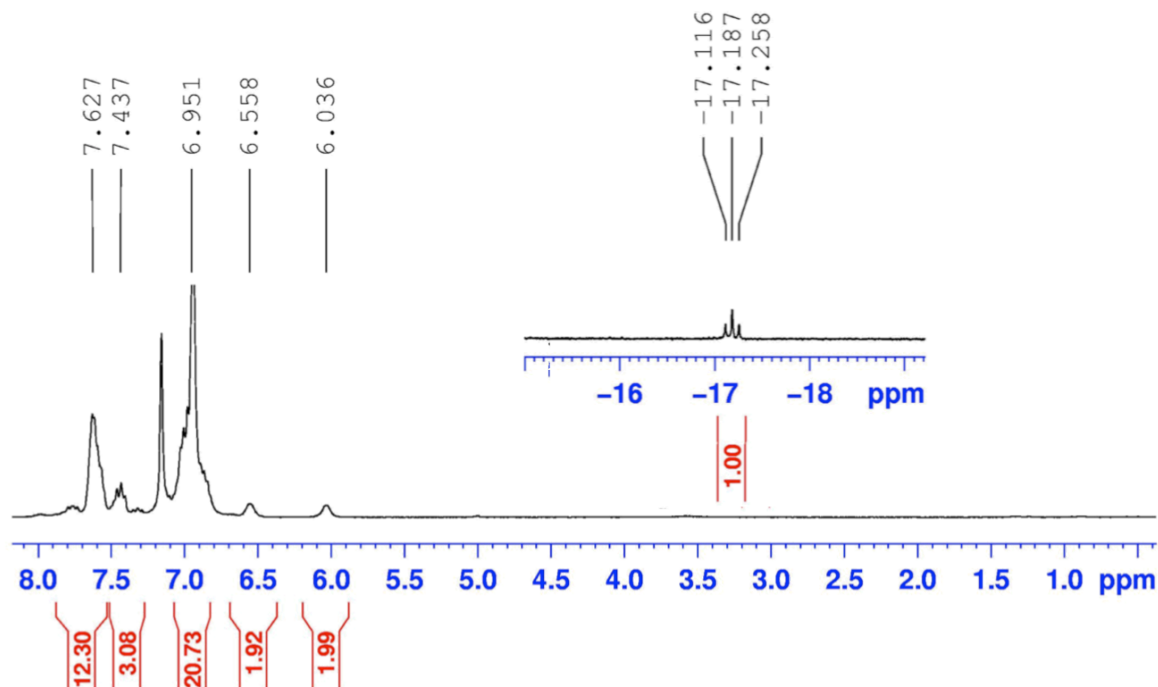


Figure A1.39. ¹H NMR spectrum for (C₆D₆, 300.3 MHz) RuH(σ-NPh₂)(CO)(PPh₃)₂ **Ru-53**. Inset shows hydride signal.

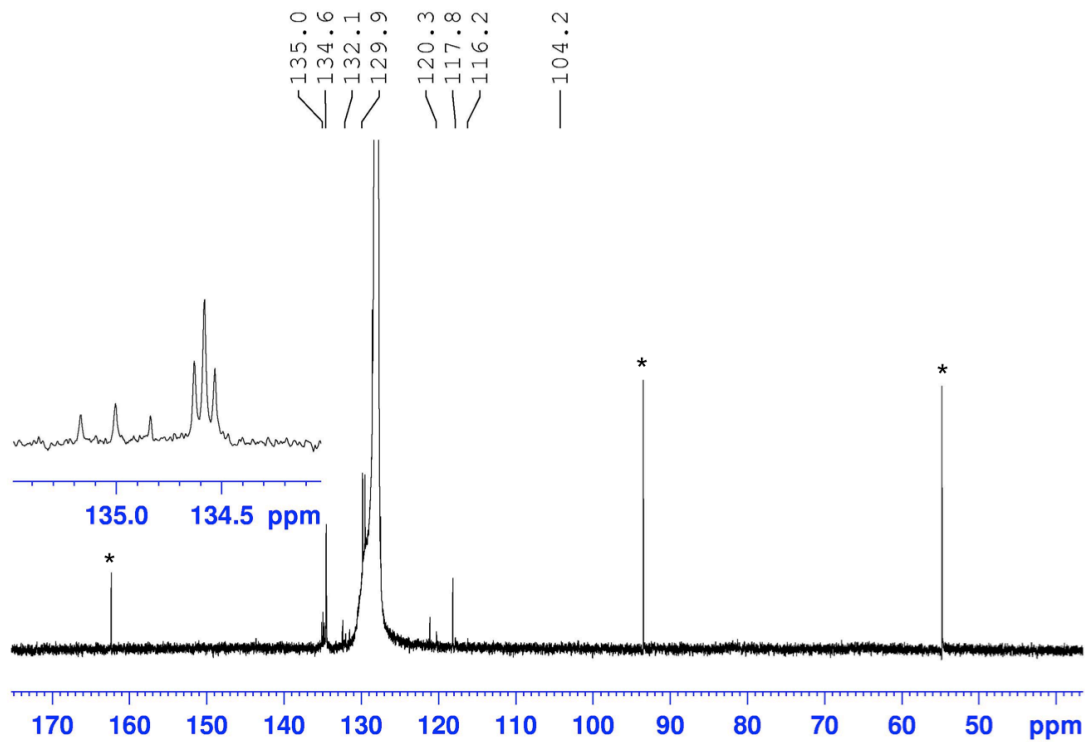


Figure A1.40. ¹³C{¹H} NMR spectrum (C₆D₆, 75.5 MHz) for RuH(σ-NPh₂)(CO)(PPh₃)₂ **Ru-53**. * denotes added 1,3,5-trimethoxybenzene.

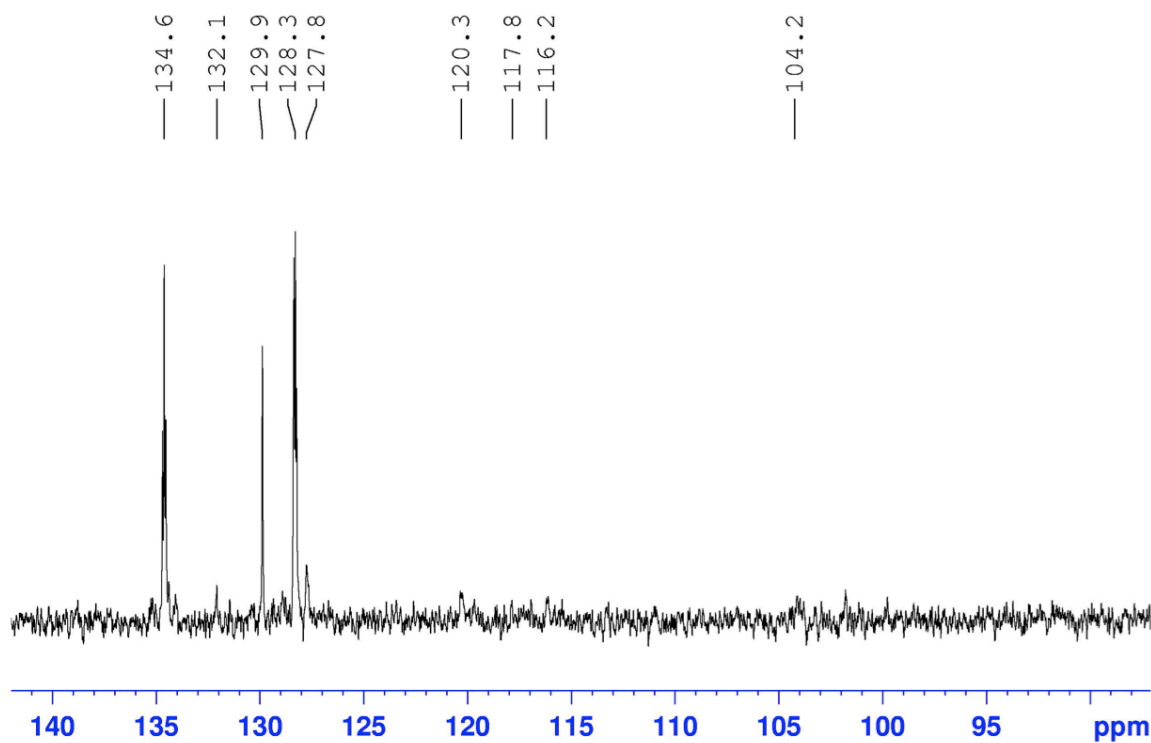


Figure A1.41. ^{13}C DEPT-135 NMR spectrum (C_6D_6 , 75.5 MHz) for $\text{RuH}(\sigma\text{-NPh}_2)(\text{CO})(\text{PPh}_3)_2$ **Ru-53**.

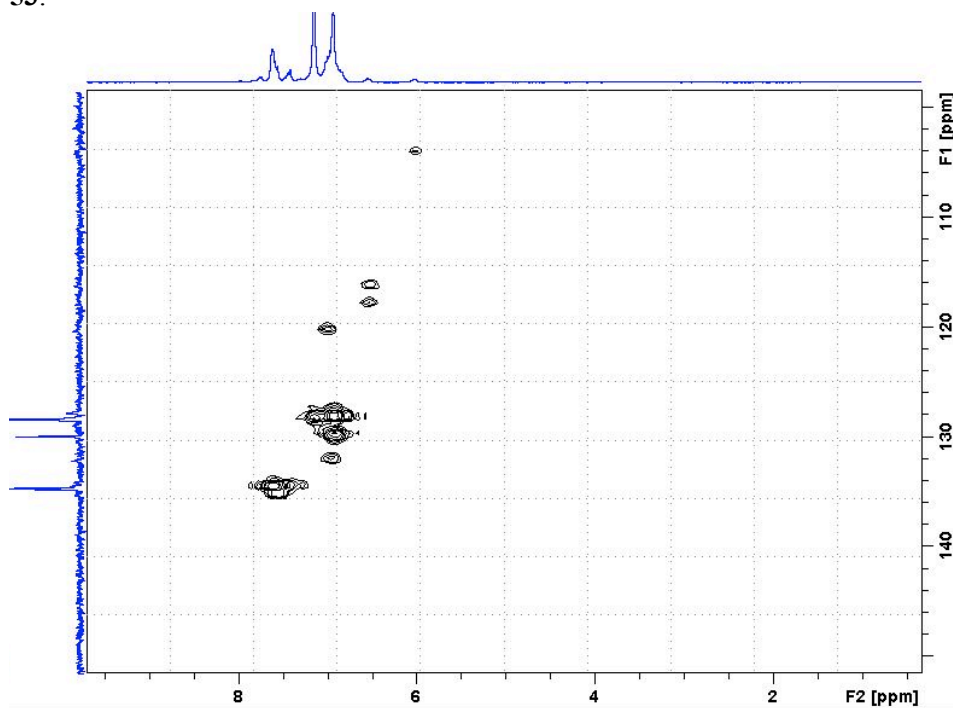


Figure A1.42. ^1H - ^{13}C HMQC correlation spectrum (C_6D_6) for $\text{RuH}(\sigma\text{-NPh}_2)(\text{CO})(\text{PPh}_3)_2$ **Ru-53**.

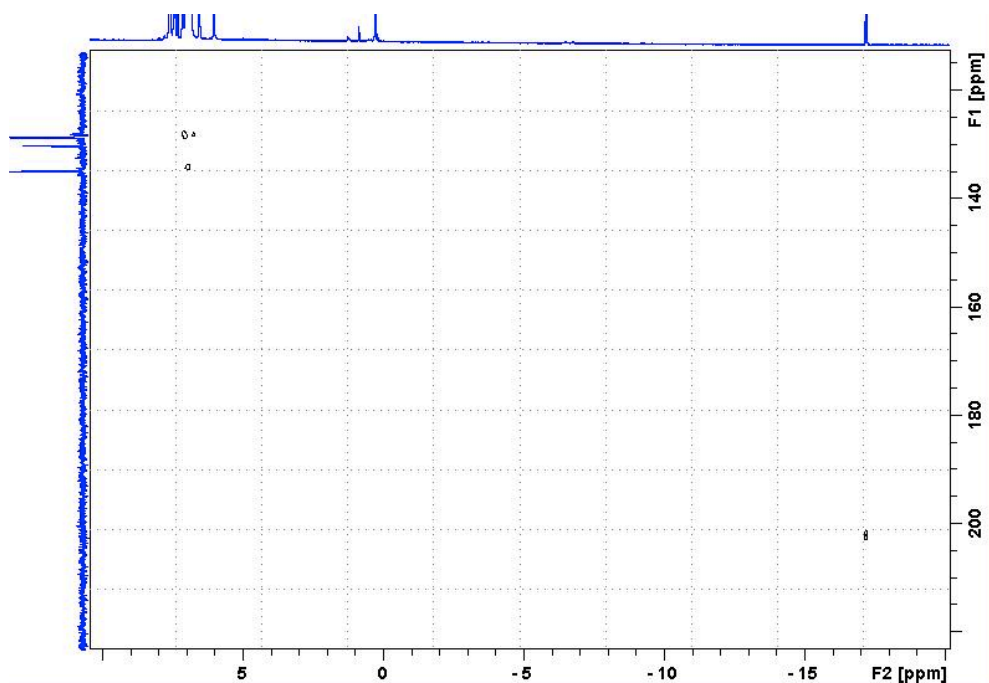


Figure A1.43. ^1H - ^{13}C HMBC correlation spectrum (C_6D_6) for $\text{RuH}(\sigma\text{-NPh}_2)(\text{CO})(\text{PPh}_3)_2$ **Ru-53**.

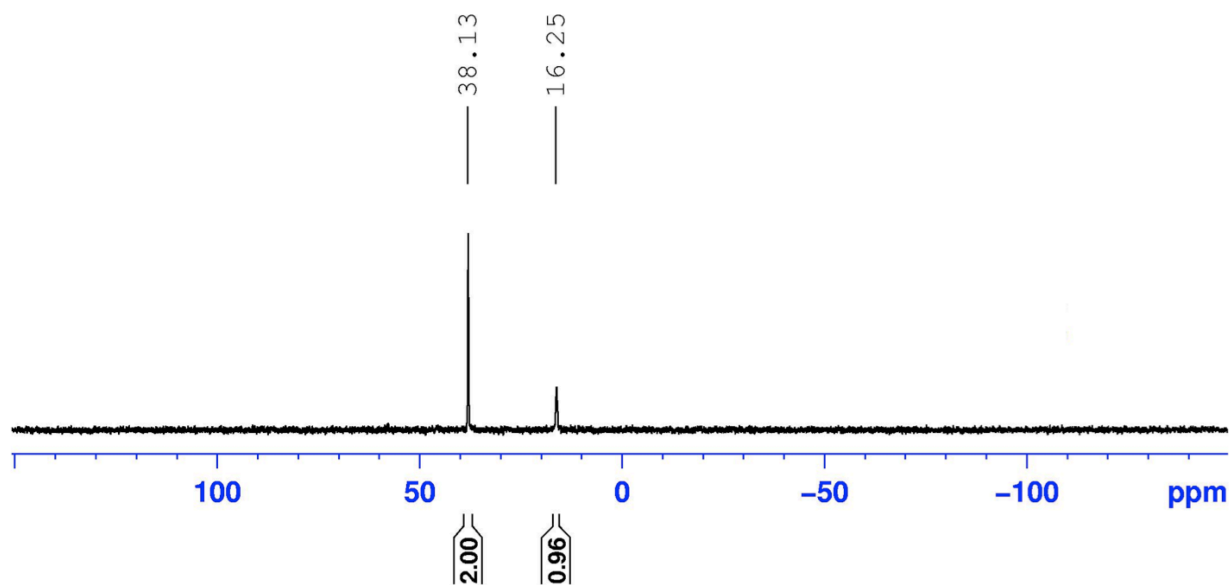


Figure A1.44. $^{31}\text{P}\{^1\text{H}\}$ NMR spectrum (C_6D_6 , 121.6 MHz) for $\text{RuH}(\sigma\text{-OPh})(\text{CO})(\text{PPh}_3)_3$ **Ru-54**.

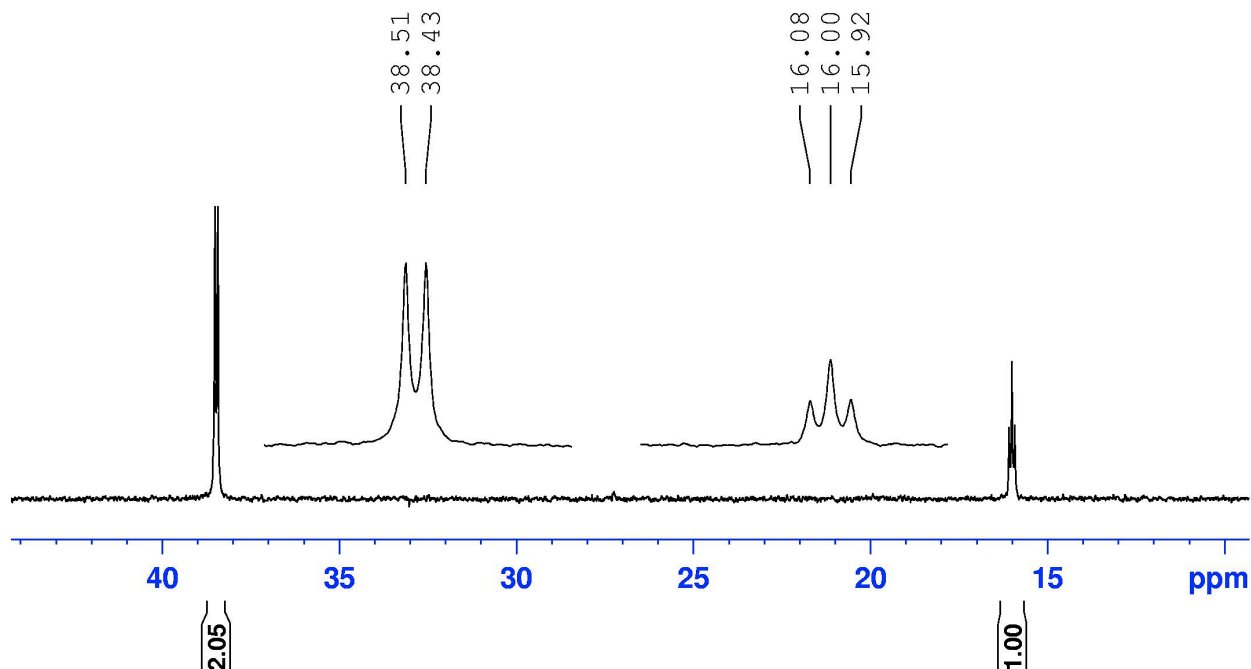


Figure A1.45. Low-temperature $^{31}\text{P}\{^1\text{H}\}$ NMR spectrum (C₇D₈, 121.6 MHz, 263K) for RuH(σ-OPh)(CO)(PPh₃)₃ **Ru-54**.

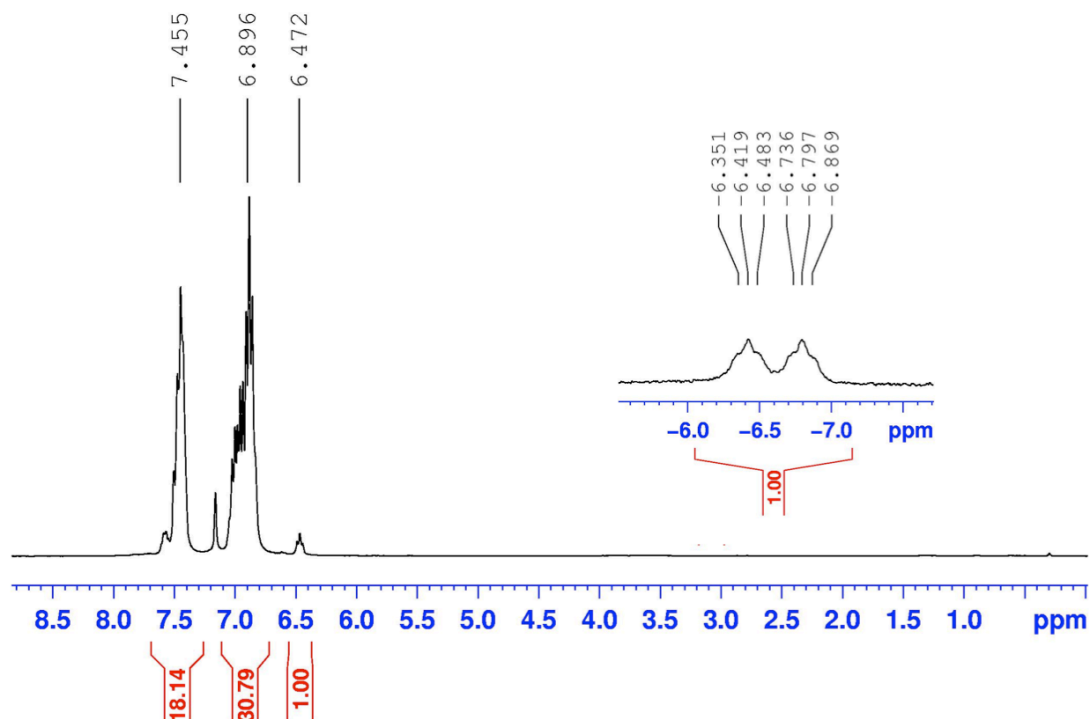


Figure A1.46. ^1H NMR spectrum (C₆D₆, 300.3 MHz) for RuH(σ-OPh)(CO)(PPh₃)₃ **Ru-54**. Inset shows hydride signal.

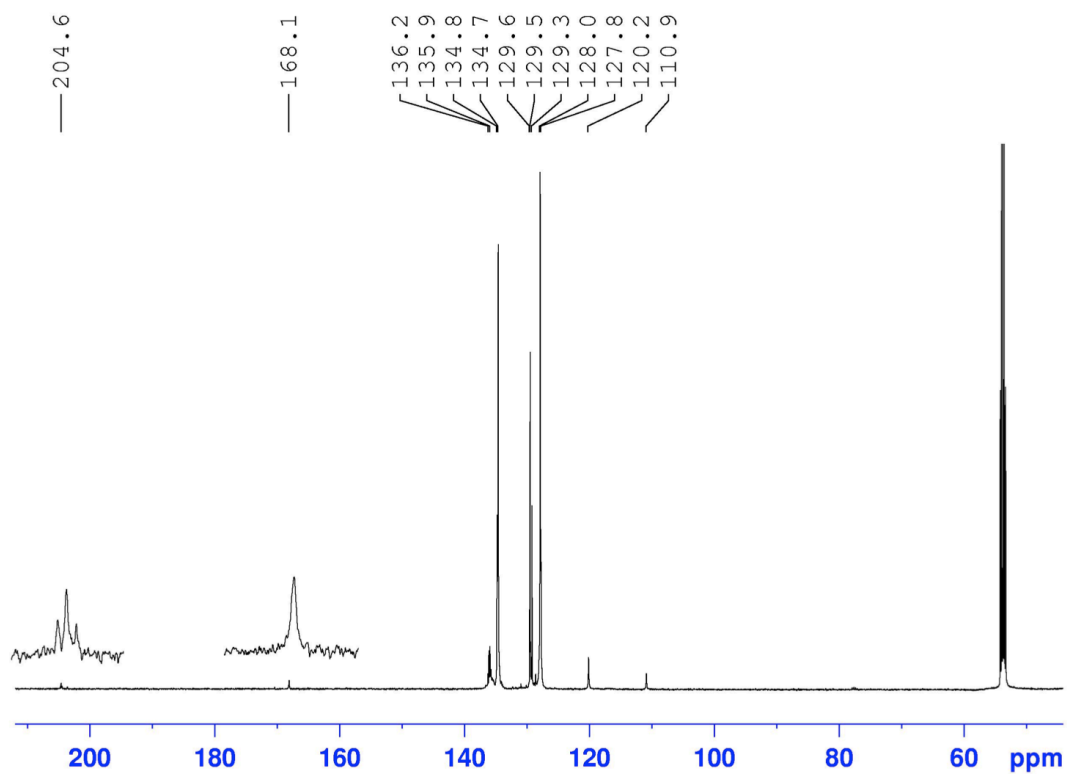


Figure A1.47. $^{13}\text{C}\{^1\text{H}\}$ NMR spectrum (CD_2Cl_2 , 202.40 MHz) for $\text{RuH}(\sigma\text{-OPh})(\text{CO})(\text{PPh}_3)_3$ **Ru-54**. Insets show RuCO (left), *ipso*-OPh (right) signals.

A1.3.4. VT-NMR Spectra for $\text{RuH}[(\eta^5\text{-C}_6\text{H}_5)\text{NPh}](\text{PPh}_3)_2$ **Ru-52a**.

Data collected subsequent to published work shown in Section A1.3.3.

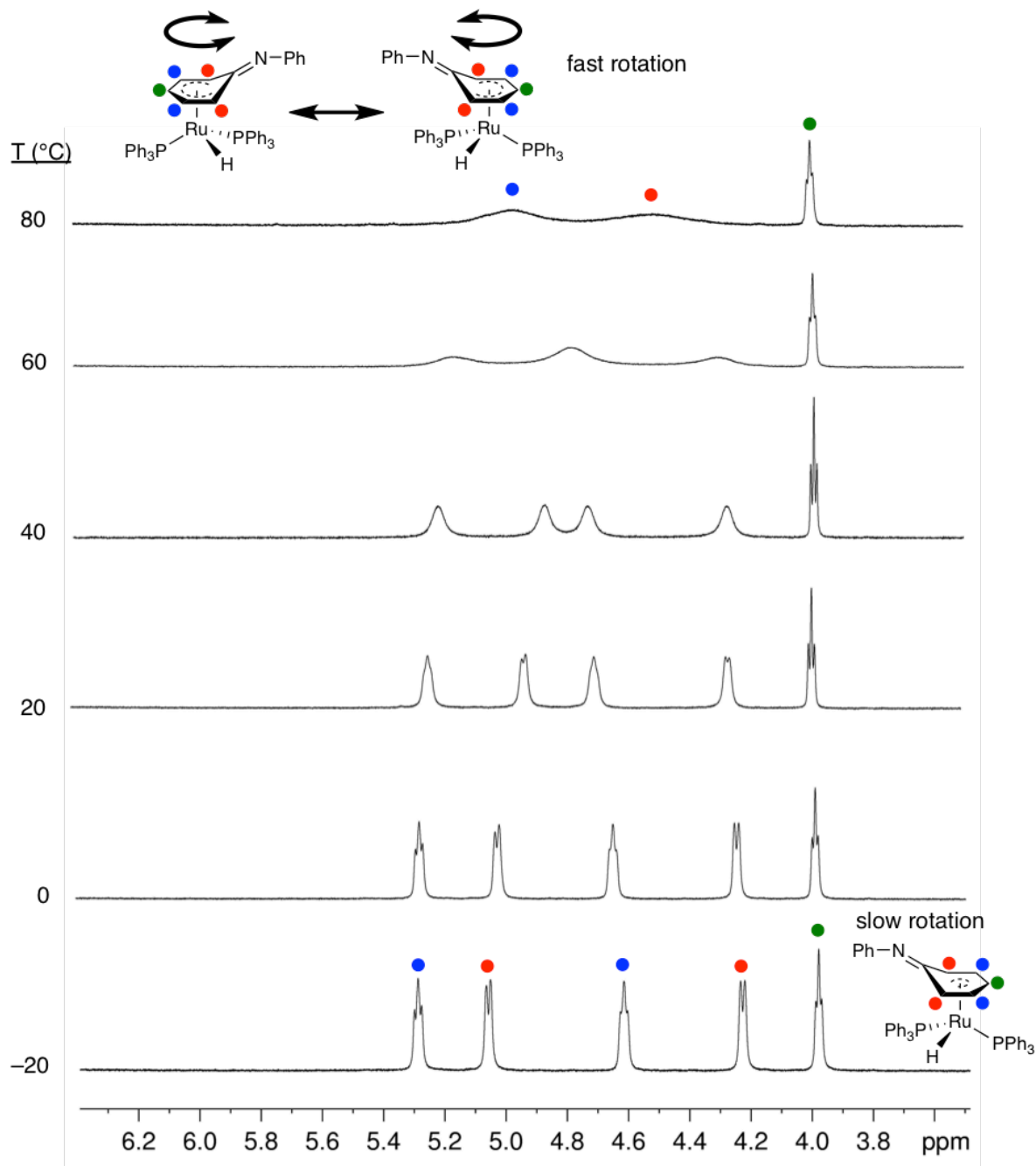


Figure A1.48. ^1H NMR spectra (C_7D_8 , 500.1 MHz) for $\text{RuH}[(\eta^5\text{-C}_6\text{H}_5)\text{O}](\text{PPh}_3)_2$ **Ru-52a** at -20 to 80 $^\circ\text{C}$. *Ortho* (red) and *meta* (blue) arene signals converge at high temperature, but are independently-resolved at RT. The *para* arene signal (green) is independently resolved across the examined temperature range.

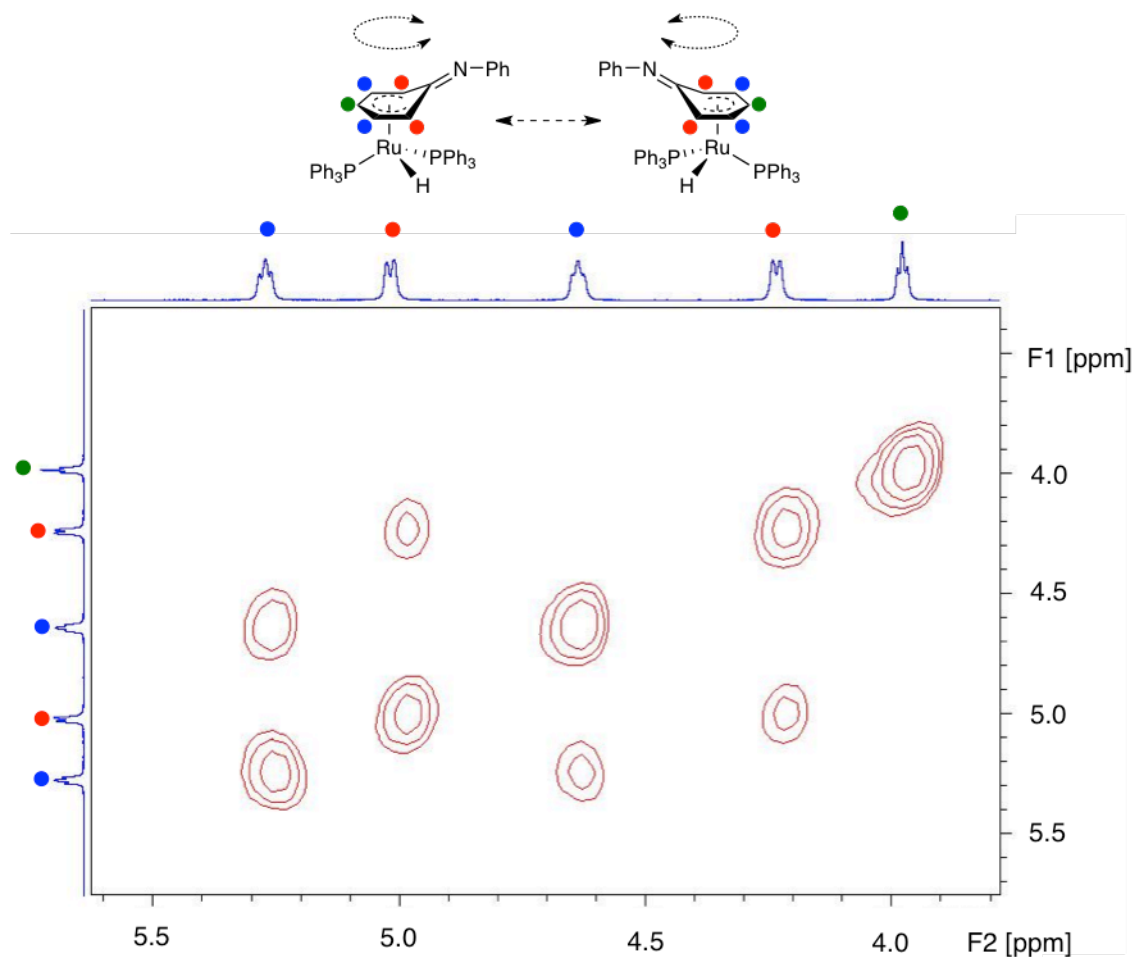


Figure A1.49. ^1H EXSY ($d_8 = 0.25$ s) NMR spectrum (C_7D_8 , 500.1 MHz, 0 °C) showing chemical exchange of *ortho* (red) and *meta* (blue) arene signals for $\text{RuH}[(\eta^5\text{-C}_6\text{H}_5)\text{O}](\text{PPh}_3)_2$ **Ru-52a**.

Appendix 2: NMR and GC-MS Spectra for In Situ Experiments

For all ^1H NMR spectra with TMB internal standard: integration normalized to $\text{Ru}=\text{CHAr}$ at t_0 .

A2.1. Spectra for Chapter 3: Decomposition of Grubbs Catalysts via Benzylidene Abstraction.

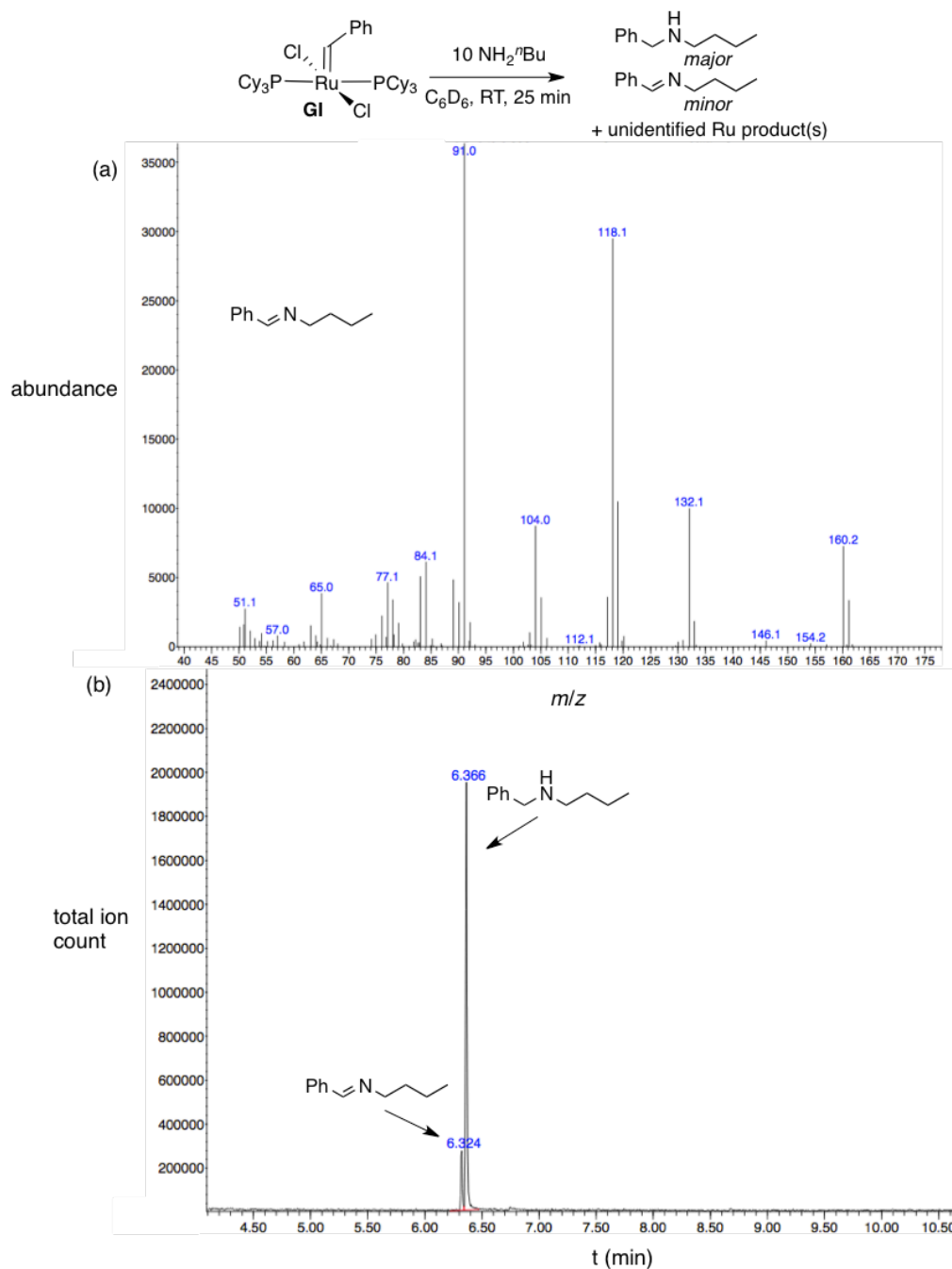


Figure A2.1. (a) EI mass spectrum for minor product $\text{PhHC}=\text{N}(\text{nBu})$ **7b** formed by reaction of **GI** with $\text{NH}_2^{\text{n}}\text{Bu}$ **NI** under the conditions depicted. (b) GC trace for the crude reaction mixture. For EI-MS spectrum of $\text{NH}(\text{nBu})(\text{CH}_2\text{Ph})$ **7a**, see Figure A2.4 (Below).

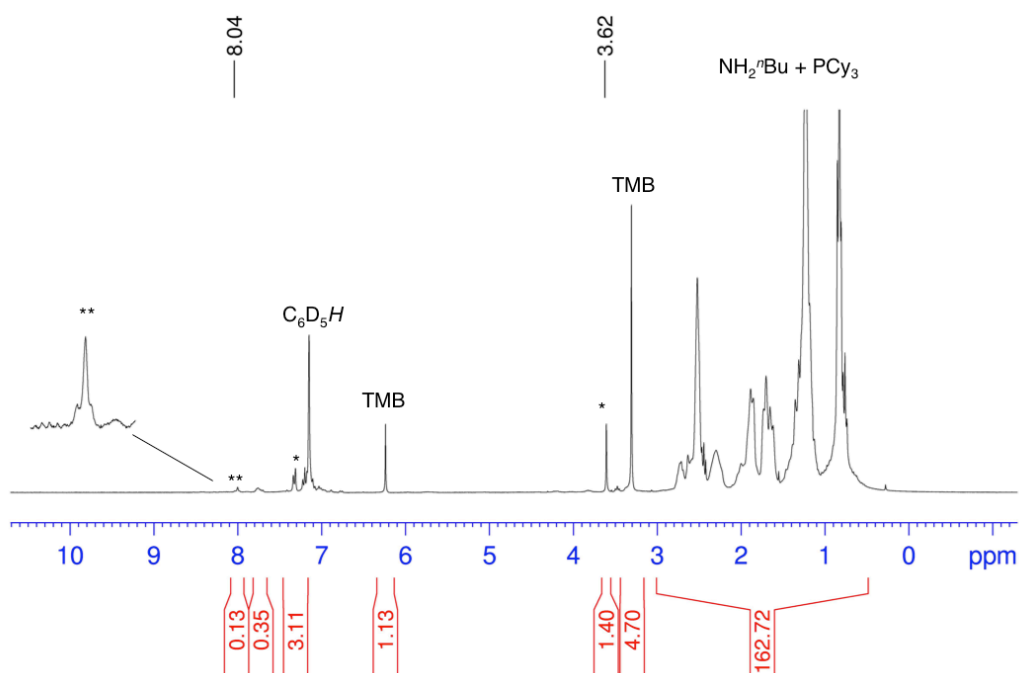


Figure A2.2. In situ ^1H NMR spectrum (C₆D₆, 300.3 MHz) for reaction of **GI** with 10 equiv **N1** NH₂ⁿBu after 30 min at RT. Signals for NH(ⁿBu)(CH₂Ph) **7a** are labeled (*). Signals for ⁿBuN=CHPh **7b** are labeled (**).

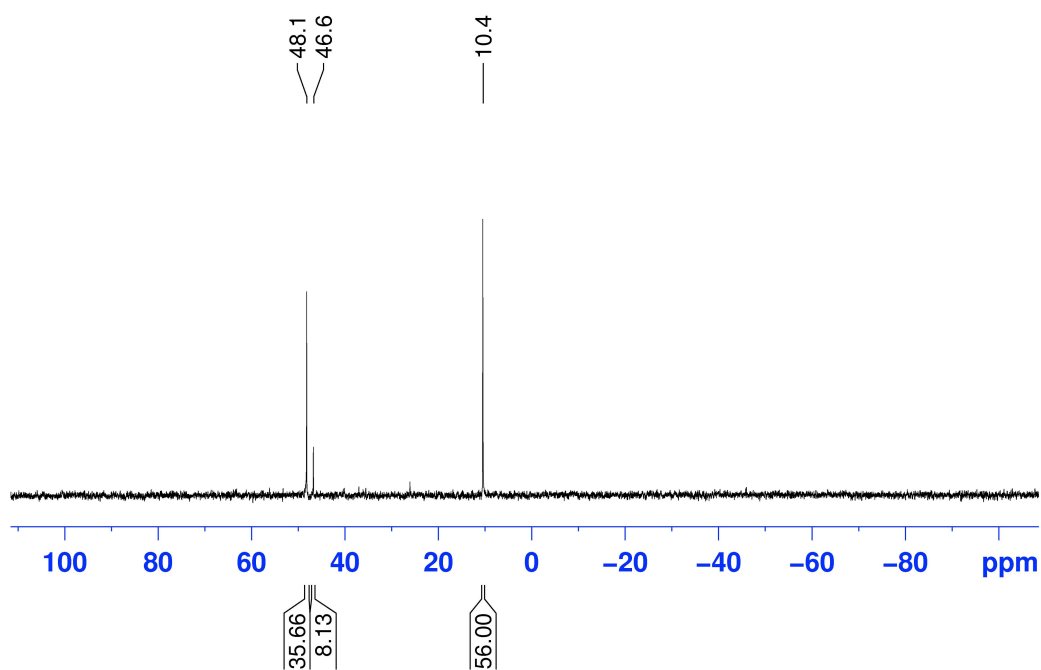


Figure A2.3. In situ $^{31}\text{P}\{^1\text{H}\}$ NMR spectrum (C₆D₆, 121.6 MHz) for reaction of **GI** with 10 equiv NH₂ⁿBu **N1** after 30 min at RT.

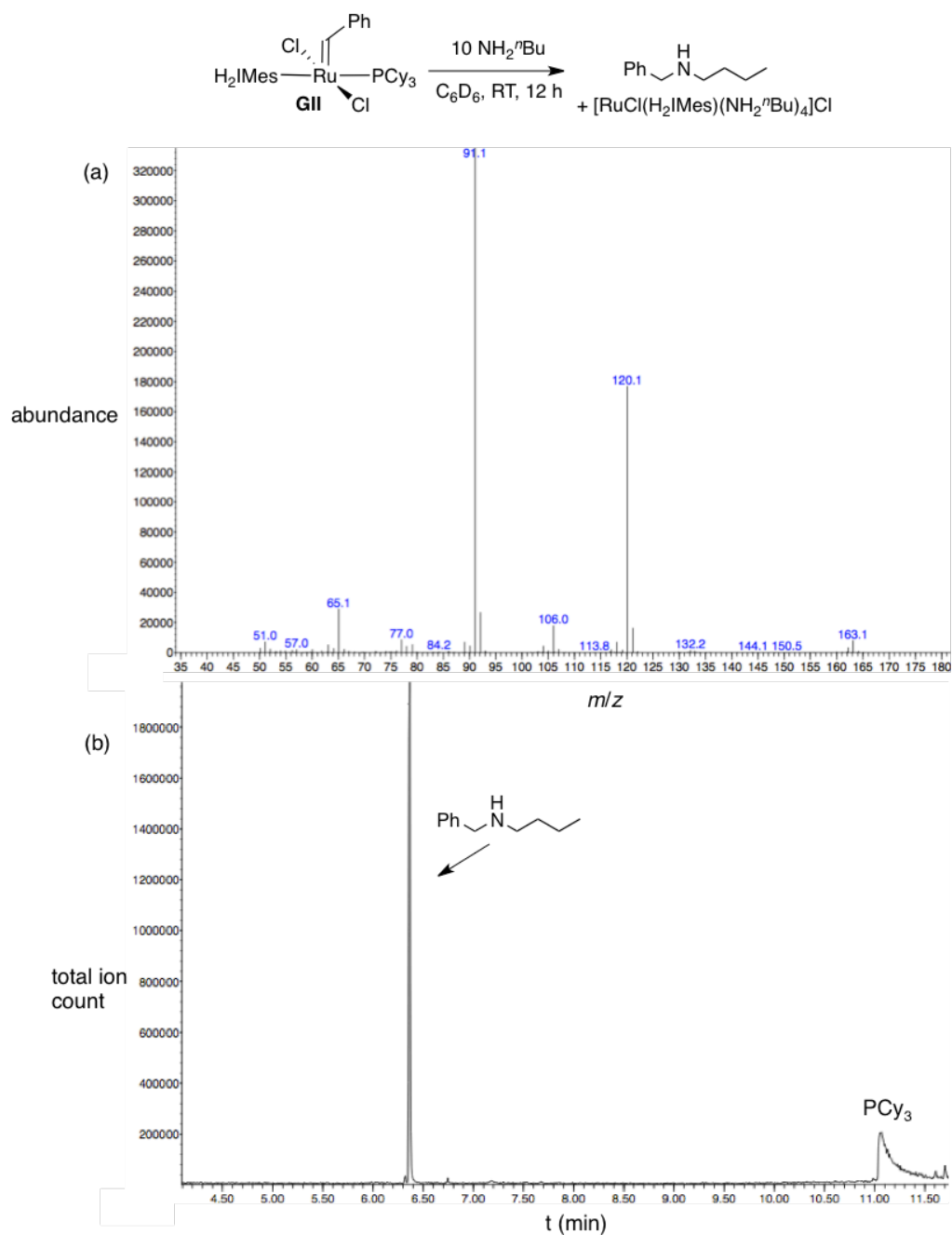


Figure A2.4. (a) EI mass spectrum for product $\text{NH}^{\text{n}}\text{Bu}(\text{CH}_2\text{Ph})$ 7a formed by reaction of **GII** with $\text{NH}_2^{\text{n}}\text{Bu}$ **N1** under the conditions depicted. (b) GC trace for the crude reaction mixture. The mass spectrum and retention time match those of a commercially-available sample (Acros).

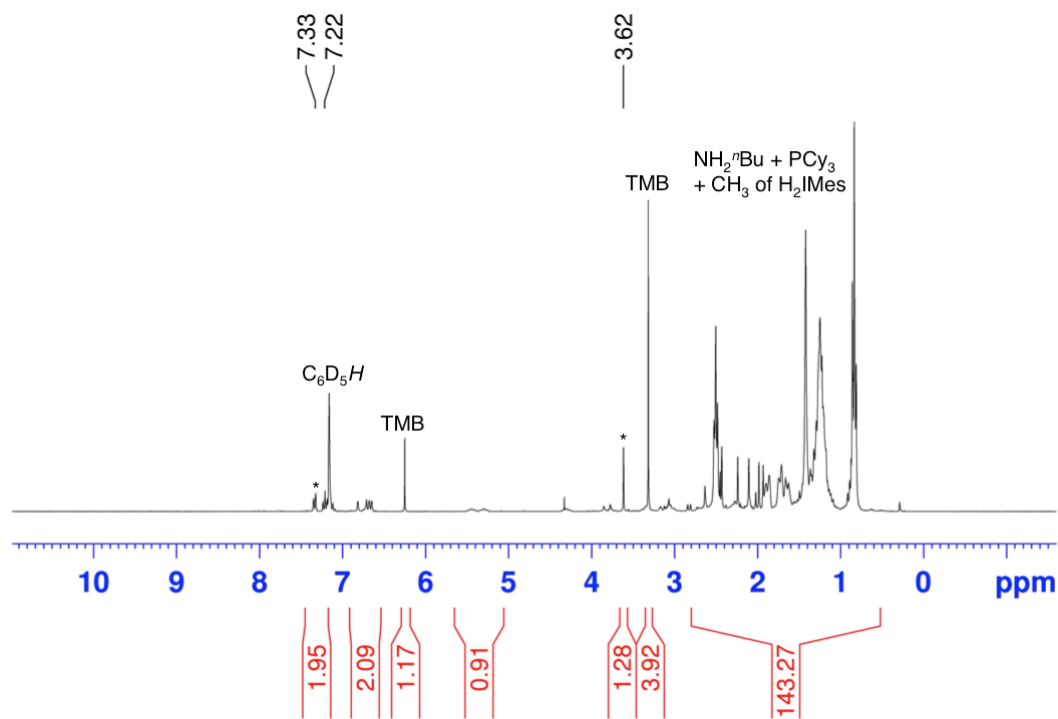


Figure A2.5. In situ ^1H NMR spectrum (C_6D_6 , 300.3 MHz) for reaction of **GII** with 10 equiv $\text{NH}_2^{\text{n}}\text{Bu}$ **N1** after 12 h at RT. Signals for $\text{NH}(\text{nBu})(\text{CH}_2\text{Ph})$ are labeled (*). Sample contained yellow precipitate.

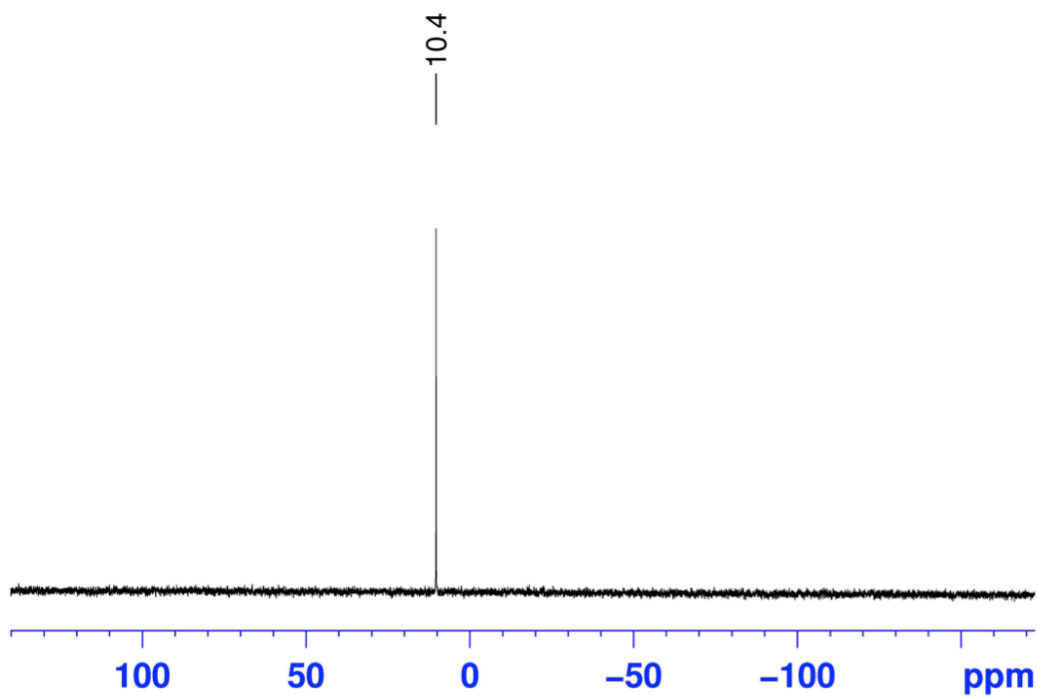


Figure A2.6. In situ $^{31}\text{P}\{^1\text{H}\}$ NMR spectrum (C_6D_6 , 121.6 MHz) for reaction of **GII** with 10 equiv $\text{NH}_2^{\text{n}}\text{Bu}$ **N1** after 12 h at RT. Sample contained yellow precipitate.

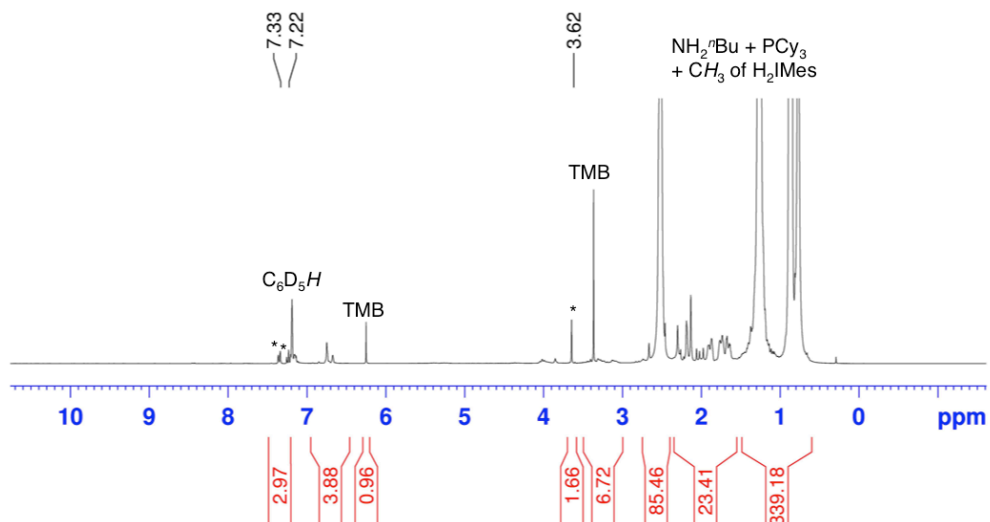


Figure A2.7. In situ ^1H NMR spectrum (C_6D_6 , 300.3 MHz) for reaction of **GII** with 40 equiv $\text{NH}_2^{\text{n}}\text{Bu}$ **N1** after 8 h at RT. Signals for $\text{NH}^{\text{n}}\text{Bu}(\text{CH}_2\text{Ph})$ are labeled (*). Fully soluble. Note increase in $\text{NH}^{\text{n}}\text{Bu}(\text{CH}_2\text{Ph})$ **7a** at 3.62 vs. Figure A2.5.

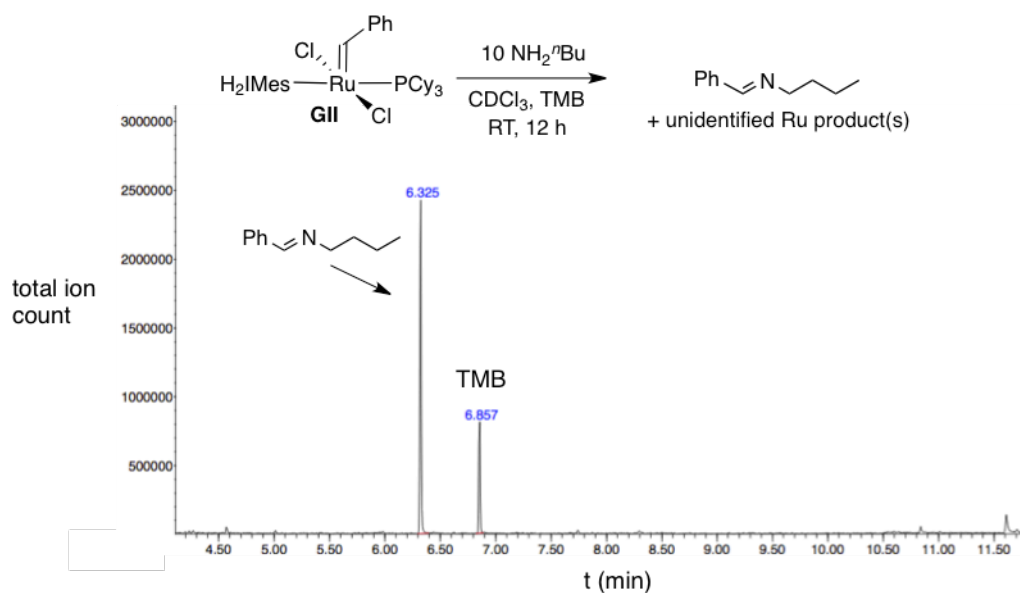


Figure A2.8. GC trace of the crude reaction mixture formed by reaction of **GII** with $\text{NH}_2^{\text{n}}\text{Bu}$ **N1** under the conditions depicted. See Figure A2.1 for EI-MS spectrum of $\text{PhHC}=\text{N}^{\text{n}}\text{Bu}$ **7b**.

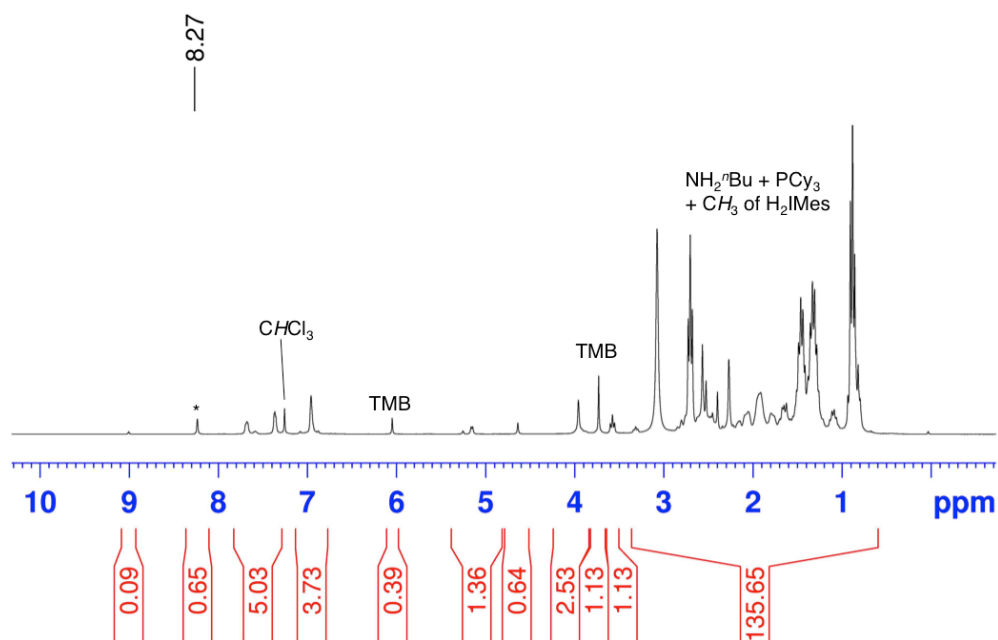


Figure A2.9. In situ ^1H NMR spectrum (CHCl_3 , 300.3 MHz) for reaction of **GII** with 10 equiv NH_2^nBu after 12 h at RT. Signal for $\text{PhHC}=\text{N}(^n\text{Bu})$ **7b** labeled (*).

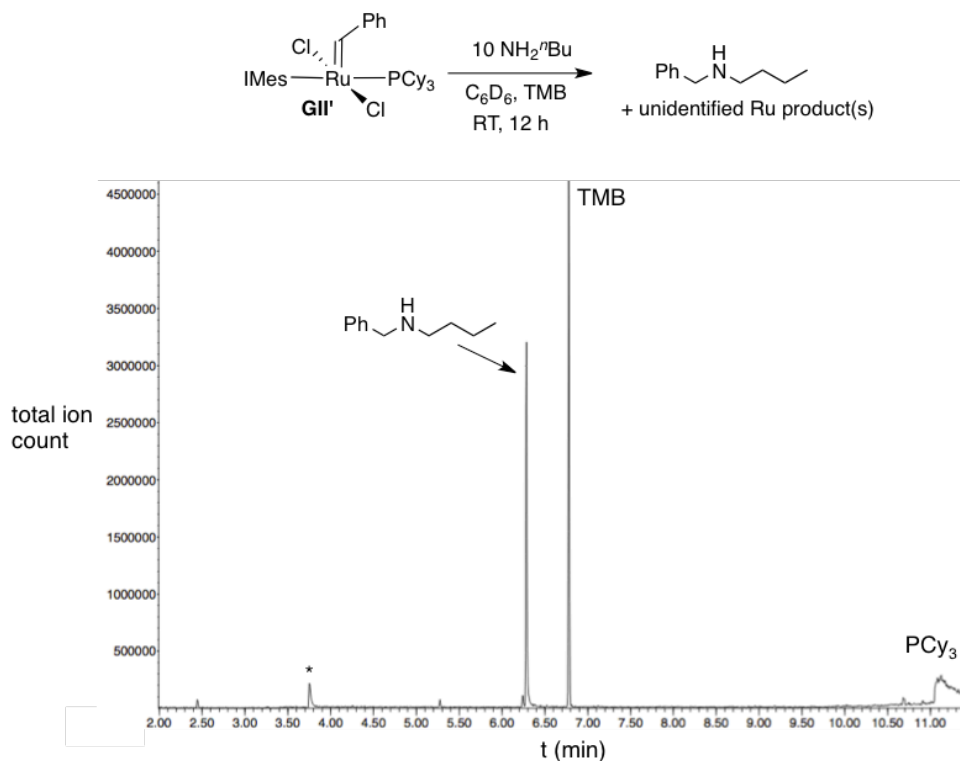


Figure A2.10. GC of the crude reaction mixture formed by reaction of **GII'** with NH_2^nBu under the conditions depicted. See Figure A2.4 for EI-MS spectrum of $\text{NH}(^n\text{Bu})(\text{CH}_2\text{Ph})$ **7a**. The peak labeled “*” is unassigned ($m/z = 112.1$).

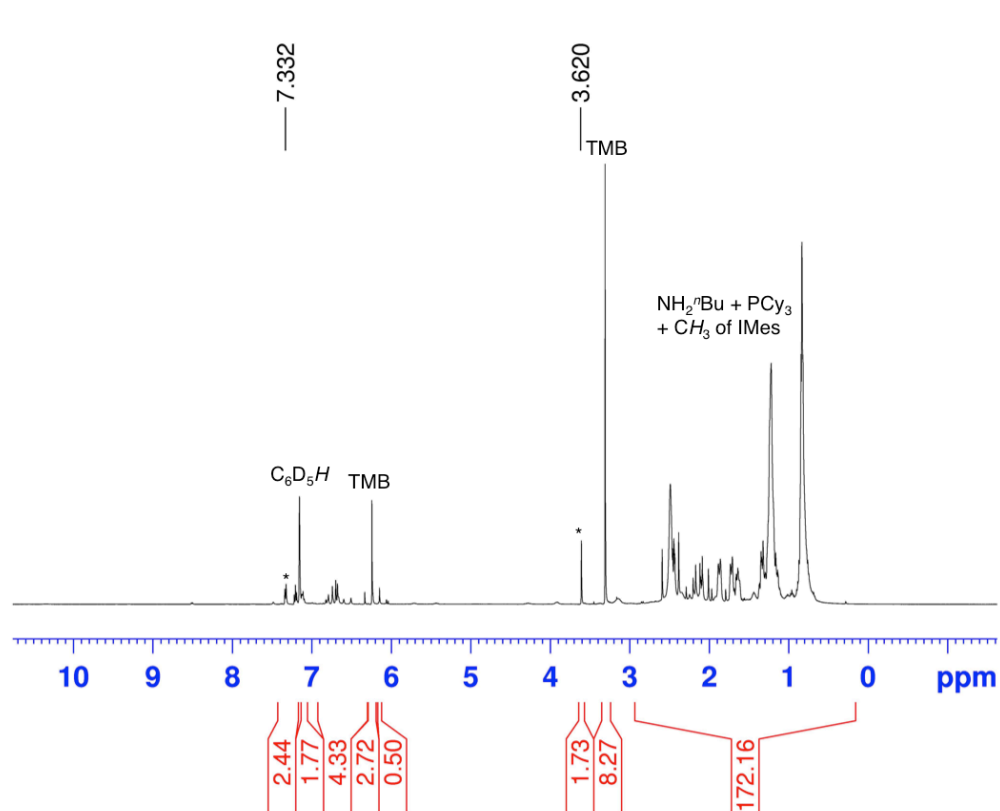


Figure A2.11. In situ ^1H NMR spectrum (C₆D₆, 300.3 MHz) for reaction of **GII'** with 10 equiv $\text{NH}_2^{\text{n}}\text{Bu}$ after 12 h at RT. Signals for $\text{NH}^{\text{n}}\text{Bu}(\text{CH}_2\text{Ph})$ **7a** are labeled (*).

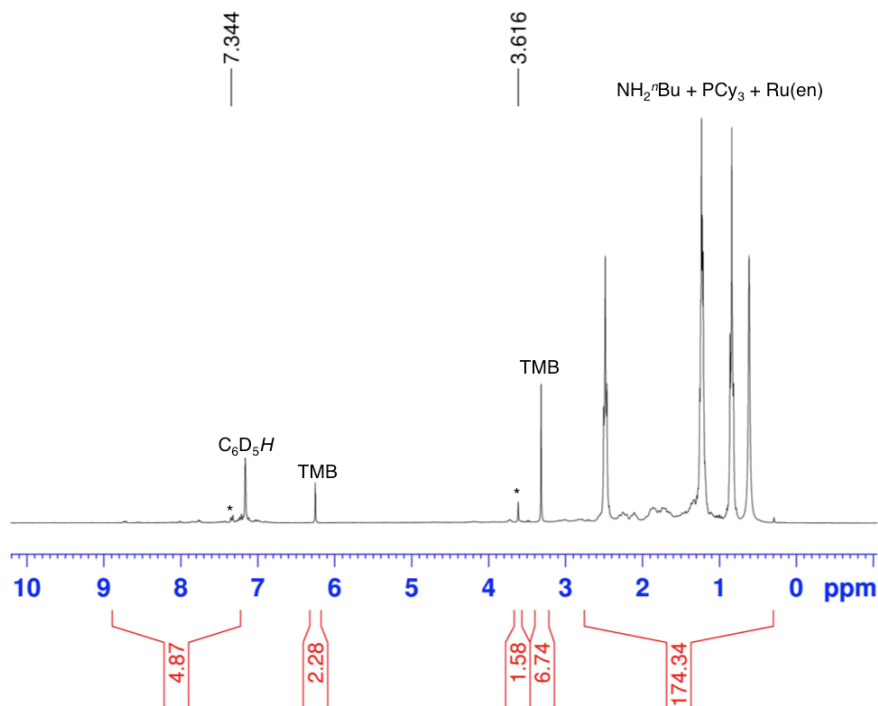


Figure A2.12. In situ ^1H NMR spectrum (C₆D₆, 300.3 MHz) for reaction of $\text{RuCl}_2(\text{PCy}_3)(\text{en})(=\text{CHPh})$ **Ru-15** with 10 equiv $\text{NH}_2^{\text{n}}\text{Bu}$ after 3 h at RT (15% **GI-10** remaining). Signals for $\text{NH}^{\text{n}}\text{Bu}(\text{CH}_2\text{Ph})$ are labeled (*).

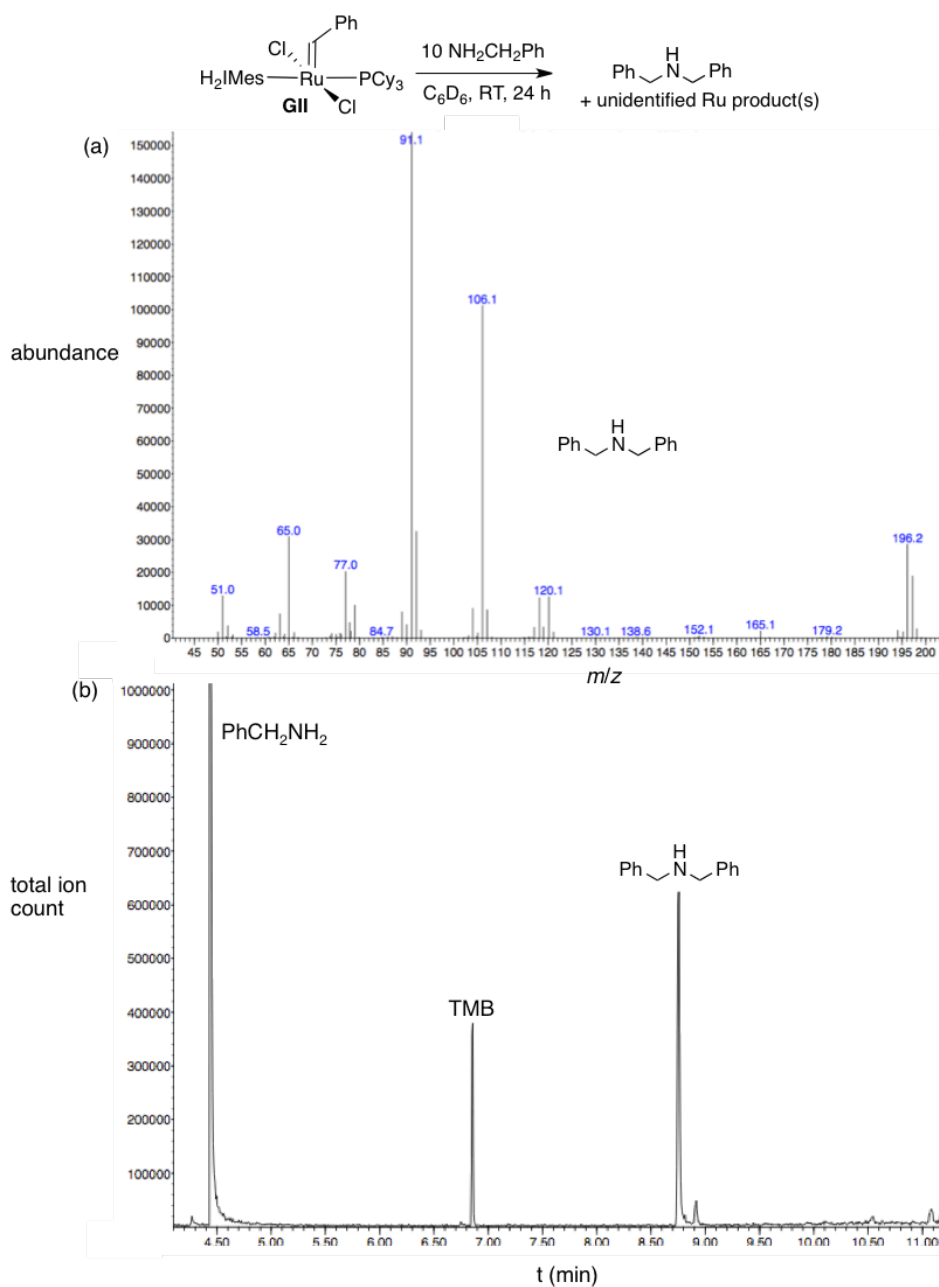


Figure A2.13. (a) EI mass spectrum for product $\text{NH}(\text{CH}_2\text{Ph})_2$ **9** formed by reaction of **GII** with $\text{NH}_2\text{CH}_2\text{Ph}$ **N3** under the conditions depicted. (b) GC trace for the crude reaction mixture. The mass spectrum and retention time match those of a commercially-available sample (Sigma Aldrich).

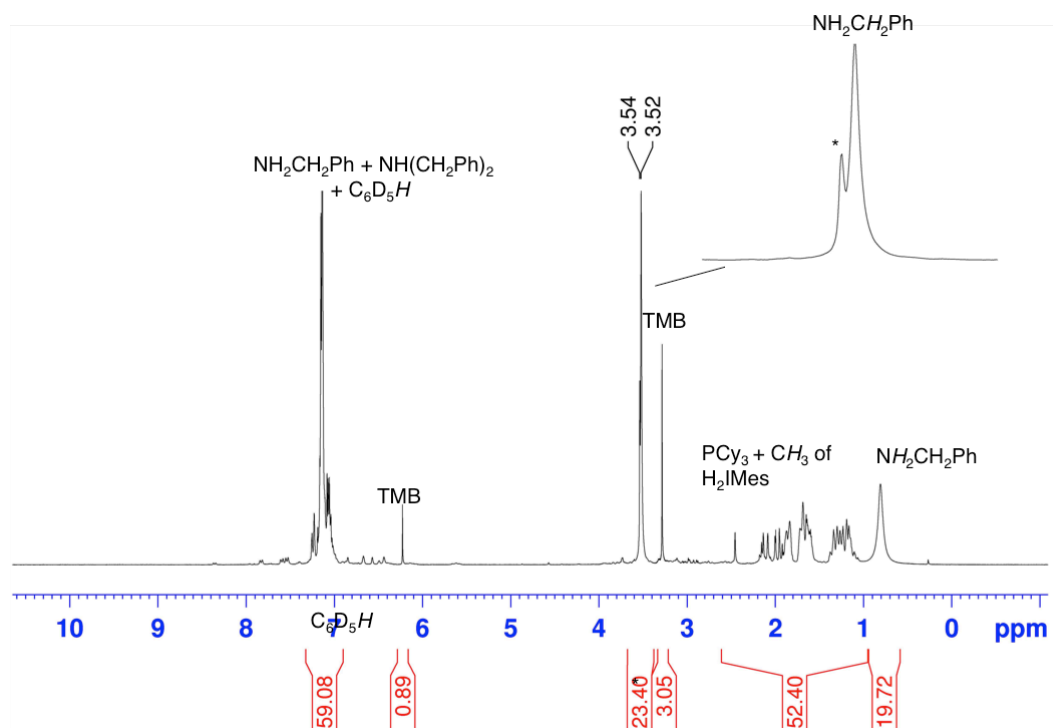


Figure A2.14. In situ ^1H NMR spectrum (C_6D_6 , 300.3 MHz) for reaction of **GII** with 10 equiv $\text{NH}_2\text{CH}_2\text{Ph}$ **N3** after 24 h at RT (9% **GII** remaining). Methylene signal for $\text{NH}(\text{CH}_2\text{Ph})_2$ **9** are labeled (*), overlaps with excess $\text{NH}_2\text{CH}_2\text{Ph}$ **N3**.

A2.2 Spectra for Chapter 4

A2.2.1. MS, GC, and NMR spectra for Chapter 4, Sections 4.1 to 4.3.

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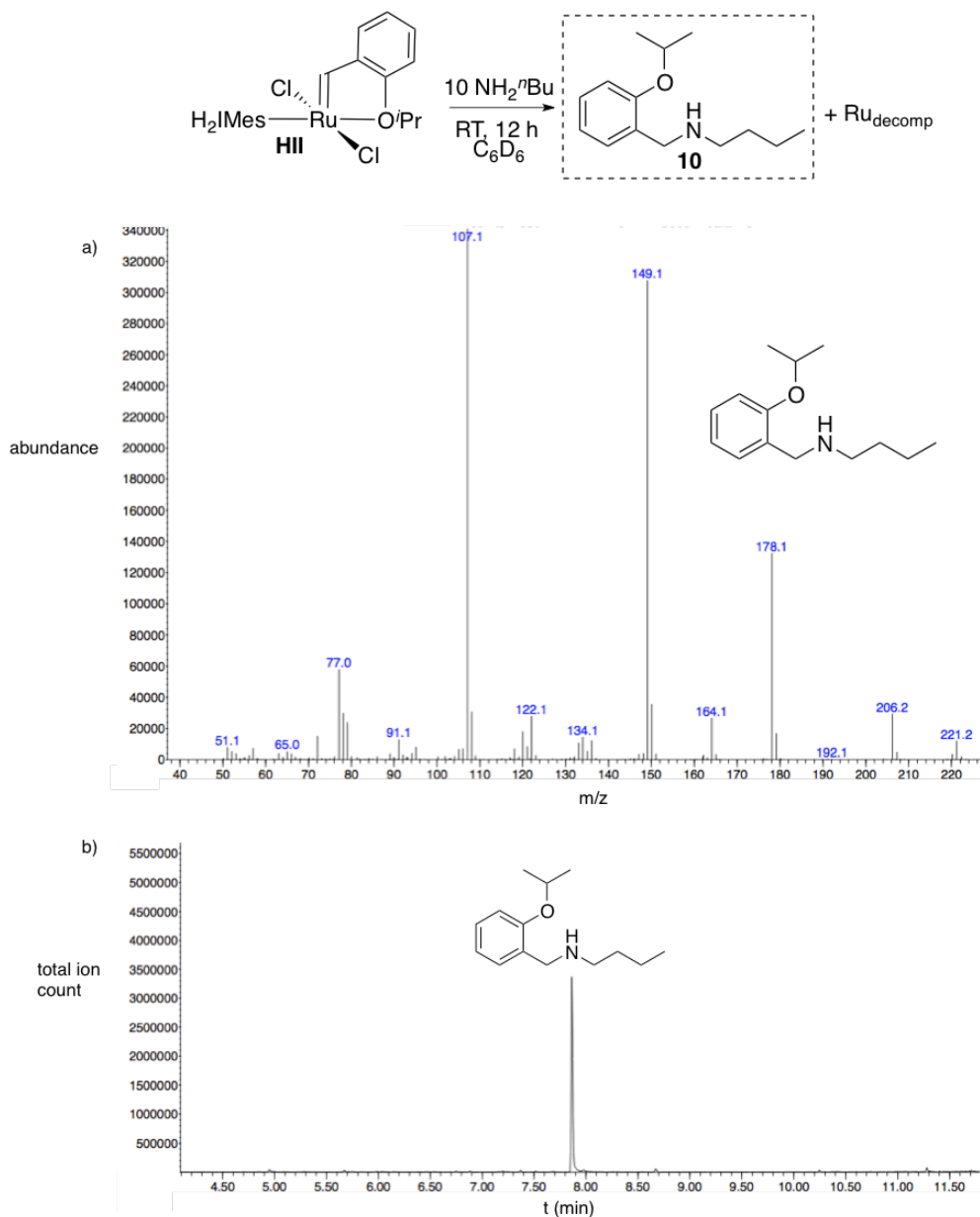


Figure A2.15. (a) EI mass spectrum for NH(ⁿBu)(CH₂Ar) **10**, formed by reaction of **HII** with NH₂ⁿBu **N1** under the conditions depicted. (b) GC trace for the crude reaction mixture. The mass spectrum and retention time match those for independently-synthesized **10**.

* Compound numbers have been modified for consistency throughout the thesis. For a Table of Compound Numbers and Structures, see p. VI.

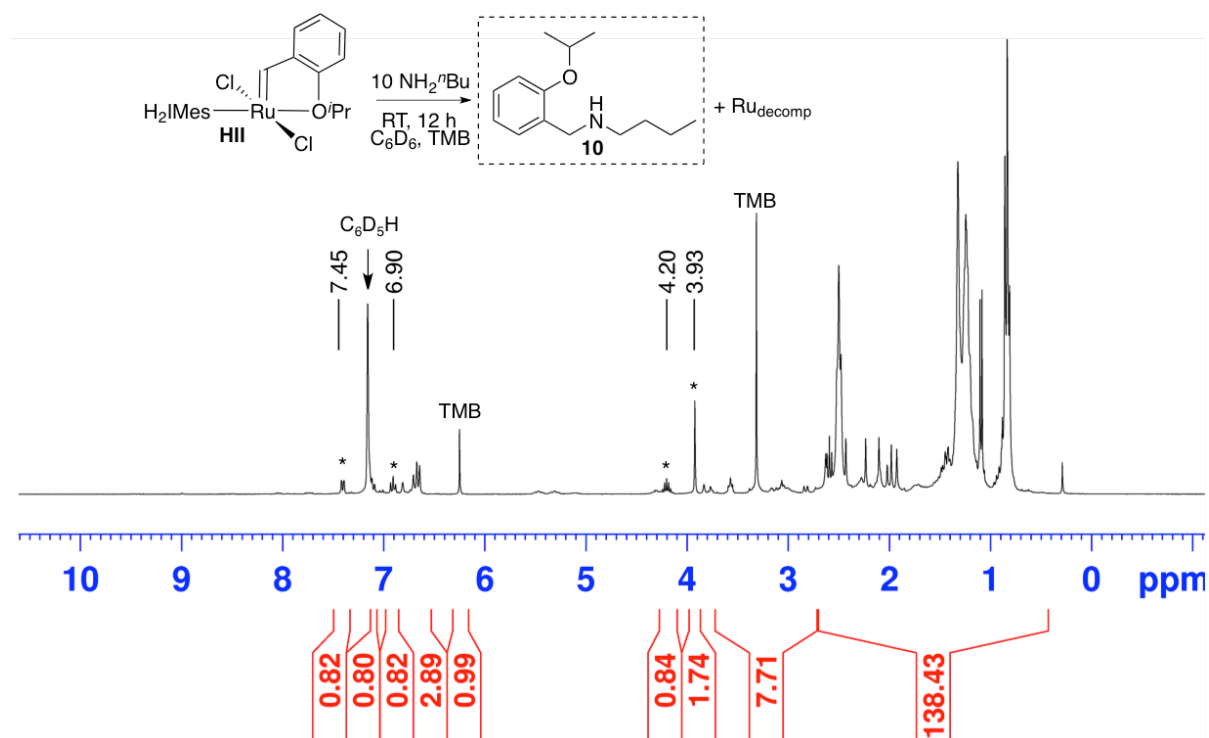


Figure A2.16. In situ ^1H NMR spectrum (C_6D_6 , 300.1 MHz) for reaction of **HII** with $\text{NH}_2^{\text{n}}\text{Bu}$ **N1** after 12 h at RT, following complete loss of alkylidene signals. Signals for $\text{NH}^{\text{n}}\text{Bu}(\text{CH}_2\text{Ar})$ **10** are labeled (*). The corresponding spectrum for independently-synthesized **10** appears in Appendix 1.

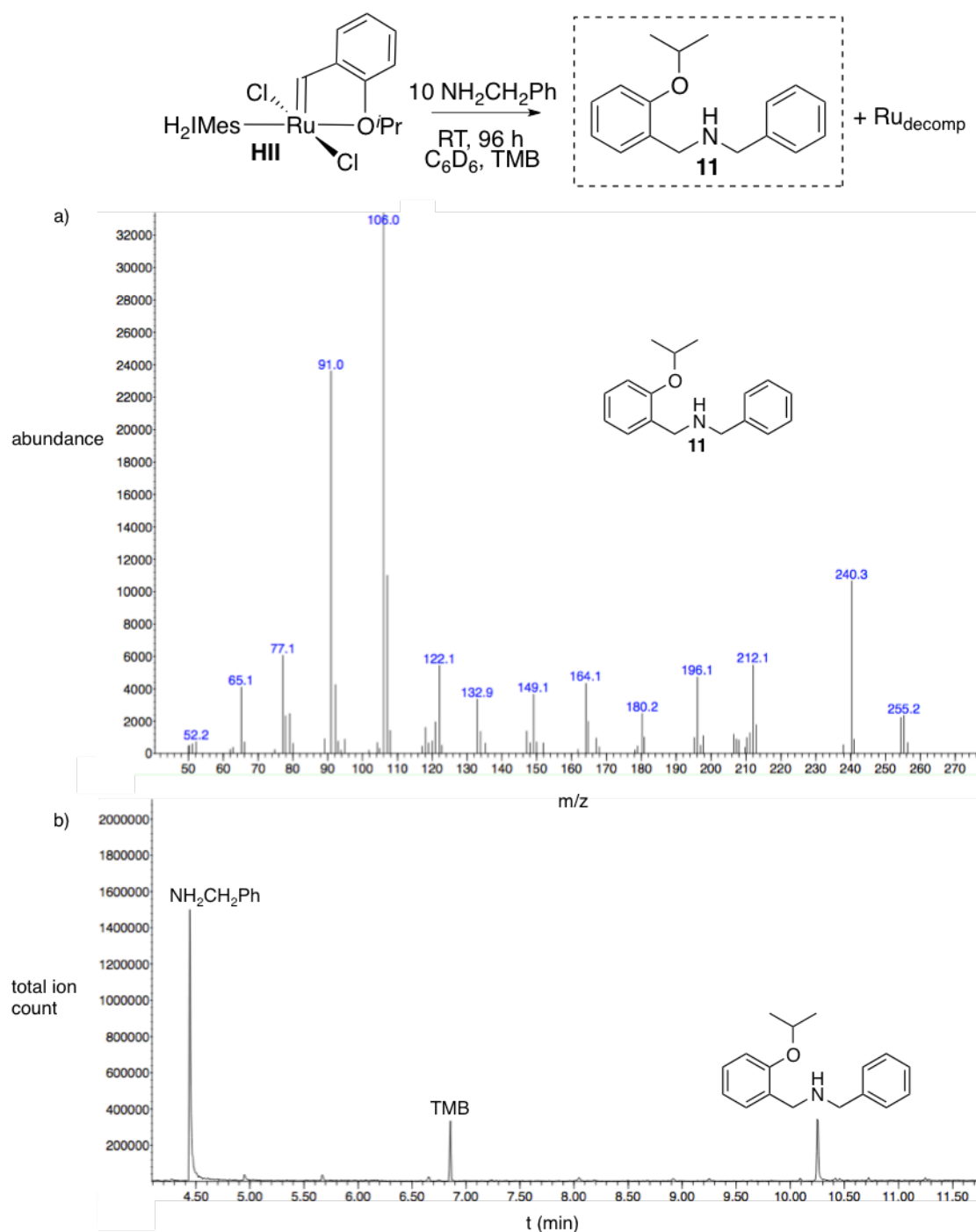


Figure A2.17. (a) EI mass spectrum for $\text{NH}(\text{CH}_2\text{Ph})(\text{CH}_2\text{Ar})$ **11**, formed by reaction of **HII** with $\text{NH}_2\text{CH}_2\text{Ph}$ **N3** under the conditions depicted. (b) GC trace for the crude reaction mixture. The mass spectrum and retention time match those for independently-synthesized **11**.

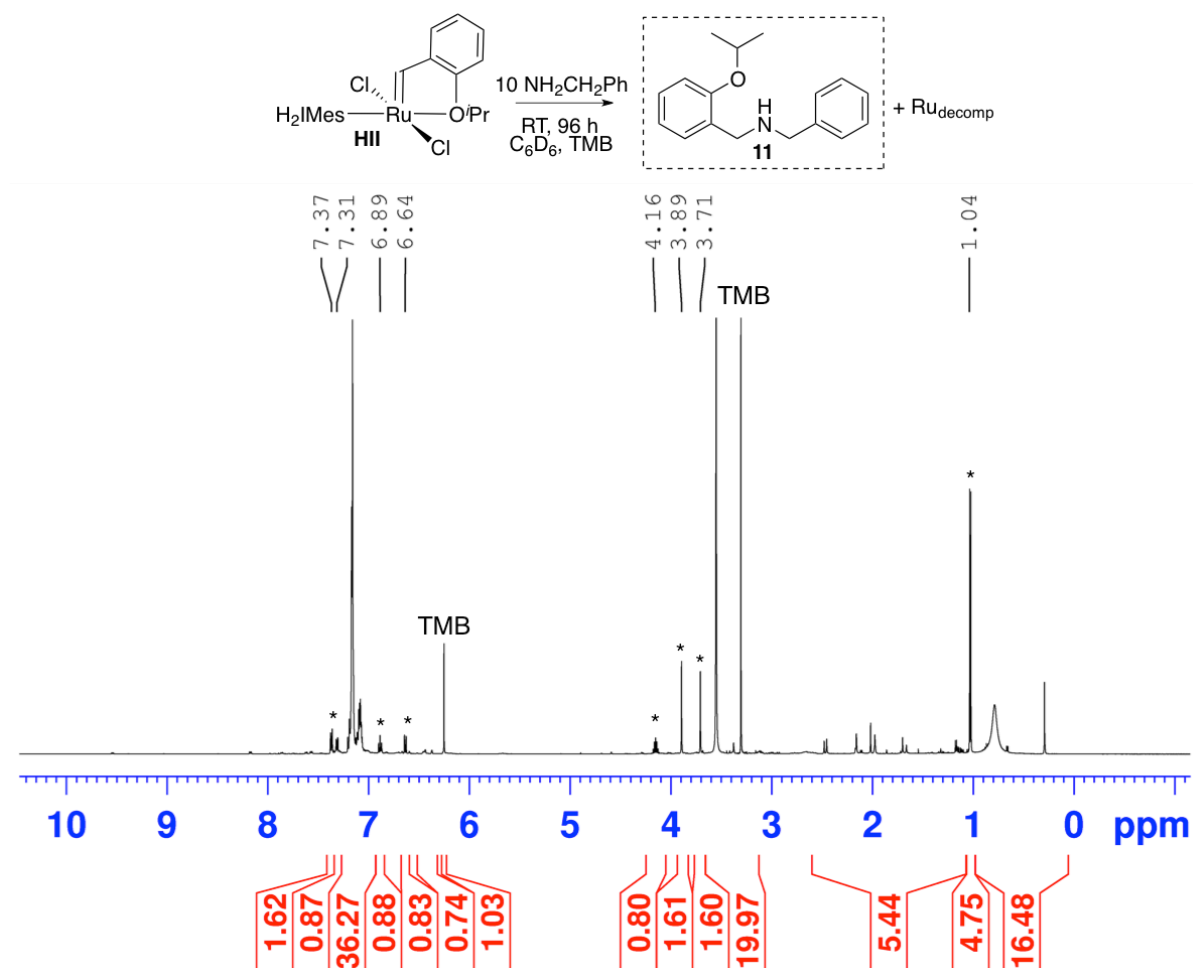


Figure A2.18. In situ ¹H NMR spectrum (C₆D₆, 500.1 MHz) for reaction of **HII** with NH₂CH₂Ph **N3** after 96 h at RT, following 94% loss of alkylidene signals. Signals for NH(CH₂Ph)(CH₂Ar) **11** are labeled (*). The corresponding spectrum for independently-synthesized **11** appears in Appendix 1.

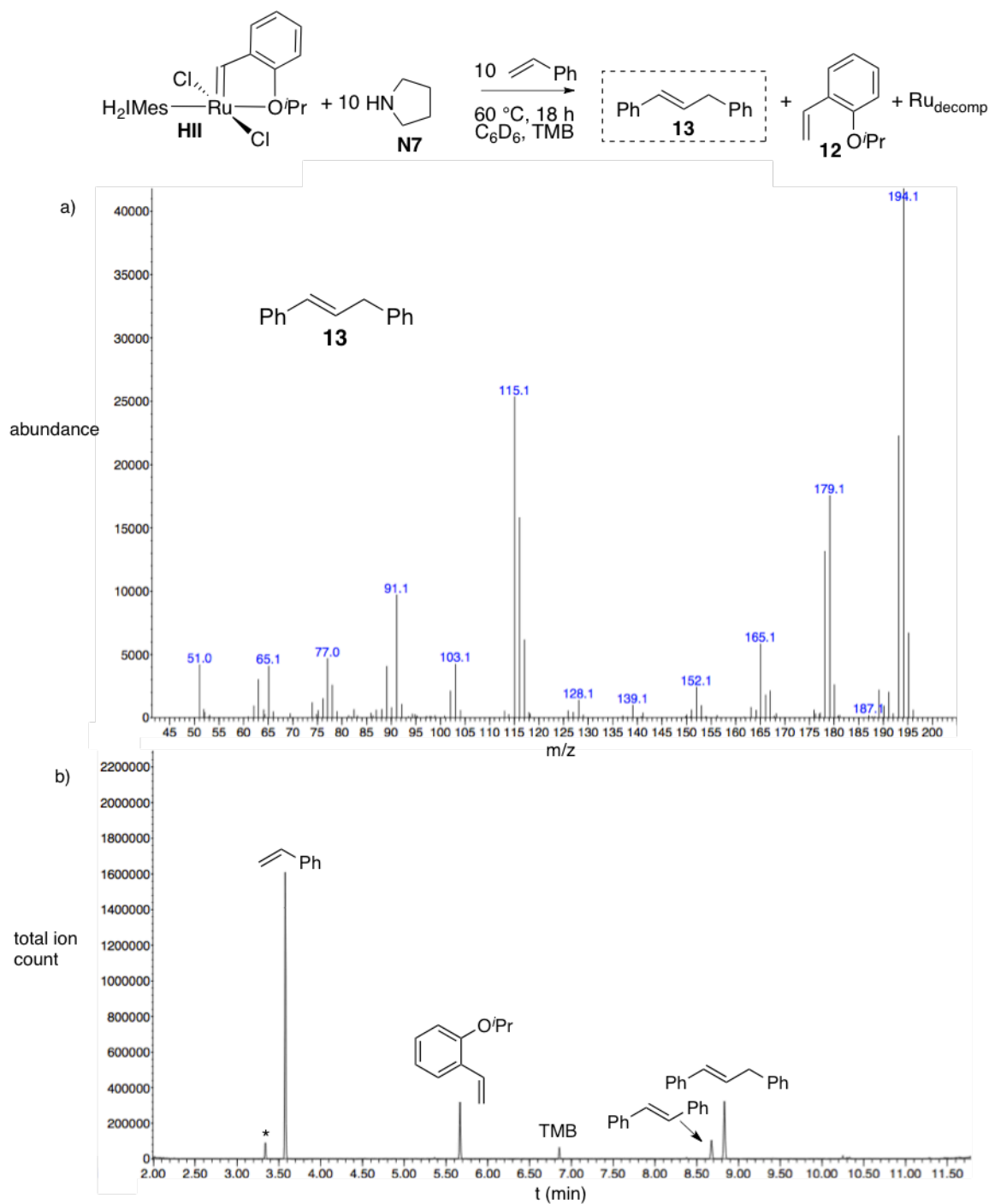


Figure A2.19. (a) EI mass spectrum for PhCH=CHCH₂Ph **13**, formed by reaction of **HII** with styrene and pyrrolidine **N7** under the conditions depicted. The spectrum of **13** matches that in the Wiley Registry of Mass Spectral Data.¹ (b) GC spectrum for the crude reaction mixture after 18 h. An unassigned signal ($m/z = 106.1$) is labeled (*). Retention times and EI-MS spectra for styrene, styrenyl ether **12**, and stilbene match authentic samples.

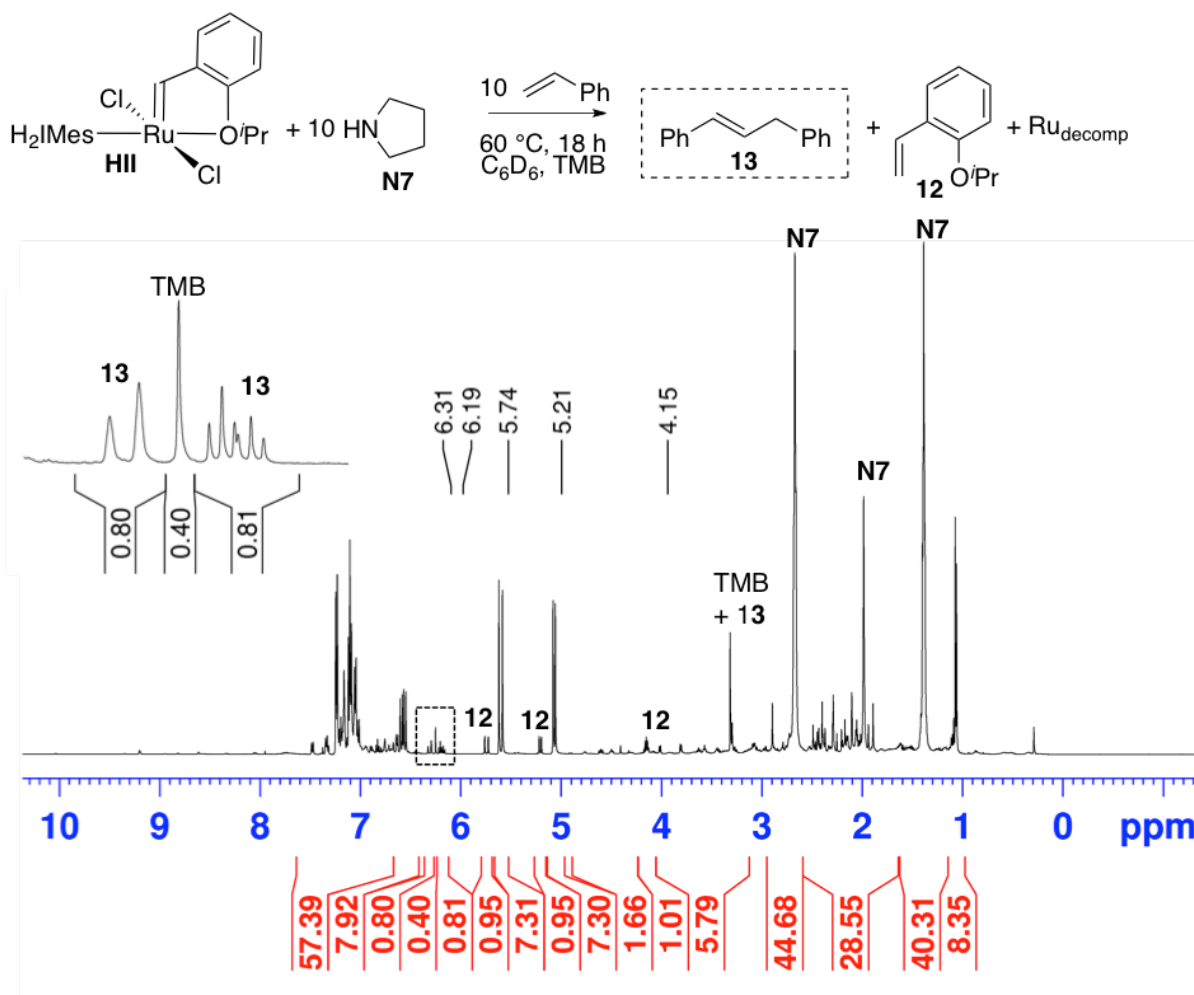


Figure A2.20. In situ ¹H NMR spectrum (C₆D₆, 500.1 MHz) showing formation of **13** via reaction of **HII** with styrene and pyrrolidine **N7** under the conditions depicted. No alkylidene signals remain. Inset shows olefinic signals for PhCH=CHCH₂Ph **13**. Values for **13** agree with those reported.²

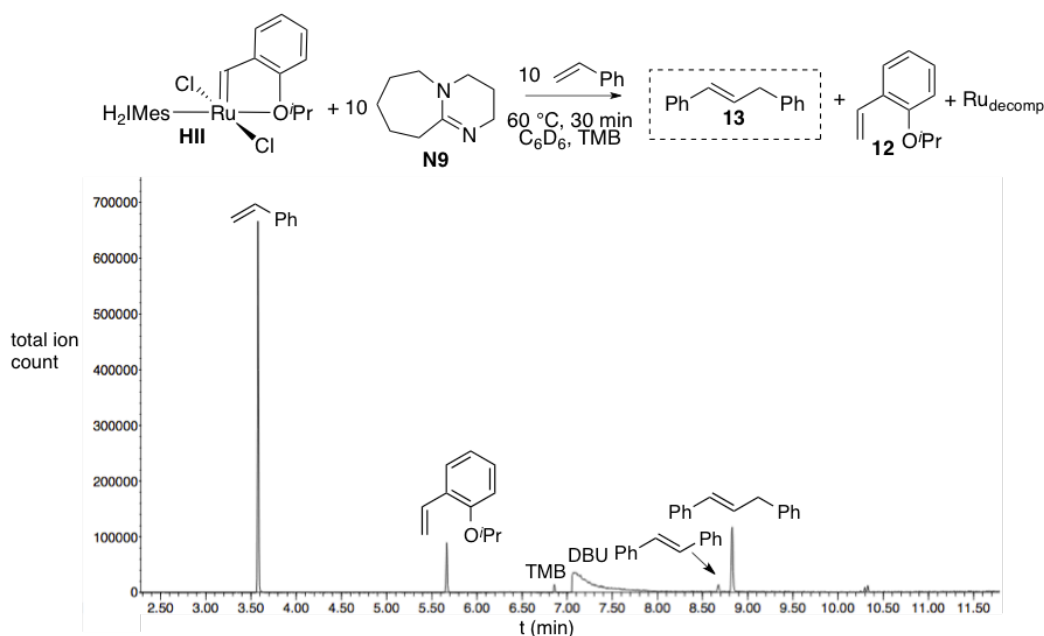


Figure A2.21. GC spectrum for the reaction of **HII** with styrene and DBU **N9** under the conditions depicted. For EI-MS of **13**, see Figure A2.19. Other values agree with authentic samples.

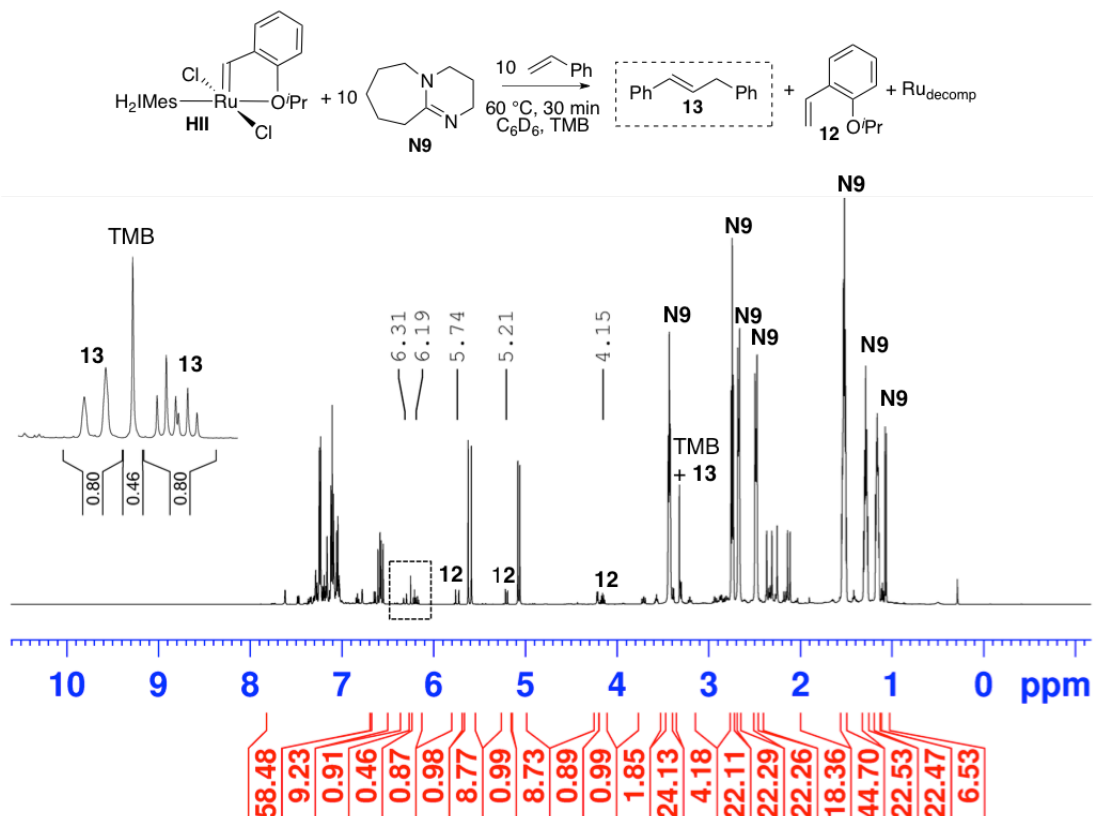


Figure A2.22. ^1H NMR spectrum (C_6D_6 , 500.1 MHz) for reaction of **HII** with styrene and DBU **N9** under the conditions depicted. No alkylidene signals remain. Inset shows olefinic signals for $\text{PhCH}=\text{CHCH}_2\text{Ph} **13**. Values for **13** agree with those reported,² as in Figure A2.20 above.$

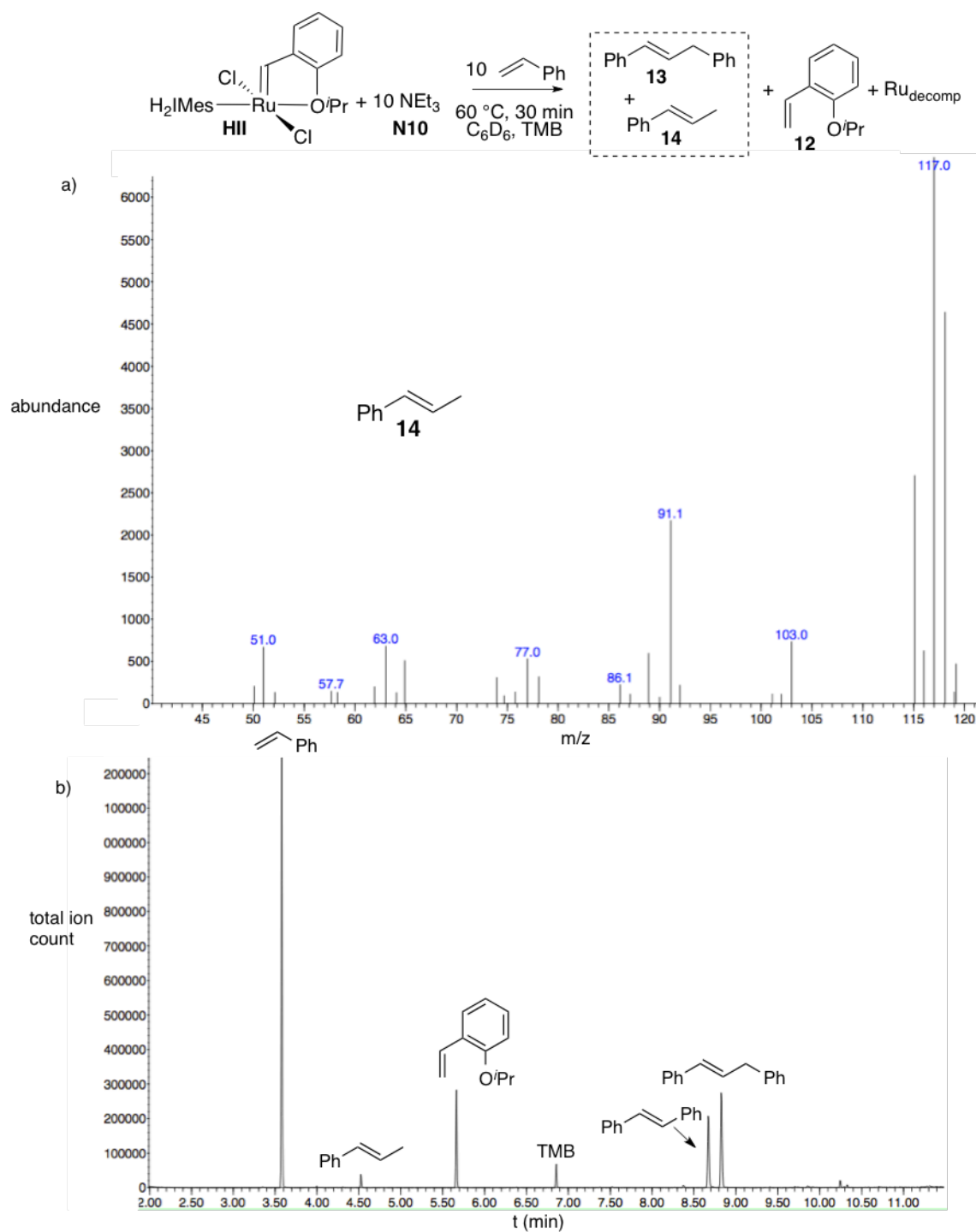


Figure A2.23. (a) EI mass spectrum for $\text{PhCH}=\text{CHCH}_3$ **14**, formed by reaction of **HII** with styrene and NEt_3 **N10** under the conditions depicted. The spectrum of **14** matches that in the Wiley Registry of Mass Spectral Data.¹ (b) GC spectrum for the crude reaction mixture. Retention times and EI-MS spectra for other components match authentic samples. See Figure A2.19 for EI-MS spectrum of **13**.

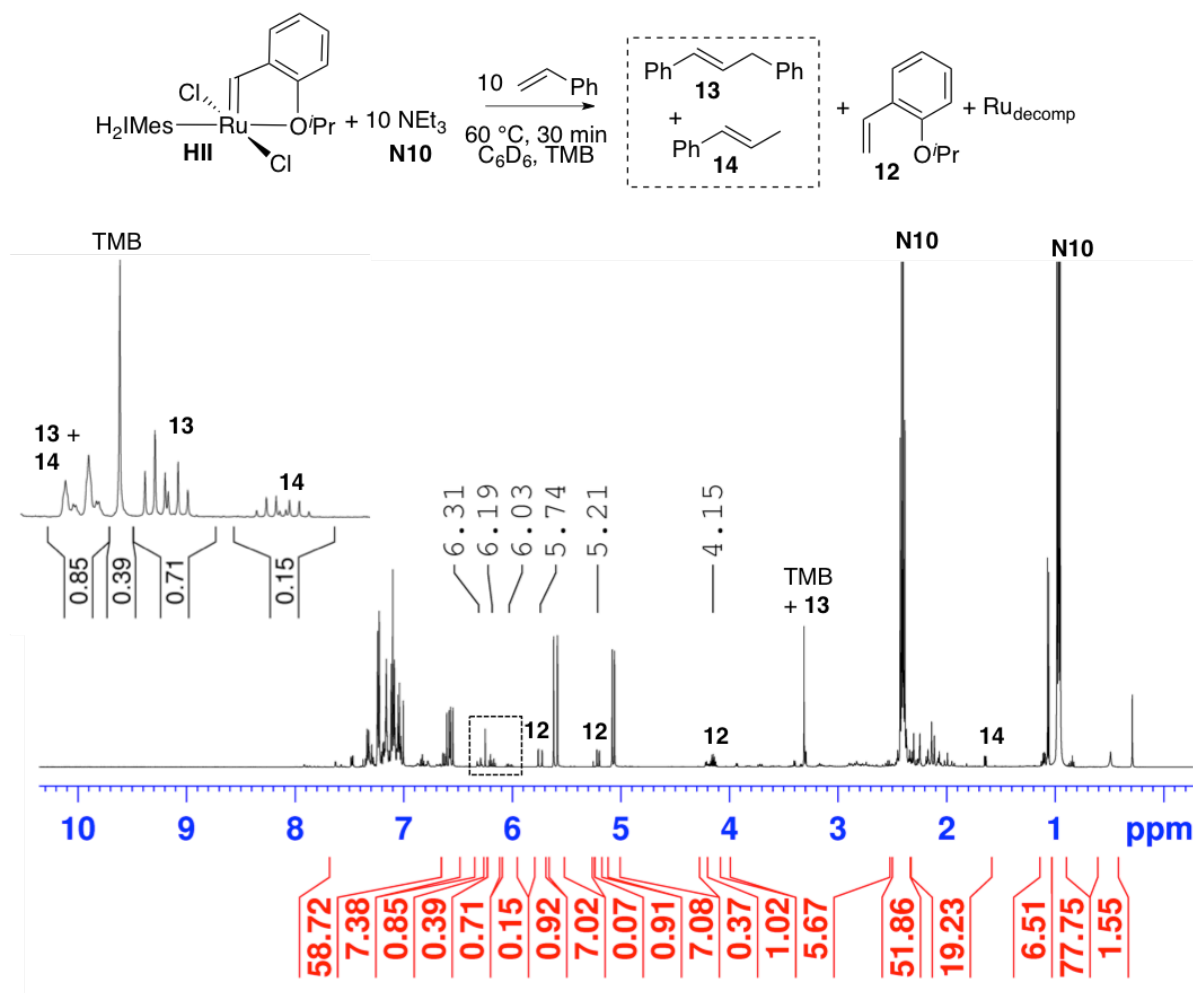


Figure A2.24. ¹H NMR spectrum (C₆D₆, 500.1 MHz) for the reaction of **HII** with styrene and NEt₃ **N10** under the conditions depicted. No alkylidene signals remain. Expansion shows olefinic signals for **13** and PhCH=CHCH₃ **14**. Values for **14** match an authentic sample. Values for **13** as above.

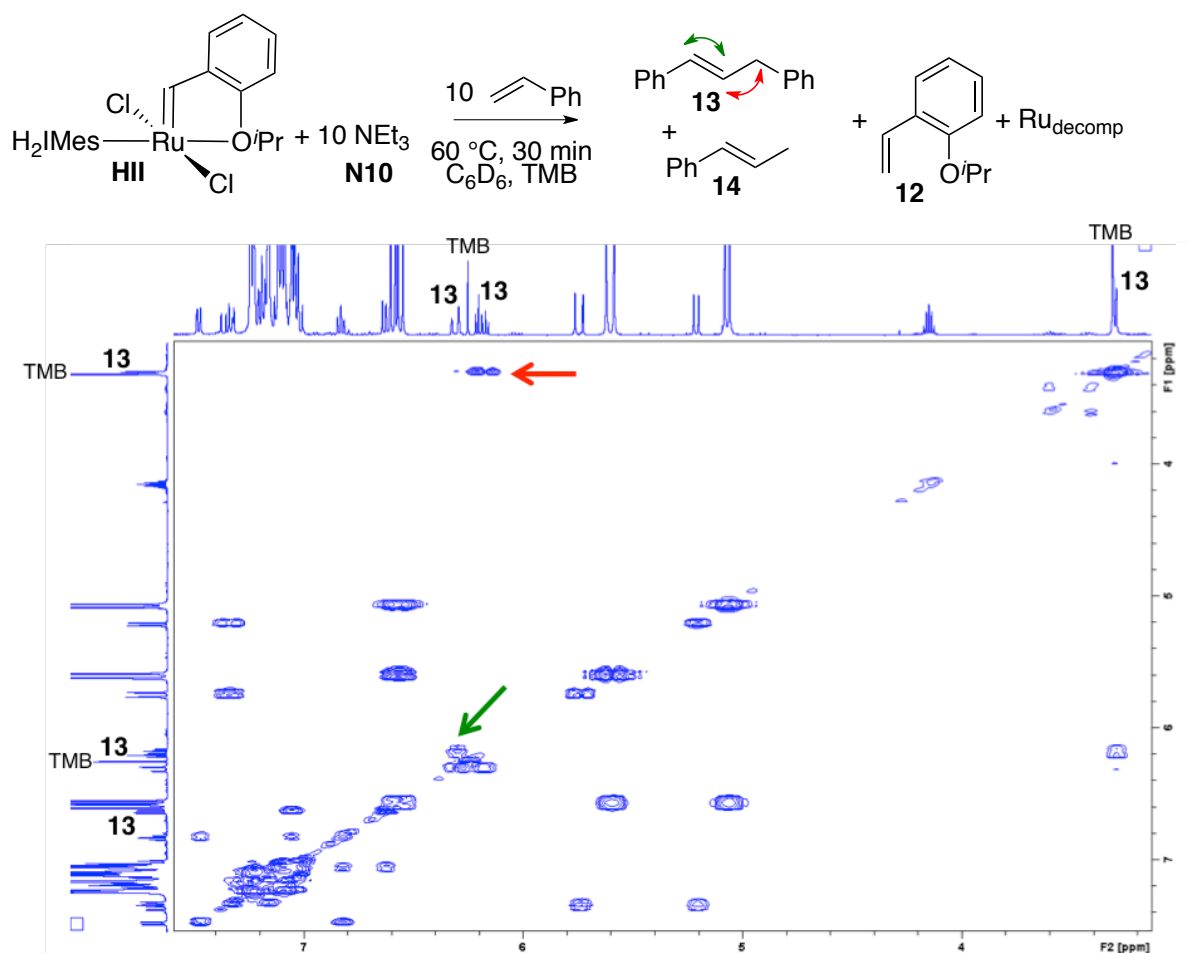


Figure A2.25. ¹H COSY NMR spectrum (C_6D_6 , 500.1 MHz) demonstrating connectivity for $PhHC=CHCH_2Ph$ **13**. Aliquot from reaction of **HIII** with NEt_3 **N10** and styrene (10 equiv each) at RT, after 1 h: no alkylidene signals remain. Red arrow shows coupling between the $CHCH_2Ph$ and $CHCH_2Ph$ protons of **13**; green arrow shows coupling between $PhHC$ and $CHCH_2Ph$ protons of **13**.

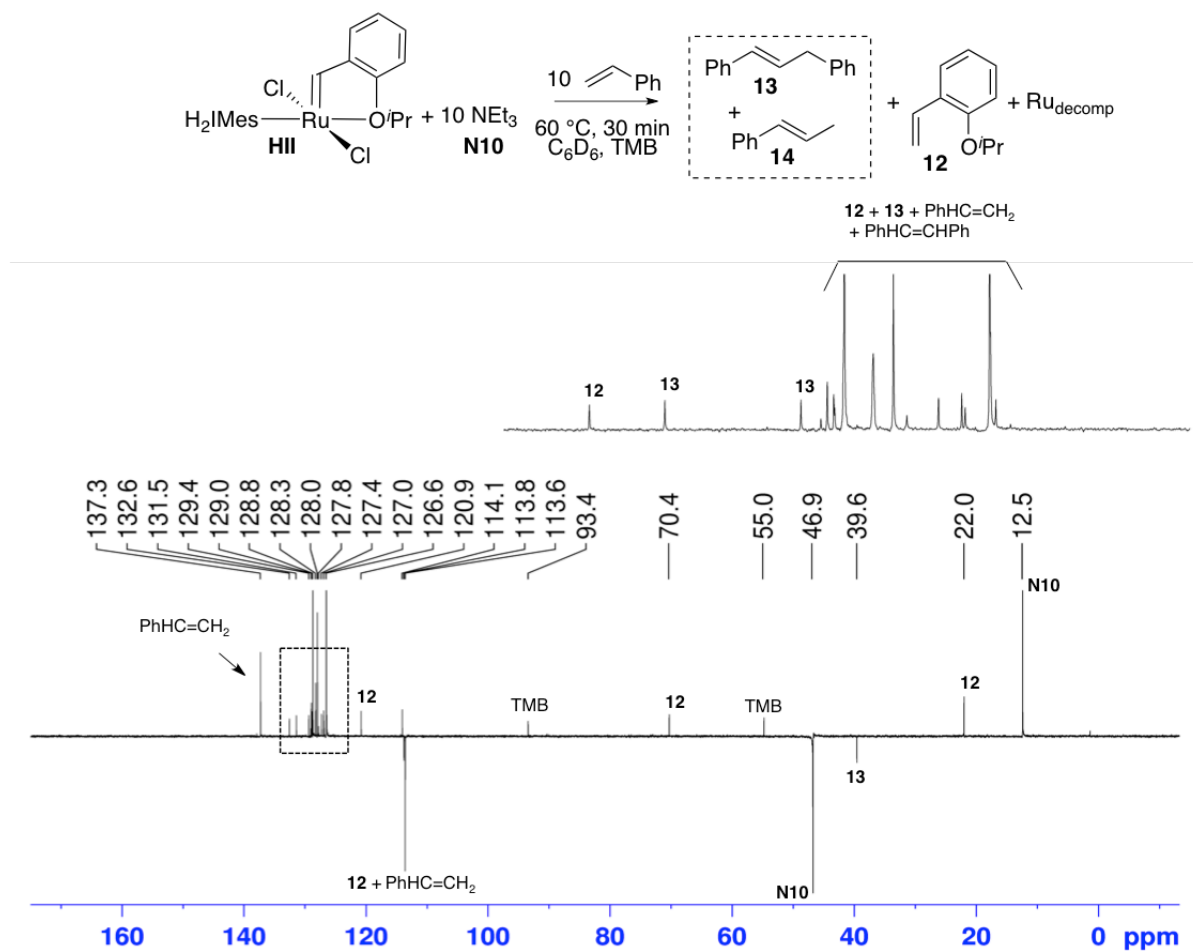


Figure A2.26. $^{13}\text{C}\{^1\text{H}\}$ DEPT-135 NMR spectrum (C_6D_6 , 125.8 MHz) for the reaction of **III** with styrene and NEt_3 **10** under the conditions depicted. No alkylidene signals remain.

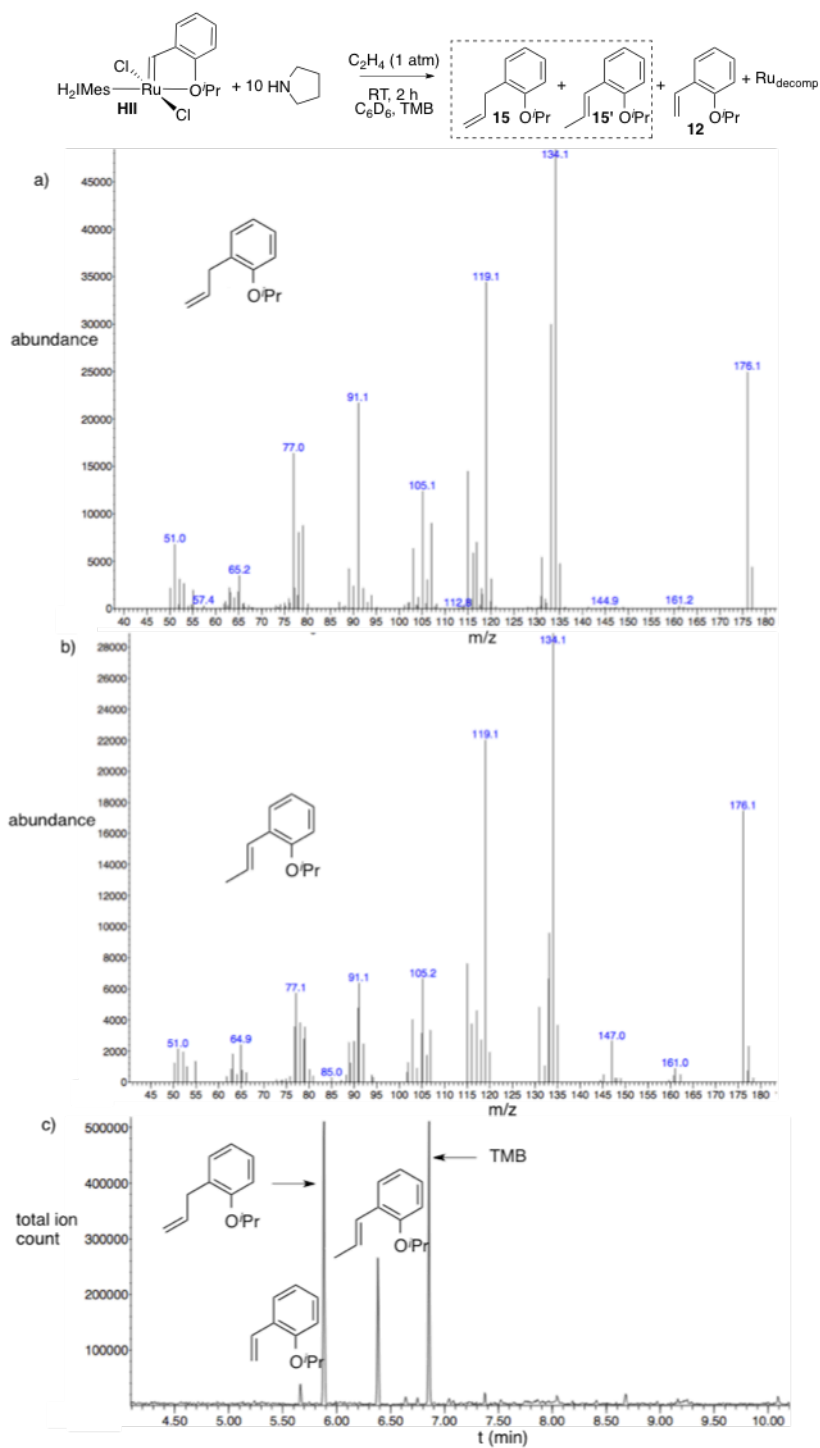


Figure A2.27. EI mass spectra of (a) $\text{H}_2\text{C}=\text{CHCH}_2\text{Ar}$ **15**; (b) $\text{H}_3\text{CCH}=\text{CHAr}$ **15'**, formed by decomposition of **HII** at RT under the conditions depicted. (c) GC spectrum for the crude reaction mixture.

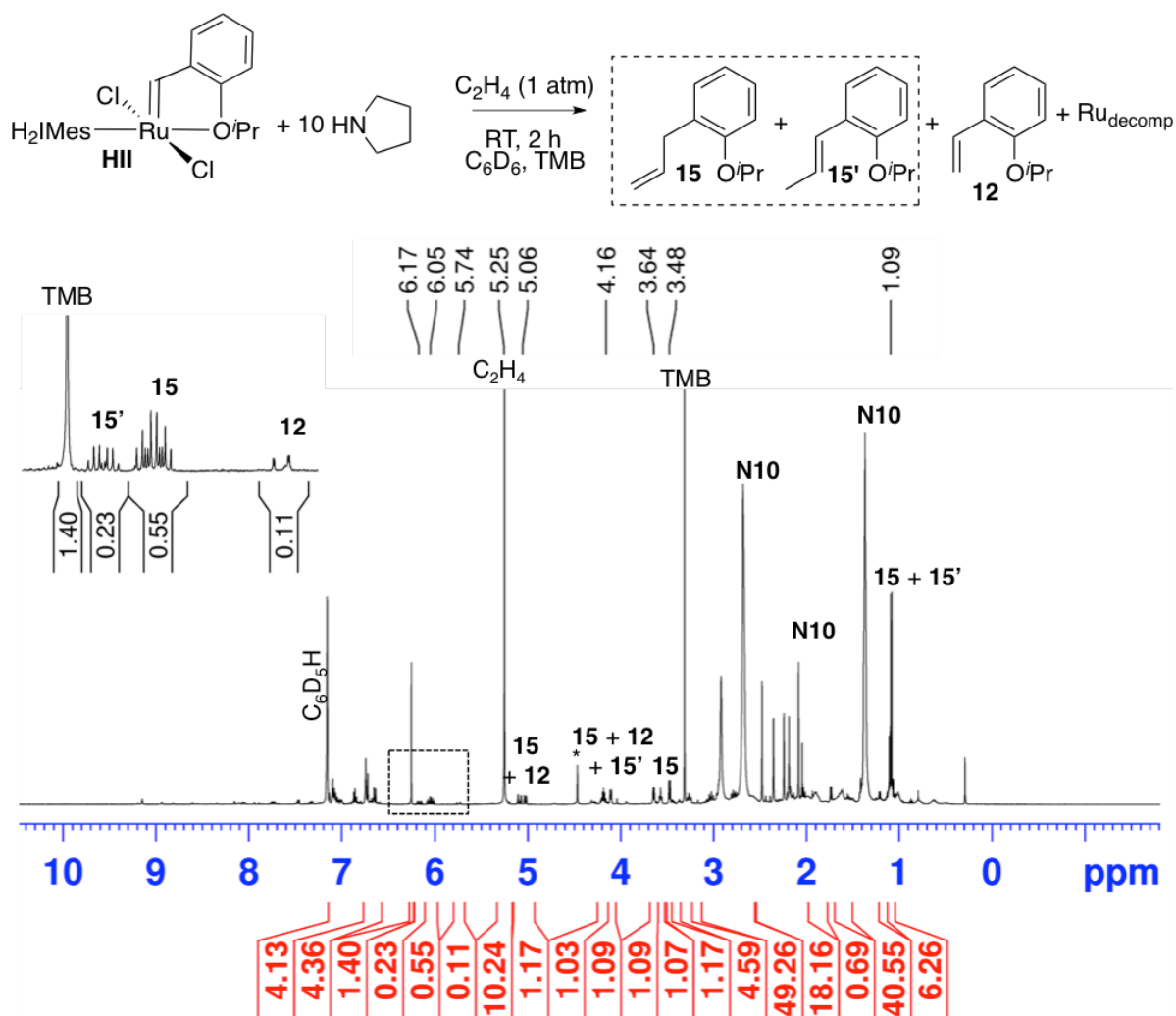


Figure A2.28. 1H NMR spectrum (C_6D_6 , 500.1 MHz) for the RT decomposition of **HII** by pyrrolidine under ethylene under the conditions depicted. Expansion shows olefinic signals for $ArCH_2CH=CH_2$ **15**, $ArCH_2CH=CH_2$ **15'** and *o*-isopropoxystyrene **12**. A CH_2Cl_2 impurity is labeled (*). Values for **15** and **15'** match those reported.³

A2.2.2. Spectra for Decomposition of **III** in by morpholine **N6** or $\text{NH}_2^{\text{n}}\text{Bu}$ **N1**.

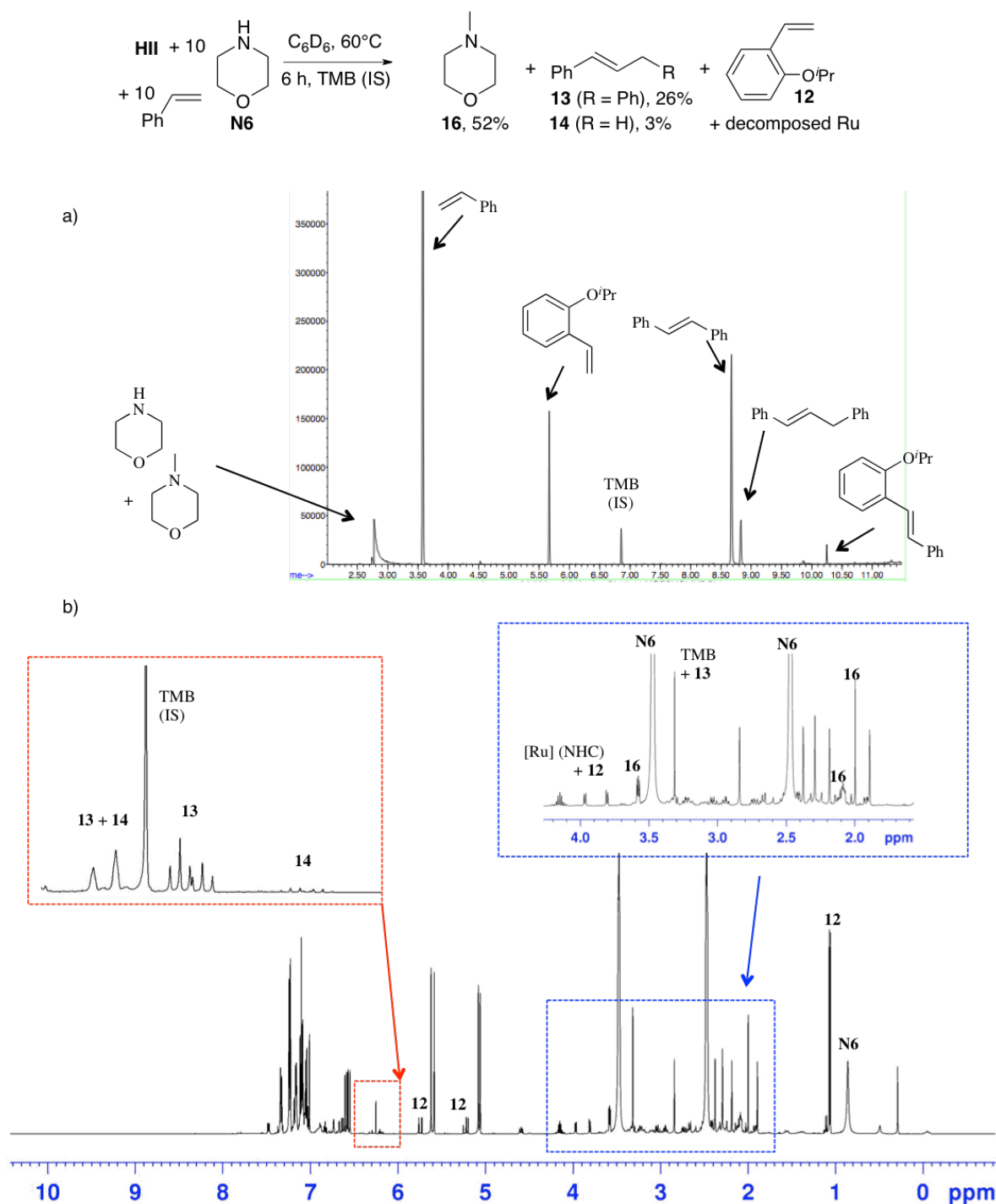


Figure A2.29. (a) GC trace for the reaction of **III** with styrene and morpholine **N6** under the conditions depicted. (b) ^1H NMR spectrum (C_6D_6 , 500.1 MHz) for the same sample. No alkylidene signals remain. Expansions show olefinic signals for **13** and $\text{PhCH}=\text{CHCH}_3$ **14** and signals for *N*-methylmorpholine **16**. Values for **14** match an authentic sample. Values for **13** as above. See figure A2.30 for comparison of **16** to an authentic sample.

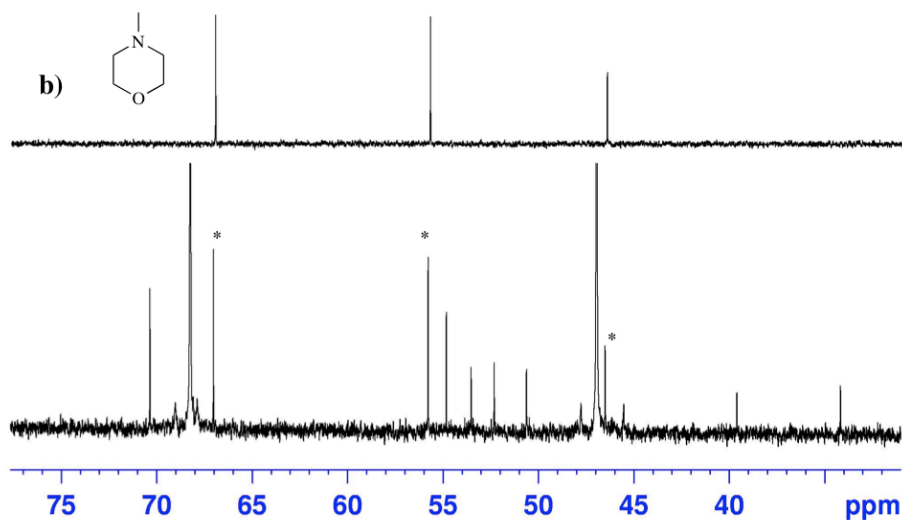
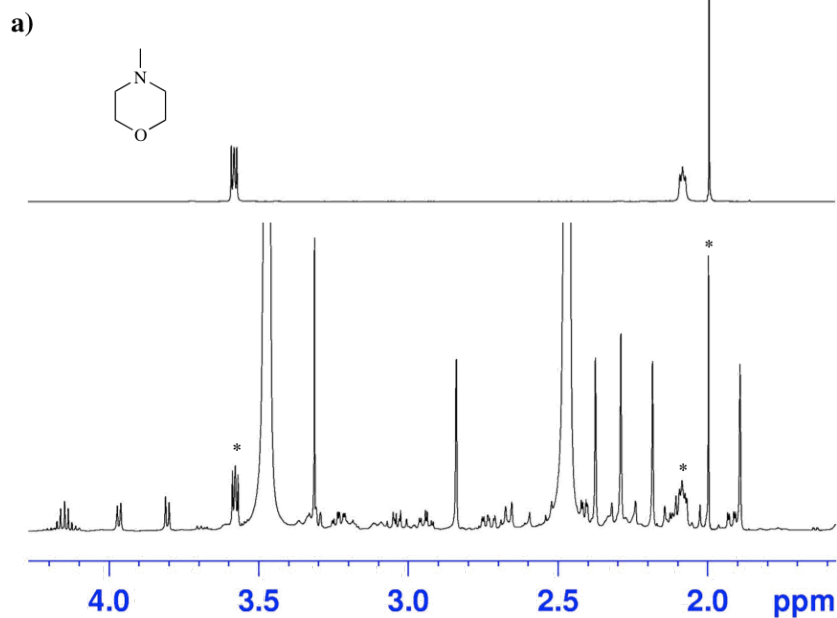
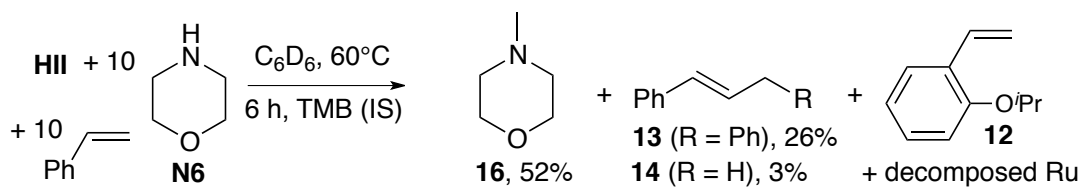


Figure A2.30. (a) ^1H (C_6D_6 , 500.1 MHz) and (b) $^{13}\text{C}\{^1\text{H}\}$ (C_6D_6 , 125.8 MHz) NMR data for an authentic sample of N-methylmorpholine **16** (above) compared to the crude reaction mixture (below) shown in Figure A2.29. The symbol “*” denotes **16** in the crude reaction mixture.

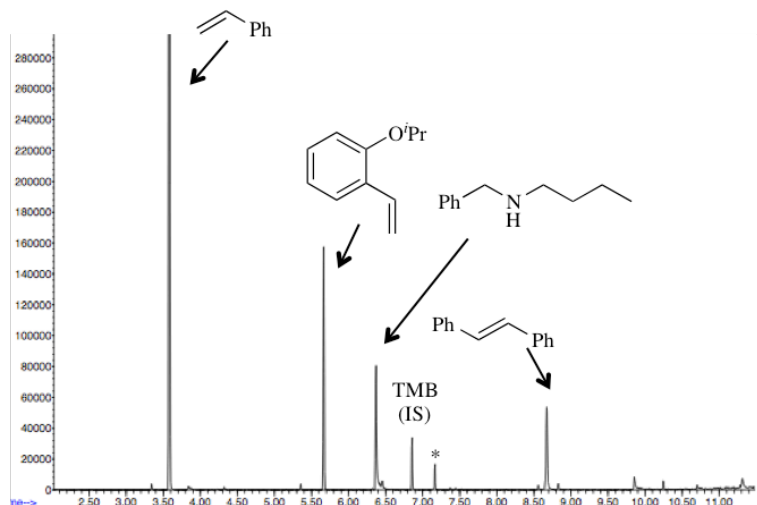
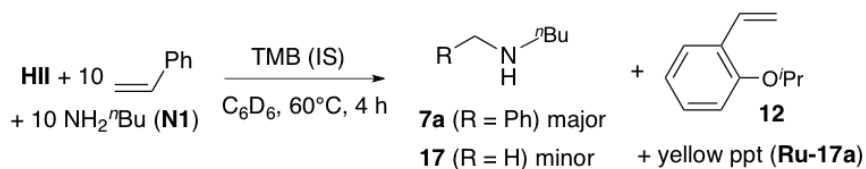


Figure A2.31. GC trace of the crude reaction mixture formed by reaction of **HII** with styrene and NH_2^tBu **N1** under the conditions depicted. See Figure A2.4 for EI-MS spectrum of $\text{NH}^t\text{Bu}(\text{CH}_2\text{Ph})$ **7a**. The peak labeled “*” is unassigned ($m/z = 123.9$).

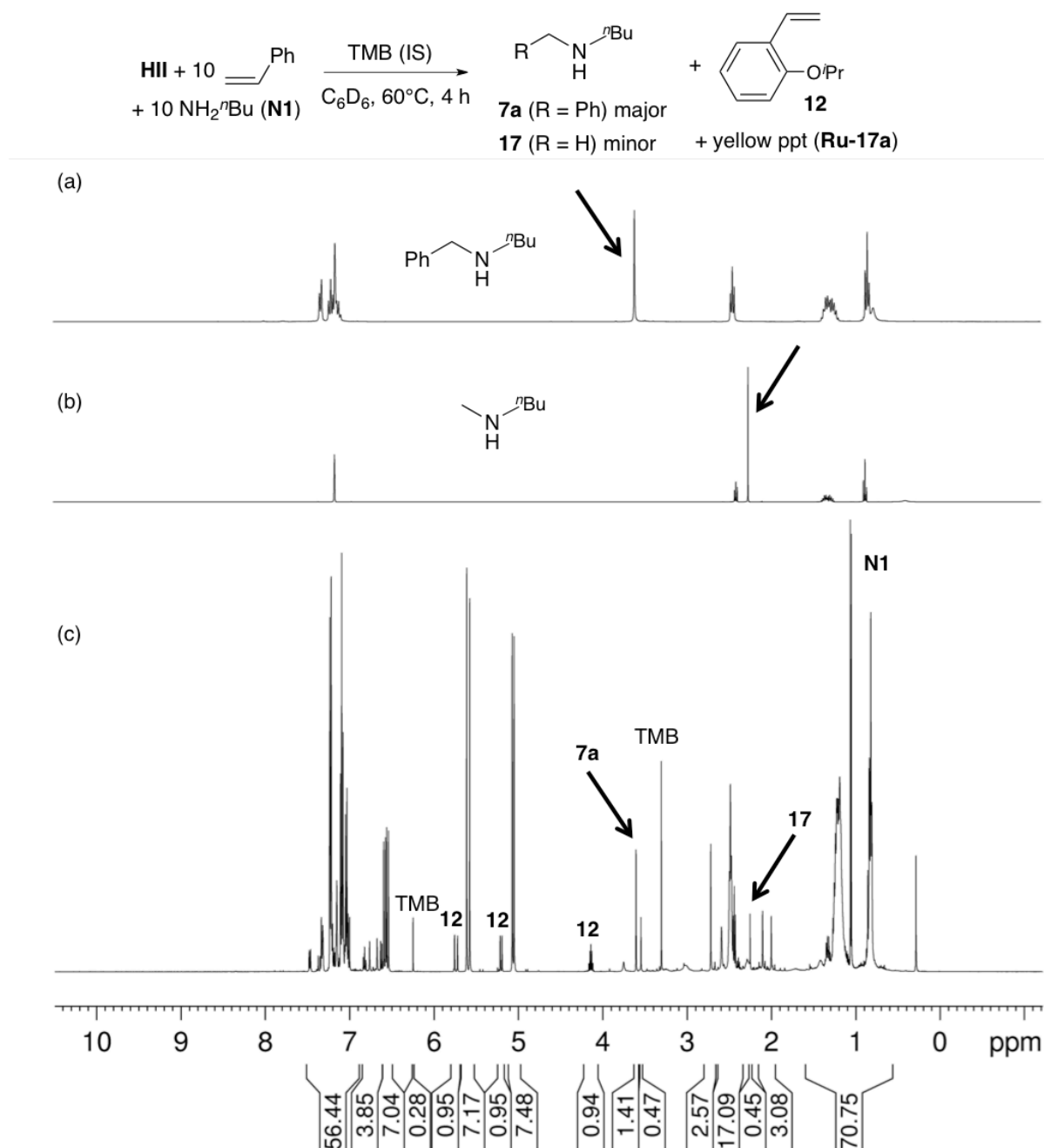


Figure A2.32. In situ ^1H NMR spectrum (C_6D_6 , 500.1 MHz) showing (a) $\text{PhCH}_2\text{NH}^n\text{Bu}$ **7a** (b) MeNH^nBu **17** (c) formation of $\text{PhCH}_2\text{NH}^n\text{Bu}$ **7a** and (proposed) MeNH^nBu **17** via reaction of **HII** with styrene and *n*-butylamine **N1** under the conditions depicted. No alkylidene signals remain.

A2.3.1. Spectra for Chapter 5, Section 5.4,2 decomposition of **Ru-42** in the presence of styrene.

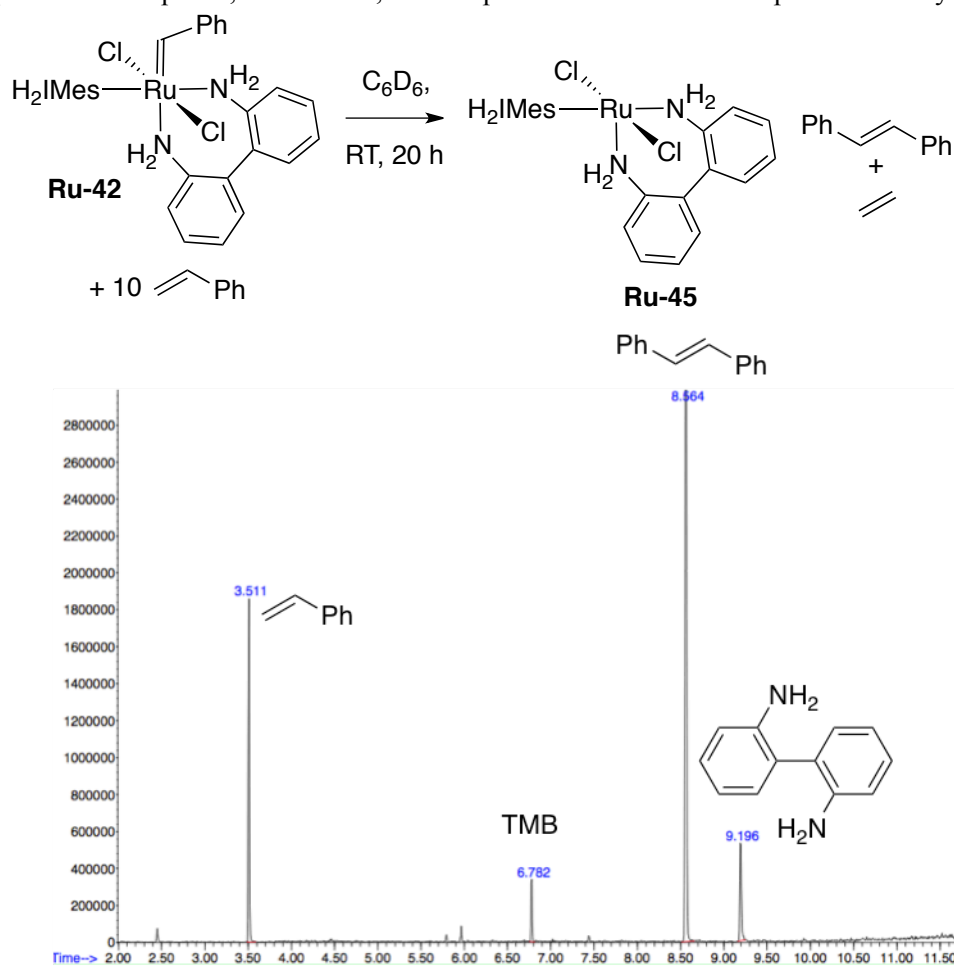


Figure A2.33. GC trace for decomposed of $RuCl_2(H_2IMes)(2,2\text{-biphenyldiamine})(=CHPh)$ **Ru-42** by styrene after 20 h at RT.

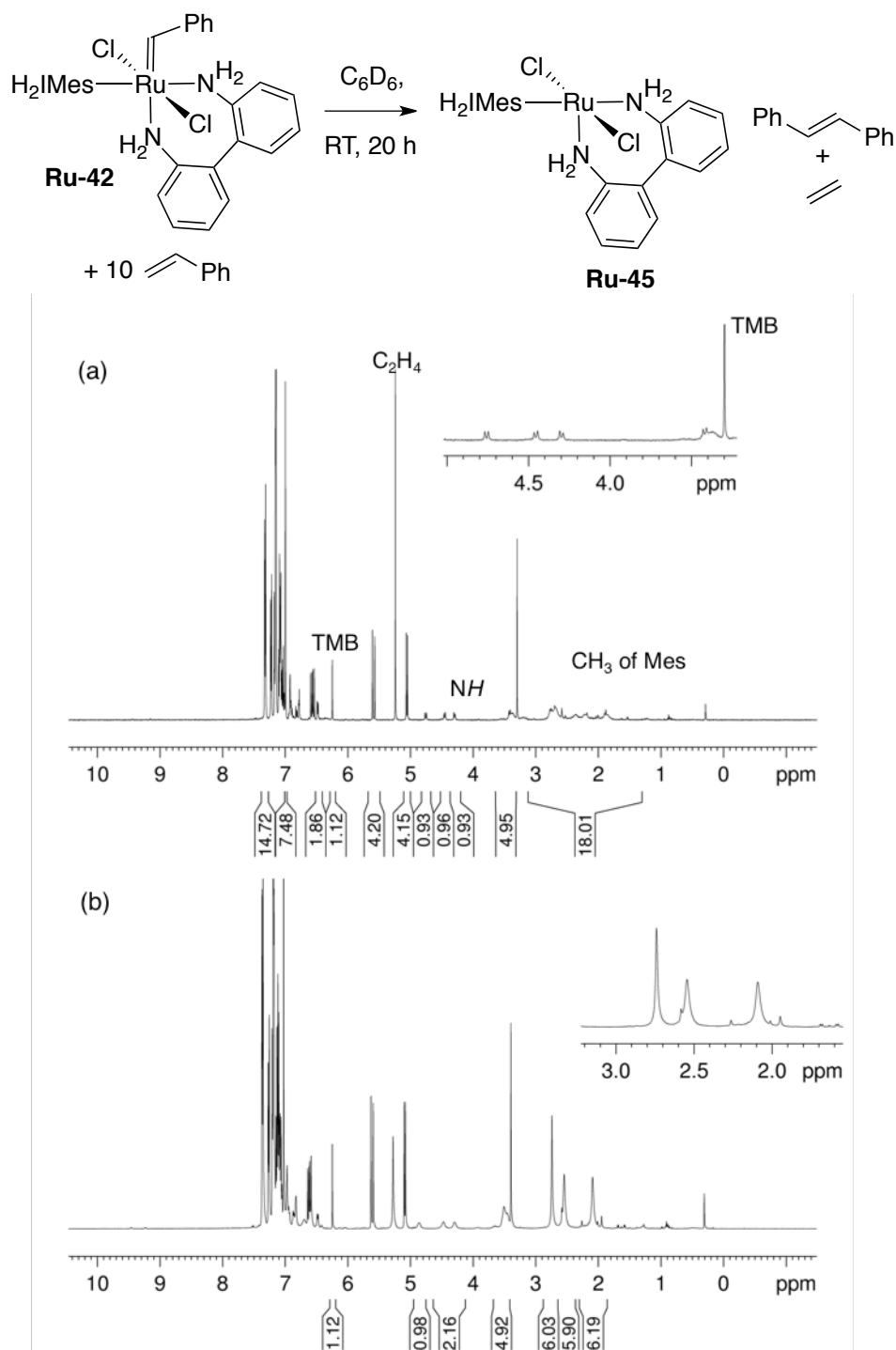


Figure A2.34. ¹H NMR spectrum (C₆D₆, 500.1 MHz) for decomposed of RuCl₂(H₂IMes)(2,2-biphenyldiamine)(=CHPh) **Ru-42** by styrene after 20 h at RT. Spectra collected at (a) RT. Inset shows NH protons. (b). 60 °C. Inset shows H₂IMes CH₃ protons (poorly resolved at RT)

A2.3.2. $^{31}\text{P}\{^1\text{H}\}$ NMR spectrum of $\text{Ru}(\text{CO})_3(\text{PPh}_3)_2$ from reductive elimination of NH on carbonylation of $\text{RuH}(\sigma\text{-NPh}_2)(\text{CO})(\text{PPh}_3)_2$.

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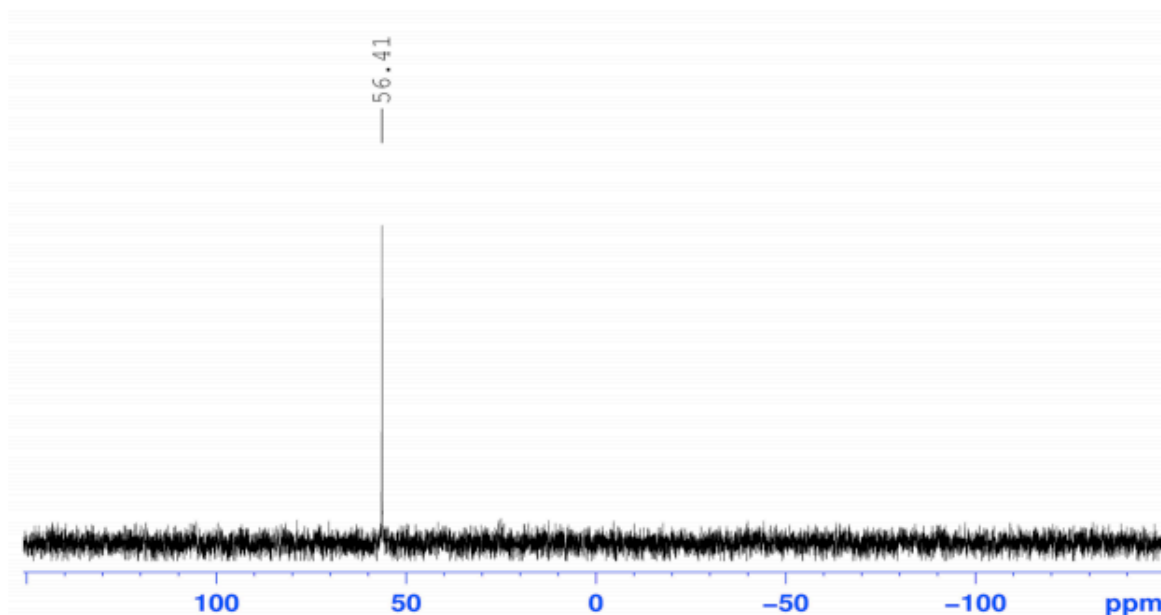


Figure A2.35. $^{31}\text{P}\{^1\text{H}\}$ NMR spectrum (C_6D_6 , 121.6 MHz), following carbonylation of $\text{RuH}(\sigma\text{-NPh}_2)(\text{CO})(\text{PPh}_3)_2$ **Ru-53** for 2h at 50 °C, showing only the singlet for $\text{Ru}(\text{CO})_3(\text{PPh}_3)_2$.

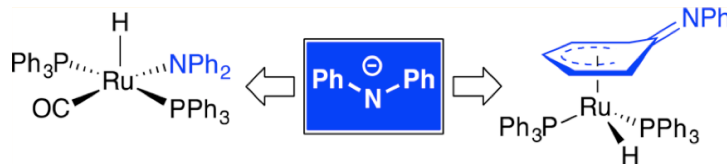
A2.4. References

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- (2) Ghosh, R.; Adarsh, N. N.; Sarkar, A. *J. Org. Chem.* **2010**, 75, 5320–5322.
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* Compound numbers and figure caption syntax have been modified for consistency throughout the thesis. For a Table of Compound Numbers and Structures, see p. VI.

Appendix 3. Published Contributions

1. "Exploring the Variable Hapticity of the Arylamide Ligand: Access to σ -Amidophenyl and π -Cyclohexadienyylimine Structure." Ireland, B. J., McDonald, R., Fogg, D. E. *Organometallics*, **2013**, 32, 4723–4725.



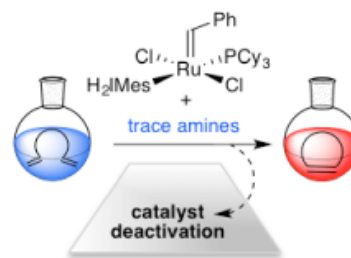
Abstract: A study of the preference for σ vs. π coordination of the arylamido ligand to a late transition metal shows that LiNPh_2 reacts with $\text{RuHCl}(\text{PPh}_3)_3$ to yield the bent-seat piano-stool complex $\text{RuH}[(\eta^5\text{-C}_6\text{H}_5)\text{NPh}](\text{PPh}_3)_2$ but with $\text{RuHCl}(\text{CO})(\text{PPh}_3)_3$ to yield the σ -amide $\text{RuH}(\eta^1\text{-NPh}_2)(\text{CO})(\text{PPh}_3)_2$. The stability of the σ -bound NPh_2 ligand in $\text{RuH}(\eta^1\text{-NPh}_2)(\text{CO})(\text{PPh}_3)_2$ reflects the π acidity of the CO ligand, which inhibits PPh_3 loss. Carbonylation of $\text{RuH}[(\eta^5\text{-C}_6\text{H}_5)\text{NPh}](\text{PPh}_3)_2$ at 50 °C affords $\text{Ru}(\text{CO})_3(\text{PPh}_3)_2$ and HNPh_2 , suggesting sequential $\pi \rightarrow \sigma$ isomerization and reductive elimination. The phenoxide ligand behaves similarly: $\text{RuH}[(\eta^5\text{-C}_6\text{H}_5)\text{NPh}](\text{PPh}_3)_2$ is formed from $\text{RuHCl}(\text{PPh}_3)_3$ but $\text{RuH}(\eta^1\text{-OPh})(\text{CO})(\text{PPh}_3)_3$ is formed from $\text{RuHCl}(\text{CO})(\text{PPh}_3)_3$, and carbonylation of $\text{RuH}(\eta^1\text{-OPh})(\text{CO})(\text{PPh}_3)_3$ gives $\text{Ru}(\text{CO})_3(\text{PPh}_3)_2$ and phenol, although more forcing conditions are required (90 °C). The crystal structure of $\text{RuH}[(\eta^5\text{-C}_6\text{H}_5)\text{NPh}](\text{PPh}_3)_2$ is reported.

Author Contributions: This manuscript was written by BJI and DEF. XRD data collection and structural refinement was performed by RM. All other experimental work was performed by BJI.

2. “Amine-Mediated Degradation in Metathesis via the Second-Generation Grubbs Catalyst.”

Lummiss, J. A. M., Ireland, B. J., Sommers, J. M., Fogg, D. E. *ChemCatChem*, **2014**, 6, 459–463.

Abstract: Amine-mediated decomposition during metathesis reactions promoted by the second-generation Grubbs catalyst is studied. For most amines, the dominant deactivation pathway involves ejection of the PCy₃ ligand by amine, followed by abstraction of the methyldiene moiety from the resting-state species RuCl₂(H₂IMes)(PCy₃)(=CH₂) as [MePCy₃]Cl. An



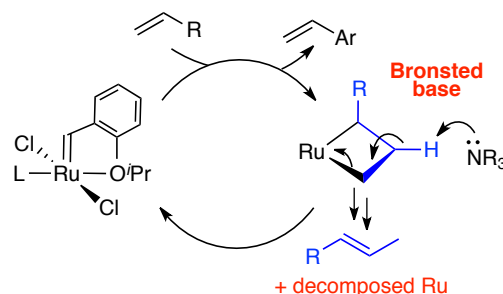
exception is highly basic DBU, which is slow to degrade the resting-state methyldiene complex, and for which the phosphonium by-product is not observed. However, DBU is shown to rapidly attack a species generated during catalysis, most probably the metallacyclobutane intermediate.

Author Contributions: Sections of this manuscript pertaining to benzylidene precatalyst studies were written by BJI and DEF. All other portions were written by JAML and DEF. JAML performed all reactions of methyldiene resting-state species **GII**, decomposition studies during RCM, as well as isolation and characterization of the DBU adduct of **GII**. BJI performed all experiments of benzylidene precatalysts, as well as isolation and characterization of pyrrolidine and morpholine adducts of **GII**. JMS assisted JAML and BJI with duplication of experimental data for publication purposes.

3. Decomposition of a Phosphine-Free Metathesis Catalyst by Amines and Other Bronsted Bases: Metallacyclobutane Deprotonation as a Major Deactivation Pathway. Ireland, B. J., Dobigny, B. T., Fogg, D. E. *ACS Catalysis*, **2015**, 5, 4690–4698.

Abstract: Reactions are described of the second-generation Hoveyda catalyst **III** with amines, pyridine, and DBU (1,8-diazabicyclo[5.4.0]undec-7-ene), in the presence and absence of olefin substrates. These nitrogen bases have a profoundly negative impact on metathesis yields, but in most cases are innocuous toward the pre-catalyst. **III** adducts were formed by primary and secondary amines (*n*-

butylamine, *sec*-butylamine, benzylamine, pyrrolidine, morpholine), pyridine, and DBU at room temperature. No reaction was evident for NEt₃, even at 60 °C. On longer reaction at RT, unencumbered primary amines abstract the benzylidene ligand from **III**. With 10 equiv NH₂^{*n*}Bu, this process was complete in 12 h, affording NH^{*n*}Bu(CH₂Ar) (Ar = *o*-C₆H₄-O^{*i*}Pr) and [RuCl(H₂IMes)(NH₂^{*n*}Bu)₄]Cl. For benzylamine, benzylidene abstraction occurred over days at RT. No such reaction was observed for *sec*-butylamine, secondary amines, NEt₃, pyridine, or DBU. All of these bases, however, strongly inhibited metathesis of styrene by **III**, with a general trend toward more deleterious effects with higher Bronsted basicity. Studies at 10 mol% **III** and 10 equiv DBU, NEt₃, and pyrrolidine (60 °C, C₆D₆) indicated that the primary mechanism for decomposition involved base-induced deprotonation of the metallacyclobutane intermediate, rather than the Lewis base-mediated decomposition pathways previously established for the Grubbs catalysts. In the corresponding metathesis of ethylene, this decomposition process is rapid even at RT, highlighting the vulnerability of the monosubstituted metallacyclobutane.



Author Contributions: This manuscript was written by BJI and DEF. Development of an optimized purification protocol for *o*-^{*i*}PrO-C₆H₄-CH₂NHCH₂^{*n*}Bu and synthesis of *o*-^{*i*}PrO-C₆H₄-CH₂NHCH₂Ph reference samples were performed by BTD. All other experiments were performed by BJI.