

**PRACTICAL AND GREEN DESIGN STRATEGIES FOR THE
CATALYTIC SYNTHESIS OF FUNCTIONAL MATERIALS**

by

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Abstract

The use of early transition metal complexes bearing *N,O*-chelating ligands for the preparation of functional materials is described within. The two central reactions explored are the hydroaminoalkylation of alkenes and the ring-opening polymerization of cyclic esters. To understand the key features of hydroaminoalkylation towards the design of more efficient catalysts, computational investigations using DFT have been used to develop a theoretical model of the catalytic cycle. The use of a sterically bulky, electron withdrawing amidate ligand leads to the formation of electrophilic metal centres that possess a plane of favorable reactivity *trans* to the amidate ligand. The steric bulk of the amidate ligand lowers the energy barrier to form catalytically active tantalaziridine species; however, it may also relieve steric congestion by accessing κ^1 bonding modes throughout the catalytic cycle. In the computed cycle, protonolysis of the 5-membered metallacycle is the turnover-limiting step and points toward a key area for optimizing reactivity through catalyst design.

N,O-chelating pyridonate ligands are used with tantalum to form highly active hydroaminoalkylation catalysts for the challenging alkylation of cyclic diene substrates. The resulting amino-norbornene and amino-cyclooctene products are then polymerized using ring-opening metathesis polymerization to prepare polyolefins containing pendant amine groups. The viscoelastic characterization of these materials is conducted by melt rheology and reveals profound and surprising physical properties that result from the association of polymer chains by dynamic hydrogen-bonding. Reduction of the polymer backbone gives saturated polymers to yield pendant amine-functionalized polyethylene analogs. These materials show interesting physical properties, including self-healing and adhesion to poly(tetrafluoroethylene).

Titanium pyridonates are used to conduct the ring-opening polymerization of cyclic esters. The modification of the ligand environment through changing the number of pyridonates or the nature of the nucleophilic ligand does not dramatically affect the resulting polymers obtained. These initiators are also used to combine *rac*-lactide and ϵ -caprolactone into random and block copolymers.

A stoichiometric reaction with methylene lactide and the ruthenium starting material $\text{RuCl}_2(\text{PPh}_3)_3$ is used to prepare a novel ring-opened ruthenium carboxylate species. This product results from the nucleophilic attack of a liberated triphenylphosphine ligand from the starting complex.

Lay Summary

A material that is functionalized is one that has been modified with a chemical group to add new function or properties. In this thesis, a primary focus was developing efficient methods to add the amine chemical group to carbon-based molecules. Amine chemical groups contain at least one nitrogen atom that is able to perform a variety of functions in a molecule, and are used prolifically by systems of life, nature, and also by humans, for example in drugs. To add the amine group, tantalum molecules, or catalysts, are used as a tool that works in one-step without creating waste. Using these molecular tools, the amine chemical group can be incorporated into carbon-based plastics to improve their functionality, for example allowing them to show self-healing behavior. The work in this thesis describes how these methods can be improved to sustainably prepare novel materials with exciting features.

Preface

The research disclosed within this thesis was carried out in part through the collaborative efforts of the Schafer Group and its members. In consultation with my supervisor, Dr Laurel Schafer, I designed and carried out the experiments described herein, with the following specific exceptions.

The theoretical calculations completed in Chapter 2 were designed and carried out under the joint supervision of Dr Eric Clot at the Institut Charles Gerhardt, Université de Montpellier (France). This was completed during an academic internship through the CREATE Sustainable Synthesis NSERC trainee program (April-July 2015).

All thermal and rheological characterization of the materials presented in Chapter 3 was conducted by Tanja Tomkovic¹ through a collaboration with Dr Savvas Hatzikiriakos in the Department of Chemical and Biological Engineering (UBC). Analysis using gel permeation chromatography was performed on an instrument operated and maintained by the Gates Group. Portions of Section 3.2.1.1 were completed in collaboration with Shou-Jen Hsiang, an undergraduate researcher (UBC), using my experimental design and supervision. Portions of Sections 3.2.2.2 and 3.2.7.2 were completed in collaboration with Hans Gildenast, a visiting Masters student (RWTH Aachen University), again under my design and supervision. The project in Chapter 4, Section 4.1 was initiated by Dr Ruth Webster, a post-doctoral fellow. Dr Webster disclosed an initial communication on this research² and continued this project by isolating the titanium pyridonate complexes described in Chapter 4. Dr Webster also contributed to the collection of their data as initiators in Sections 4.1.2-4.

A portion of Chapter 2 was published by the American Chemical Society: Gilmour, D. J., Lauzon, J. M. P., Clot, E., Schafer, L. L. "Ta-Catalyzed Hydroaminoalkylation of Alkenes:

Insights into Ligand-Modified Reactivity Using DFT.” *Organometallics* **2018**, 37, 4387-4394. Lauzon conducted initial theoretical studies that inspired this investigation. Theoretical calculations were performed by myself and Prof Clot through collaboration at the Institut Charles Gerhardt, Université de Montpellier (France). Experiments were conceived through this collaboration together with Prof Schafer and I wrote the manuscript for the published paper.

A portion of Chapter 4 was published by the Royal Society of Chemistry: Gilmour, D. J., Webster, R. L., Perry, M. R., Schafer, L. L. “Titanium pyridonates for the homo-and copolymerization of rac-lactide and ϵ -caprolactone.” *Dalton Trans.* **2015**, 44, 12411-12419. Dr Webster isolated the titanium pyridonate complexes described in Chapter 4. Dr Webster, Perry, and I contributed to the collection of their data as initiators in Sections 4.1.2-4. I interpreted the data and wrote the manuscript for the published paper.

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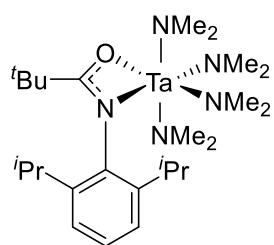
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List of Compounds

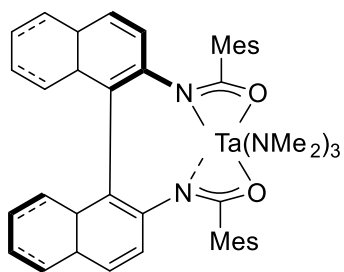
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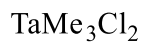
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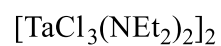
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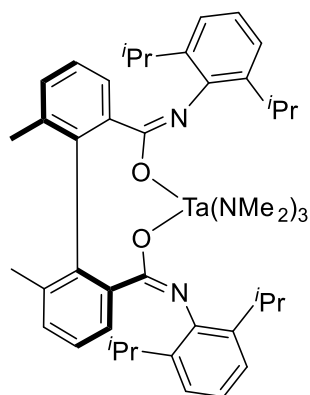
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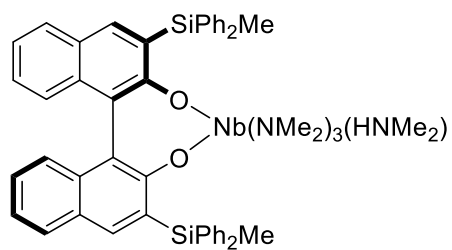
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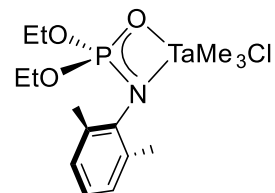
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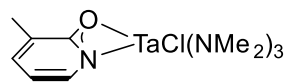
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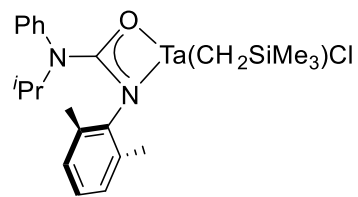
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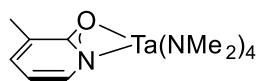
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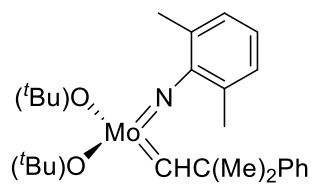
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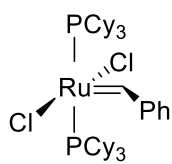
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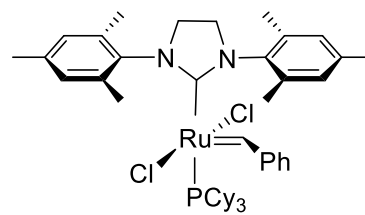
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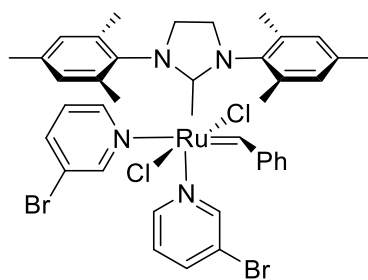
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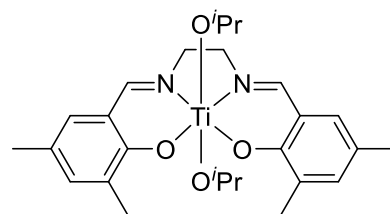
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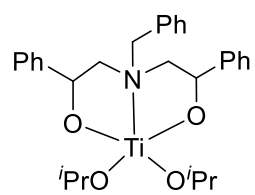
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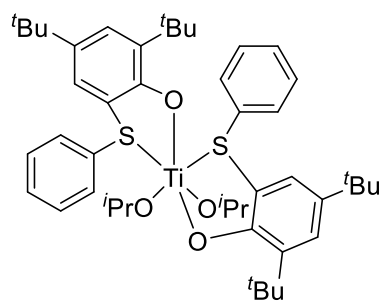
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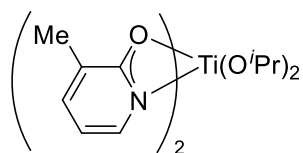
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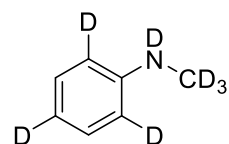
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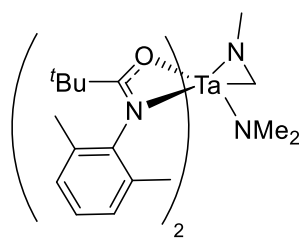
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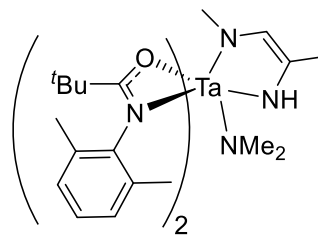
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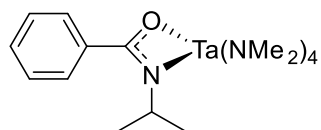
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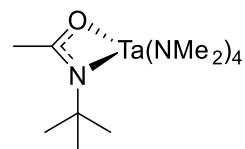
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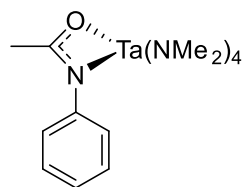
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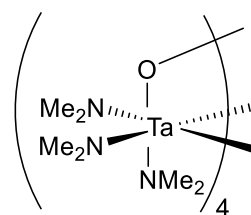
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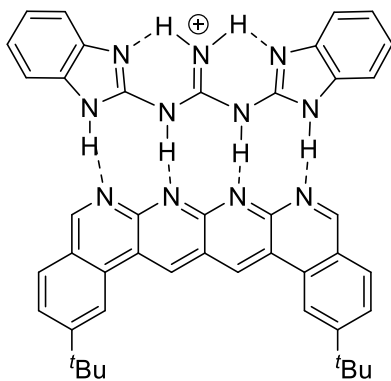


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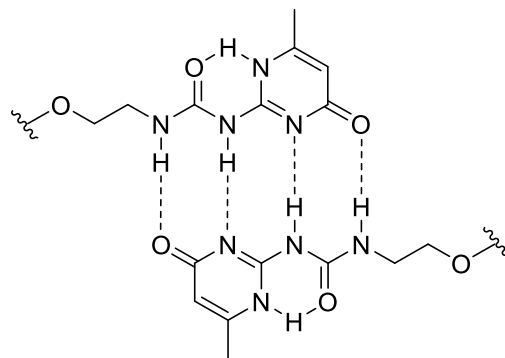


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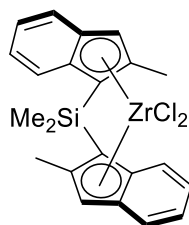
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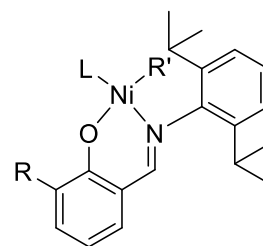
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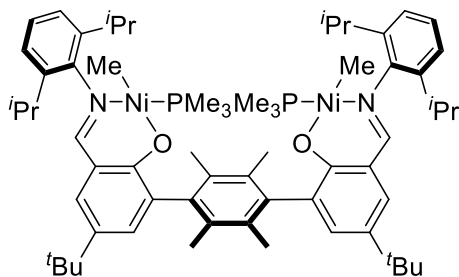


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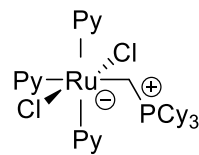


L = PPh₃, NCCH₃
R = H, alkyl, aryl
R' = Ph, CH₃

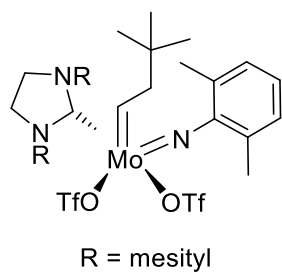
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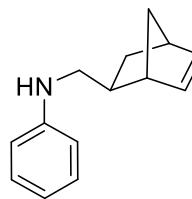
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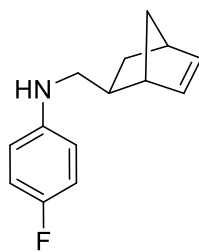
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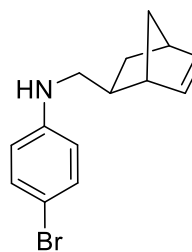
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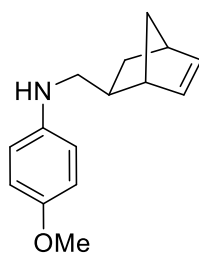
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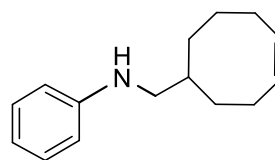
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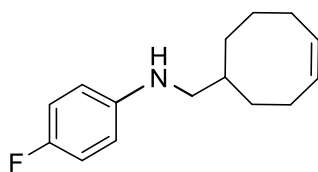
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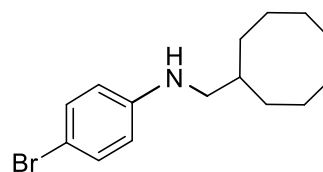
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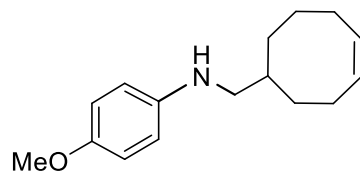
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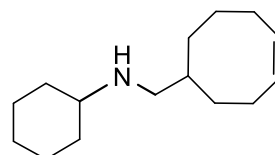
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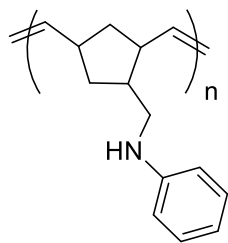
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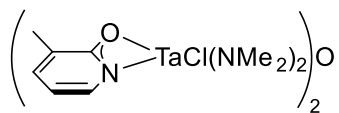
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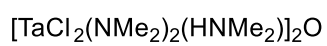
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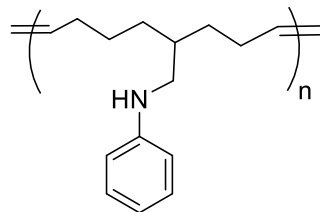
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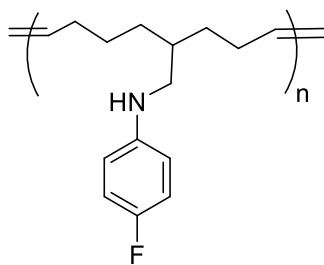
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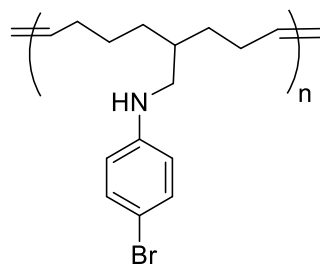
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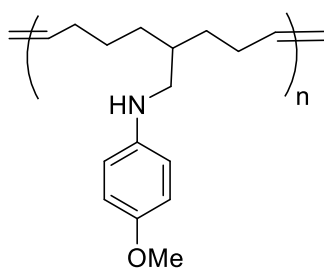
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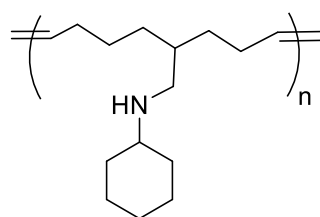
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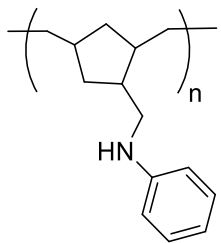
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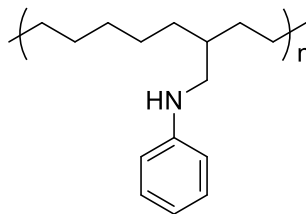
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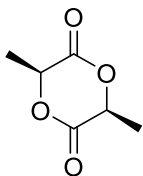
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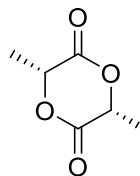
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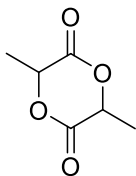
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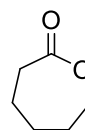
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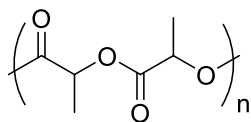
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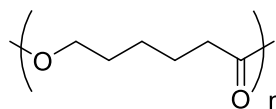
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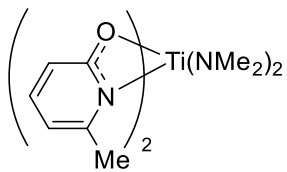
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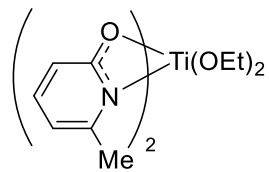
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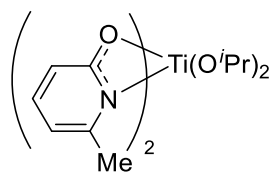
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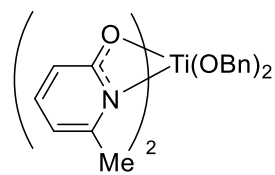
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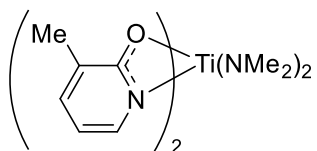
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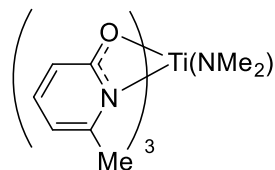
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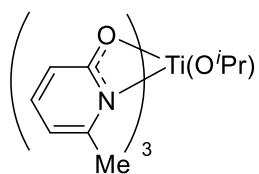
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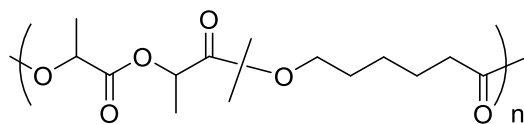
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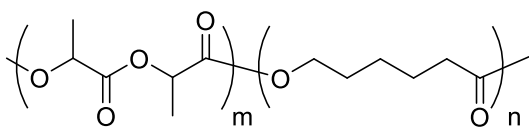
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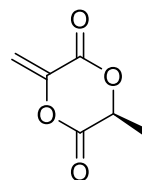
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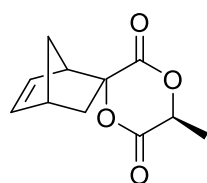
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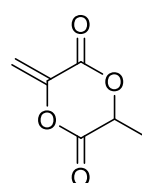
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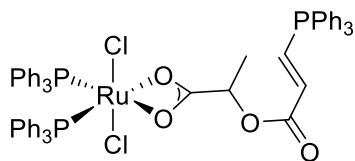
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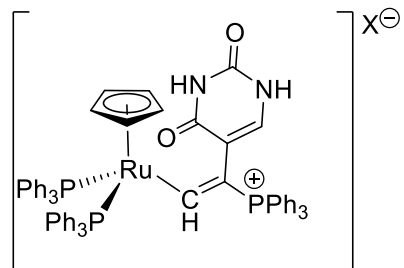
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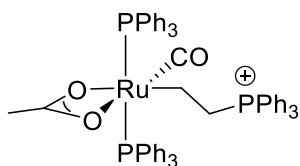
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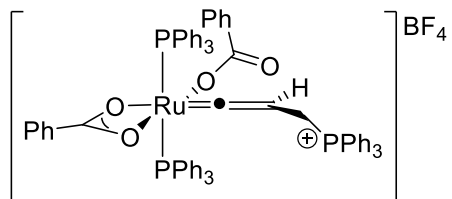
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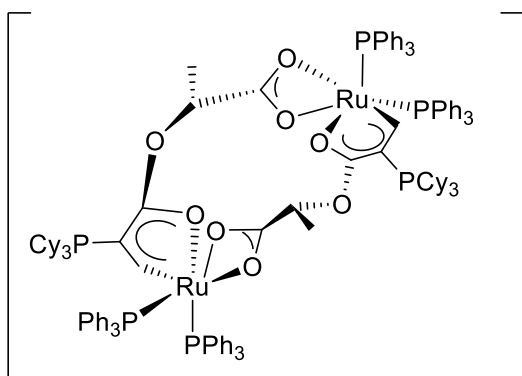
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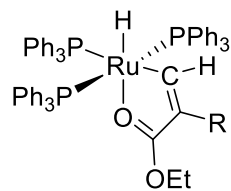
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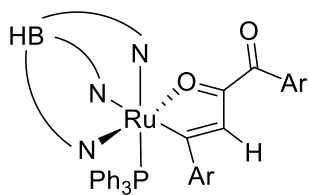
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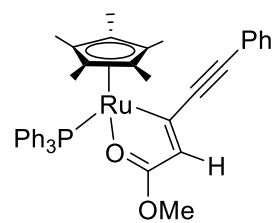
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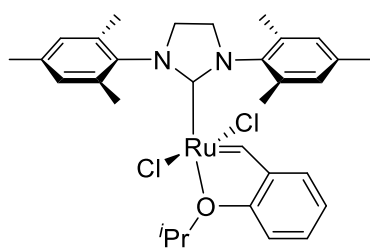
5.7



5.8



5.9



HG-2

List of Abbreviations

ACC	amine-containing cyclooctene
ACN	amine-containing norbornene
ADMET	acyclic diene metathesis
aq	aqueous
Ar	aryl
ATR	attenuated total reflectance
<i>ca.</i>	circa
calcd	calculated
CDCl ₃	chloroform-d
CL	ϵ -caprolactone
CM	cross-metathesis
COD	cyclooctadiene
COE	cyclooctene
Đ	dispersity
DCM	dichloromethane
DFT	density functional theory
DLS	dynamic light scattering
DOSY	diffusion ordered spectroscopy
DSC	differential scanning calorimetry
<i>e.g.</i>	exempli gratia
eq.	equivalent

ESI	electrospray ionization
etc.	et cetera
ETM	early-transition metal
exp.	experimental
FID	flame ionization detection
GPC	gel permeation chromatography
h	hour
HA	hydroamination
HAA	hydroaminoalkylation
HRMS	high resolution mass spectrometry
<i>ie.</i>	id est
IR	infrared
κ	kappa
KIE	kinetic isotope effect
LA	lactide
LS	light scattering
LTM	late-transition metal
M:I	monomer-to-initiator ratio
<i>m/z</i>	mass-to-charge ratio
MAH	maleic anhydride
MHz	megahertz
M_n	number-average molecular weight

MS	mass spectrometry
NBD	norbornadiene
NBE	norbornene
NHC	<i>N</i> -heterocyclic carbene
NMA	<i>N</i> -methyl aniline
NMR	nuclear magnetic resonance
PCL	poly(ϵ -caprolactone)
PCOE	polycyclooctene
PE	polyethylene
PLA	poly(lactic acid)
P_m	probability of <i>meso</i> enchainment
ppm	parts per million
ROMP	ring-opening metathesis polymerization
ROP	ring-opening polymerization
RT	room temperature
SHOP	Shell higher olefin process
SMD	solvent model based on density
T_g	glass transition temperature
TGA	thermogravimetric analysis
theo.	theoretical
TLS	turnover-limiting step
tol	toluene

TS	transition-state
USD	United States Dollar
<i>vide infra</i>	see below
<i>vide supra</i>	see above
vs.	versus

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Dedication

To my parents,
John and Karen Gilmour;

And my grandmothers,
Margaret Gilmour
and
Shirley Skinner

Chapter 1: Introduction

1.1 Principles of green chemistry

Since its conceptualization in the early 1990's, green chemistry has received increasing global interest from both academia and industry, influencing chemical innovation towards a sustainable balance of environmental and economic goals.³ Formally defined as the “Design of chemical products and processes to reduce or eliminate the use and generation of hazardous substances, and beyond”⁴ it can also be seen as a framework that strives to maximize sustainability at a molecular level. Green chemistry is sub-divided into twelve key principals, with an emphasis that the cohesive application of all principles is desired for a truly sustainable process (Figure 1.1). Many connections are readily apparent, for instance a process that possesses high atom economy likely also reduces derivatives such as stoichiometric co-reagents or additives. An overarching goal of this thesis has been the consideration of this cohesive framework as additional criteria during the design of all experiments, specifically, the use of catalysis to improve the efficiency of chemical synthesis. While these principals are limited to a qualitative analysis in this thesis, quantitative tools could be used to interrogate the sustainability of these methods further. E-factor is an important metric that describes how much waste is generated per kilogram of product.³ Another measure would be a full life-cycle assessment, which would entail a comprehensive analysis of the overall environmental impact of the processes from raw starting materials to the demands of production, distribution, use, and waste management.⁵

1. Waste Prevention vs. its treatment/disposal
2. Atom Economy maximizes incorporation of all materials in final products
3. Less Hazardous Synthesis pose minimal toxicity to human health and environment
4. Safer Chemicals maintain efficacy while reducing toxicity
5. Safer Solvents that are innocuous and avoid auxiliaries
6. Energy Efficiency to minimize environmental and economic impact
7. Renewable Feedstocks prevents depletion of non-renewable resources
8. Reduce Derivatives that require additional steps and increase waste
9. Catalysis vs. stoichiometric reagents
10. Degradation to innocuous products that do not persist in environment
11. Real-time Analysis enables process monitoring prior to formation of hazardous substances
12. Safer Chemistry that minimize potential for chemical accidents

Figure 1.1 Twelve Principles of green chemistry³⁻⁴

While catalysis does not take priority over any principle of green chemistry, its utilization allows several principles to be satisfied. For example, the reduction of waste can be achieved using catalysis to complete a transformation without the need for stoichiometric co-reagents that can plague traditional syntheses. Catalysis can also result in superior selectivity, improved yields, and obtain products that in some cases are not otherwise accessible in using traditional methods.

1.2 Schafer Group catalysis: *N,O*-ligated early transition-metal complexes

A central platform of Schafer Group research is the development of homogeneous early transition-metal catalysts bearing *N,O*-chelating ligands. The principle objective with these systems is the development of methods for bond activation that enable challenging transformations such as carbon-carbon and carbon-nitrogen bond-forming reactions. This methodology permits the preparation of a variety of amine-containing molecules, from small molecules to polymeric materials, which can be designed for application in fine chemical, petrochemical, agrochemical, and pharmaceutical industries.⁶

The focus on the development of highly active *homogeneous* catalysts typically enables a more nuanced molecular understanding of the overall reaction mechanism than in heterogeneous systems. Heterogeneous systems are typically very reactive, can be easily removed, and are commonly used industrially; however the active site is difficult to characterize, preventing a clear understanding of reaction mechanism that in turn also hampers rational catalyst development.⁷ Since homogeneous systems exist in the same phase as the reactants, molecular changes and interactions between catalyst and substrate may be observed, therefore enabling more direct comparisons between structure and activity. By studying this relationship, one can realize improvements in reactivity, control, and selectivity. Furthermore, clear elucidation of reaction mechanisms in homogeneous systems may also provide indirect insight into heterogeneous systems that catalyze similar or analogous reactions.

Another goal in the Schafer group is the use of catalysts that are based upon abundant and low-toxicity metals. In contrast to late transition metals (LTM), early transition metals (ETM) are generally more abundant, reducing their cost. For example, titanium, *ca.* 0.5 wt % of the Earth's crust, is approximately two orders of magnitude more abundant than copper.⁸ From the perspective of sustainability, the development of systems based on more abundant metals is critical for reducing our reliance on precious metals.

The foundation of catalyst development in the Schafer Group is the preparation of 1,3-*N,O*-chelating ligands for coordination to metal complexes. A variety of 1,3-*N,O*-chelating ligands, including amidates, ureates, 2-pyridonates, phosphoramidates, and sulfonamides, have been installed on metal complexes and used for a range of transformations, from stoichiometric bond formation to catalysis (Figure 1.2).⁹ These ligand motifs can provide a range of steric and electronic environments about the metal centre, allowing for systematic studies of the relationships

between catalyst structure and reactivity. Furthermore, these ligands are modular and readily synthesized, enabling further tuning of the ligand backbone through structural variation, allowing the rapid formation of ligand libraries for catalytic screening.

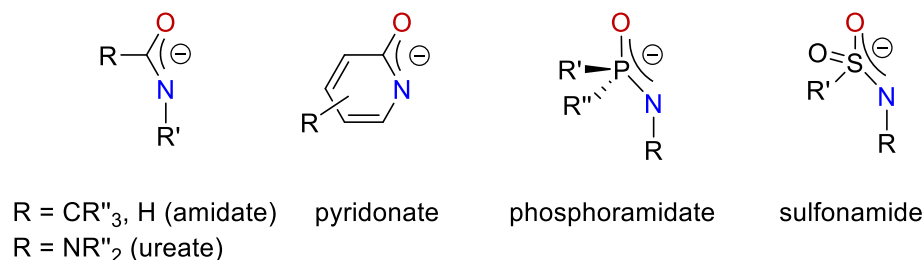


Figure 1.2 *N,O* chelating ligands explored in the Schafer Group (depicted as anions)⁹

These ligands demonstrate good compatibility for complexation with ETMs. Typically, these ligands are installed onto a metal centre using relatively straightforward substitution reactions such as protonolysis with a proteo-ligand or salt metathesis with a ligand salt. As predicted by hard/soft acid/base theory, the hard *N,O* donor is commonly observed to bind as hard ETMs in a 1,3- κ^2 fashion (Figure 1.3). However, κ^1 modes through *N* and *O* may also be observed, especially when these modes alleviate steric congestion about the metal centre. In some cases, bridging modes between two metal centres are also be observed, ie. $\mu_2\text{-}N,O$.¹⁰ These ligands are therefore hemilabile: a property where an atom from a chelated ligand dissociates while the other atom remains bound to the metal centre.¹¹ Critically, this property is believed to permit coordinative unsaturation about the metal centre and in some systems has been proposed as a key feature of catalytically active species.¹¹⁻¹²

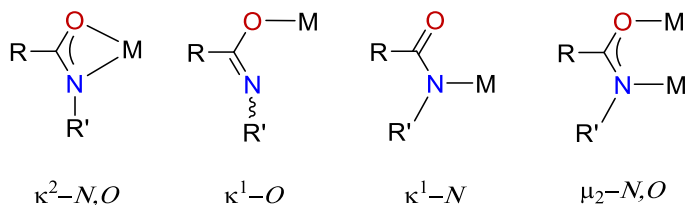


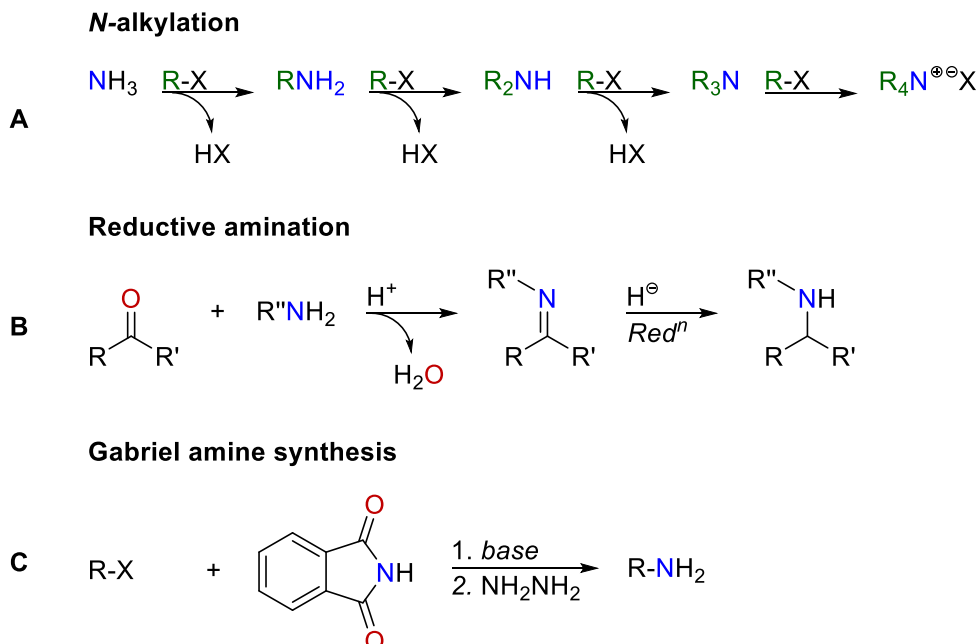
Figure 1.3 Variable binding modes observed with *N,O*-chelates

N,O-chelated ETM catalysts have been applied in the Schafer Group to a wide variety of transformations. Intersecting organic, organometallic, and polymer chemistry, this research development has enabled the synthesis of amines, heterocycles, ethers, and polymeric materials from biodegradable polyesters to polyethylene. The goal is to develop catalytic methodology that can replace or provide alternatives to traditional synthesis, thereby reducing waste and adding versatility to the practical chemists' toolbox.

1.3 Challenges in traditional amine synthesis

The high demand for amines can be partially understood by the massive energy cost associated with ammonia production, where fixation of nitrogen by the Haber-Bosch process consumes approximately 1-2 percent of the world's energy.⁶ Approximately 70% of ammonia production is used for the manufacture of agrochemicals, while the production of synthetic amines requires 3-4% of the total worldwide output (~5-7 mT per year). The global amines market between 2015 and 2020 has a forecasted compound annual growth rate of 8.3%, reaching a valuation of approximately 20B USD by 2020.¹³

There have been a number of methods developed to synthesize amines (Scheme 1.1). While these routes have been long-used as synthetic tools, they have inherent drawbacks that fundamentally limit their efficiency.



Scheme 1.1 Common stoichiometric synthesis of amines¹⁴⁻¹⁶

N-alkylation represents a straightforward example of an S_N2 nucleophilic substitution reaction, but this reaction suffers from poor selectivity (Scheme 1.1 A).¹⁶ Once the secondary amine is formed, it can continue to act as a substrate, giving a mixture of amine products due to over-alkylation. Even in cases where large excesses of the amine are used, difficult-to-separate product mixtures result in poor yields. Reductive amination constitutes an important strategy in synthetic organic chemistry (Scheme 1.1 B).¹⁴ Beginning with an aldehyde or ketone, an imine is formed as an intermediate, which can then be reduced to give the new amine. This sequence prevents over-alkylation, thus providing control over nitrogen-carbon bond formation. However, this method is not able to form N-Csp² or N-Csp hybridized bonds. While an equivalent of water as waste is environmentally benign, its removal from reaction mixtures can be energy intensive. Further, while catalytic reductions using hydrogen are known, stoichiometric reductants such as sodium cyanoborohydride are commonly employed for practical reasons, lowering atom economy.

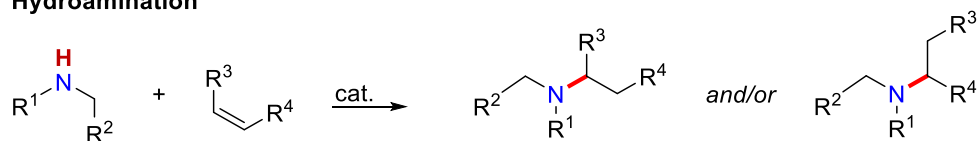
The Gabriel synthesis of amines also uses alkyl halides as electrophiles, however phthalimide is used as a masked source of ammonia (Scheme 1.1 C).¹⁵ While phthalimide is nucleophilic, its alkylated product is much less so, therefore the selective formation of primary amines in high yield is possible. However, similar drawbacks as noted in other traditional methods are observed: halogenated substrates are typically from non-renewable feedstocks and stoichiometric reagents that are not incorporated into the final product lower overall atom economy.

While these are only three of the numerous traditional methods that have proved useful in amine synthesis, these examples highlight critical challenges remaining in minimizing waste and maximizing selectivity. To overcome these challenges, catalytic methods to prepare amines have also been developed. Whereas traditional synthetic pathways rely on the reactivity of organic functional groups, transition-metal catalyzed routes possess the capability of furnishing novel covalent bond formations through the activation of less reactive bonds.¹⁷ This can enable the formation of valuable products from readily available starting materials. The disparate connection strategies offered through catalytic bond activation can also form novel structural motifs that may reveal interesting and new profiles of reactivity. Thus, catalysis offers a powerful means to address the fundamental limitations of traditional synthesis.

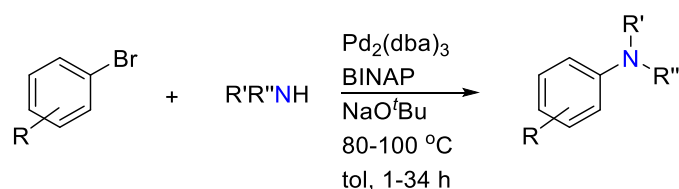
A vast number of metal-catalyzed reactions have been investigated towards the synthesis of amines (Scheme 1.2). As a direct hydrofunctionalization of an olefin with an amine, hydroamination (HA) is the addition of an N-H bond across a C-C unsaturation. A variety of ETM and LTM systems have been investigated towards this transformation, including extensive catalyst development in the Schafer Group. However, this reaction remains challenging, in particular for intermolecular functionalization.¹⁸⁻²⁰ Two other very noteworthy amination catalytic reactions are

Buchwald-Hartwig amination²¹ and hydroaminomethylation.²²⁻²³ These strategies have been the subject of extensive research, but are only a few of the strategies present among a large class of metal-catalyzed reactions.

Hydroamination

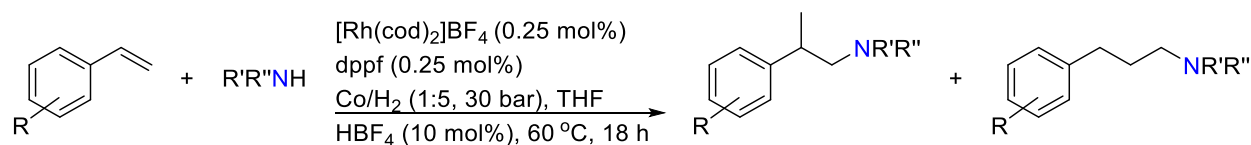


Buchwald-Hartwig Amination



R/R' = alkyl
R'' = alkyl, aryl, H
dba = dibenzylideneacetone

Hydroaminomethylation

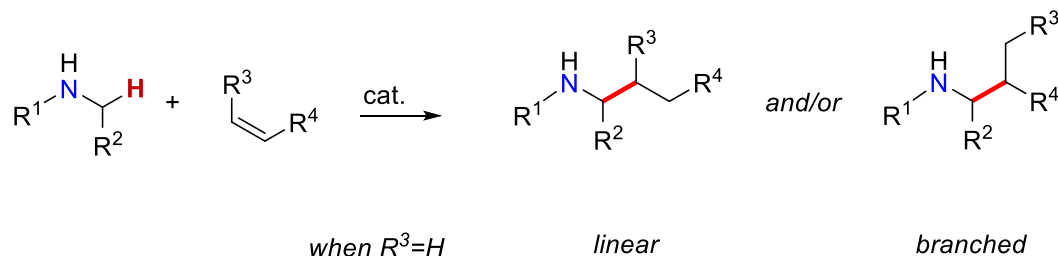


Scheme 1.2 Common catalytic routes for amine synthesis¹⁹⁻²²

While hydroamination catalysis has seen significant progress, relying on C-N bond formation provides challenges because of a low thermodynamic driving force. In HA, breaking the C=C π bond to form a C-N single bond can be practically ergo-neutral (depending on substrates).²⁴ As such, intermolecular reactions between alkenes and amines that proceed *via* N-H addition are somewhat rare and typically require the use of strained alkenes or amine activation, for example through oxidation by a photoredox catalyst.²⁵ However, over the last decade a complementary strategy has emerged from dormancy that circumvents this fundamental limitation.

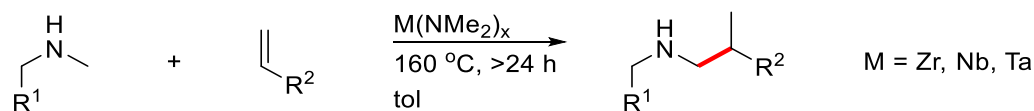
1.4 Amine synthesis through catalytic C-C bond formation: Hydroaminoalkylation

An alternative connection strategy in the catalytic assembly of amine-containing molecules is hydroaminoalkylation (HAA), in which C-C bond formation provides a driving force for reactivity. This reaction furnishes one-step functionalization in which a carbon-carbon bond is formed α to an amine across a C-C unsaturation (Scheme 1.3):



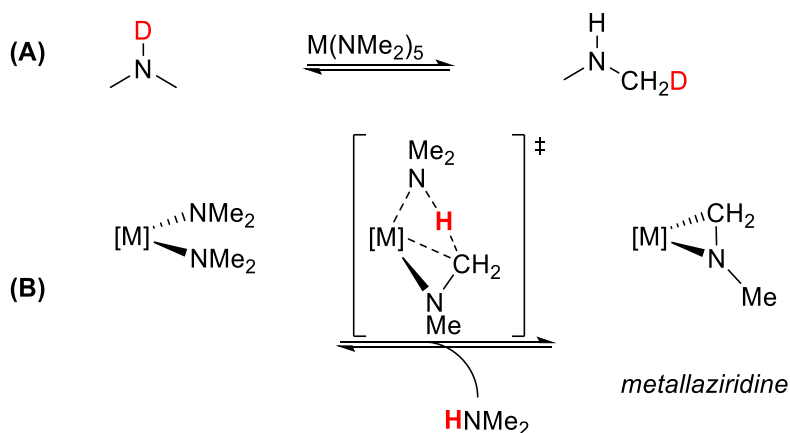
Scheme 1.3 Hydroaminoalkylation coupling a secondary amine with an alkene

To date, a variety of ETM and LTM catalyzed systems have been developed for this transformation. While LTM systems are mostly observed to be selective for linear products,²⁶⁻²⁸ ETMs in contrast give branched products (certain exceptions discussed *vide infra*).²⁹ Published in the literature in 1980, this reaction was first reported using homoleptic zirconium, niobium, or tantalum amido compounds to couple dimethylamine with 1-octene (Scheme 1.4).³⁰ These seminal reactions required high temperatures ($> 160\text{ }^{\circ}\text{C}$) and long reaction times, with a maximum yield of 38% after one week. Rapid deactivation of these systems was also observed if they were not kept under certain reaction conditions; the authors note that even heating a tantalum solution in toluene in the absence of an excess of amine leads to degradation. This report offered the first glimpse of the potential for ETMs to activate simple amines, while also demonstrating the importance of ligand design to provide kinetic stability to prevent catalyst decomposition.



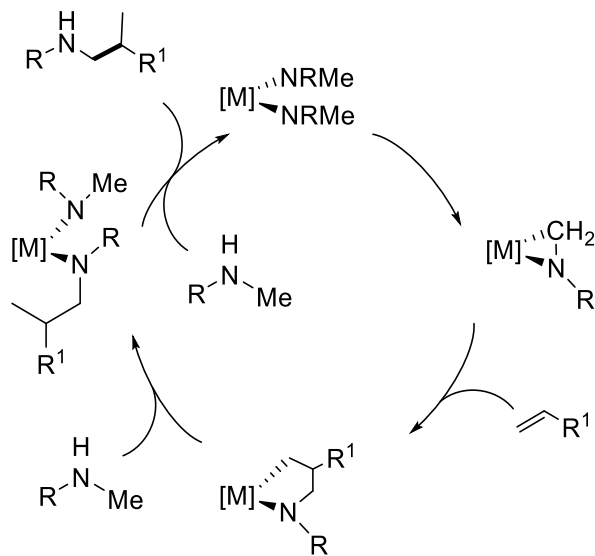
Scheme 1.4 Maspero's seminal report of reactivity³⁰

This report was followed by work by Nugent *et al.* in 1983 that sought to further understand the mechanism of this transformation.³¹ Using *N*-deutero dimethylamine, elevated temperature caused deuterium scrambling into the methyl group as observed by gas-phase IR spectroscopy and ¹H NMR spectroscopy. This was proposed from the formation of a key metallaziridine intermediate (Scheme 1.5):



Scheme 1.5 Observed deuterium scrambling leading to proposed metallaziridine³¹

This proposal was broadly relevant, as to that point the cyclometallation of d⁰ ETM complexes was rare. Based upon this key intermediate, catalysis was proposed to proceed *via* the “trapping” or insertion of an olefin into the metallaziridine, followed by product release *via* protonolysis by an incoming amine substrate (Scheme 1.6):



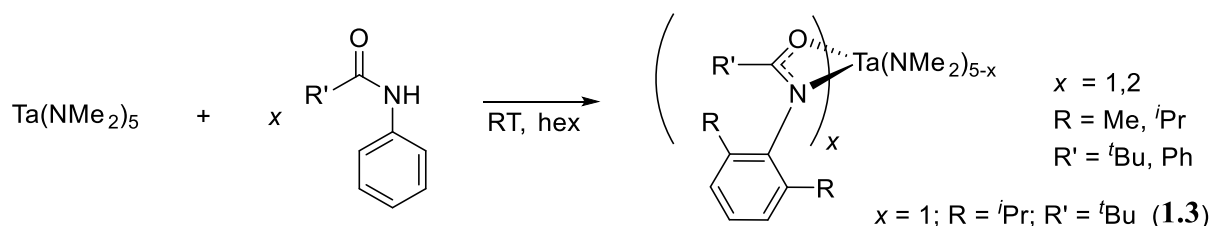
Scheme 1.6 First proposed mechanism for C-H amine alkylation³¹

While these initial reports demonstrated promising reactivity, development of this reaction with ETMs remained somewhat dormant until 2007. It was then reported by Hartwig that using *N*-aryl secondary amines, rather than dialkylamines, improved reactivity using group 5 tantalum catalysts. Using these substrates, synthetically useful yields (>60%) of the branched isomer were obtained using the same homoleptic tantalum amido complex Ta(NMe₂)₅ (**1.1**) as initially disclosed by Nugent.³² The higher observed reactivity of this substrate was foreshadowed by a previous report by Whitby, which experimentally showed that C-H activation at the α -carbon of an *N*-alkyl arylamido group is more facile than in an *N*-dialkylamido group.³³ Furthermore, this functionalization was selective for Csp³ over Csp² C-H bonds. Intriguingly, norbornene (NBE) was alkylated in high yield (96% at 4 mol% [Ta]), suggesting that this transformation can be applied to cyclic alkene substrates.

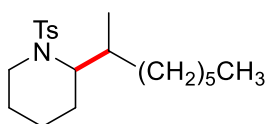
One year later, Hartwig reported that a dimeric complex [TaCl₃(NEt₂)₂]₂ (**1.2**) was more efficient for this reaction. As three amido groups have been effectively replaced with less electron donating halides, the generation of a more electrophilic metal centre was proposed to prompt

improved reactivity.³⁴ Using this catalyst, the reaction temperature was lowered to 90 °C and the scope of the reaction in amine was extended to less reactive dialkylamine substrates. Inspired by this work, catalyst development towards the formation of electrophilic, sterically protected metal centres began in earnest.

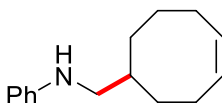
In 2009, the Schafer group reported a new class of amidate-supported tantalum complexes that were well-suited for this transformation.^{12, 35} A straightforward protonolysis reaction with easily prepared amide ligands enabled the facile formation of a series of electrophilic complexes with variable steric bulk (Scheme 1.7). Both mono- and di-amidate complexes were reported, where in the latter case the isolation and solid-state molecular structure of a tantallaziridine was observed (*vide infra*). Steric bulk at the *N*-aryl position was found to be important for reactivity, with optimized yield for the 2,6-diisopropylphenyl substituent (**1.3**).



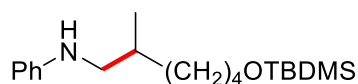
Expanded product scope of 1.3:



74 % yield
130 °C, 134 h



83 % yield
165 °C, 96 h



85 % yield
130 °C, 11 h

Scheme 1.7 Facile synthesis of mono-amidate Tantalum complexes and expanded product scope of 1.3³⁵

The mono-amidate catalysts ultimately proved superior for reactivity, with the substrate scope in amine expanded to include piperidines and silyl-protected alcohols using **1.3**. In addition

to demonstrating high yield and excellent diastereoselectivity (20>1 *exo*) in the alkylation of norbornene, this system also tolerated the less strained cyclic alkene cyclooctadiene (COD), albeit requiring 96 hrs at higher reaction temperatures (165 °C). This report also included a tethered, axially chiral ligand targeting enantioselectivity (complex **1.4**, Figure 1.4). Using a bridged, C₂-symmetric biphenyl di(amidate), an *ee* (enantiomeric excess) up to 61% was obtained.

Further efforts to develop enantioselective group V catalysts for HAA were provided by Zi and Hultzsich (Figure 1.4). Shortly thereafter our disclosure of Ta-amidate catalysts, Zi used a binaphthyl bridged di-amidate ligand to obtain *ees* up to 93% (**1.5**).³⁶ Their group subsequently disclosed complexes with various other chiral ligands, however no significant increase in enantioselectivity was observed.³⁷ Using a 3-3' silylated binaphtholate ligand on niobium (**1.6**), Hultzsich has demonstrated enantiomeric excess up to 98% in the coupling of *N*-methyl aniline (NMA) with trimethyl(vinyl)silane.³⁸ In contrast to Zi's work in which improved reactivity was observed with tantalum, Hultzsich's systems showed improved reactivity with niobium. This difference highlights how optimization of ligand design with choice of ETM are necessary for achieving optimal reaction selectivity and/or reactivity.

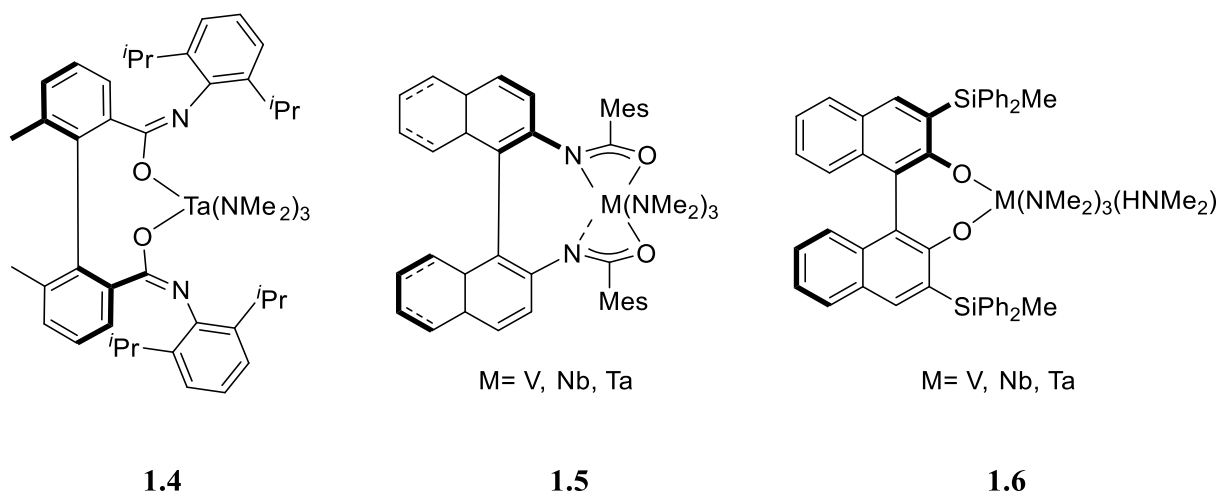


Figure 1.4 Group V complexes for enantioselective HAA from Schafer³⁵ (L), Zi³⁶ (M), Hultzsich³⁸ (R)

As these prior reports noted improved reactivity through the generation of an electrophilic metal centre, the already known and accessible starting material TaMe₃Cl₂ (**1.7**) was explored as a precatalyst.³⁹ While the methyl group is a σ electron donor, in the presence of amine substrate the driving force of releasing methane can presumably form highly reactive species. Correspondingly, this precursor shows modest reactivity as a stand-alone catalyst.³⁹ In 2013, it was found that using this starting material in conjunction with an *N,O*-chelating phosphoramidate ligand gave a catalytic system that was operative at room temperature (**1.8**, Figure 1.5).⁴⁰ When paired with this starting material, the increased steric bulk and electron withdrawing character imposed by the phosphoramidate ligand was proposed to provide improved reactivity in contrast to amidate complexes. With select substrate combinations, the reaction could also be performed solvent-free, which in combination with low temperatures renders this reaction relatively more Green. However, while showing broadly improved reactivity, this system was restricted to NBE and norbornadiene (NBD) as cyclic alkene substrates, possibly because of the large steric congestion about the metal centre. The starting material and catalysts were also observed to decompose rapidly when stored above freezing temperatures (> 20 °C) and in the presence of visible light, thereby limiting their practical use. This is proposed to originate from kinetic lability of the Ta-C bond, which has several pathways that lead to decomposition.

In recognition of this challenge, in 2014 a series of mixed chloro, amido-tantalum complexes supported with pyridonate ligands were reported with a broader scope of internal alkenes (**1.9**, Figure 1.5).⁴¹⁻⁴² Pyridonate ligands were installed with the goal of forming relatively more sterically accessible metal centres than related amidate and phosphoramidate complexes. While requiring higher reaction temperatures (>140 °C), this system can catalyze the alkylation of sterically demanding alkenes, including cyclic alkenes. In comparison to the mono-amidate system

1.3 that required a week at 165 °C to alkylate COD, this system could alkylate the more challenging cyclooctene in less than 24 hrs.

While the tantalum methyl complexes exhibit the lowest reaction temperatures known for this transformation, their lack of robustness has limited their practical use. To address this, Ta(CH₂SiMe₃)₃Cl₂ was investigated as a catalyst precursor. When combined *in-situ* with ureate ligands, this catalyst platform demonstrates unprecedented turnover frequency (TOF) and turnover number (TON) (**1.10**, Figure 1.5).⁴³ While heating above room temperature is required, divergent reactivity for terminal or internal alkenes can be obtained by variation of the ureate ligand used. Encouraged by these promising initial results, these systems are currently undergoing further optimization and mechanistic study.

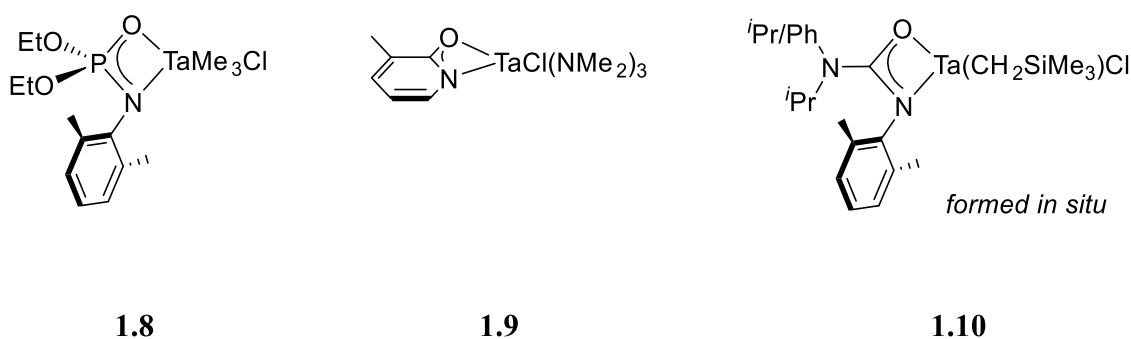


Figure 1.5 Recent leading examples of Ta HAA catalysts developed in the Schafer Group^{40-41,43}

These breakthroughs in catalyst development have transformed the field of HAA from seminal reports of fundamental reactivity to a diverse toolbox of catalytic systems. While no single combination of metal starting material and ligand is universally superior as a catalyst, a plethora of *N,O*-chelated systems are accessible that can be selected depending on reaction substrates. As gains in the practicality and versatility of this reaction have been realized, the products it can furnish have been explored as synthetic building blocks in organic and materials chemistry.

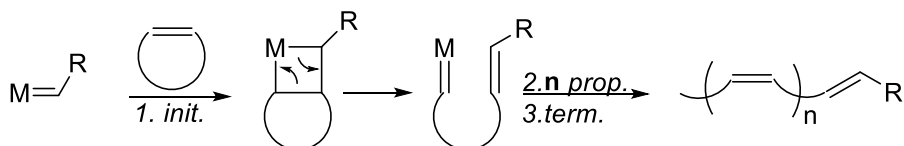
Recently, it has been demonstrated that HAA may be used to generate compounds that are highly relevant to medicinal chemistry. In 2013, **1.3** was used for the preparation of a variety of α -alkylated *N*-heterocycles.⁴⁴ This report also demonstrated this reaction in a one-pot alkylation/cyclization reaction to obtain large quantities of β -methylated *N*-heterocycles. In 2017, it was demonstrated that combining Ta(NMe₂)₅ with 3-methyl pyridone *in situ* generates a system (**1.11**) that can form a variety of α - and β -alkylated amines, which could then be cyclized towards the preparation of a variety of pharmaceutically relevant building blocks.⁴⁵ By utilizing commercially available catalytic starting materials, this method provided a practical route to the use of hydroaminoalkylation without the need of specialized equipment.

HAA products have recently been explored as precursors to polymerization towards the generation of amine-functionalized materials.⁴⁶ While initial reports of HAA were limited to the alkylation of terminal alkenes, new and more powerful generations of catalyst possess the reactivity to alkylate challenging internal alkenes. This allows the preparation of cyclic amine-containing alkenes as monomers for ring-opening metathesis polymerization (ROMP) to prepare polyolefinic materials bearing pendant amines (*vide infra*).

1.5 Application of HAA towards synthesis of precursors for polymerization

Advances in HAA have provided novel amine-containing monomers for the development of polymers through the use of ROMP. ROMP is a sub-category of olefin metathesis, a rearrangement reaction in which olefins are redistributed through the scission and regeneration of π bonds (Scheme 1.8).⁴⁷ The remarkable versatility and utility of olefin metathesis led to the recognition of Grubbs, Schrock and Chauvin with the Nobel Prize in 2005 for its discovery and mechanistic elucidation.⁴⁸ This reaction can be used to form polymers from the successive 'opening' of cyclic olefins. As a sub-category of olefin metathesis reactions, ROMP is a powerful

tool that can permit polymerization with defined molecular weight and moderate to high control (Scheme 1.8).⁴⁷



Scheme 1.8 General ring-opening metathesis polymerization (ROMP)

In the development of olefin metathesis catalysts, two dominant classes have emerged; Schrock⁴⁹ systems based upon molybdenum and tungsten, and Grubbs⁵⁰ systems based upon ruthenium (Figure 1.6). While the Schrock systems generally show higher reactivity, the use of ETM complexes lowers their stability to air and moisture and in general their lower functional group tolerance. Grubbs systems are less reactive overall but more easily handled and broadly functional group tolerant. As polymerization is entropically disfavored, the reaction requires strained cyclic alkenes to provide thermodynamic driving force through release of ring-strain.

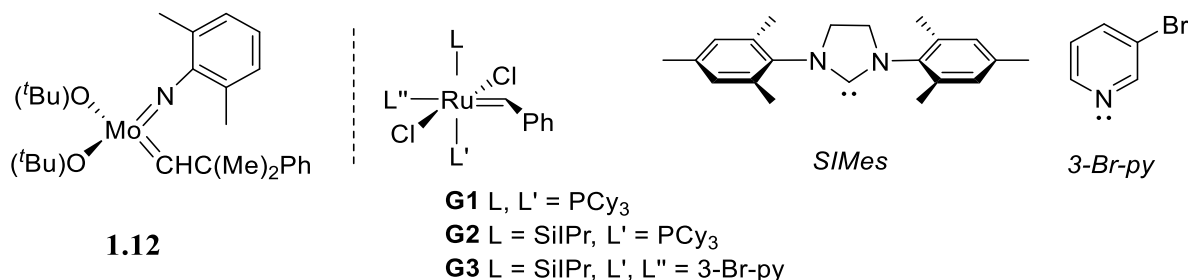
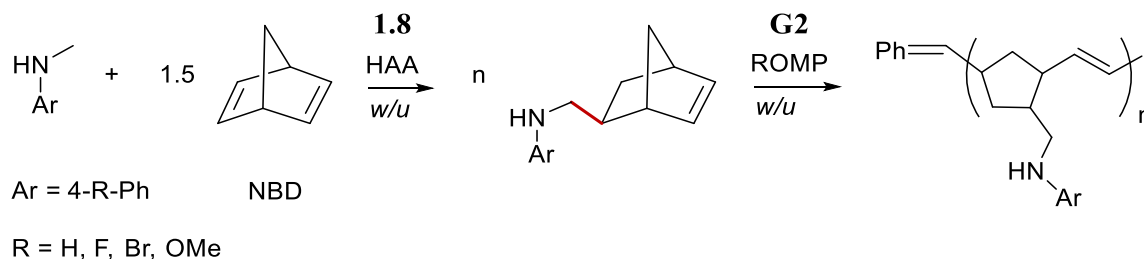


Figure 1.6 Representative examples of (L) Schrock⁴⁹ and (R) Grubbs⁵⁰ metathesis catalyst

In 2016, work in our group led by Dr Mitchell Perry demonstrated the catalytic synthesis of secondary amine-containing polymers using hydroaminoalkylation followed by ROMP.⁴⁶ Using **1.8**, NBD was selectively alkylated with a variety of secondary aryl amines at room temperature under solvent free conditions (Scheme 1.9). These amine-containing norbornenes (ACNs) were

shown to polymerize under living conditions using **G2** to obtain high molecular weight with narrow dispersity.



Scheme 1.9 Synthesis of amine-containing polymers by HAA followed by ROMP⁴⁶

The rheological properties of these poly(ACN) materials were investigated in collaboration with the Hatzikiriakos Group in Chemical and Biological Engineering (UBC). In comparison to polynorbornene, the presence of the secondary aryl amine substituent was found to have profound effects on viscoelasticity through the formation of hydrogen-bonded networks. Furthermore, varying the *para* substituent on the aryl ring allows for subtle tuning of these hydrogen-bonded features that may lead to different rheological properties. These polymers have potential application to materials science, wherein amine-containing materials have been used to fulfill a myriad of specialized roles, for example as compatibilizers,⁵¹ semiconductors,⁵² anti-microbials/anti-biofouling,⁵³⁻⁵⁵ gas uptake,⁵⁶⁻⁵⁷ and as coatings.⁵⁸

1.6 ETM initiators for ring-opening polymerization of cyclic esters

While a significant focus in the Schafer group has been towards the synthesis of amines, the large family of *N,O*-chelated ETM catalysts that have been explored have proven useful to other transformations. One such transformation is the ring-opening polymerization (ROP) of cyclic esters.⁵⁹ These polyesters as a general class demonstrate rapid degradation in comparison to traditional polyolefin plastics and have been investigated as biodegradable materials.⁶⁰⁻⁶¹ Owing

to the large and ever-growing interest in sustainable materials, a vast number of initiator systems spanning the periodic table have been investigated for this transformation.⁶²⁻⁶³

The investigation of titanium complexes as initiators^{2, 64-85} for the ring-opening polymerization of cyclic esters has been largely driven by the minimal cost, high abundance, and low toxicity⁸⁶ of the source metal. Titanium examples include species ligated with tetradentate amino-phenolates,⁸⁷ salen ligands,⁸⁸ catecholates,⁸⁹ aminodiols,⁶⁶ thio-etherphenolates,⁸⁵ sulfur or tellurium bridged bimetallic species,⁸³ and sulfonamide supported complexes.⁷⁵ Typically, these complexes range from tetra- to hexa-coordinate species with bulky ancillary ligand(s) to vary the steric and electronic environment about the metal center. In addition, they also possess one or more ‘reactive’ ligands (alkoxide, aryloxy, and halogen initiating ligands^{78, 90-91}) that function as the nucleophilic ligand for polymerization initiation. Select examples of titanium complexes bearing bulky ancillary ligands are shown in Figure 1.7.

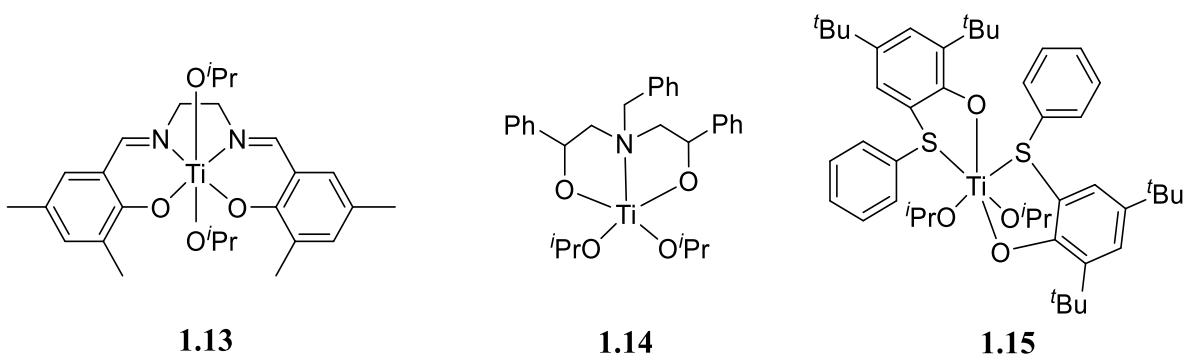
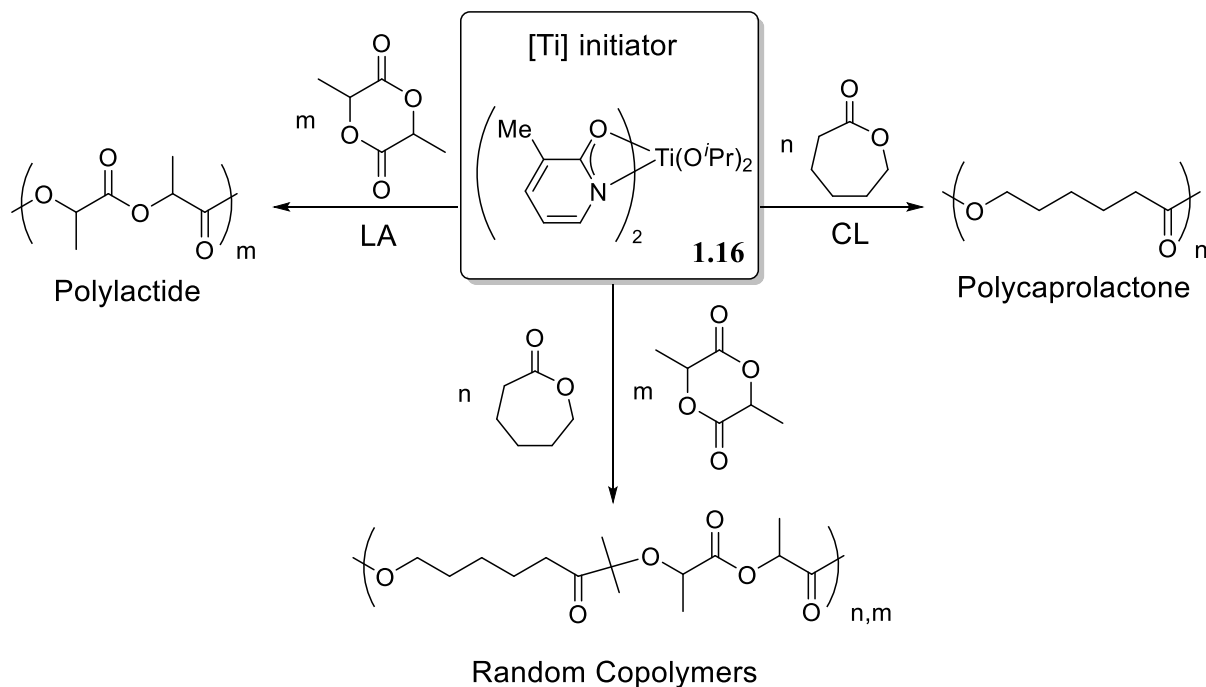


Figure 1.7 Select examples of titanium ROP complexes^{66, 85, 88}

In 2013, we communicated that titanium pyridonate complexes were suitable initiators for ROP of *rac*-lactide (LA) and ϵ -caprolactone (CL) (Scheme 1.10).² These systems are competitive with other leading examples of titanium-initiated ROP of cyclic esters.^{66-67, 71-72, 74, 92} From this initial report, a variety of titanium pyridonates were rigorously screened for the homo and co-polymerization of these cyclic esters, with the goal of obtaining an initiator that demonstrates

greater control over the reaction (Scheme 1.10). Examples of desirable control would be the ability to afford precise molecular weight under living conditions or control the stereochemistry of lactide polymerization.⁵⁹



Scheme 1.10 Preparation of polyesters of lactide (LA) and caprolactone (CL) and a typical titanium pyridonate initiator²

1.7 Scope of thesis

The central theme of this research is the development of catalytic methodology that can be applied to the synthesis of polymeric materials. The focus for catalyst development has been the use of homogeneous early-transition metal complexes bearing *N,O*-chelating ligands. The hydroaminoalkylation reaction has been mechanistically investigated to inform the development of amine-containing small molecules as precursors to ring-opening metathesis polymerization (ROMP). The ability of these different monomers to undergo polymerization has then been probed, and the physical properties of resultant materials studied. Another transformation that has been

explored with *N,O*-chelated ETM complexes is the ring-opening polymerization of cyclic esters to form biodegradable polyesters.

As a method to access amine-functionalized small molecules, the mechanism of tantalum-catalyzed hydroaminoalkylation has been probed in Chapter 2. In the development of this reaction, the Schafer Group has disclosed a series of tantalum-based catalyst systems bearing *N,O*-chelating ligands. Within this class, a tantalum mono-amidate complex has among the broadest scope in substrate reported in the literature. To better understand its reactivity and understand key features of its potential energy surface, theoretical modelling using density functional theory has been performed. This was followed by the development of an experimental method to corroborate predictions generated from calculations. Challenges in experimental studies highlight the complexity in examining this important transformation.

With a more sophisticated understanding of HAA, it has been utilized in Chapter 3 to generate amine-containing monomers for polymerization. The application of this methodology to produce amine-functionalized polyethylene derivatives has been compared to current methods of preparation in the literature. Using insight gained from Chapter 2, optimized routes for monomer synthesis have been explored to improve the efficiency and practicality of this reaction. This enables the synthesis of amine-containing cyclic olefins, which are polymerized using ROMP. A series of amine-functionalized polyethylene analogs have been prepared and are observed to have dramatic physical properties, including self-healing.

In Chapter 4, the formation of biodegradable polymers using titanium-catalyzed ring-opening polymerization of cyclic esters has been examined. A series of titanium pyridonate complexes have been prepared and tested for their effectiveness in the ROP of two different monomers, *rac*-lactide and caprolactone. Various polymer architectures, including linear

homopolymers and block and random copolymers, have been prepared and characterized. As polymers containing ester groups as hydrogen-bond acceptors, the compatibility of these polymers with those prepared in Chapter 3 has been briefly investigated.

Chapter 5 has disclosed initial investigations of reactivity with the cyclic ester methylene lactide. In stoichiometric reactions with ruthenium, novel complexes have been serendipitously discovered that may prove highly relevant as catalysts and/or mechanistic probes.

Chapter 6 has summarized key conclusions in this thesis and the future outlook of this research. Opportunities to take advantage of new advances in the field of reaction monitoring have been discussed for their potential to gain further insight into the HAA reaction. With novel amine-containing polymers in hand, future directions in the application of these new materials have been highlighted.

Chapter 2: Insights into the mechanism for Ta-catalyzed hydroaminoalkylation using experimental and computational methods

2.1 Introduction: Probing the mechanism of hydroaminoalkylation

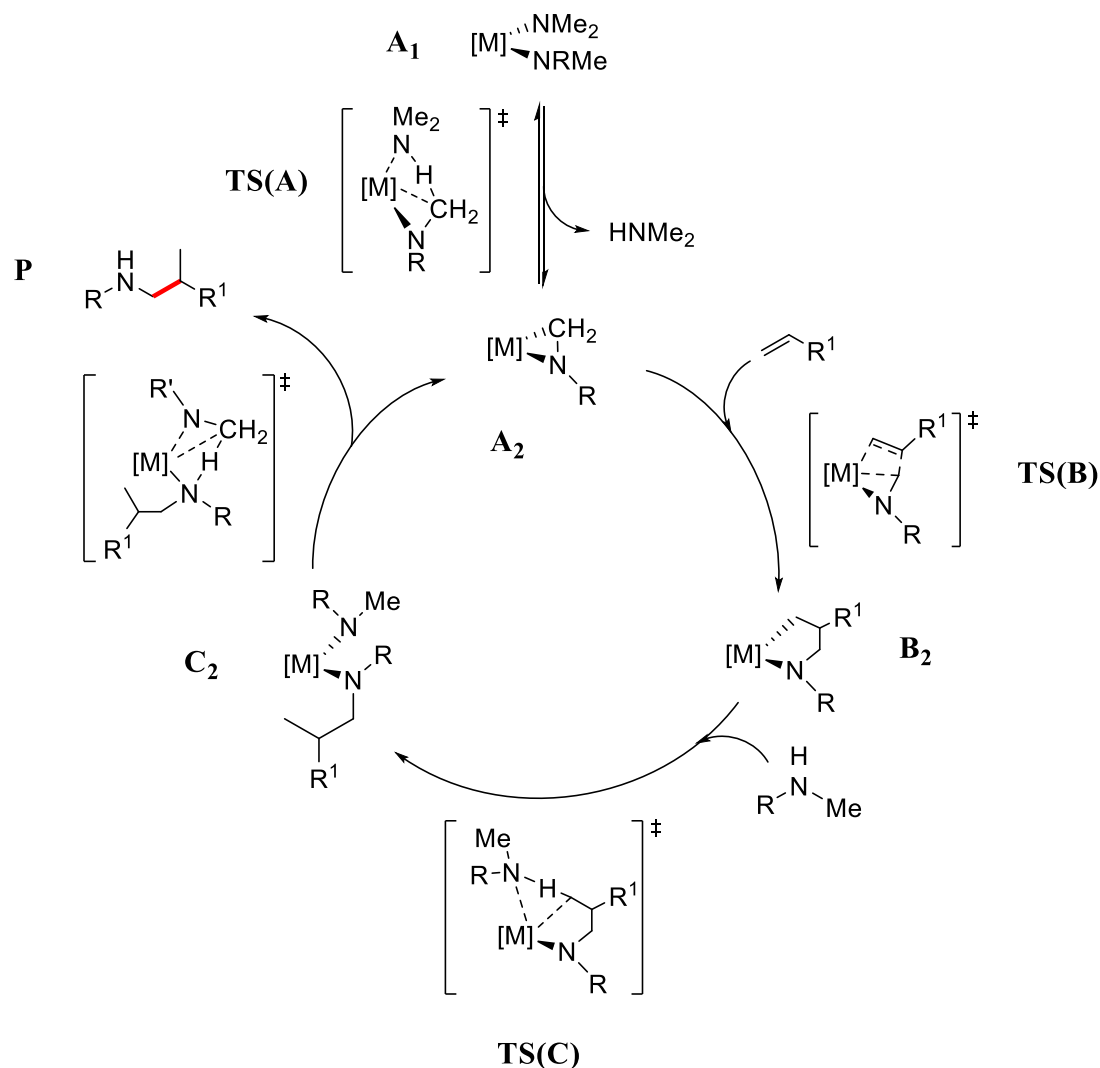
Hydroaminoalkylation (HAA) has developed into a useful reaction for the catalytic synthesis of amines, however, certain aspects of the reaction mechanism remain unclear. Experimental approaches have provided some clues into the nature of the reaction; for example, Nugent's deuterium labelling studies in 1983 proposing metallaziridines as catalytically active species remains the foundation upon which the reaction is envisioned.³¹ However, a clear elucidation of the reaction mechanism remains fleeting. As a catalytic reaction, several steps and side-equilibria are taking place simultaneously, obscuring the identification of any one species or intermediate experimentally. As early-transition metal systems are sensitive to air and moisture, the variety of analytical techniques that can be used is limited to those that can be conducted while maintaining inert reaction conditions, which proves challenging in sampling or measuring without perturbing the system.

While fraught with these limitations, the quest for insight to guide catalyst development has prompted a variety of approaches to probe the reaction mechanism.^{12, 42, 93-95} Deuterium labelling studies have proven highly useful in predicting rate dependencies and the relative energetics of reaction steps. Isolation of reaction intermediates or decomposition products can also provide valuable clues as to how the reaction proceeds. Kinetic studies to determine order of reaction in various substrates can enable assignment of rate-limiting steps. The rapid growth of computing power has also seen the development of various computational approaches, including density functional theory, to probe reactions.⁹⁵ Most importantly, a combination of all these

approaches is required to assemble the necessary information to understand the reaction. The goal is to develop a synergy between experiment and theory that can identify the key features of optimized catalyst structure and reactivity.

2.1.1 Experimental methods

The principal objective in this chapter is the interrogation of the HAA mechanism proposed by Nugent in 1983 using computational and experimental approaches. While this mechanism is generally accepted, its simplicity fails to account for the origin of improved reactivity and selectivity. As a multi-step reaction, the overall rate of all steps is limited by the slowest, turnover-limiting step (TLS). Thus, the identification of this step is critical to enable logical structural modifications towards improved catalytic efficiency. Scheme 2.1 depicts the proposed transition state structures for the catalytic cycle of the HAA of a terminal olefin with a secondary amine.

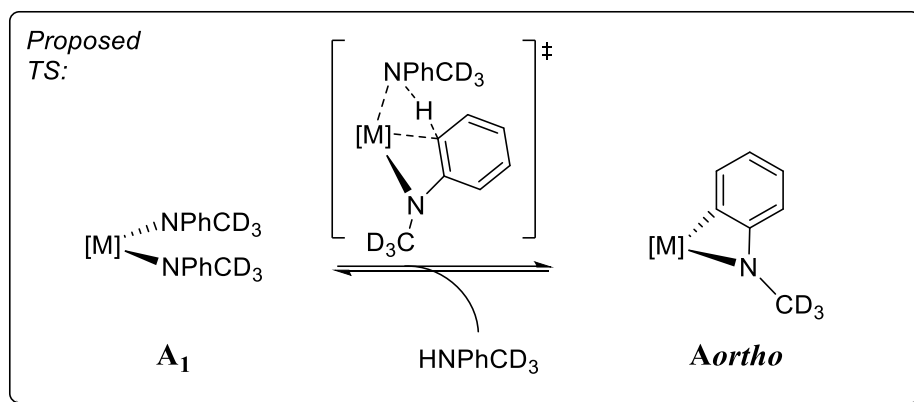
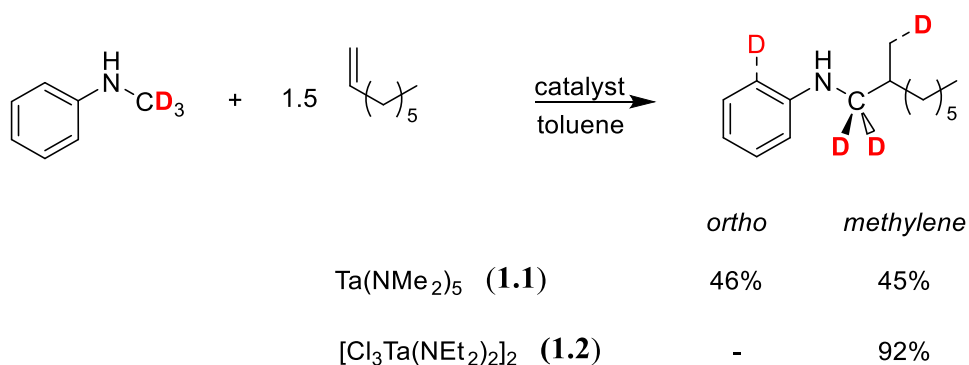


Scheme 2.1 Key transition states proposed in the general HAA mechanism²⁹

The proposed catalytic cycle for HAA is comprised of three key steps: C-H activation transition-state A (TS(A)), alkene insertion TS(B), and protonolysis TS(C). C-H activation of **A₁** results in metallaziridine formation (**A₂**), liberating an equivalent of neutral amine. The resulting 3-membered metallaziridine is then primed for alkene insertion, resulting in a five membered metallacycle (**B₂**). Another equivalent of amine then liberates the M-C bond by protonolysis. Product release was proposed by Nugent to occur through exchange with another equivalent of

amine (transamination).³¹ Alternatively, the product may be released by a similar C-H activation as in TS(A), re-generating the metallaziridine for the next turnover (as depicted in Scheme 2.1).

As previously discussed, Hartwig's report in 2007 re-invigorated interest in HAA by demonstrating that *N*-alkyl aryl amines showed enhanced reactivity compared to dialkylamine substrates, reducing reaction times from one week to a more practical 24 hrs.³² To probe the reversibility of tantallaziridine formation, the isotopically labelled *N*-(methyl-*d*₃) aniline was used as an amine substrate under catalytic reaction conditions (Scheme 2.2). Upon measuring the relative incorporation of deuterium in different positions in the product amine, significant loss of deuteration at the methylene position was observed, indicating that tantallaziridine formation is a reversible process. Another key observation is the incorporation of deuterium at the *ortho* position on the aryl ring. As no products with functionalization at this position are observed, this result suggests *ortho*-metalation is a side-equilibrium off the catalytic cycle.

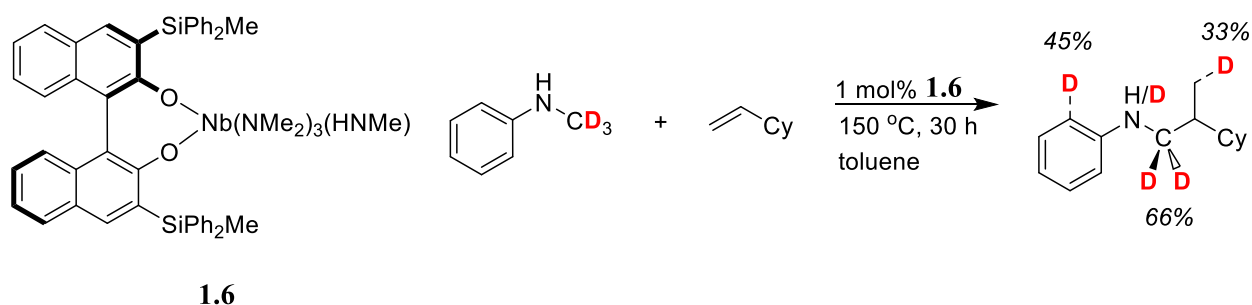


Scheme 2.2 Deuterium incorporation with d_3 -NMA and corresponding proposed TS structure for *ortho*-metalation of **A₁**^{32, 34}

The same deuterium-labelling experiment was completed with $[\text{TaCl}_3(\text{NEt}_2)_2]_2$ (**1.2**) in 2008.³⁴ With this catalyst, the methylene position retains >90% of its deuterium, suggesting that reversion of the tantalaziridine is not significant compared to alkene insertion. No deuteration was observed at the *ortho* position, suggesting *ortho*-metalation is not a competing side-reaction. Compared to **1.1**, the avoidance of off-cycle equilibria could partly account for the improved reactivity observed with this catalyst. Furthermore, this difference also demonstrates how changing the electronics of the metal centre can result in significant changes to the relative energetics of the cycle.

A significant mechanistic investigation was conducted by the Hultsch group to explore the origin for improved reactivity with their platform of binaphtholate-bridged tantalum and

niobium complexes.⁹³ Using *N*-(methyl-*d*₃) aniline with their tantalum system, loss of deuterium incorporation at the methylene position suggested that tantallaziridine formation was reversible in this system (Scheme 2.3). Significant incorporation at the aryl *ortho* carbon (45%) suggests *ortho*-metalation is also a competing pathway in this system; this was also observed in the amine in the absence of alkene, providing evidence this side-equilibria is occurring prior to alkene insertion. Using their analogous niobium complex (**1.6**) under the same conditions, no significant deuterium is depleted from the methylene position (95%), nor is any significant *ortho*-metalation observed. As higher reactivity is generally observed when pairing niobium with their ligand-set, they attribute the absence of extensive off-cycle equilibria as an important factor for improved catalysis.



Scheme 2.3 Observed deuterium incorporation in **1.6**⁹³

Empirical rate laws were determined for their niobium complex. Using either vinylcyclohexene or 1-octene as amine substrates, they determined a rate law that was first order in catalyst and amine. This dependence in catalyst validates a mono-metallic pathway. Different orders in alkene were observed: with the less bulky 1-octene no rate dependence was observed, while with the bulkier vinyl-cyclohexylamine first-order kinetics were observed at low alkene concentrations. Therefore, the rate can depend on alkene concentration when bulky alkene substrates are used.

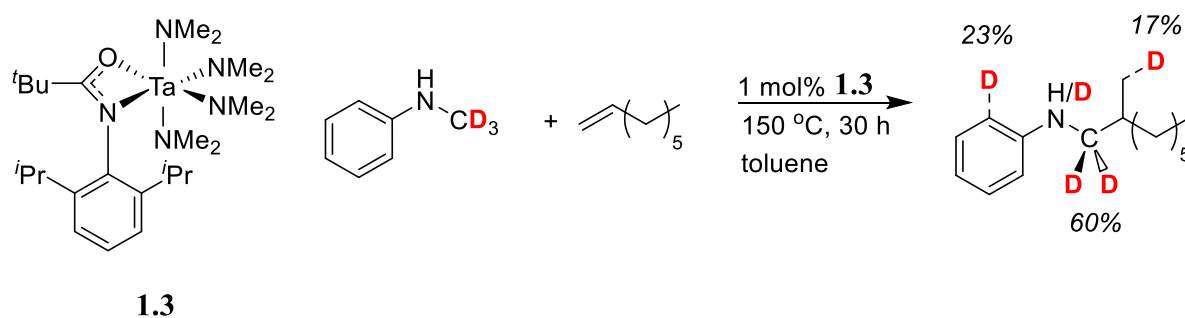
Kinetic isotope effect (KIE) experiments were also performed to probe substrate dependence on rate. Using their niobium catalyst, no KIE was observed using *N*-(methyl- d_3) aniline, suggesting metallaziridine formation is not turnover-limiting. However, *N*-deutero methyl aniline had a KIE of 1.6 ± 0.1 , which led the authors to propose amido exchange as turnover-limiting in cases when alkenes lacking steric bulk are used.

This work from Hultsch represents key findings of the HAA cycle while also demonstrating the challenges in studying this reaction. With a focus on their more reactive niobium catalyst, they were able to derive rate laws that agreed well with reaction simulations. However, this work also showed that trends in reactivity with a given metal-ligand environment depend heavily on both the steric and electronic properties of the substrates. This work also demonstrated the challenges in probing the mechanism of catalysts that contain amido ligands, which upon liberation can coordinate to the metal as neutral amines in non-productive resting states, or act themselves as substrates, thus obscuring the key steps of interest.

Related efforts have been conducted in our group towards understanding the mechanism of mono-amidate tantalum catalyst **1.3**. This catalyst has among the broadest substrate scope of all group V catalysts, tolerating a broader scope of amine and alkene substrates than reported for **1.2**.^{12, 35, 44, 96} Thus, a variety of experimental techniques have been applied with the goal of uncovering the key features that enable this system's improvement on reactivity.

As was observed in Hultsch's work, the presence of amido groups on catalyst **1.3** heavily complicates reaction analysis. During catalysis, isolable quantities of byproducts formed from unwanted reactivity between 1-octene and liberated dimethylamine are obtained, including mono- and di-alkylated amines. While only formed in minor quantities, these unwanted side reactions prevent accurate monitoring of alkene consumption.

Deuterium incorporation was also investigated with complex **3** using *N*-(methyl-*d*₃) aniline as a labelled substrate along with 1-octene under catalytic conditions (Scheme 2.4). Significant deuteration was observed in the *ortho* position (23%), while depletion was observed at the methylene position (60% D). As was observed in the homoleptic Ta(NMe₂)₅ system, this suggests reversible tantallaziridine formation and competing *ortho*-metallation side-equilibria. When this substrate was also reacted with **1.3** in the absence of alkene, free dimethylamine was detected at room temperature by ¹H NMR spectroscopy, suggesting facile aziridine formation and/or transamination. When this same sample is heated to 65 °C, substantial scrambling of hydrogen into the *d*₃-methyl group is noted, and integrations assigned to *ortho* C-H protons decrease. While no catalysis has been noted at these lower temperatures, this observed reactivity at sub-catalytic temperatures suggests tantallaziridine formation is not turnover-limiting. Some kinetic isotope effects were observed when investigating the initial rates of *N*-(methyl-*d*₃) aniline and of *N*-*D*-(methyl-*d*₃) aniline with 1-octene (*k*_H/*k*_D = 1.4 ± 0.1 and 1.5 ± 0.1 respectively). With these experiments, it should be noted that *ortho*-metalation is likely ‘diluting’ the deuterium label, as *ortho* hydrogen atoms can be exchanged with deuterium on the nitrogen, and, ultimately, the methyl group as well.



Scheme 2.4 Observed deuterium incorporation in **1.3**¹²

Kinetic studies were conducted to probe the reaction order in amine, alkene, and catalyst. Using pseudo-first order conditions, in which a ten-fold excess of catalyst and alkene are used, the amine substrate was consumed linearly, suggesting zero-order dependence on amine. The reaction was found to be first-order in catalyst concentration up to 5 mol%, suggesting a mono-metallic complex effects catalysis. No increases in rate are observed with higher catalyst loading, this is proposed to be due to the formation of unproductive multi-metallic species. When the reaction was compared at different absolute concentrations (concentration of catalyst/substrates constant with respect to one another) the observed rates were indistinguishable. This suggests that variable catalyst loading relative to the substrates affects reaction rate, but that the concentration of the reaction solution does not.

Pseudo-first order conditions could not be adopted to monitor the rate dependence on alkene. As the *ortho* C-H proton of the *N*-methyl aniline substrate is used as a diagnostic handle in the ^1H NMR spectrum to probe reaction conversion, using a large excess of amine causes reactant and product peaks to overlap, preventing their comparison. Analysis of alkene consumption is likewise complicated by the formation of by-products with dimethylamido groups on the catalyst starting material. A series of catalytic runs were prepared where the alkene concentration was varied while the other reagents/catalyst remained constant. These runs showed a dependence of rate on alkene concentration, leading to assignment of alkene order as “non-zero”.

Together, these experiments led to the description of the rate law for HAA with mono-amidate tantalum complexes as zeroth order in amine, first order in catalyst, and non-zero order in alkene. Additionally, to investigate whether one-electron radical chemistry may be operative with these systems, an alkene substrate bearing a cyclopropyl moiety was prepared. The ring-opening of cyclopropyl rings is a well-known radical process; the detection of ring-opened products under

catalytic conditions can be used to detect radical species. As no ring-opening is observed in the full consumption of this alkene, a one-electron process as part of the HAA mechanism was disregarded with mono-amidate tantalum complexes.¹²

2.1.2 Computational methods to probe the mechanism

Seeking to complement the experimental data, the use of computational methods has become increasingly powerful as a means of corroborating and predicting results. As computing power has rapidly expanded and easy-to-use software has become available, the use of density functional theory (DFT) calculations to rationalize empirical observations has become common.⁹⁷ The speed and accuracy of these calculations have also enabled predictions about how a chemical system may behave. Computations may also be used to predict species that are short-lived and/or very challenging to detect physically. Thus, the interplay of experimental and theoretical techniques offers a synergistic and promising approach to molecular design.

DFT has become a preeminent and versatile tool in the theoretical investigation of transition-metal catalyzed reactions.⁹⁸⁻⁹⁹ It can be used to calculate the electronic structure of an atom, molecule or phase by considering them as bodies of electrons. A functional expression can then be used to approximate spatially-dependent electron density. These functionals can be calculated for a multi-body system such as a molecule, giving a total density functional that can approximate the total ground state energy.

DFT has been used as a tool in the field of ETM-catalyzed HAA as a means of understanding reaction mechanism and informing catalyst design. Calculations have been carried out on Group 3 scandium-catalyzed HAA of tertiary amines with alkenes.⁹⁵ This study proposed a turnover-limiting step of C-H activation that agreed well with KIE experiments. The charge distribution of fifteen different alkene substrates was also calculated and shown to be an effective

means for predicting the regioselectivity of alkene insertion. Doye and coworkers have also used computational tools to probe the intramolecular HAA of primary aminoalkenes using group 4 catalysts.⁹⁴ In their system, they found C-H activation to be turnover-limiting, which is in agreement with their KIE experiment suggesting the RDS involves breaking a C-H bond.

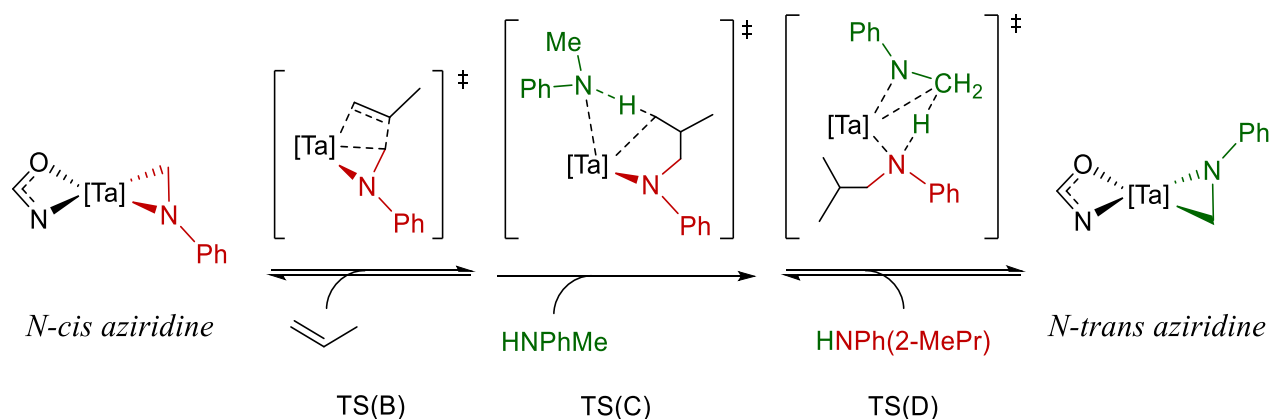
Efforts in the Schafer Group have likewise sought to provide corroboration of experimental trends of reactivity with theoretical calculations. This investigation was initiated by former graduate student Dr Jean Michel Lauzon, beginning with using DFT to interrogate the mechanism of HAA put forth by Nugent with catalyst **1.3**.⁹⁶ This cycle was modelled using *N*-methyl aniline and 1-octene as model substrates. Using B3LYP as a hybrid functional, transition states were found for the proposed key steps in the mechanism.

The calculation of this mechanism provided several key findings. In the initial C-H activation step TS(A), the formation of the catalytically active tantallaziridine was found in the plane of the chelating amidate, suggesting that this ligand promotes catalysis in the equatorial plane. The amidate ligand is bound to the metal in a $\kappa^1(O)$ fashion; this suggests the hemilability of the ligand to provide steric relief about the metal centre could be an important property of active systems. The turnover-limiting step was found to be protonolysis, with an activation energy of 47.7 kcal•mol⁻¹.

This proposed cycle represents the first known mechanism for group 5 HAA supported by computational calculations. However, this theoretical cycle does not completely align with experimental results. Computationally, protonolysis was predicted to be turnover-limiting, with a transition state over 7 kcal•mol⁻¹ higher than any other TS in the pathway. However, experimentally the reaction was found to be zero-order with respect to amine. Instead, alkene

insertion was proposed as the TLS, which theoretically was predicted to have a much lower barrier (24.6 kcal•mol⁻¹).

In the proposed cycle, it was also unclear how the catalytically active species was regenerated. After one turnover of catalysis, the tantallaziridine would be in an opposite orientation from the chelate than which it began, with *N* of the tantallaziridine *trans* to *N* of the amidate (Scheme 2.5). The subsequent steps in the cycle were calculated for this orientation; protonolysis was still found to be the RDS (+0.9 kcal•mol⁻¹) while alkene insertion had a much higher barrier than the first cycle (+ 12.5 kcal•mol⁻¹). From these calculations it was undetermined whether the cycle flips geometry on every turnover or whether there exists a cross-over point where the geometries isomerize at any point in the cycle.



Scheme 2.5 Reversion of tantallaziridine geometry after a catalytic cycle

The methodology used in this proposed theoretical cycle was applied appropriately; however, it was limited to one functional method, B3LYP. The use of one DFT method in combination with the high magnitude of the TLS (over 45 kcal•mol⁻¹) caused the theoretical results to be treated with some skepticism. With the large variety of computational resources available today, increasing the scope of methodology with respect to DFT functional, basis-set, and inclusion of interactions such as solvent and dispersion was sought to validate the accuracy of the

obtained calculations. In search of alternative pathways with lower energy, every step in the proposed mechanism was re-interrogated with different possible geometries or transformations to rule out alternative mechanisms. These efforts were conducted during an academic internship under the supervision of Professor Eric Clot of the Université de Montpellier II and comprise the leading topics discussed in Chapter 3.¹⁰⁰

2.1.3 Scope of Chapter

This chapter explores the mechanism of tantalum-catalyzed HAA of terminal olefins with secondary amines using computational and experimental approaches. To date improved catalysts for this transformation have been discovered empirically. Generalized ligand design parameters for early transition metal reaction development is an active area of research.¹⁰¹ Thus, a theoretical understanding of the mechanistic details of this reaction could provide useful insights for the ongoing development of improved ligands for Ta HAA catalysts. A computational model of the proposed mechanism for tantalum catalyzed hydroaminoalkylation has been sought to provide a mechanistic rationale for why *N,O*-chelated complexes show improved reactivity over other reported systems. DFT calculations have been performed on modelled transition state structures and intermediates of the proposed catalytic cycle. The key goals of this theoretical cycle were to determine turnover-limiting steps, visualize molecular structure during these steps to inform catalyst design, and probe the origin of improved reactivity using *N,O*-chelating amidates as supporting ligands.

Based upon the report by Hartwig in 2008, it has been established that improved reactivity over homoleptic Ta(NMe₂)₅ species is obtained upon replacement of spectator amido ligands with chloro groups. This report suggests that improved reactivity is obtained when the electronic properties of the complex is tuned to create a more electrophilic metal centre. To test this

hypothesis, modelling has also been performed on $\text{TaR}(\text{NPhMe})_2\text{Cl}_2$ with R as either an electron donating (methyl) or electron withdrawing (chloro) ligand. The results from these models have been compared with that of the tantalum mono-amidate catalyst, **1.3**.

These theoretical investigations have been followed by the development of a new methodology to experimentally explore kinetic isotope effects, with the goal to compare experimental trends with theoretical predictions. This new method has utilized GC-FID as a means of separating and quantifying reaction analytes, thus providing a complement to previous strategies using NMR spectroscopy. These experiments included the synthesis of a novel deuterium-labelled amine substrate that prevents experimental error from *ortho*-metallation. This method has then been applied to the HAA of 1-octene with *N*-methyl aniline using mono-amidate tantalum complex **1.3**.

Theoretical calculations have also provided a predicted low-energy intermediate whose isolation was attempted experimentally. This intermediate has been proposed to be a non-productive resting state that can be accessed by tantalum amidate complexes bearing minimal steric protection. During these efforts, a tantalum-oxo cluster compound has been obtained serendipitously as a proposed decomposition product.

2.2 Results and Discussion

2.2.1 Modelling HAA of terminal olefins with secondary amines using DFT

Initial efforts into developing a new theoretical understanding of the mechanism first required selection of DFT method and basis set. To reduce the computational cost and time required for initial calculations, a structurally more simple amidate-supported tantalum catalyst bearing only dimethylamido ligands was chosen as a model system for **I** (Figure 2.1)

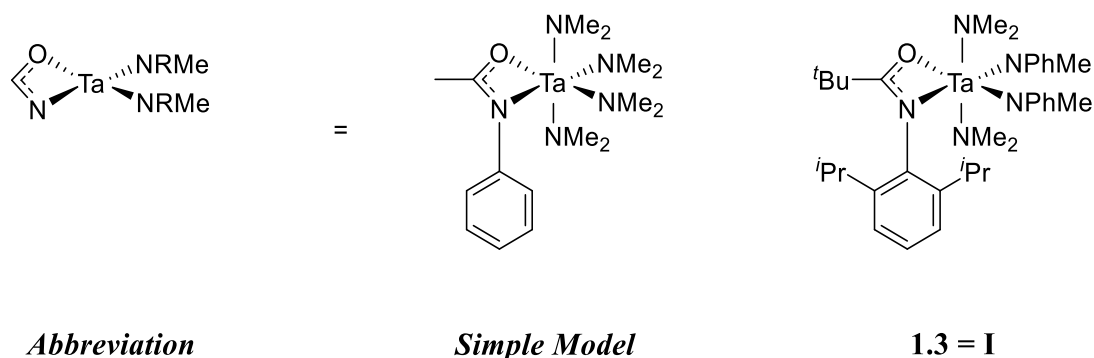


Figure 2.1 Simple model used for rapid comparative calculations to build to the fully calculated model (I) for system 1.3

Using this simple model, the first TS (tantallaziridine formation, TS(A)) was located and calculated using a variety of DFT methods with progressively larger basis sets. Within computational calculations, the opportunity exists for error from methodology and basis set.¹⁰² To minimize error associated with methodology, nine different functional methods were used to calculate the energy barrier of TS(A). B3PW91 and M06 were selected based on the interpretation of their output by Prof. Clot. Errors from basis set can occur when the basis set is not sufficiently large for a calculation to provide an accurate approximation. To ensure our basis sets were sufficient, the calculation for each method was repeated at progressively larger basis sets and compared to ensure optimizations had reached convergence.

Using this methodology, the ‘simple model’ system enabled rapid and inexpensive calculations to be performed on the proposed TS structures as well as explorations of alternative steps and/or transformations. Optimizations from the simple model were then optimized (B3PW91) with the full catalyst system **I** using *N*-methyl aniline and propene as substrates. The single-point energy (SPE) of these optimizations was then calculated at a high level of theory including solvent interactions and dispersion (B3PW91/Def2-QZVPP + SMD(Toluene)). In this discussion, all ΔG values were calculated using this full calculation in reference to system **I**. The energy of all species in a cycle is given with respect to the initial species at 0.0 energy; however, the individual activation energy barrier for each TS is described with respect to the lowest point in the potential energy surface. Calculations explicitly referring to this ‘simple model’ were sufficiently high in energy to not warrant full calculation in **I**.

A key trend in Ta-catalyzed HAA is the observation of improved reactivity when the electronics of the complex are tuned to create a more electrophilic metal center. To test this hypothesis, modelling was also performed on $\text{TaR}(\text{NPhMe})_2\text{Cl}_2$, with R as either an electron-withdrawing (chloro) (**II**) or electron-donating (methyl) (**III**) ligand (Figure 2.2). Modelling on **II** can be related to the known catalyst $[\text{Cl}_3\text{Ta}(\text{NEt}_2)_2]_2$ (**1.2**), which is presumed to effect HAA after breakup of the dimer.³⁴ These calculations were compared with **I** to explore the effect of the sterically bulky, electron-withdrawing amidate ligand on catalysis.

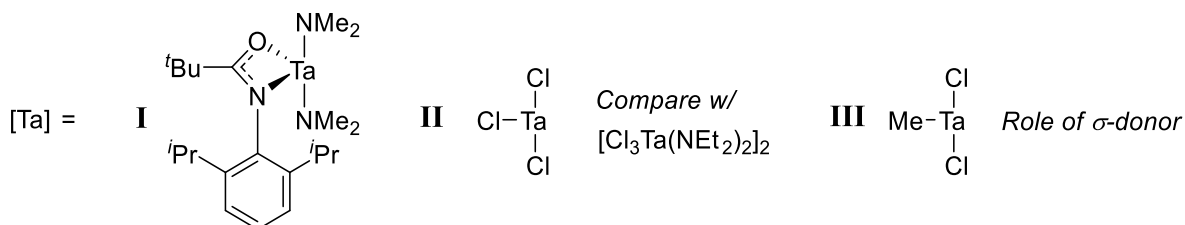


Figure 2.2 Complexes modelled as HAA catalysts

The resulting energy profiles for **I-III** are depicted as a potential energy surfaces in (Figure 2.3). These are followed by an in-depth discussion of each individual step.

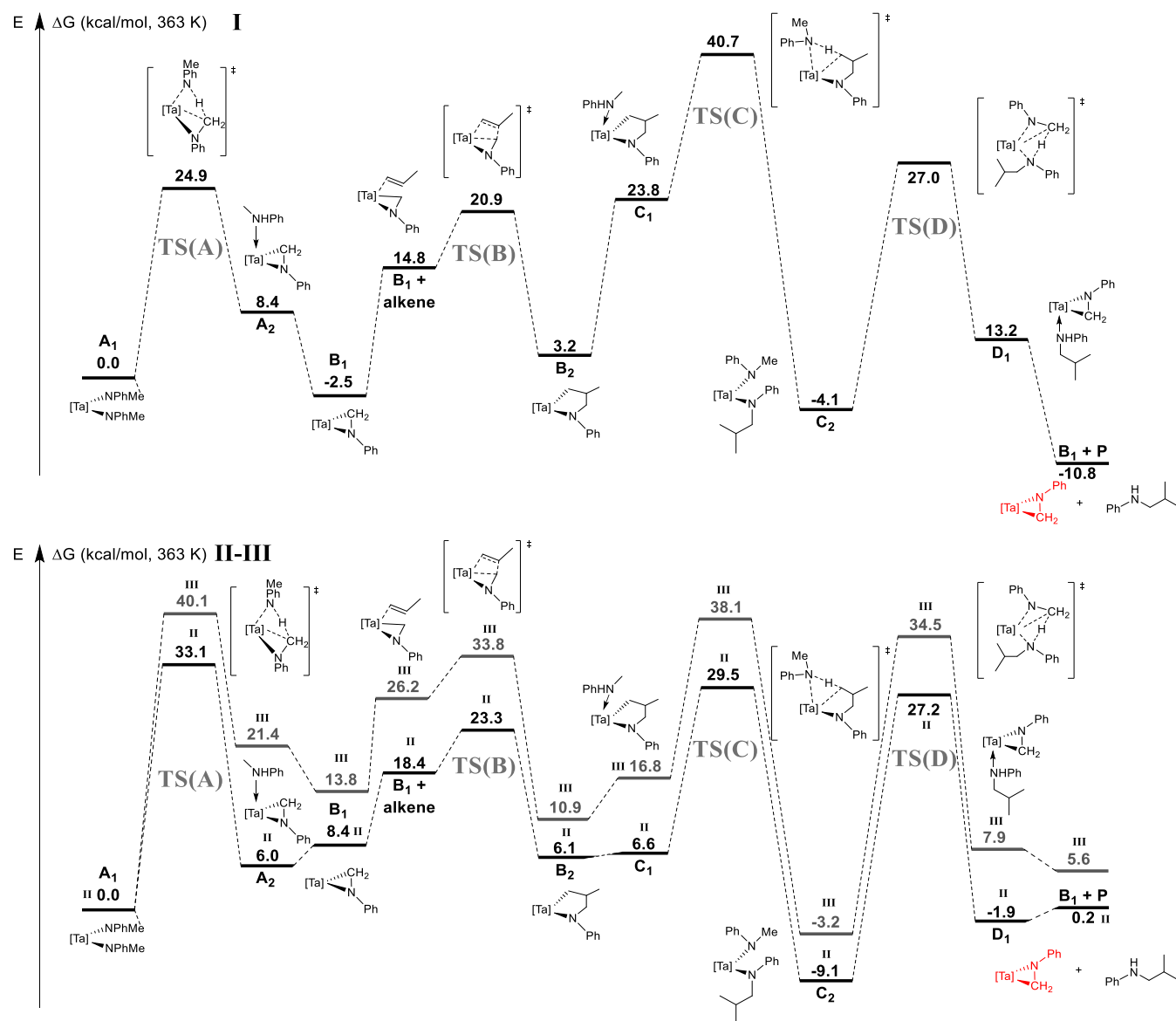
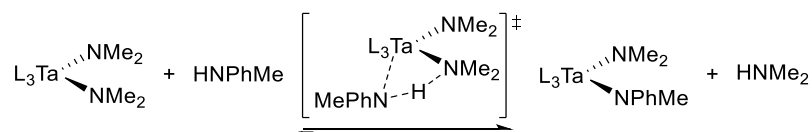


Figure 2.3 Energy Profile of the Gibbs free energy (kcal•mol⁻¹, 363 K, 1 atm) of the proposed mechanism for hydroaminoalkylation catalyzed by (T) I and (B) II and III. Backbone atoms omitted for clarity.

Optimizations performed using B3PW91-D3 level with an SVP basis set; single point energies calculated with the Def2-QZVPP basis (toluene)

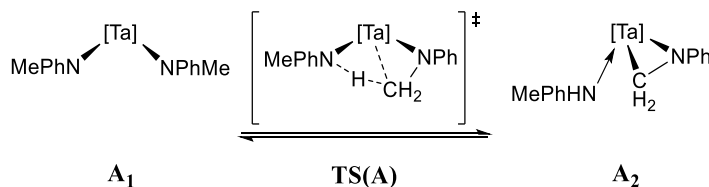
2.2.1.1 Tantallaziridine formation

In all proposed cycles for HAA, the catalytically active species, the tantallaziridine, must first be formed from the starting complex. In the catalysts bearing dimethylamido groups, amine exchange *via* transamination or reversible tantallaziridine formation is proposed to obtain the catalyst bearing the amine substrate as amido groups (Scheme 2.6).



Scheme 2.6 Transamination for amido ligand exchange

To form the active species, tantallaziridine formation is proposed to occur from the C-H activation of a $-CH_3$ proton of the amido group to the nitrogen atom of another bound amido, thus forming a three-membered metallaziridine while forming an equivalent of amine that remains bound to the metal centre (Scheme 2.7).



Scheme 2.7 Formation of tantallaziridine via TS(A)

Beginning with **II** and **III**, transition states were located corresponding to intramolecular proton abstraction (Scheme 2.7). Relaxation of this TS gave a three-membered tantallaziridine with a coordinated neutral amine. As predicted, the energies calculated were more favorable with **II** than **III** (33.1 and 40.1 kcal•mol⁻¹ respectively). Release of the free amine gives five-coordinate complexes with the axial chloro ligands bent down towards the equatorial plane (**B1-II** and **B1-III** in Figure 2.4).

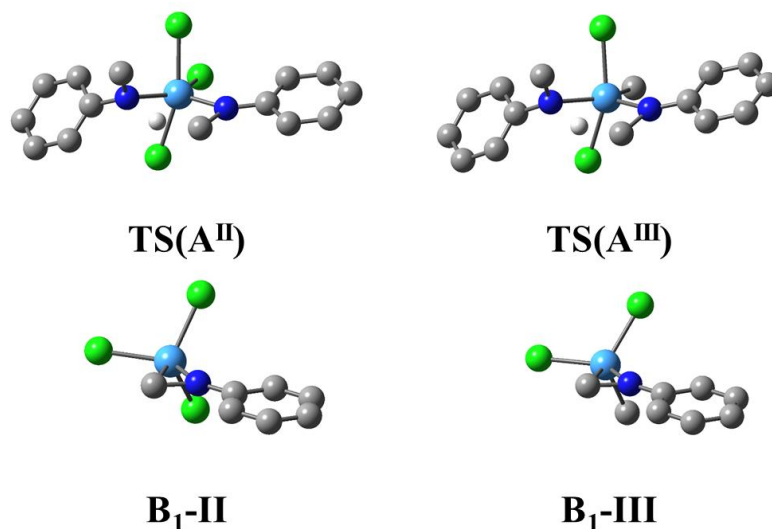
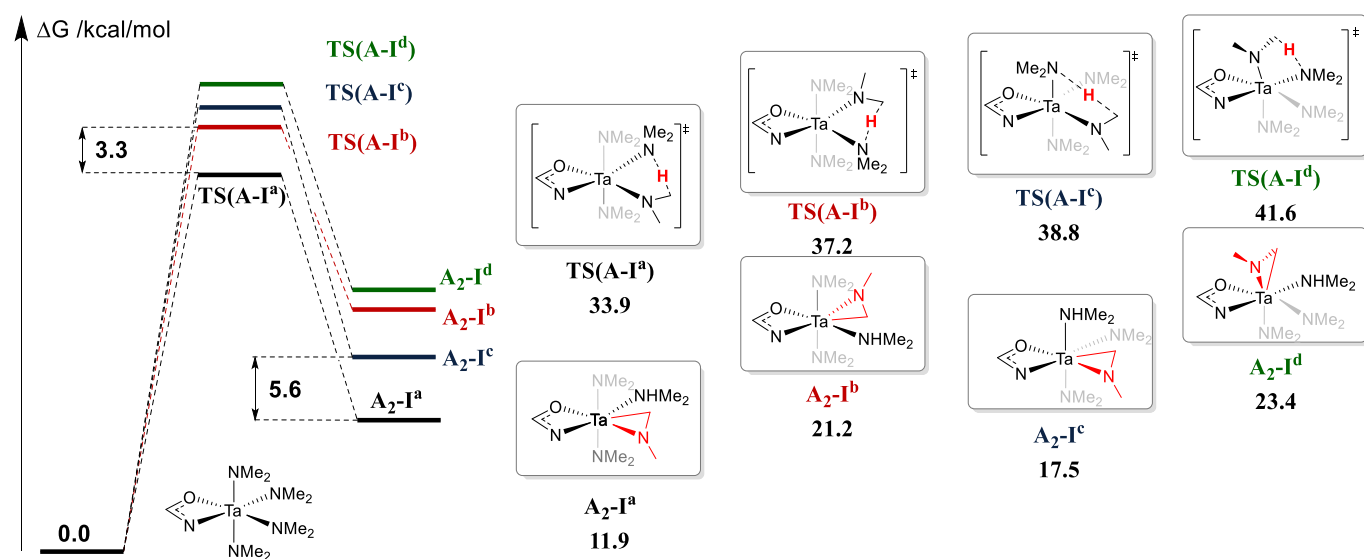


Figure 2.4 Optimized TS(A) and B₁ species for complexes I and II. Hydrogen atoms omitted for clarity.

B3PW91-D3/Def2-QZVPP + SMD(Toluene) // B3PW91/svp

Complex **I** has four bound amido groups; therefore enabling several possible intramolecular C-H activation steps to form the catalytically active aziridine. While initial studies conducted by Dr Lauzon proposed most favorable energetics in the plane of the amidate ligand, alternate geometries of aziridine formation could not be located as stationary points, preventing their calculation as transition-states. Here, various TS were calculated for **I** between the four starting dimethylamido groups (Scheme 2.8).



Scheme 2.8 Comparison of selected C-H activation steps in the ‘simple model’ system. Associated free energy values (ΔG) given in kcal $\cdot$ mol $^{-1}$. M06/Def2-QZVPP // M06/svp

Formation was found to be most energetically favorable in the plane of the electron withdrawing *N,O*-chelating amidate ligand, with the nitrogen of the metallaziridine lying *cis* to the nitrogen of the *N,O* chelate ($\text{A}_2\text{-I}^{\text{a}}$). The flipped geometry, in which the metallaziridine is formed with its nitrogen *trans* to the nitrogen of the chelate, was found to be *ca.* 3 kcal $\cdot$ mol $^{-1}$ higher in energy (see $\text{TS(A-I}^{\text{b}}\text{)}$). Alternative pathways involving participation of axial ligands were also explored. Proton transfer from an equatorial amido group to liberate an axial amido group as a free amine was found to be *ca.* 5 kcal $\cdot$ mol $^{-1}$ higher in energy (see $\text{TS(A-I}^{\text{c}}\text{)}$). Proton transfers from axial to equatorial amidos, thus forming axial tantallaziridines, were likewise found to be *ca.* 7 kcal $\cdot$ mol $^{-1}$ higher in energy than geometries which put the metallaziridine and *N,O* chelating amidate in the same plane (see $\text{TS(A-I}^{\text{d}}\text{)}$ as one example).

This suggests that the bulky, electron withdrawing *N,O* chelate provides a plane of more favorable reactivity for formation of the catalytically active species. To explore the origin of this favored reactivity, the molecular orbitals of the starting complex **A**₁ were visualized (Figure 2.5).

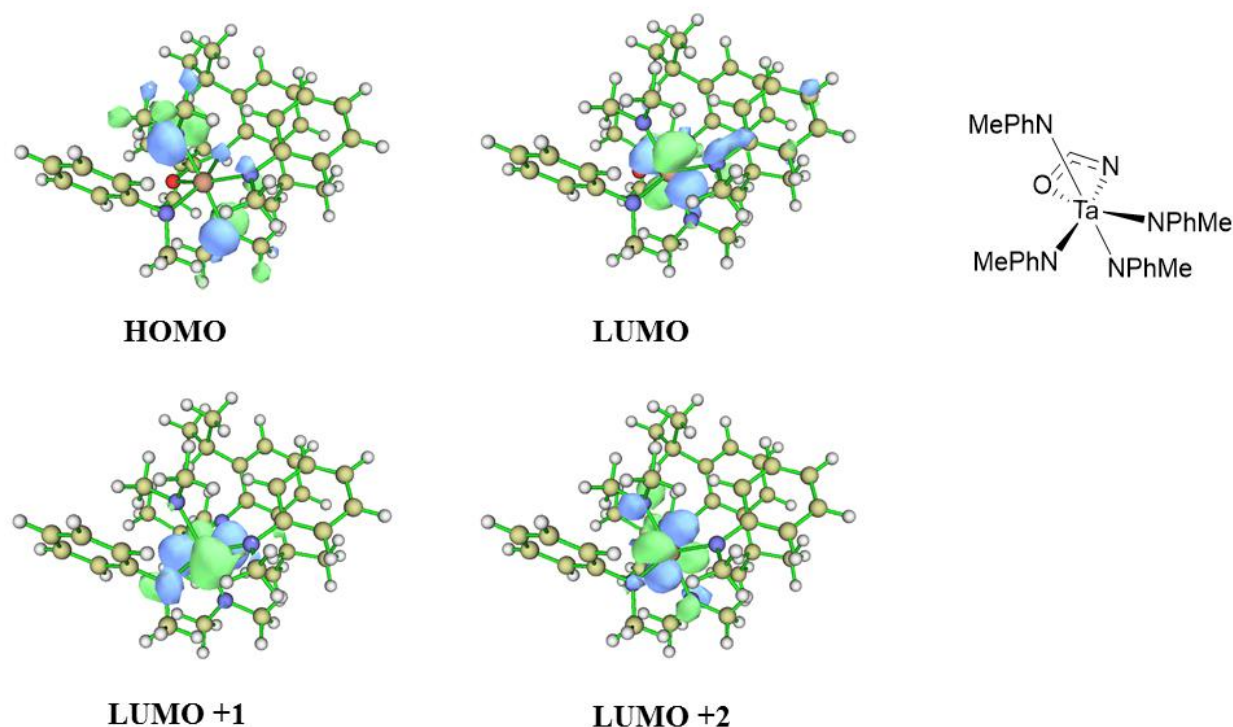


Figure 2.5 Molecular orbitals for **A**₁ in **I**. B3PW91-D3/Def2-QZVPP// B3PW91/svp

The **LUMO** to **LUMO+2** correspond to M-L π anti-bonding combinations, of which the “N-*cis*” amido in the plane of the chelate is the lowest lying in energy. The **LUMO +1** corresponds to the M-L interaction with the other amido in the plane of the chelate (N-*trans*). The **LUMO+2** is the interaction with the axial amidos. As the O of the *N,O* chelate is the strongest donor to the metal, *trans* to it the anti-bonding interaction of the lone pair of the N-*cis* amido with the metal centre is accessed more readily than in the other amidos. During the TS, the diminished π character in the M-N bond allows the lone pair to greater delocalize into the N-C bond, increasing its π character and making the proton to be abstracted more “acidic”.

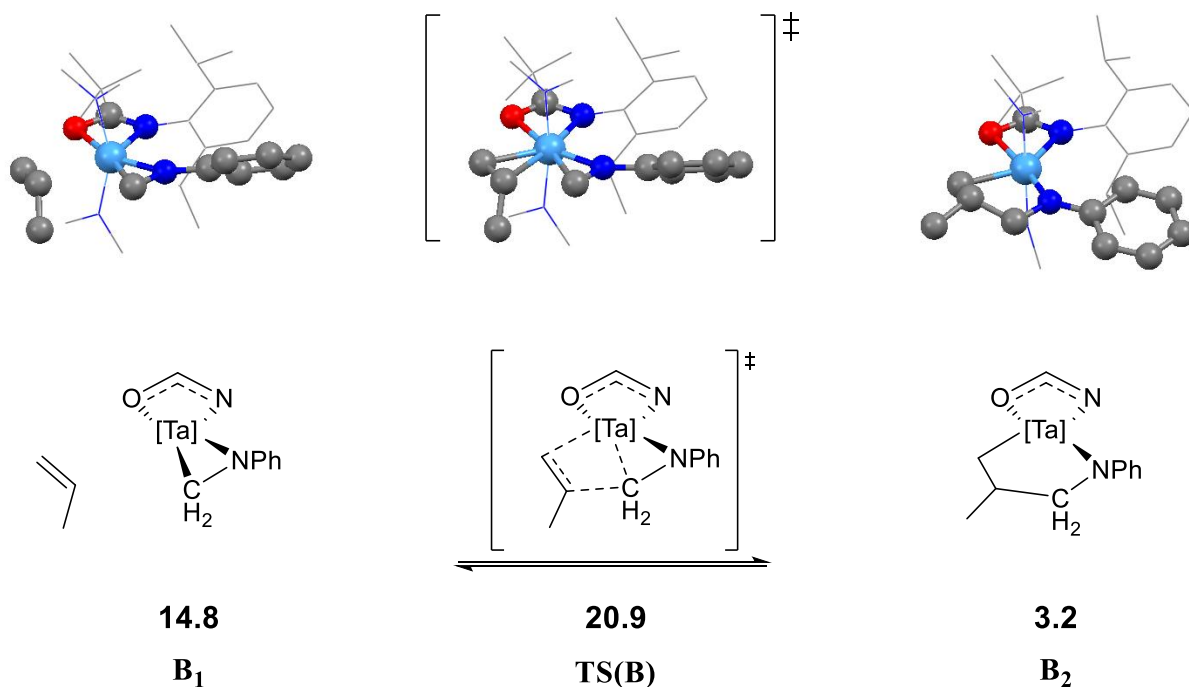
Figure 1 illustrates the reaction scheme for the [2+2] cycloaddition of a Ta complex with a furan derivative. The scheme shows the reactant (A₁), the transition state (TS(A)), and the product (A₂). The energy levels are 0.0 for A₁, 24.9 for TS(A), and 8.4 for A₂. The reaction is exothermic, as the product is at a lower energy than the reactant.

Scheme 2.9 TS(A) showing tantallaziridine formation in I. Associated free energy values (ΔG) given in kcal•mol⁻¹. Backbone atoms and non-participating ligands shown in skeletal form (T) or omitted (B) for clarity

2.2.1.2 Alkene Insertion

44

stereocenter in this reaction. In **I**, this TS was located in the plane of the chelate with a relatively low energy barrier of 23.4 kcal•mol⁻¹ (Scheme 2.10).



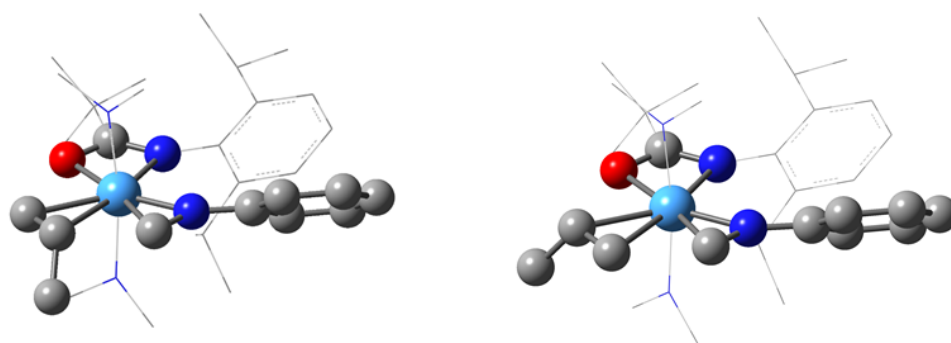
B3PW91-D3/Def2-QZVPP + SMD(Toluene) // B3PW91/svp

Scheme 2.10 TS(B) showing alkene insertion in **I. Associated free energy values (ΔG) given in kcal•mol⁻¹.**

Backbone atoms and non-participating ligands shown in skeletal form (T) or omitted (B) for clarity

This transition state for 1,2 insertion was located showing simultaneous Ta-C and C-C bond formation across the propene unsaturation with breakage of the metallaziridine Ta-C bond. A transition state was also located for 2,1 insertion and found to be higher in energy (+ 4.0 kcal•mol⁻¹). These results match experimental findings, in which almost exclusive formation of the branched vs. linear product suggests terminal alkene insertion occurs in a 1,2, rather than 2,1, fashion.²⁹ Whether the origin of this difference is in electronics or sterics is unclear. It can be argued that greater steric repulsion of the methyl group exists near the metal centre in 2,1 insertion, compared to its positioning away from the metal centre in 1,2 insertion. However, a visual

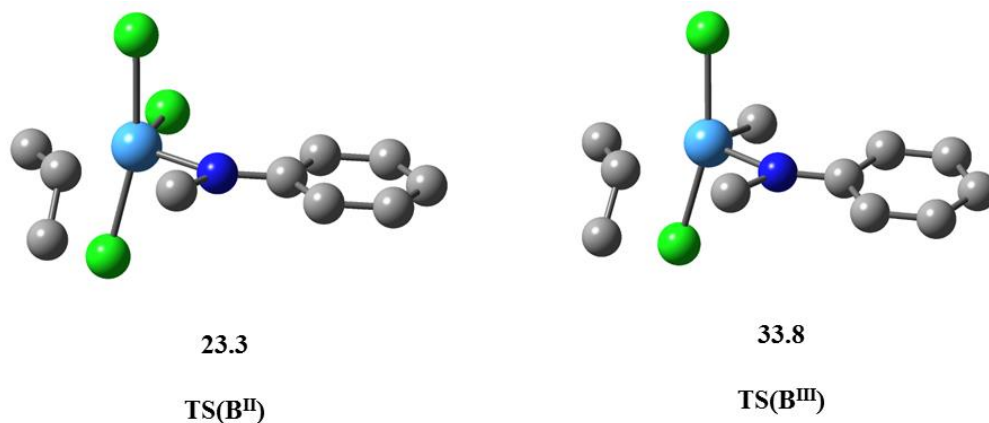
inspection of the optimized TS structures does not provide a clear rationale for how this subtle change in sterics accounts for a relatively large energy difference (Figure 2.6). The use of the unsymmetric *N,O*-chelating ligand results in no significant steric interactions of the alkene with the metal complex, thereby suggesting that regioselectivity during the insertion step is under electronic control, and is defined by preferential polarization of the alkene in the TS. This also clarifies how electronic control of regioselectivity can be substrate dependent. Indeed, a related *N,O*-chelated Ta phosphoramidate complex **1.8**, which exploits the use of an even more electron-withdrawing ligand, displays reversed regioselectivity with vinylsilane substrates.⁴⁰ These results are consistent with recent computational and experimental findings for group 3 catalysts.⁹⁵



B3PW91-D3/Def2-QZVPP + SMD(Toluene) // B3PW91/svp

Figure 2.6 Divergent alkene insertion regioselectivity in TS(B) for I. Backbone atoms omitted or shown in skeletal form for clarity

In the transition states calculated for the methyl and chloro complexes, the same trend was observed as in TS1, where alkene insertion is less favorable with **II** (+ 2.4 kcal•mol⁻¹) and much less so with **III** (+ 12.9 kcal•mol⁻¹) in contrast to **I** (Figure 2.7). In contrast to TS(A) however, differences between the chloro and amidate systems are more subtle, with the methyl group far higher in energy. This suggests that electron deficiency at the metal centre is critical to favor alkene insertion at this TS.



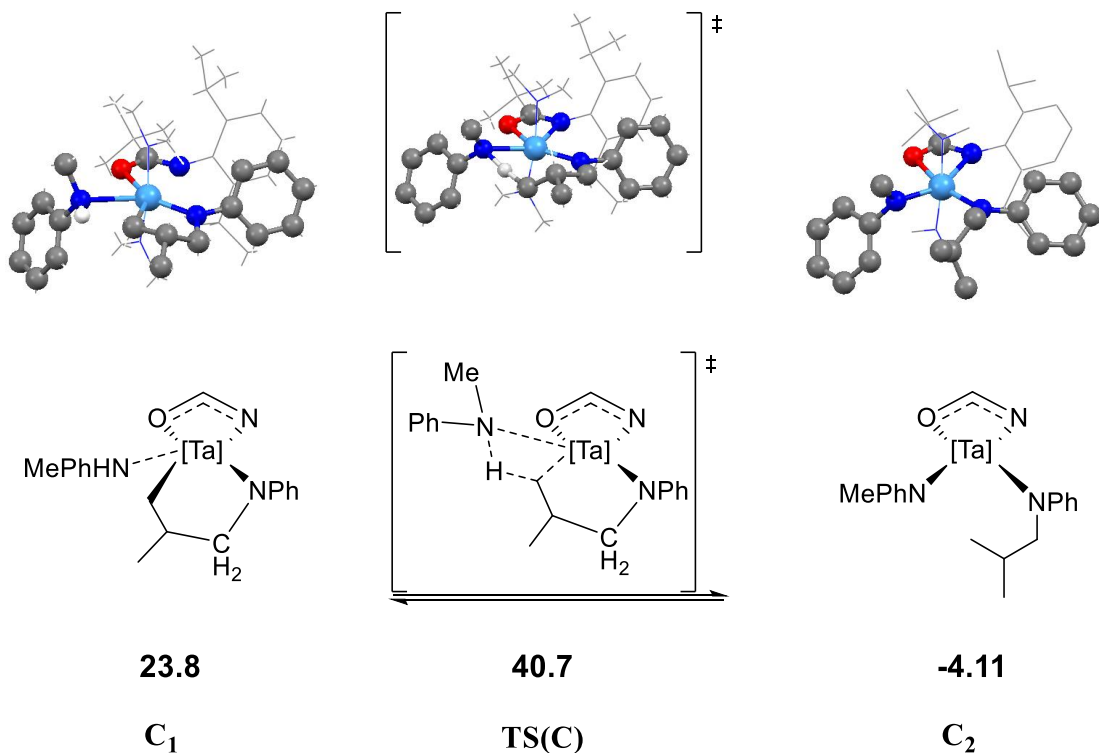
B3PW91-D3/Def2-QZVPP + SMD(Toluene) // B3PW91/svp

Figure 2.7 TS of alkene insertion in TaRCl₂(NPhMe)₂. Associated free energy values (ΔG) given in kcal•mol⁻¹.

Ball and stick structures omit hydrogens for clarity

2.2.1.3 Protonolysis

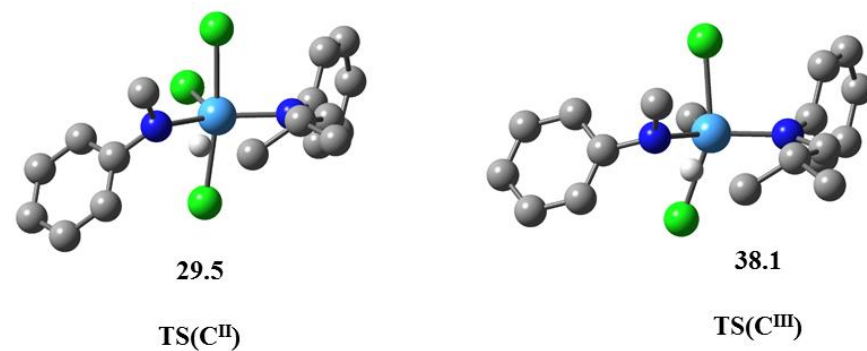
Upon olefin insertion, an incoming amine is proposed to pre-coordinate to Ta then break the Ta-C bond of the metallacycle by transfer of its proton (TS(C)). For **I**, this transition state as calculated is the most energetically costly of the cycle (an effective barrier of 43.2 kcal•mol⁻¹). In visualizing this TS, this is proposed due to the significant crowding about the equatorial plane for proton transfer (Scheme 2.11).



B3PW91-D3/Def2-QZVPP + SMD(Toluene) // B3PW91/svp

Scheme 2.11 TS(C) showing protonolysis of the metallacycle by neutral amine in **I**. Associated free energy values (ΔG) given in $\text{kcal}\cdot\text{mol}^{-1}$. Backbone atoms and non-participating ligands shown in skeletal form (T) or omitted (B) for clarity

In contrast to TS(A) and TS(B), the chloro species **II** demonstrates a more favorable activation energy for this transformation (Figure 2.8). The six-coordinate TS broadly resembles an octahedral geometry, perhaps accounting for the stabilization of this TS relative to the formally seven-coordinate species in TS(C) for **I**. The energy for **III** is unsurprisingly higher, as observed generally with less electrophilic complexes.



B3PW91-D3/Def2-QZVPP + SMD(Toluene) // B3PW91/svp

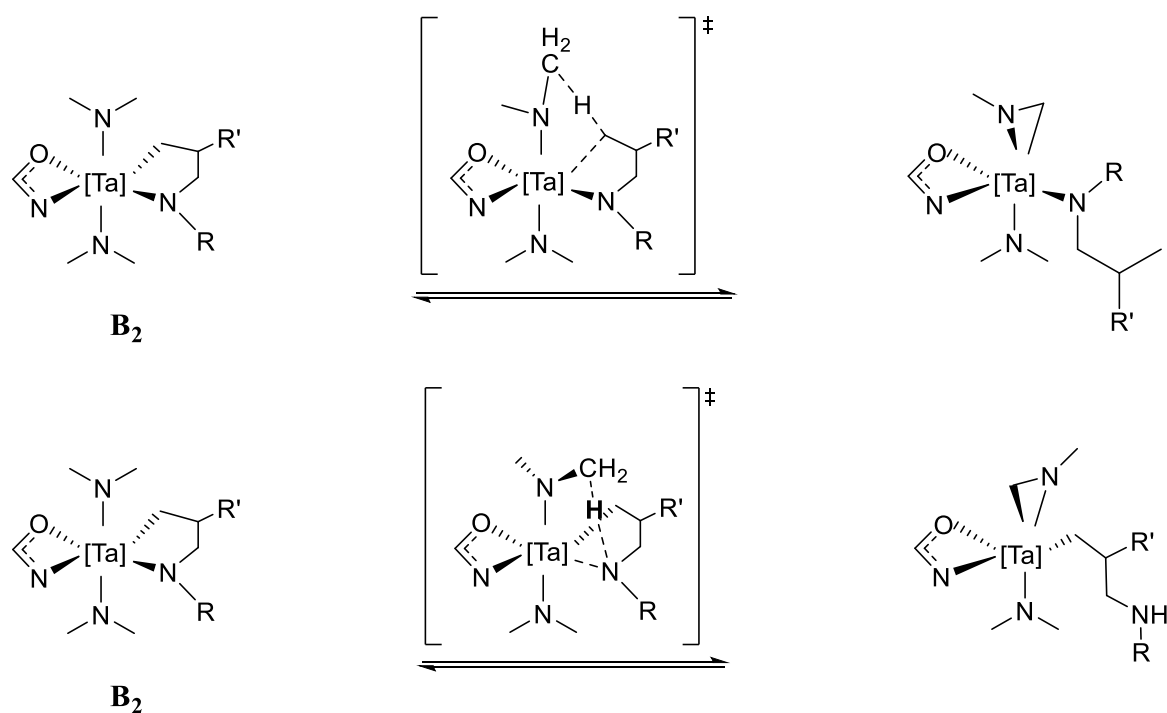
Figure 2.8 TS of protonolysis in TaRCl₂(NPhMe)₂. Associated free energy values (ΔG) given in kcal•mol⁻¹.

Ball and stick structures omit hydrogens for clarity (with exception of transferred proton)

These results suggest that the steric environment about the metal centre imposed by the amidate ligand is detrimental to this step, where the less bulky complexes **II** and **III** are better able to accommodate the incoming amine substrate into the inner coordination sphere. As this step is the highest energy barrier yet calculated for **I** in the cycle, various alternatives were explored in search of a lower energy pathway.

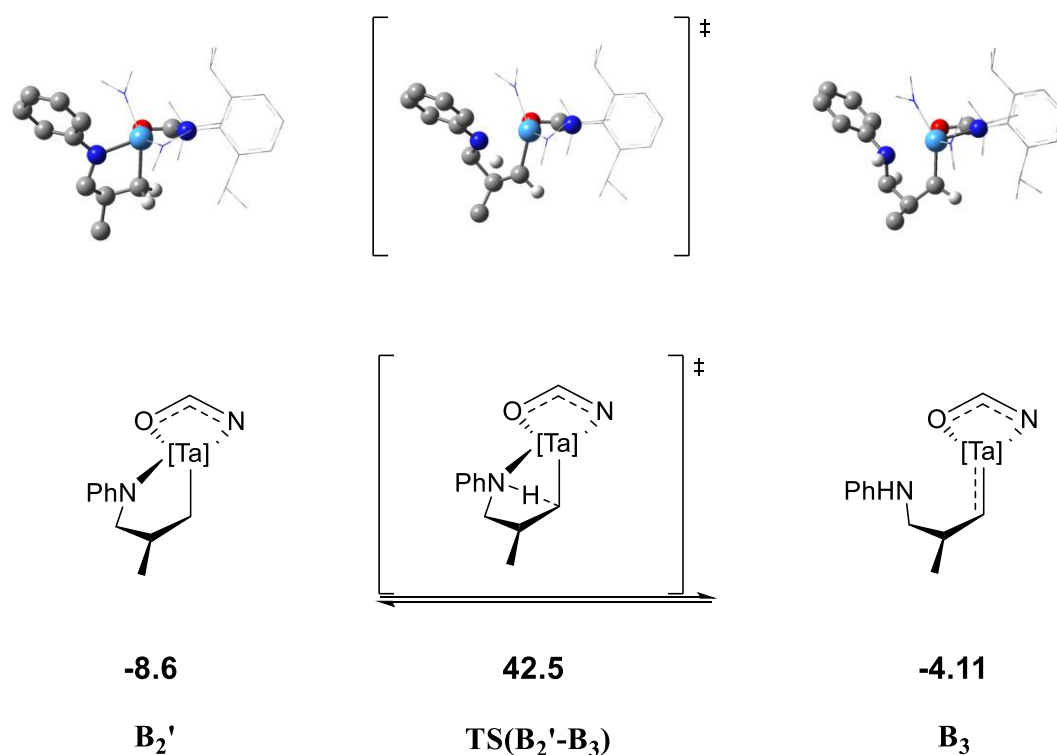
2.2.1.3.1 Alternative mechanisms to protonolysis

A variety of alternative mechanisms to liberate the metallacycle were explored. Efforts to identify a transition state species with a κ^1 binding mode of the amidate were not successful. In a step similar to the formation of the tantallaziridine, a transition state in which a proton was transferred from the methyl group of the amido (thus forming an axial tantallaziridine) to liberate the nitrogen or carbon of the equatorial metallacycle was sought (Scheme 2.12). These TS were located in the simple model system, however they were found to be significantly higher energy pathways (approximately 8 kcal•mol⁻¹ over TS(C)). This finding again suggests that the plane of the *N,O*-chelating amidate provides the most favorable site for reactivity.



Scheme 2.12 TS corresponding to proton transfer from an axial amido group to liberate carbon (T) or nitrogen (B) of **B₂** in the simple model system

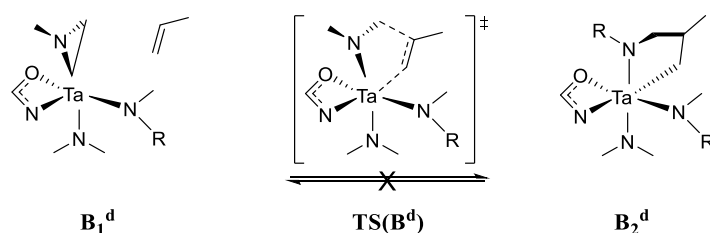
Tantalum alkylidenes represent a well known structural motif.¹⁰³ In considering a possible Ta alkylidene intermediate, proton transfer from carbon to nitrogen within the metallacycle to liberate the Ta-N bond was also considered. Unfortunately, this TS could not be modelled in the plane of the chelate in **B₂**. A TS for formation of a tantalum alkylidene was located for an isomer of **B₂**, in which a proton was transferred from an axial carbon to liberate the nitrogen bound to the tantalum centre (Scheme 2.13). However, this TS was higher in energy than TS(C), and no TS could be located to account for the formation of proposed **B₂'**.



B3PW91-D3/Def2-QZVPP + SMD(Toluene) // B3PW91/svp

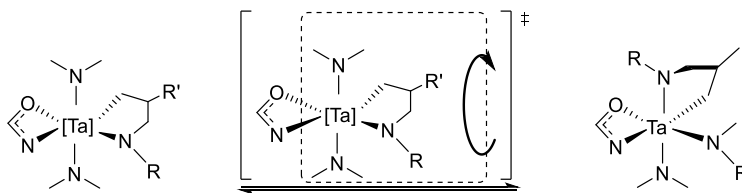
Scheme 2.13 TS(C) showing *intramolecular* proton transfer within metallacycle to form tantalum alkylidene in I. Associated free energy values (ΔG) given in kcal•mol⁻¹. Backbone atoms and non-participating ligands shown in skeletal form (T) or omitted (B) for clarity

As no lower-energy alternative could be found for in-plane protonolysis TS(C), the first TS was re-visited, in which the various tantallaziridine formations were calculated. Although the formation of the “*N-cis*” aziridine **A2-I^a** was found to be the lowest energy pathway, there are transition states to other aziridines with energies that are competitive with protonolysis. Therefore, it was considered whether the reaction could proceed from the formation of a less stable aziridine, such as **A2-I^d** (Scheme 2.14). This axial tantallaziridine is less stable than **A2-I^a**, however upon alkene insertion a metallacycle would result that is perpendicular to the chelate. This would then enable a much less sterically congested plane of reactivity for an incoming amine to liberate the Ta-C bond by protonolysis.



Scheme 2.14 Alternative TS(B) showing alkene insertion into an axial aziridine

Unfortunately, no TS could be located in which an alkene inserts into an axial aziridine intermediate (**A2-I^d** and other geometries). However, during the course of those attempts, an axial metallacycle intermediate akin to **B2^d** was successfully optimized, with a ground-state energy lower than any other point on the potential energy surface ($-7.7 \text{ kcal}\cdot\text{mol}^{-1}$). Based on the magnitude of this energy minima, this theoretical axial metallacycle is considered to possess too low of a ground-state energy to be a key intermediate, as significant energy would be required to catalytically turn-over from this stabilized intermediate. Interestingly, re-optimizing TS(C) in the simple model after completely removing the substituents on the amidate, thereby dramatically reducing steric bulk, causes the metallacycle to isomerize (Scheme 2.15). When the diisopropyl phenyl group is on nitrogen of the amidate, the isopropyl substituents block this rotation.



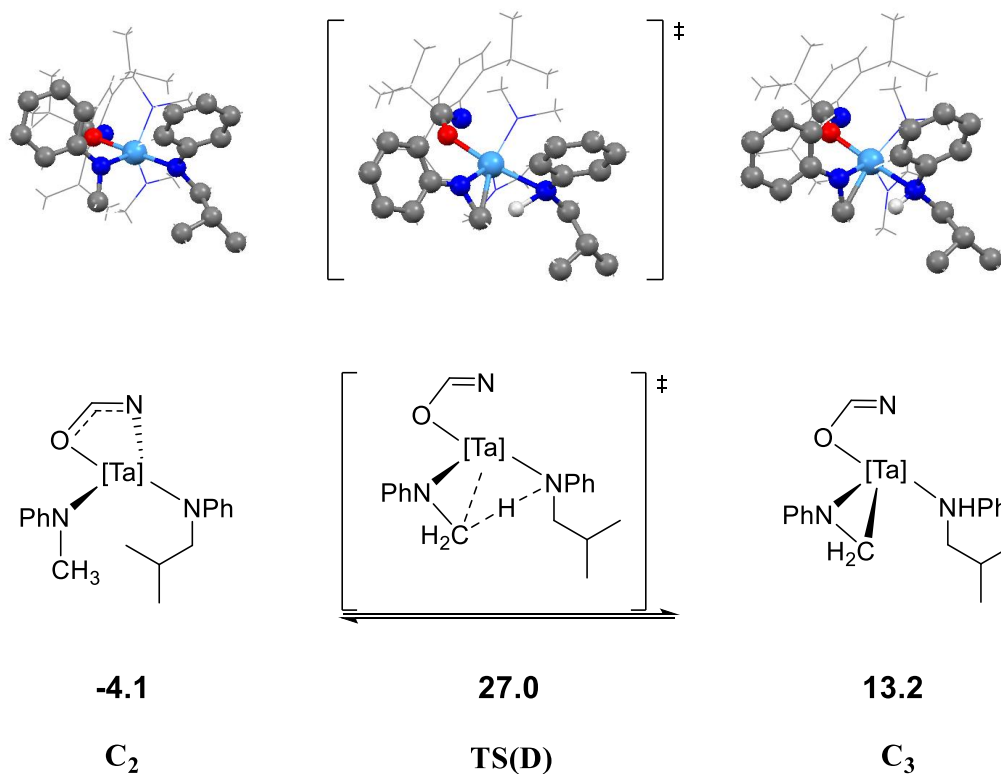
Scheme 2.15 Isomerization of B₂ to B₂' from rotation of metallacycle

Experimentally, improved catalytic activity has been reported with increasingly bulky amidates; it is proposed that this increased bulk may prevent this isomerization which is considered detrimental to productive catalysis. Experimental attempts to detect and isolate axial metallacycles are discussed later in this chapter.

Based upon these computational efforts, in-plane protonolysis as calculated in TS(C) is proposed as the TLS. While the calculated energetic barrier is high energy, it is conceivable under the reaction conditions, which require temperature in excess of 110 °C and thus take place in superheated and pressurized solutions of toluene.

2.2.1.4 Product Release

Liberation of the alkylated amine product and restoration of the catalytically active species is proposed to occur *via* proton abstraction from the equatorially bound amido group. This TS was found in the plane of the chelating ligand with an overall barrier of 31.1 kcal•mol⁻¹ from C₂ (Scheme 2.16).



B3PW91-D3/Def2-QZVPP + SMD(Toluene) // B3PW91/svp

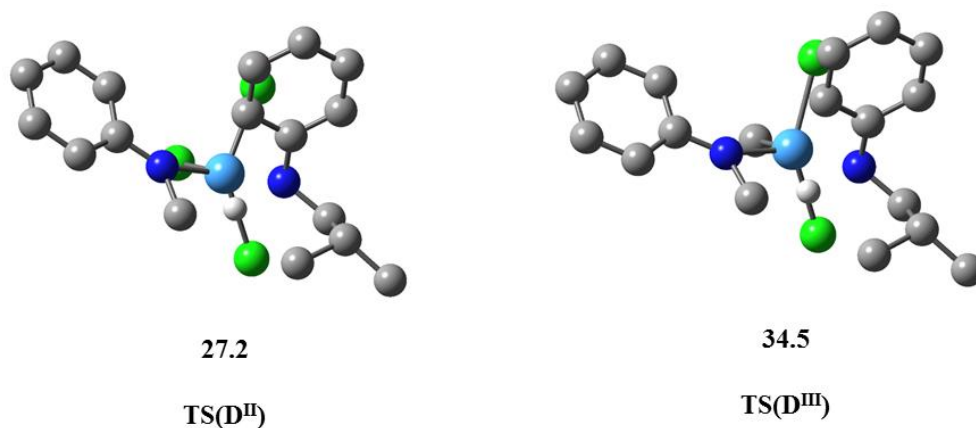
Scheme 2.16 TS(C₂-C₃) showing C-H activation to liberate product as a neutral amine in **I**. Associated free energy values (ΔG) given in kcal•mol⁻¹. Backbone atoms and non-participating ligands shown in skeletal form (**T**) or omitted (**B**) for clarity

Notably, this transition state shows the amide ligand bound κ^1 through oxygen with the C-N bond bent away from the tantalum centre. This highlights the hemilabile coordination of the amide ligand, which can alleviate inner sphere steric interactions while maintaining a protected centre of reactivity. This step generates a tantallaziridine in which the nitrogen of the aziridine is oriented *trans* to the nitrogen of the *N,O* chelate (which reverts to κ^2 coordination upon liberation of the product).

As discussed previously, it remains unclear whether catalysis proceeds with this flipped aziridine or whether catalysis only proceeds with the favorable *N-cis* aziridine. Based on Scheme

2.8, the difference between the TS energies of these aziridines to revert to bis amido species is *ca.* 3 kcal•mol⁻¹. It is proposed based on these subtle differences in energetics that subsequent turnovers proceed through the most favored *N-cis* aziridine after proton transfer equilibria with excess equivalents of amine. This is opposed to proceeding with the former '*N-trans*' aziridine and having the cycle in fact be two alternating cycles, which is ruled out because of more costly energetics with the less favorable '*N-trans*' aziridine than the required equilibria to return to the catalytically active '*N-cis*' species.

Modelling with **II** gave a TS of the comparable energy (effective barrier of 36.4 kcal•mol⁻¹), while **III** unsurprisingly requires higher energy (effective barrier of 45.3 kcal•mol⁻¹) (Figure 2.9). Optimization of these complexes after removal of the amine product gives the same optimized tantallaziridines as obtained after the first C-H activation in the bis amido complexes.



B3PW91-D3/Def2-QZVPP + SMD(Toluene) // B3PW91/svp

Figure 2.9 TS of product release via C-H activation in TaRCl₂(NPhMe)₂. Associated free energy values (ΔG) given in kcal•mol⁻¹. Ball and stick structures omit hydrogens for clarity (with exception of transferred proton)

In the presence of a large excess of amine substrate, amine exchange *via* transamination to liberate the product has also been proposed as a mechanism for product release.¹⁰⁴ In **1.3**, ligand exchange occurs readily at sub-catalytic temperature, suggesting this process is facile.^{12, 96}

Combined with the fact that product release *via* C-H activation is not implicated in the theoretical TLS for **I-III**, the differences between these mechanisms of product release were not scrutinized.

2.2.1.5 Off-cycle equilibria

In addition to the cycle modelled herein, computations were also performed to examine off-cycle equilibria that could be occurring during catalysis with amidate tantalum catalysts. In experimental deuterium labelling studies with **1.3**, the incorporation of deuterium in the *ortho*-position on the aromatic ring in *N*-methyl aniline was observed and thus suggests an off-cycle pathway. This is presumably an *ortho*-metallation event similar to **TS(A)** and can occur in the starting material or in the post-protonolysis intermediate (see Scheme 2.2). Transition states that can rationalize the formation of these cyclometalated species were located; it was found that *ortho*-metalation from the starting bis amido **A₁** (33.8 kcal•mol⁻¹) is more likely than in the bis amido in which one is the bound product (**C₂**) (47.7 kcal•mol⁻¹) (Scheme 2.17). This difference is presumably due in part to forming a cyclometalated species with **C₂** in the less favored orientation in which its nitrogen lies *trans* to the nitrogen of the *N,O*-chelating amidate. The starting complex is returned upon protonolysis by an amine; if it is an *N*-deuterated amine, a deuterium will have been incorporated *ortho* in the aryl ring. The calculated energy of this transition state from **A₁** is lower than the overall TLS of protonolysis, therefore accounting for the experimentally observed deuterium incorporation at this position.

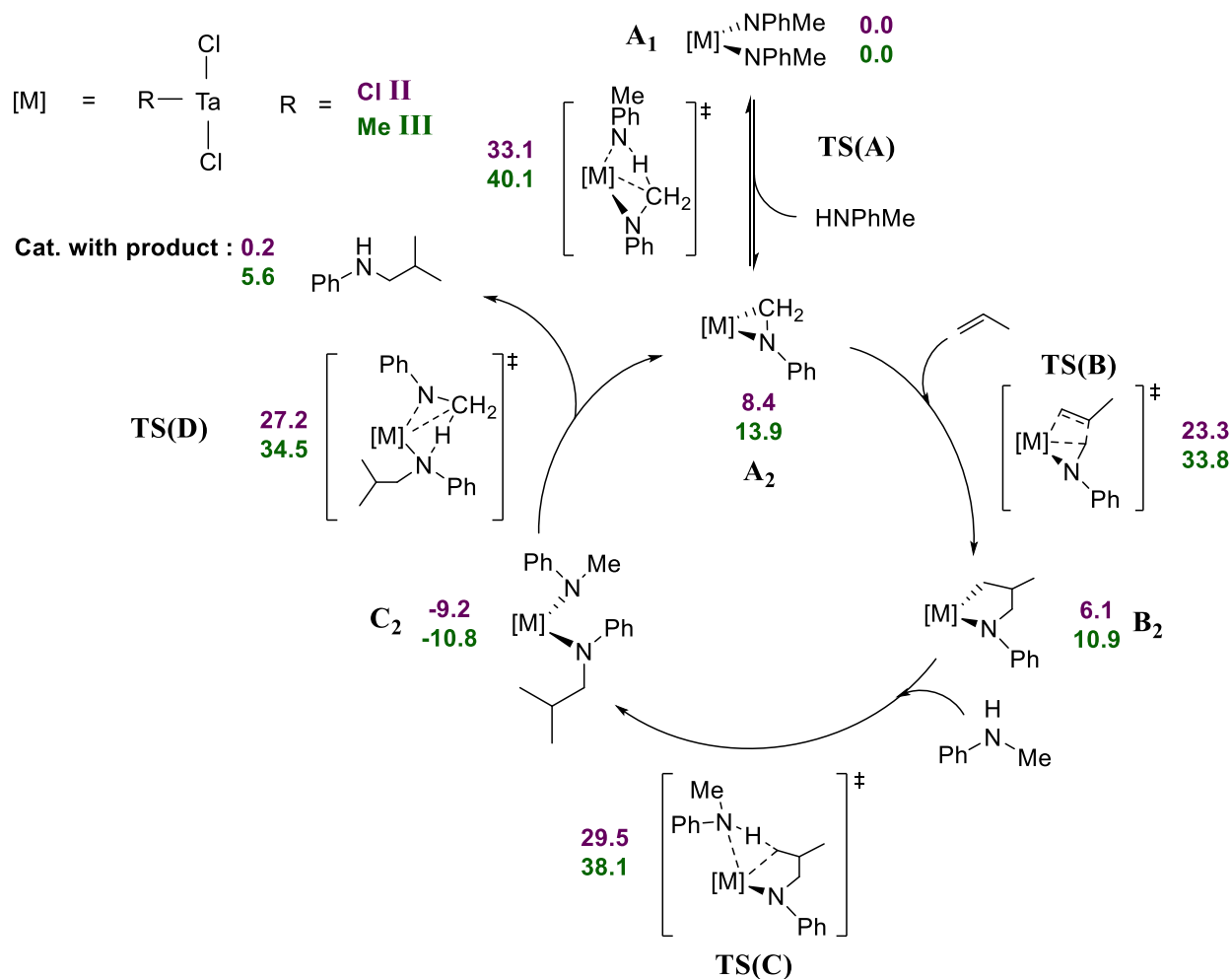
Table 2.1 Bond lengths and angle of the amidate ligand to Ta in I. (*) indicates κ^1 coordination mode.

Entry	Ta-O / Å	Ta-N / Å	O-Ta-N / °
A ₁	2.10	2.44	56.6
TS-A	2.12	2.29	58.8
A ₂	2.16	2.26	59.0
B ₁	2.25	2.19	58.8
B ₁ + alkene	2.18	2.21	59.6
TS-B	2.15	2.27	58.7
B ₂	2.25	2.21	57.9
C ₁	2.14	2.56	54.5
TS(C)	2.11	2.44	56.3
C ₂	2.13	2.43	56.5
TS(D)	2.02	3.32*	-
C ₃	1.97	3.44*	-

The precursor amido complex **A₁** begins with a much shorter Ta-O bond than Ta-N bond, yet in **TS(A)** the Ta-N contracts to 2.29 Å. Throughout the PES, the Ta-N bond length varies depending on the steric properties and electron density at the metal: from contraction in **TS(A)** to facilitate amine release to elongation in **TS(C)** to make space for amine approach (2.44 Å). Significant changes are also observed in the Ta-O bond length, wherein the κ^1 **TS(C)** this bond is shortest (2.02 Å) This electronic feature of 1,3-*N,O*-chelating ligands thus offers flexibility in the donation to these highly reactive, electrophilic metal centers.

2.2.1.7 Overall cycles and comparison to experimental trends

The catalytic cycle for **II-III** is shown in Scheme 2.18.

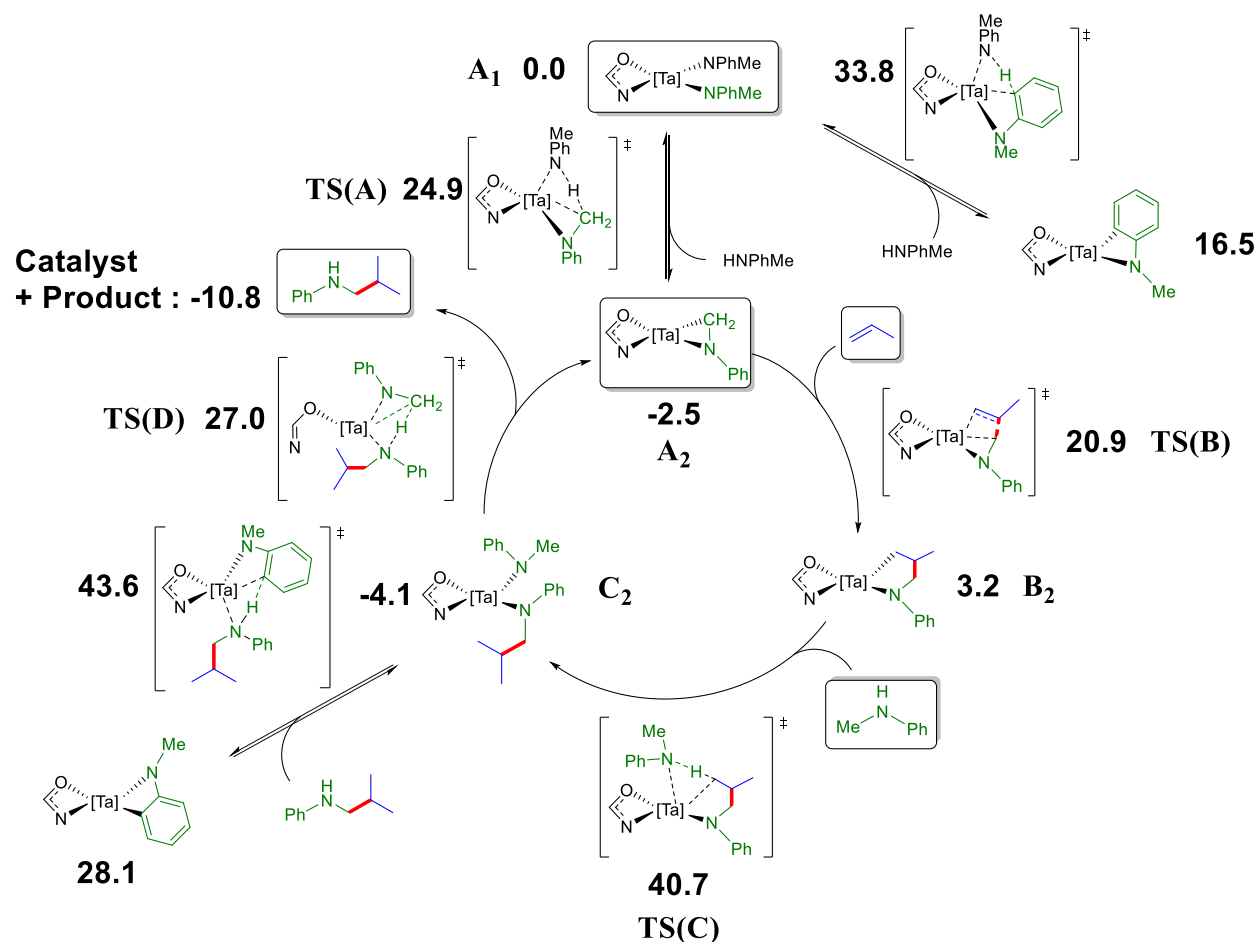


Scheme 2.18 Overall cycles of HAA of 1-octene with NMA using $TaRCl_2(NPhMe)_2$. Associated free energy values (ΔG) given in $\text{kcal}\cdot\text{mol}^{-1}$. Backbone atoms omitted for clarity

Comparison of the energetics between **II** and **III** reveals several key differences. As hypothesized, the energetics with **II** are more favorable than **III** by a minimum of $7 \text{ kcal}\cdot\text{mol}^{-1}$ in every calculated transition state. This corroborates the expected trend with increased reactivity being observed with more electrophilic metal centres. In **II** and **III**, the proposed turnover-limiting step is formation of the catalytically active tantallaziridine, at a minimum of $33.1 \text{ kcal}\cdot\text{mol}^{-1}$, compared to $24.9 \text{ kcal}\cdot\text{mol}^{-1}$ with **I**. This compares favorably with reported deuterium labeling experiments using $[Cl_3Ta(NEt_2)_2]_2$ (**1.2**) as a pre-catalyst, where limited deuterium scrambling

from *N*-(methyl-*d*₃) aniline was observed, leading the authors to propose that C-H activation was not reversible under catalytic conditions.³⁴

The full cycle for **I** is shown in Scheme 2.19:



Scheme 2.19 Overall cycle for HAA catalyzed by **I**. Associated free energy values (ΔG) given in kcal•mol⁻¹ (363 K, 1 atm). Backbone atoms omitted for clarity. Optimizations performed using B3PW91-D3 level with an SVP basis set; single point energies calculated with the Def2-QZVPP basis (toluene)

In contrast to **II** and **III**, **I** showed a significantly reduced barrier to C-H activations and the formed tantalaziridine is similar in energy to the starting complex **A₁**. Related deuterium labelling experiments with **I** showed fast and reversible C-H activation, and a small kinetic isotope

effect (KIE) in comparative rate experiments.¹² It is proposed that one contributing factor to the improved reactivity with N,O-chelated complexes arises from the more facile entry into the active catalytic cycle. This is attributed to the steric bulk imposed in the electronically defined equatorial plane of reactivity. This bulk also favors the loss of free amine upon C-H activation.

Theoretically, 1,2 insertion is favored over 2,1 alkene insertion by *ca.* 4 kcal•mol⁻¹. Also, 2,1 insertion is expected to raise the energy of TS(C), as the substituent on C-2 of the alkene would hamper the approach of an incoming amine. As protonolysis is considered to be the TLS, regioselectivity will be under Curtin-Hammett control and it is this turnover limiting protonolysis step that will ultimately define the branched product selectivity observed. Future efforts towards altering regio- and stereoselectivity in these reactions will require the design of a ligand/metal combination optimized for the two possible insertion products.

With **I**, protonolysis (TS(C)) is the highest energy barrier (43.2 kcal•mol⁻¹), owing to significant steric interactions. This is in contrast to **II** and **III**, in which their TS structures are in a less sterically congested, pseudo-octahedral geometry. The protonolysis TS shows that the sterics imposed by the amidate ligand prove detrimental to facile protonolysis of the Ta-C bond and point toward an opportunity for ligand design to enhance catalytic activity.

KIE studies have shown only a small KIE when investigating the initial rates of *N*-(methyl-*d*₃) aniline and *N-D*-(methyl-*d*₃) aniline with 1-octene ($k_H/k_D = 1.4 \pm 0.1$ and 1.5 ± 0.1 respectively).¹² A complicating factor in interpreting these kinetic experiments is the fact that because of various reversible equilibria including *ortho*-metalation and transamination it is anticipated that the deuterium label is “diluted” over the course of the reaction. Furthermore, experimental kinetic studies have shown the reaction has a non-zero order dependence on alkene and a zero-order dependence on amine.¹² These kinetic observations could be consistent with the

mechanism if **A**₁ is the resting state of the catalyst and transamination reactions are rapid and reversible. Experimental results are consistent with rapid transamination, as precatalyst conversion to the substrate bound analogue of **A**₁ is observed by NMR spectroscopy at room temperature within minutes.¹² Experimental work with mono-pyridonate tantalum catalyst **1.9** has likewise shown that the equilibrium between the bis-amido and tantallaziridine species is heavily shifted to the former.¹⁰⁴ If this is the case the reaction is expected to be zero-order in amine overall as an amine is consumed in TS(C) but released in TS(A). As the TLS occurs after alkene insertion, the reaction is non-zero order in alkene.

2.2.2 Experimental monitoring of rates using GC-FID

With theoretical predicted energies for a proposed catalytic cycle, experimental trends in reactivity were further explored. Previous experimental methods using NMR spectroscopy have been challenged by the nature of the reaction. In deuterium labelling experiments conducted by Hultsch⁹³ and Lauzon,¹² the scrambling of deuterium into the *ortho* carbon in the aryl ring dilutes the deuterium label, potentially underestimating the KIE, and thus limiting the interpretation of KIE experiments with these substrates.

The reaction conditions also pose challenges to monitoring the reaction by NMR spectroscopy. Typically HAA reactions are conducted at high temperature (> 110 °C), preventing the use of variable temperature NMR spectroscopy. In rate experiments with **1.3**, samples were heated in an external heating bath and cooled prior to collecting spectra.⁹⁶ Unfortunately, heating and cooling cycles were also shown to have a detrimental effect on rate, which is proposed to be due to the formation of inactive catalyst decomposition products, such as metal aggregates, upon cooling. Therefore, spectra were only collected in hourly intervals to minimize catalyst

degradation, which unfortunately limits how much data can be collected, and on-going degradation diminishes the accuracy of the measurements as they are collected.

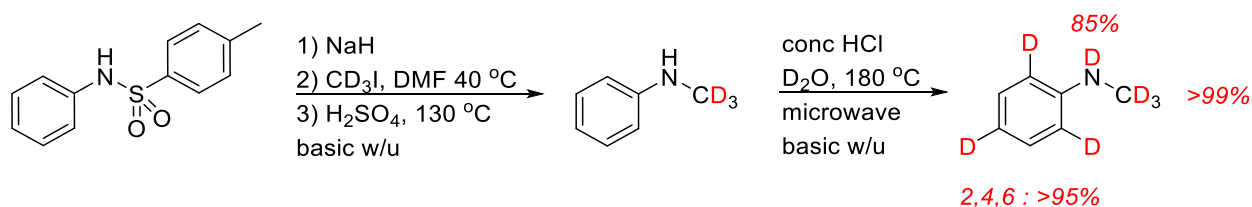
Using ^1H NMR spectroscopy to monitor the reaction is also limited to the number of characteristic signals that can be uniquely assigned to product and substrate. Comparing the integration of the aryl C-H protons of *N*-methyl aniline and its product is commonly used with this substrate combination, however these integrations overlap when using a large excess of amine (for example in *pseudo*-first order experiments probing alkene dependence). The formation of by-products between starting dimethylamido ligands and alkene prevents accurate monitoring of alkene consumption. Rate experiments on substrates other than *N*-methyl aniline and 1-octene will necessitate locating new NMR resonances for each substrate combination to probe the reaction. For example, an *N*-methyl aniline derivative that is fully deuterated (*ie.* C_7ND_9) could not be monitored using the integration of *ortho* C-H protons using ^1H NMR spectroscopy.

In consideration of these challenges, a new kinetic method was targeted using gas-chromatography flame-ionization detection (GC-FID). Using GC enables the separation of all reaction components, allowing more straightforward identification of all reaction species. These can be accurately identified using reference samples and quantified using flame-ionization detection with an internal standard. With the goal of further exploring the KIE in this reaction, the synthesis of another deuterated *N*-methyl aniline was undertaken.

2.2.2.1 Synthesis of a new isotopically labeled *N*-methyl aniline substrate

To avoid the loss of deuterium into the aryl ring, a fully deuterated *N*-methyl aniline molecule was sought. However, the lack of commercial availability required lab synthesis. In 2008, the Lautens group reported a simple method for the 2,4,6 deuteration of anilines using electrophilic aromatic substitution in D_2O with stoichiometric acid catalyst.¹⁰⁵ It was envisioned that this

reaction could be used to further deuterate *N*-methyl-*d*₃ aniline substrates in the desired *ortho* position (Scheme 2.20).



Scheme 2.20 Preparation of deuterated substrate 2.1

Using this route, the deuterated substrate **2.1** was prepared. To retain incorporation of deuterium on the nitrogen atom, a work-up was conducted using NaOD and ethyl acetate. As the reaction uses HCl as a stoichiometric catalyst to activate the aniline as an anilinium salt, the reaction was necessarily conducted under dilute conditions in D₂O (*ca.* 2 mM). The microwave reactor limited the maximum vessel size to 10 mL, therefore the synthesis was conducted in six batches. All batches were combined for sufficient quantities for purification by distillation *in vacuo*. Comparing residual signals in the ¹H NMR spectrum with the *meta* C-H protons allowed for calculation of deuterium incorporation, with over 95% substituted in each of the 2/6 and 4 positions on the aryl ring.

2.2.2.2 GC-FID method development

GC-FID method development was conducted to establish instrument parameters that allowed for the effective separation of analyte peaks. This included adjustment of volumes (*eg.* injected/split volumes, dead volume) and the temperature profile through the chromatographic separation. Using pure samples of protonated substrates as standards, effective separation and identification of the amine substrate, HAA product, and internal standard (2,4,6-trimethoxybenzene, TMB) was achieved. These conditions also enabled the separation and

identification of the amide pro-ligand, allowing its quantification to be used to verify catalyst concentration. Using a series of these standard compounds at varying concentration, the instrument response was validated over the relevant concentration range used in catalysis.

The method procedure is illustrated in Figure 2.10:

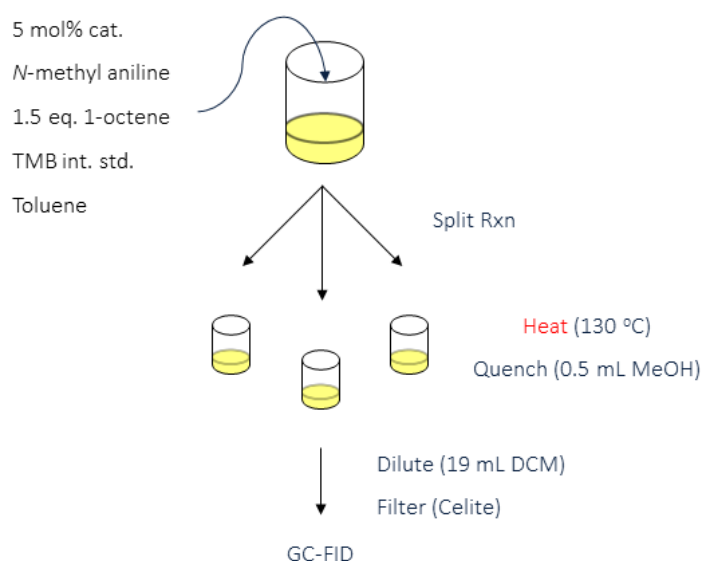


Figure 2.10 Reaction set-up for monitoring HAA reactions by GC-FID

First, a “stock” catalytic HAA reaction was prepared with *N*-methyl aniline (*proteo*- or **2.1**), 1-octene, 5 mol % catalyst **1.3**, and TMB in toluene. This stock was used to prepare a series of identical samples in 20 mL scintillation vials at a concentration relevant to typical NMR screening reactions (*ca.* 0.2 M). Practical limitations in distributing even heat to all vials in the oil-bath limited the experiment to 6 reaction vessels (in addition to one non-heated “t-zero”). These vials were removed from the box, heated, and quenched at a given reaction time. After being quenched, the samples were filtered to remove metal oxides and diluted for direct injection into the GC. By only measuring the reaction progress once quenched, it was hoped that errors associated with repeated sampling from the same vial were avoided. While sampling a single reaction vessel multiple times over a reaction window using syringe techniques was considered,

the comparative volatility of 1-octene and toluene (121 and 111 °C respectively) causes partitioning of the alkene between the solution and vapor phase. Thus, piercing the reaction septum under nitrogen flow to maintain pressure could cause loss of alkene, and without maintaining pressure within the reaction vessel the results could be affected.¹⁰⁴

2.2.2.3 Monitoring initial rates

With experimental design in hand, the consumption of *N*-methyl aniline and formation of its product with 1-octene during Ta-catalyzed HAA was monitored. After one hour, a reaction was quenched. Surprisingly, the measured concentration of *N*-methyl aniline was approximately equal to the measured concentration in the t-zero sample (Figure 2.11). However, a small amount of product was observed as well. Obviously, some *N*-methyl aniline must have been consumed to form the small amount of detected product. The product of the functionalization of 1-octene with the starting dimethylamido ligand has a different retention time (as observed with a standard reference sample) and this product is known not to form if the reaction has sufficient head space (as in the case in a 20 mL vial with *ca.* 0.5 mL reaction volume).⁴⁵ Two reactions were quenched at an equal reaction time (2 hours). The percent difference between the measured values of *N*-methyl aniline and the HAA product were within 0.5 % (see Figure 2.11, product data points overlap). While these two reactions showed minimal differences they are only two data points and are not sufficient to conclude reproducibility. To assess the precision of the measurement, 3 different samples were measured four times each; the average %RSD from these 3 quadruplicate runs was 0.199%. The amidate ligand can also be quantified to assess the precision of the overall method (as the pro-ligand post-quench); in a run with n=28 reactions (*vide infra*) the %RSD of the measured ligand concentration was 0.70%. After all samples were measured, the initial consumption of amine appears linear if the first hour is treated as an induction window:

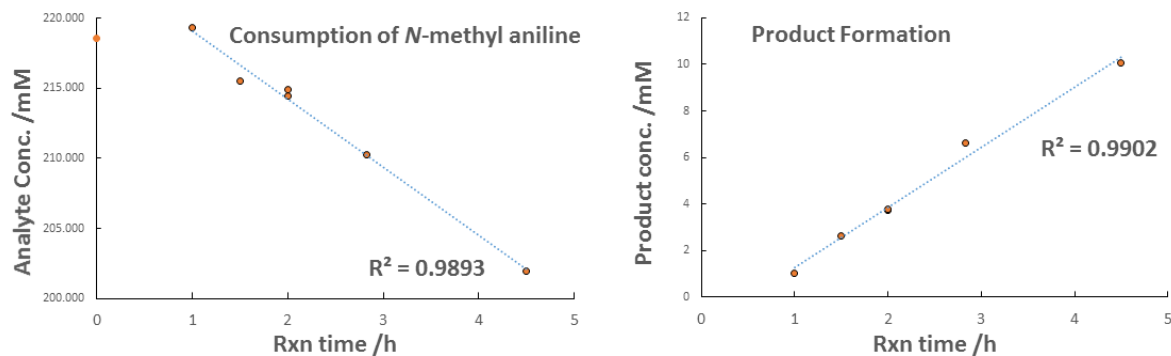


Figure 2.11 Monitoring by GC-FID of *N*-methyl aniline and the product of the HAA of 1-octene as a function of time

More runs were conducted and measured to assess the viability of the method. The reactions were observed to have a variable induction period, with the observation over several repeat experiments that the onset of consumption of *N*-methyl aniline took up to an hour. Qualitatively, this could be observed in visualizing the reaction color; initially, the reaction color is pale-yellow, and is observed to go bright yellow after some heating. Comparing these notes with quantification from GC-FID, it was found that samples with intense yellow color had begun to turn-over, while some samples that remained pale yellow even with heating showed negligible *N*-methyl aniline consumption.

Surprisingly, the measured concentration of *N*-methyl aniline was observed to *increase* by as much as 5% in samples (relative to the “time-zero” sample) that were quenched during the induction period. This observation was observed across several experimental runs and is in slight excess of the error of the method. How the concentration of amine in these samples relative to the “time-zero” solution is increasing remains mysterious. These samples are heated, where the time-zero solution is simply a sample from the stock solution that is quenched when heating is begun. Ideally, a true t-zero sample would undergo heating just up to the catalytic temperature along with the other samples, but have zero reaction time at the temperature of catalysis. Unfortunately, this

is practically challenging. Quenching the solution should fully liberate all ligands, substrates, and products from any coordination with tantalum and not depend on whether the sample was heated. It can only be concluded at this point that control has been lost in one or more unknown variables between the heated and unheated samples.

As the accuracy of the method was limited by the small number of measured samples, smaller reaction vials (4 mL) were used to accommodate the preparation of 28 identical reactions. This enabled four samples for every time point to allow for comparison of ‘identical’ reactions at these times. Visualizing the consumption of *N*-methyl aniline in this series led to the clear observation that these reactions have a problematic and variable induction period (Figure 2.12)

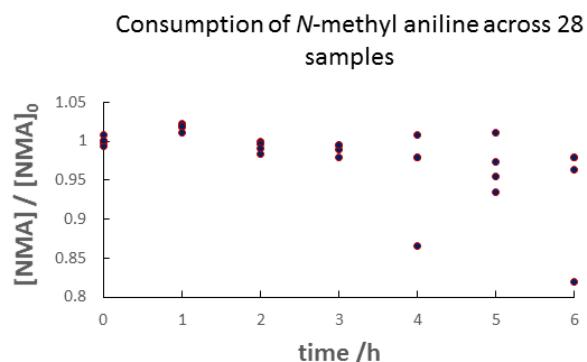


Figure 2.12 Consumption of *N*-methyl aniline across 28 samples

Unfortunately, the variable induction of the reactions prevented a highly accurate determination of the reaction rate. Since the induction period and time required for 20% amine consumption are on the same time scale (hours), attempts to monitor the latter are obscured by the former. While the initial consumption of amine proceeds linearly once the reaction begins to turn-over, the onset of catalysis is unpredictable. To date, the origin of this inductive effect is poorly understood; it is proposed that it may be related to the autocatalytic formation of active species before catalytic turnover. In a further complication, rates of product formation are observed to be

less than the rate of amine substrate consumption. This further suggests inaccuracy in determining reaction rate, as these rates should be equivalent in that no other reaction products from the amine substrate are noted.

Nonetheless, the rates of amine consumption and product formation were determined and an approximate KIE was determined using the deuterated substrate **2.1** (Figure 2.13). Due to the variable induction period, the rate of product formation across three runs with unlabeled *N*-methyl aniline varied from 1.57-2.90 mM•h⁻¹. With substrate **2.1**, product formation was significantly suppressed, with an observed rate of 0.79 mM•h⁻¹ that correlates to an average KIE of approximately 3.

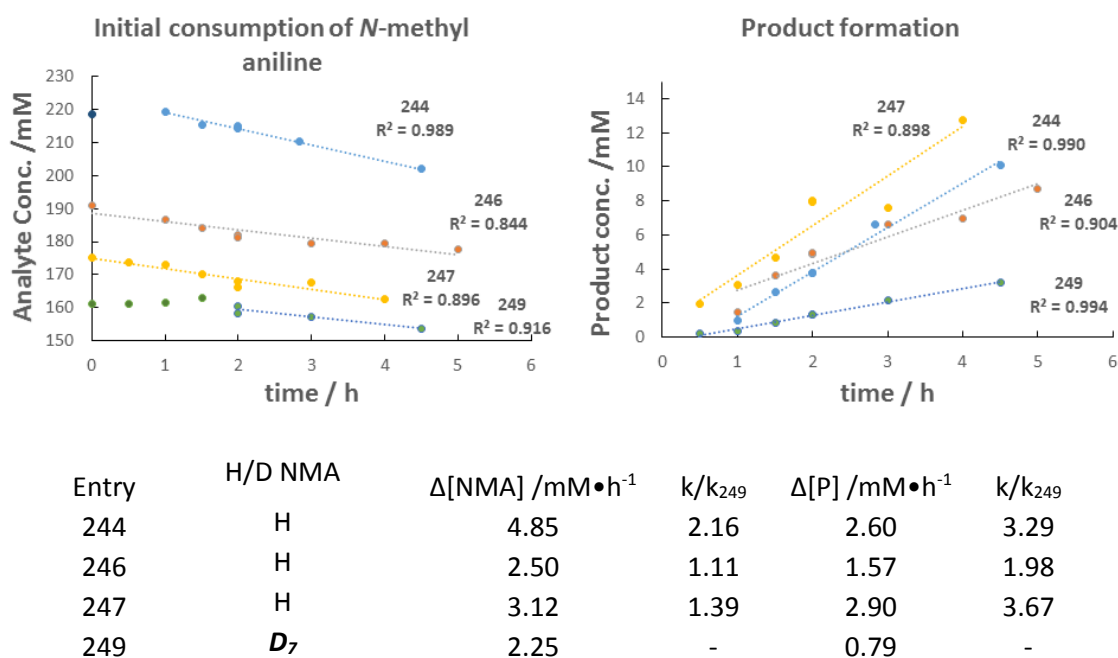


Figure 2.13 Comparing initial rates of *N*-methyl aniline consumption and product formation across four kinetic runs. Note that last entry 249 was performed with *d*₇-*N*-methyl aniline **2.1**

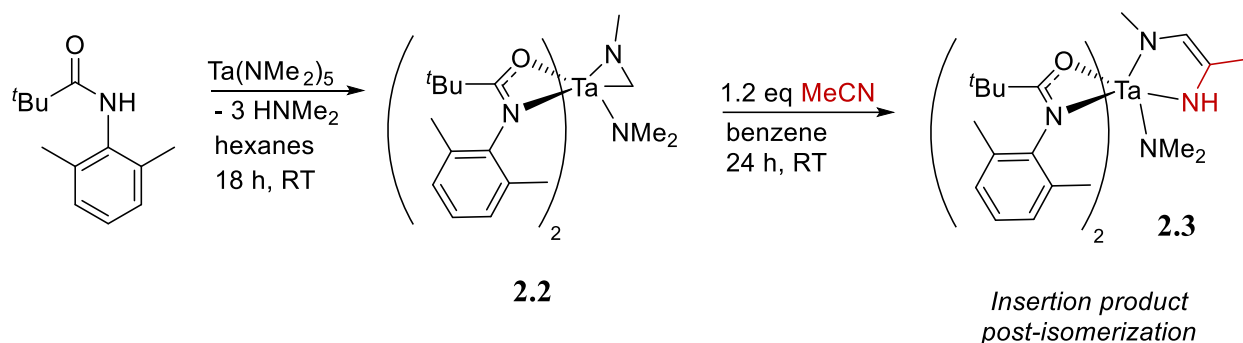
A key assumption with this developed methodology was that reactions that were performed in parallel would proceed in synchronization with each other. Unfortunately, the observed

variation in induction before the onset of catalysis has demonstrated that this assumption is not valid with this reaction. While this unfortunately prevents the highly accurate determination of a KIE, the general trends observed in these kinetic experiments are not in conflict with theoretical predictions. The observed increase in KIE with *d*₇-*N*-methyl aniline **2.1** is consistent with the theoretically proposed dependence of amine concentration on the TLS.

2.2.3 Attempts to experimentally isolate reaction intermediates

The isolation of reaction intermediates from a catalytic cycle can provide valuable information about the operative mechanism. Where possible, the identification and characterization of active species using X-ray crystallography is a powerful means of corroborating or refuting key proposed steps. However, the isolation of catalytic intermediates is inherently challenging, as efficient catalysis has rapid turnover and thus these intermediates are reactive and presumably only present fleetingly.

Efforts to isolate intermediates from HAA with tantalum catalysts has been met with limited success. The reaction takes place in an excess of amine, and extensive equilibria with these amines results in a mixture of metal complexes in solution. Somewhat surprisingly, all efforts to isolate a pre-catalyst bearing *N*-methyl anilido groups exchanged for dimethylamido (using an excess of amine) have been unsuccessful. Using a bis-amidate tantalum catalyst, Lauzon was able to isolate a tantallaziridine **2.2** (Scheme 2.21).



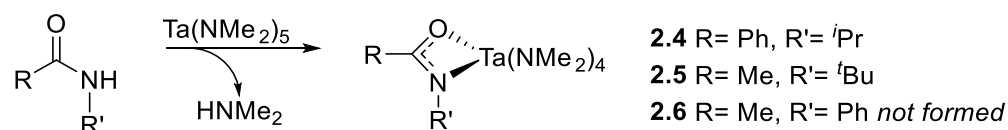
Scheme 2.21 Spontaneous formation of tantallaziridine (**2.2**) and subsequent insertion product (**2.3**) with acetonitrile obtained by Lauzon.^{12, 35, 96}

This formation is thought to be driven by steric relief of the congestion around the metal imposed by the two bulky amidates. This complex displays sluggish reactivity, with 71% conversion of 1-octene with *N*-methyl aniline at 130 °C for 168 h.³⁵ Despite the formation of the catalytically active tantallaziridine as the starting complex, the steric congestion is thought to preclude efficient catalysis. Lauzon was also able to isolate the metallacycle insertion product **2.3** from the addition of acetonitrile (Scheme 2.21).^{12, 96} However, no insertion products were obtained with various alkenes, internal alkynes, or conjugated ketones, even with heating to 90 °C.

2.2.3.1 Attempts to form an axial metallacycle

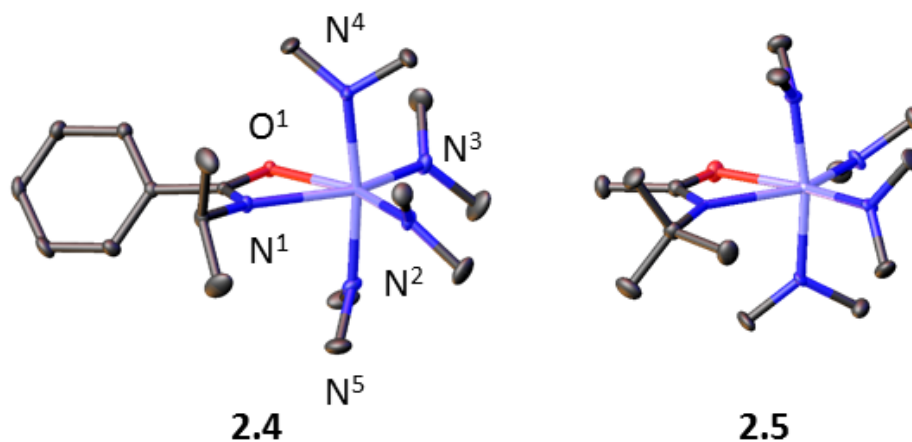
During the computational modelling of the catalytic cycle, a low energy axial metallacycle was identified. This proposed theoretical species is the product intermediate from the insertion of an alkene into an axial tantallaziridine (see Scheme 2.14). Due to its low ground state energy relative to the starting tantalum complex **A1**, this species is proposed to be a non-productive resting state. It was hypothesized that the steric bulk imposed by the amidate ligand prevents isomerization of the equatorial metallacycle to this resting state. Thus, using a mono *N,O*-chelated complex with minimal steric bulk, it is predicted that if this axial metallacycle is formed in sufficient quantities it could be isolable.

To experimentally isolate such a species, a series of mono-*N,O*-chelating amidate tantalum complexes were prepared (Scheme 2.22). The amidate pro-ligands for complexation were selected with the intention to form mono-amidate complexes with a minimal steric profile. Using 1:1 stoichiometry, complexes **2.4** and **2.5** were obtained in high yield (> 90%). Attempts to form complex **2.6** as a mono-amidate were not successful; the outcome of this reaction will be discussed later.



Scheme 2.22 Formation of tantalum mono-amidates with minimal steric bulk

Complexes **2.4** and **2.5** were characterized by ^1H NMR spectroscopy and in the solid-state by X-ray diffraction. Unsurprisingly, the amidate is observed to bind in all cases κ^2 to tantalum through the 1,3-*N,O*-chelate (Figure 2.14). Compared to the more bulky **1.3**, the Ta-O and Ta-N contacts are more symmetric, with Ta-O bonds expanding by *ca.* 0.1 Å and Ta-N bonds contracting by *ca.* 0.15 Å. It is proposed that diminished steric bulk on the *N* substituent enables this closer contact, resulting in a more symmetrically delocalized κ^2 binding mode.

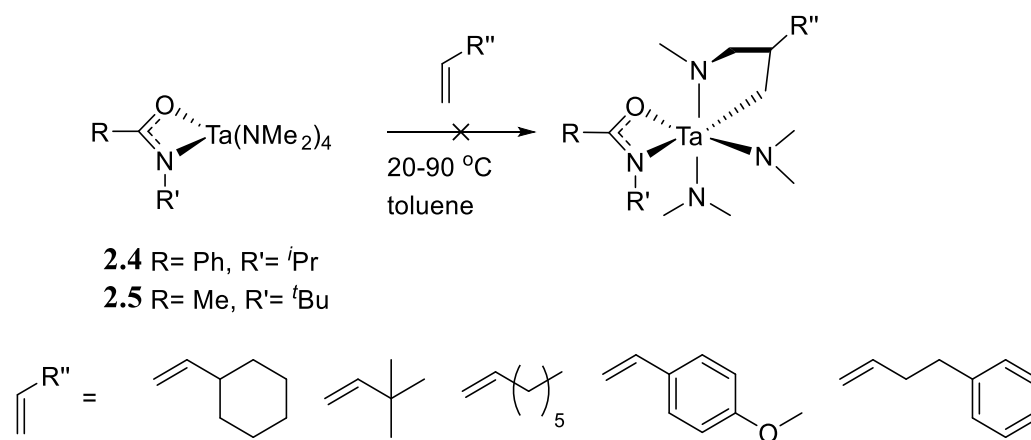


Entry	Ta-O	Ta-N ¹	Ta-N ²	Ta-N ³	Ta-N ⁴	Ta-N ⁵	O ¹ -Ta-N ¹
1.3	2.099(3)	2.447(3)	1.970(3)	1.996(4)	2.037(4)	2.050(4)	56.9(1)
2.4	2.203(1)	2.301(1)	1.997(1)	1.994(2)	2.040(1)	2.028(1)	58.3(5)
2.5	2.211(6)	2.289(6)	2.007(7)	1.980(7)	2.040(7)	2.043(7)	58.0(2)

Figure 2.14 Solid-state molecular structures and selected bond metrics of tantalum mono-amidate complexes 2.4-2.5. Thermal ellipsoids shown at 30% probability, H-atoms omitted for clarity. Compared with reported data for complex 1.3³⁵

With minimal steric bulk imposed by these amidates, complexes **2.4** and **2.5** are predicted to be poor HAA catalysts. To test this hypothesis, simple catalytic screening was performed with *N*-methyl aniline and 1-octene. After 16 hours at 130 °C, minimal conversion was observed, with 21% and 16% for **2.4** and **2.5**, respectively. This observation of sluggish catalytic performance supports the well-accepted notion that the steric environment imposed by the amidate is important for reactivity. Further, the lack of turnover was considered encouraging for the purposes of capturing intermediates.

With these complexes in hand, stoichiometric experiments were conducted with terminal alkenes (Scheme 2.23).



Scheme 2.23 Attempted formation of an axial metallacycle

As the goal is to crystallize an insertion product, vinyl cyclohexane was specifically among the alkenes chosen as the cyclohexyl substituent may impart crystallinity. Initial reaction attempts were set-up in the glovebox at room temperature, but no physical observations to suggest reactivity were observed, nor were crystals obtained upon attempts to crystallize the reaction mixture. Selected reactions were monitored by ^1H NMR spectroscopy. Unfortunately, monitoring these stoichiometric reactions in the olefinic region did not show any diagnostic shifts that may indicate insertion products, even when the reaction was heated. In reactions with **2.4**, the signal at δ 3.96 assigned to the *N*-isopropyl $\text{CH}(\text{CH}_3)_2$ is lost upon heating. The product of this reaction is unknown, however this reactivity at the amidate suggests **2.4** is not a suitable candidate for these experiments. Regrettably, no high quality crystals were obtained from any of these attempted reactions with various alkenes.

Reflecting upon these attempts to isolate a metallacycle, it is proposed that the extensive equilibria taking place during the reaction prevents the formation of meaningful quantities of product. Although the metallacycle is predicted as the lowest point in the PES, there are multiple equilibria present in solution. As the metallaziridine is formed, an equivalent of neutral amine is

released, which can act as a substrate in the reverse reaction. Therefore, future experiments should be designed to remove this equivalent of neutral amine.

2.2.3.2 Isolation of tantalum cluster decomposition product

During attempts to form the less bulky Ta complexes in the previous section, an unusual product was obtained from the attempted protonolysis of the tantalum starting material to form compound **2.6** (Scheme 2.22). As with prior reactions, the 1:1 stoichiometry of ligand and metal is expected to give a tantalum mono-amidate complex. After the reaction, re-crystallization in a mixture of toluene and hexanes gave bright yellow crystals. These crystals were investigated by ^1H NMR spectroscopy, however, only two overlapping singlets were observed at δ 3.61 and 3.58. No other signals were observed which could be logically assigned to the amidate ligand. Fortunately, the crystals were of sufficient quality for X-ray diffraction. The solid-state structure is shown in Figure 2.15.

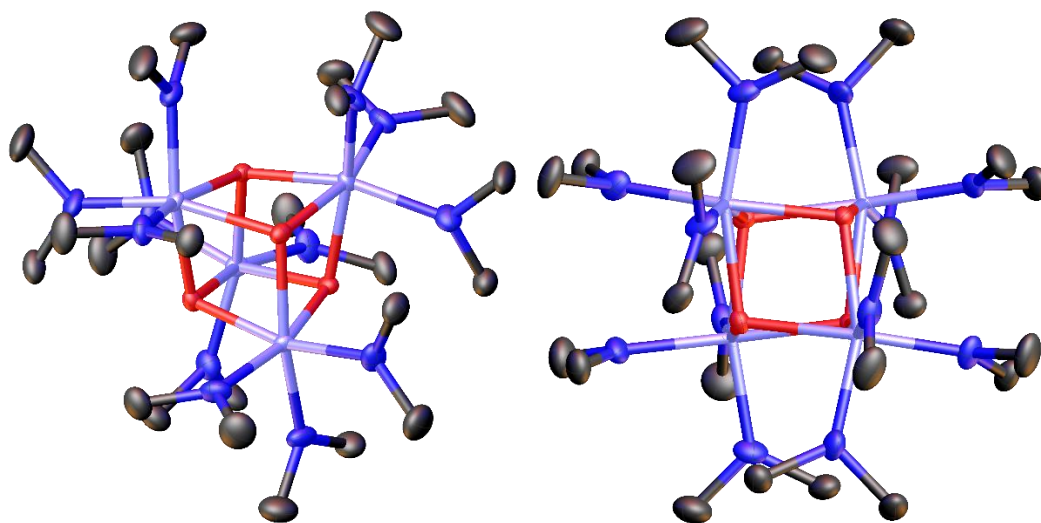


Figure 2.15 Solid-state molecular structure of tantalum-oxo complex **2.7** from two perspectives. Thermal ellipsoids shown at 30% probability, H-atoms omitted for clarity

The solid-state structure indicates the product of the reaction was a cubane-like tantalum oxo tetramer (**2.7**). A search of this compound reveals that this is a reported structure, however it was crystallized in a different unit cell.¹⁰⁶ In that report, the authors were able to prepare the complex in 11.6 % yield using a careful addition of H₂O/THF at – 78 °C. This complex is therefore considered a product of decomposition, where one equivalent of water liberates two amido ligands in a protonolysis mechanism, while the oxygen bridges between three tantalum atoms. Under the reaction conditions, water could have entered the reaction from solvent, the ligand, or the glove-box atmosphere. As this complex was prepared from the same solvent as the other protonolysis reactions in which this product was not observed, this was not considered the source of water. It is proposed that the ligand is the source of the water as a mono-hydrated molecule. This ligand was purified for the glovebox *via* sublimation, which normally removes all traces of water, however the ability of the amidate to hydrogen-bond makes it possible for water to be retained in the sublimate. This proposed hypothesis is also supported by the isolation of a product resulting from a 1:1 stoichiometric reaction between water and the tantalum starting material. If an excess of water were provided to this starting material, it is predicted that a complex mixture of tantalum oxo species would be obtained with all amido ligands liberated.

Complex **2.7** was screened for catalytic activity in the HAA of 1-octene with *N*-methyl aniline. No conversion was noted upon heating to 130 °C for 24 hrs. This complex is proposed to be too stable to form catalytically active species. While this molecule was not investigated further, this reaction may be of relevance to microelectronics; homoleptic Ta(NMe₂)₅ has been used as a pre-cursor to chemical vapor deposition and atomic layer deposition to prepare metal nitride and metal oxide films using both oxygen and water as oxygen sources.¹⁰⁷⁻¹⁰⁹

2.3 Conclusions

The use of computational and experimental tools have been applied to gain valuable insight into the mechanism of Ta-catalyzed HAA of olefins with secondary amines. This development of more efficient catalysts has greatly improved the practicality and versatility of this reaction towards the synthesis of amines, however the inherent oxophilicity of group 5 complexes has prevented a corresponding development of mechanistic knowledge.

This chapter first explored the origin of improved reactivity that is observed using tantalum complexes supported by an amidate ligand. Using DFT, the modelling of experimentally relevant complexes was conducted and compared with known experimental trends. Modelling of **I** was performed for the mono-amidate tantalum complex **1.3**, while modelling of **II** ($\text{Ta}(\text{NPhMe})_2\text{Cl}_3$) is related to $[\text{TaCl}_3(\text{NEt}_2)_2]_2$ (**2**). Comparison of experimentally relevant complexes **I** and **II** has revealed key differences in the potential energy surface depending on the ligand environment. The steric congestion in amidate-supported **I** favors the formation of the catalytically active tantallaziridine, in contrast to the more sterically accessible **II** and **III** ($\text{TaMe}(\text{NPhMe})_2\text{Cl}_2$). However, this steric bulk proves to be detrimental to the turnover limiting step, protonolysis.

These predictions were compared with deuterium labelling and KIE experimental studies, as well as comparative results from related catalytic investigations. These studies have suggested a kinetic isotope effect with deuterated amine substrates, consistent with the theoretical turnover-limiting step, protonolysis. This theoretical mechanism is also consistent with catalytic observations, rationalizing the regio-selective formation of branched products and the competition of hydroaminoalkylation with non-productive *ortho*-metallation.

These results point toward attractive features of *N,O*-chelated catalysts as being bidentate to promote catalyst stability while maintaining a highly electrophilic character. Ligand

hemilability and electron delocalization through the ligand backbone also contribute to effective catalysis. Future catalyst development should focus on the importance of an electrophilic, yet sterically-supported environment about the metal center for hydroaminoalkylation catalysis.

The inherent challenges in monitoring HAA reactions by NMR spectroscopy motivated the development of an alternative methodology using separation and detection by GC-FID. This method was also necessary to explore kinetic isotope effects with a novel *N*-methyl aniline substrate that is deuterated in the *ortho* position, preventing reaction monitoring by ^1H NMR spectroscopy. Method development enabled the measurement of several HAA reactions. Unfortunately, these reactions were observed to have a variable induction time with a period on the same time order as 20% amine consumption, limiting the accuracy of the determined rates. Nonetheless, an approximate KIE was determined with the labelled substrate that qualitatively matches the predicted RDS of protonolysis in the computational model.

Attempts to isolate a metallacycle intermediate that is a predicted resting state were conducted with sterically accessible mono-amidate complexes. Two such complexes were prepared, characterized, and shown to be poor HAA catalysts, matching known trends in the importance of sterics about the metal centre. Various alkene insertions were attempted, unfortunately no such metallacycle was obtained. During these efforts, a tantalum-oxo cluster compound was obtained from the attempted protonolysis of the tantalum starting material with an amide proligand. This cubane-like molecule is proposed to be a product of partial decomposition from the reaction of the starting material with one equivalent of water. Experimentation with this complex was limited to HAA screening, in which no conversion was noted.

2.4 Experimental

2.4.1 Computational details

Calculations have been carried out with the hybrid B3PW91¹¹⁰ or M06¹¹¹ density functional as implemented in the Gaussian 09 package.¹¹² An SVP¹¹³⁻¹¹⁴ basis set was used with Dolg's pseudo potential¹¹⁵⁻¹¹⁶ and associated basis sets for Ta. Single point calculations have been carried out with the Def2-QZVPP¹¹⁷⁻¹¹⁸ basis including dispersion¹¹⁹ and solvent interactions (toluene) using the SMD model.¹²⁰ The geometry optimizations were performed without constraints and transition states were checked by internal reaction coordinate forward and reverse relaxations. The energies given are Gibbs free energy values G in kcal•mol⁻¹ computed with Gaussian 09 at catalytically relevant conditions: $T = 363$ K and $P = 1$ atm.

2.4.2 Materials and Methods

General All reactions were performed under an inert atmosphere using a Schlenk double manifold equipped with N₂ and high vacuum (10⁻³ mbar) or a glovebox filled with N₂, unless otherwise stated. All glassware used was heated above 160 °C in an oven prior to use. Reactions were performed in threaded scintillation vials (4 or 20 mL) equipped with a poly(tetrafluoroethylene)-coated magnetic stir bar and a poly(tetrafluoroethylene)-lined polypropylene screw-cap. NMR spectra were collected in poly(tetrafluoroethylene)-capped J-young NMR tubes.

Reagents All reagents were purchased from commercial sources. N-methyl aniline (Aldrich) and 1-octene (Aldrich) were stirred over CaH₂ for a minimum of 2 h, separated by distillation, then manipulated using standard Schlenk techniques. Trimethoxybenzene (TMB) was purchased from Aldrich and sublimed prior to use. The amidate pro-ligands for complexes **1.3**, **2.3-2.5** and alkenes in section 2.2.3 were purified by sublimation. Ta(NMe₂)₅ (Strem) was used as received. For the preparation of *D*₇-N-methyl aniline, *p*-toluenesulfonanilide (Aldrich), NaH (60%, Aldrich), and

d_3 -iodomethane (Aldrich) were used as is. Toluene and hexane were purified by passing over activated alumina columns prior to collection and storage in the glovebox. Common solvents and work-up reagents were used as is.

Instrumentation

NMR spectroscopy ^1H NMR spectra were collected using a Bruker Avance instrument operating at 300 or 400 MHz. Chemical shifts, δ , are reported in parts per million (ppm) and coupling constants J are given in Hertz (Hz). Abbreviations for NMR assignments are as follows: s = singlet; d = doublet; dd = doublet of doublets; t = triplet; q = quartet; m = multiplet; br = broad; appt = apparent.

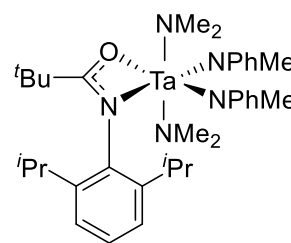
GC-FID Measurements were conducted on an Agilent 7890B GC with an FID detector, utilizing methane as the ionization gas and hydrogen as for the FID flame.

X-ray diffraction Diffraction data was collected on either a Bruker X8 Apex or Bruker Apex DUO diffractometer. Cell determination and integration were carried out using SAINT. Refinement of integrated data was conducted with OLEX2 using SHELXL.¹²¹

2.4.3 Synthesis and Characterization

(N-[2,6-Diisopropylphenyl]pivalamidate)tetrakis(dimethylamido)tantalum (1.3)³⁵

$\text{Ta}(\text{NMe}_2)_5$ (0.200 g, 0.5 mmol) and N-(2,6-diisopropylphenyl)pivalamide (0.130 g, 0.5 mmol) were combined in hexane (5 mL) resulting in a heterogeneous suspension. Upon stirring overnight, the initially yellow, cloudy mixture became a yellow, clear

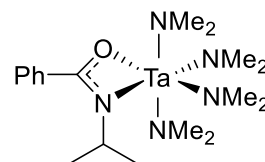


solution. Volatiles were removed *in vacuo* and the resulting yellow solid was recrystallized from a minimum of hot hexanes (*ca.* 1 mL) to afford pale yellow crystals (0.276 g, 90%). ^1H NMR (300 MHz, d_8 -tol): δ 7.00 (s, 3H, ArH), δ 3.49 (m, 2H, $\text{CH}(\text{CH}_3)_2$), δ 3.31 (s, 24H, $\text{N}(\text{CH}_3)_2$), δ 1.34 (d,

6H, CH(CH₃)₂), δ 1.26 (d, 6H, CH(CH₃)₂), δ 1.08 (s, 9H, C(CH₃)₃). Characterization was consistent with previously reported values.

(N-[isopropyl]benzamidate)tetrakis(dimethylamido)tantalum (2.4)

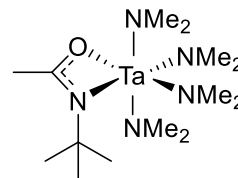
Ta(NMe₂)₅ (0.100 g, 0.25 mmol) and N-(isopropyl)benzamide (0.040 g, 0.25 mmol) were combined in hexane (5 mL) resulting in a heterogeneous suspension. Upon stirring overnight, the initially yellow, cloudy mixture



became a yellow, clear solution. Volatiles were removed *in vacuo* and the resulting yellow solid was recrystallized from a minimum of hot hexanes (*ca.* 1 mL) to afford pale yellow crystals (0.110 g, 85%). ¹H NMR (300 MHz, d₈-tol): δ 7.49 (m, 2H, ArH), δ 7.10 (m, 3H, ArH), δ 3.97 (quartet, 1H, CH(CH₃)₂), δ 3.49 (s, 24H, N(CH₃)₂), δ 1.11 (s, 6H, CH(CH₃)₂).

(N-[tert-butyl]methamidate)tetrakis(dimethylamido)tantalum (2.5)

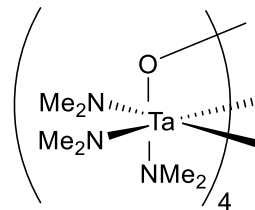
Ta(NMe₂)₅ (0.100 g, 0.25 mmol) and N-(tert-butyl)methamide (0.029 g, 0.25 mmol) were combined in hexane (3 mL) resulting in a heterogeneous suspension. Upon stirring overnight, the initially yellow, cloudy mixture



became a yellow, clear solution. Volatiles were removed *in vacuo* and the resulting yellow solid was recrystallized from a minimum of hot hexanes (*ca.* 1 mL) to afford pale yellow crystals (0.100 g, 86%). ¹H NMR (300 MHz, d₈-tol): δ 3.43 (s, 24H, N(CH₃)₂), δ 1.77 (s, 3H, CH₃), δ 1.20 (s, 3H, CH₃).

(OTa(NMe₂)₃)₄ (2.7)¹⁰⁶

Ta(NMe₂)₅ (0.200 g, 0.5 mmol) and N-(phenyl)methamide (0.067 g, 0.25 mmol) were combined in hexane (5 mL) resulting in a heterogeneous suspension. Upon stirring overnight, the initially yellow, cloudy mixture became an orange, clear solution. Volatiles were removed *in vacuo* and

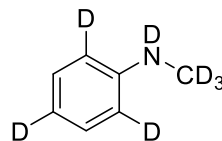


the resulting yellow solid was recrystallized from a minimum of hot hexanes (*ca.* 1 mL) to afford lustrous yellow crystals. ^1H NMR (300 MHz, $\text{d}_8\text{-tol}$): δ 3.61 (s, 36H, $\text{N}(\text{CH}_3)_2$), δ 3.58 (s, 36H, $\text{N}(\text{CH}_3)_2$). Characterization was consistent with previously reported values.

***N*- D d_3 -methyl 2,4,6- d -aniline (2.1)** *p*-toluenesulfonanilide (10 g, 0.040

mmol) in 30 mL DMF was added to NaH (2.05 g, 0.044 mmol) in 130 mL

DMF with a few drops of hexane. The reaction was heated to 60 $^\circ\text{C}$, then



cooled to 40 $^\circ\text{C}$, upon which CD_3I (5.7 g, 0.040 mmol) was added (no immediate observations).

The reaction was left to stir overnight at 40 $^\circ\text{C}$. Upon removal of the volatiles *in vacuo*, 40 mL of

water was added, followed by three successive extractions with ether (30 mL each). The ether

layers were then collected. Concentrated H_2SO_4 was added to the residue and the heterogeneous

mixture was heated to 130 $^\circ\text{C}$, with swirling and stirring until all solids were dissolved. The

homogeneous mixture was cooled down, water (50 mL) was added, and the pH was adjusted to 14

using 3 M NaOH. The product was extracted with ether (30 mL each), then washed with brine,

and dried over Na_2SO_4 . Removal of the volatiles gave a clear, colorless liquid (2.94 g, 67%). After

checking the resulting *N*- d_3 -methyl aniline by ^1H NMR, it was used as is for the next step. *N*- d_3 -

methyl aniline (0.1 g, 0.9 mmol) was added to a 10 mL microwave reactor tube, followed by 4 mL

of a solution of $\text{HCl}/\text{D}_2\text{O}$ (0.225 M, 1 equiv. HCl with respect to amine) and a stir bar. The tube

was capped and heated in a microwave reactor at 180 $^\circ\text{C}$ for 30 mins. This was repeated with five

tubes to obtain reasonable quantities of material; after 30 mins, reactions had variable color, from

pale grey to blue to purple. The 6 tubes were combined and 30 mL of a solution of $\text{NaOH}/\text{D}_2\text{O}$

(0.225 M, 1.2 equiv.) was added, followed by extraction with 30 mL ether. The volatiles were

removed *in vacuo* overnight, followed by distillation under vacuum (10^{-2} mbar, 40 $^\circ\text{C}$) to give a

clear, colorless liquid (0.48 g, 77% yield). ^1H NMR (300 MHz, $\text{d}_8\text{-tol}$): δ 7.13 (s, 2H, 3,5- ArH).

^2H NMR (60 MHz, tol) δ 6.72 (s, 1D, 4-ArD), δ 6.37 (s, 2D, 2,6-ArD), δ 2.87 (s, 1D, ND), δ 2.29 (s, 3D, CD_3).

2.4.4 Methods

Reaction Screening

An example reaction screen is as follows: To a poly(tetrafluoroethylene) capped J-young NMR tube was added a given catalyst (10 mol%) in d^8 -toluene (*ca.* 1 mL). To this was added 10 equiv. *N*-methyl aniline and 15 equiv. 1-octene. The tube was capped and heated at a specified temperature and time in an external oil bath. Conversion was measured comparing the integration of the aryl C-H *ortho* protons, in which the product is observed at δ 6.57 relative to δ 6.47 .

GC-FID Methodology

To prepare a “stock” reaction, **1.3** (0.016 g, 0.025 mmol) was added to a 20 mL scintillation vial along with *N*-methyl aniline (0.056 g, 0.5 mmol), 1-octene (0.122 g, 0.75 mmol) and trimethoxybenzene (0.012 g, 0.08 mmol) in toluene (0.7 mL). This mixture was swirled, with all components rapidly dissolved as a pale yellow solution. 100 μL of this stock was then added to seven 20 mL scintillation vials using an auto-pipettor. To each of these seven reactions, 0.35 g of toluene was added to reach a total reaction volume of 0.5 mL. A stir bar was added to each reaction, then each was capped with a poly(tetrafluoroethylene)-lined cap. These vials were removed from the glovebox and heated in an external heating bath (130 $^\circ\text{C}$), with the exception of one sample (the t-zero) which was not heated but immediately quenched. Reactions were quenched by adding 0.5 mL methanol, upon which the yellow color immediately disappeared and a white precipitate was observed. 19 mL of dichloromethane was added to bring total volume to *ca.* 20 mL, which was pre-calculated as an appropriate concentration for the GC-FID (*ca.* 500 of *N*-methyl aniline in the t-zero sample). These samples were filtered through celite into vials for injection in the GC.

At a given time point, a given reaction was quenched and prepared for GC measurement. Once all samples were prepared for analysis, they were all run consecutively in a single GC run. Within the run, periodic blanks were inserted into the sequence to confirm a clean background is obtained after each individual run.

The concentration of analytes were quantified by integration of the peak area of the analyte relative to the internal standard (1,3,5-trimethoxybenzene). Data was analyzed using Microsoft Excel's built-in linear regression analysis. See Appendix B for a representative data set.

Chapter 3: Synthesis of amine-pendant polyolefins with dynamic hydrogen bonding

3.1 Introduction: Established routes to prepare amine-functionalized polyolefins

Polyethylene (PE) has emerged as the world's most common plastic, with annual production on the order of one hundred million tonnes annually.¹²²⁻¹²³ As a broad class of materials, PE offers a plethora of advantageous properties that have allowed for its exploitation in a tremendously wide variety of applications. The high commodity of PE is partially derived from its versatility in processing and use, combining a low glass-transition ($T_g < -100$ °C) with a high melting point ($T_m > 100$ °C) while demonstrating excellent mechanical and chemical stability. On-going research efforts have sought to further improve the properties of PE by modification to properties such as density.

While polyolefins such as PE are physically useful and inexpensive materials, their inert, non-polar backbone also limits their scope of function. Their low surface energy prevents compatibility with polarized molecules, preventing them from interacting with paints, adhesives, coatings etc.¹²⁴ This property also prevents their incorporation into hybrid materials with polar synthetic polymers or conventional materials like wood, glass and metal. As passive materials, they are not capable of “smart” behaviors in which they are responsive to internal or external stimuli such as stress, temperature, pH, radiation, other molecular interactions, etc. In recognition of these limitations, a long-standing goal has been the expansion of material properties *via* the installation of polar functional groups onto polyolefin backbones.¹²⁴

Due to their unique and broad range of applications, amine-functionalized polymers have become an important class of specialized materials.¹²⁵⁻¹²⁹ Their reactivity can be harnessed to

realize a myriad of functions, such as metal-scavenging,¹³⁰ CO₂ uptake,¹³¹⁻¹³² water-treatment,¹³³ drug-delivery,¹³⁴ and anti-microbial activity.^{53, 55, 135} As specialized materials they have found application in the electronics industry as components in membranes.¹³⁶ They can also be incorporated into other polymers to modify their properties or function, with one example being compatibilizers for polymer blends.⁵¹

Inspired by supramolecular systems in biology,⁶ nitrogen-containing molecules designed to participate in hydrogen-bonding interactions¹³⁷⁻¹³⁸ have shown novel features as responsive materials, for eg. self-healing polymers.¹³⁹ Motivated in part from well-known base pairing between purine and pyrimidine in DNA, synthetic efforts have sought to prepare supramolecular donor (D)-acceptor (A) arrays that enable directional and selective self-assembly.¹⁴⁰ One of many promising advances was reported in 2011, in which Leigh *et al.* reported an AAAA-DDDD quadruple hydrogen bond array (Figure 3.1 A).¹³⁸ These D-A interactions were able to confer outstanding stability to the intermolecular complex; the binding free energy is calculated to be 20% in excess of a carbon-carbon covalent bond (as determined by its association constant in dichloromethane). These interactions also permit stability in a variety of solvents. In 2014, Lewis *et al.* demonstrated the effects these hydrogen-bonded pairs could produce in the viscoelastic behavior in a series of model butyl acrylate copolymers (one such complementary group shown in Figure 3.1 B).¹⁴¹ Depending on the nature and degree of hydrogen bonding, varying entanglement of polymer chains resulted in modified material bulk properties such as shear response, glass-transition temperature, and shape memory. Most critically, the presence of hydrogen bonds resulted in the formation of thermo-reversible supramolecular networks with technologically useful viscoelasticity.

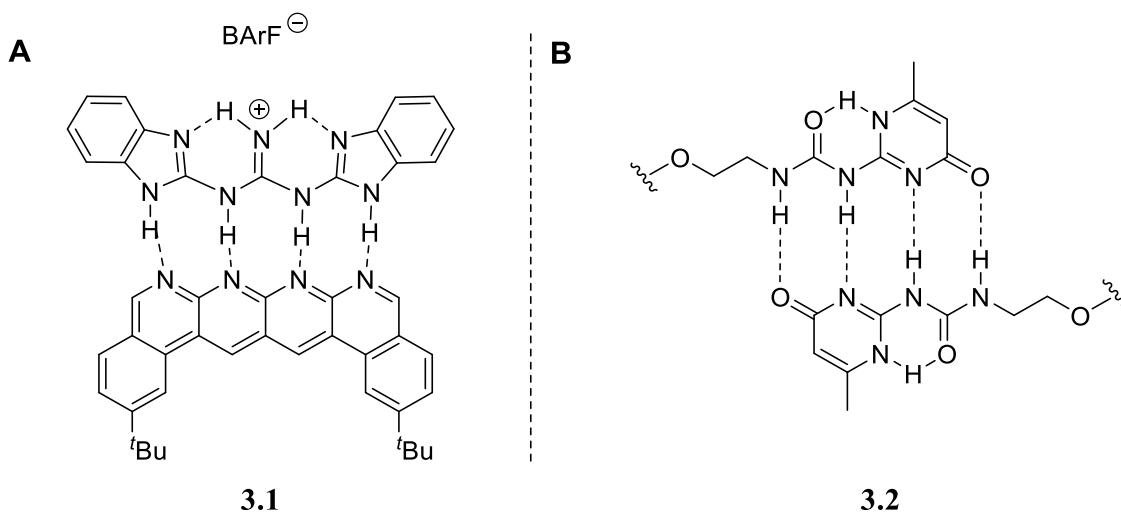
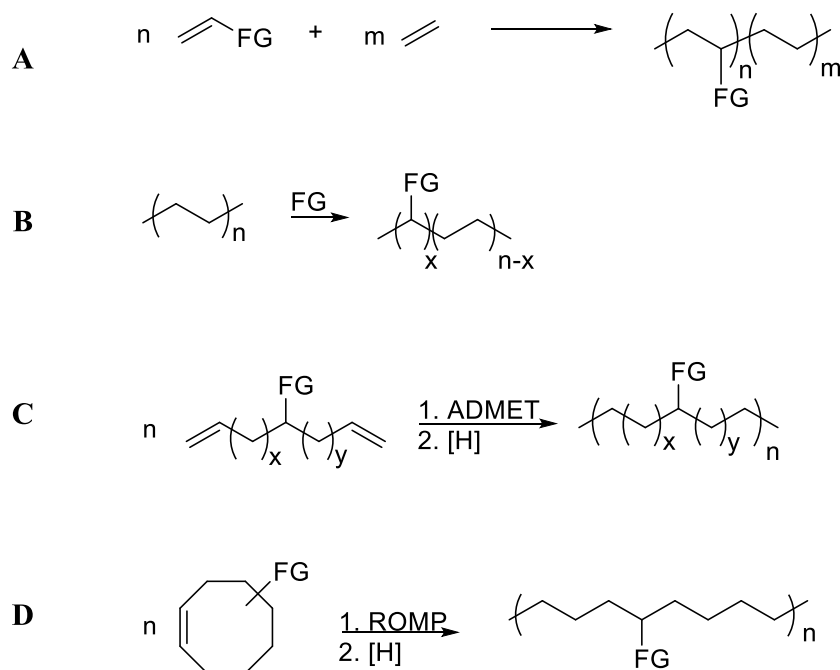


Figure 3.1 (A) DDDD-AAAA hydrogen bond array¹³⁸ (B) DDAA-AADD hydrogen bond array in a butyl acrylate copolymer¹⁴¹

The precedent for amines as a component of these advanced materials has validated the potential for this functional group to impart superior and novel properties. However, highly efficient routes for their controlled incorporation into PE remains a challenge.¹²⁴ The inherent physical and chemical stability of the PE backbone that provides such robust practical advantages also prevents straightforward installation of functional groups using chemical synthesis. The general strategies that have emerged to prepare functionalized polyethylene derivatives are shown in Scheme 3.1.



Scheme 3.1 General strategies for the synthesis of functionalized polyethylenes (A) Radical/TM-catalyzed copolymerization (B) Post-polymerization modification (C) ADMET followed by hydrogenation (D) ROMP followed by hydrogenation

The introduction of functionalized monomers during conventional olefin polymerization would constitute the most direct method for the assembly of functionalized polyolefins. However, radical¹⁴²⁻¹⁴³ or transition metal catalyzed¹⁴⁴⁻¹⁵⁶ pathways typically demonstrate poor compatibility with polar functional groups (Scheme 3.1 A). Post-polymerization modification is the most commonly used functionalization method industrially; however these typically employ harsh reaction conditions, often leading to material defects because of chain scission/branching (Scheme 3.1 B).^{51, 157-160} Two other methods using metathesis may also be used to prepare PE derivatives when followed by hydrogenation. Acyclic diene metathesis (ADMET) is a somewhat specialized technique that forms polymeric materials by metathesis polycondensation (Scheme 3.1 C).¹⁶¹⁻¹⁶⁷ Alternatively, in recent years Hillmyer and others have shown that ring-opening metathesis polymerization (ROMP) of pre-functionalized cyclooctene (COE) followed by reduction can be a

powerful tool for functionalized polyethylene synthesis (Scheme 3.1 D).¹⁶⁸⁻¹⁷⁰ This route can allow precise control over functional group incorporation and polymer microstructure. However, a challenge in ADMET and ROMP reactions are that metathesis catalysts are often poorly compatible with amine-containing substrates.^{47, 171} These routes in the context of amine-functionalized PE will be discussed in further detail in the following sections.

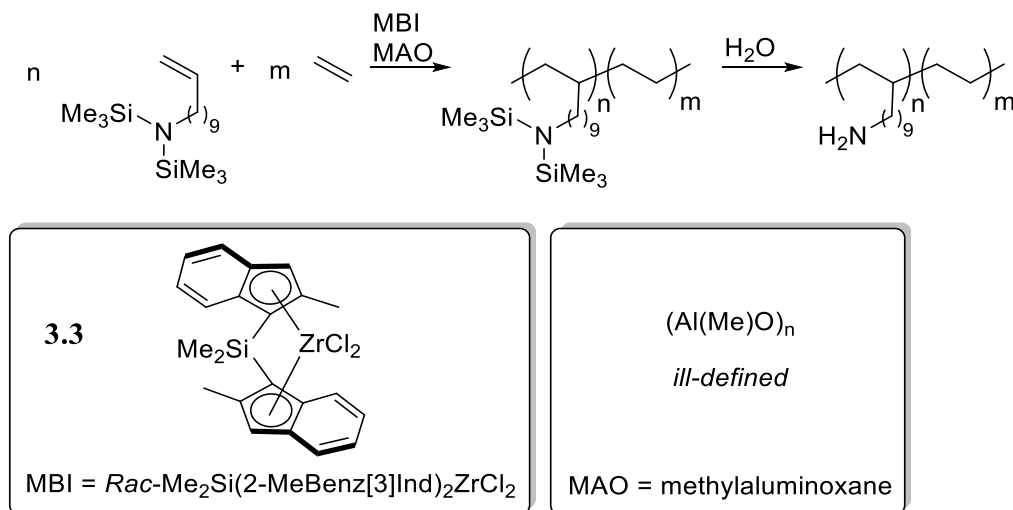
3.1.1 Catalytic copolymerization

The most direct means to produce amine-functionalized polyolefins would be the introduction of amine-functionalized co-monomers directly along with α -olefins during conventional polyolefin production. A major class of catalysts for olefin polymerization are Lewis-acidic ETM complexes that show poor tolerance with monomers containing a Lewis-basic amine. For example, Ziegler-Natta systems based upon titanium suffer from poisoning in the presence of nitrogen even in an excess of methyl aluminum oxide (MAO).¹⁵¹ The fundamental challenge with this method exists in developing catalysts that show similar reactivity profiles towards electronically dissimilar olefins while avoiding deactivation.¹⁷²

In spite of these challenges, examples of metal-catalyzed routes to copolymerize olefins with amino-olefins to form copolymers bearing pendant amines are known.^{144-156, 173} Earlier, work by Giannini explored the polymerization of various diisopropylamine derivatives with Ziegler-Natta type catalysts.¹⁵⁶ This report successfully polymerized amine derivatives by separating the functional group from the terminal olefin with methylene “spacers” and sterically protecting the nitrogen atom as a tertiary amine (see a related example in Scheme 3.2). The use of silyl groups as “masking” agents to generate passivated amines as poorer electron donors is also a noted strategy.¹⁵⁶ A detailed study completed later by Waymouth *et al.* with zirconocene and Ziegler-

Natta catalysts showed that significant steric bulk about the amine group is a more important factor than electronics in maintaining high polymerization activity.^{153, 155}

Using a combination of these design strategies, in 1997 Schneider *et al.*¹⁵⁴ reported a metallocene-catalyzed ethene copolymerization to produce primary amine-functionalized PE with variable amine % incorporation (Scheme 3.2).



Scheme 3.2 Metallocene-catalyzed ethene copolymerization¹⁵⁴

While this report represents a proof-of-concept of this methodology, drawbacks remain in the limitations with respect to monomer synthesis and product scope. The amine-functionalized monomer requires four stoichiometric steps to produce; as polymerizations are very sensitive to trace impurities, three of the steps require distillation to obtain pure materials. Post-polymerization deprotection of the silyl group with water is also required to afford the pendant free amine.

In recognition of the challenges of amines with early-transitional metal catalysts, systems have also been developed with late-transition metals in pursuit of broad functional group tolerance. A prominent industrial reaction is the Shell higher olefin process (SHOP) for the production of linear ethylene oligomers (C₄-C₂₀).¹⁷⁴ This reaction, using O,P-chelating nickel catalysts, can be

performed in the presence of polar solvents and has thus also been adopted for PE synthesis.¹⁷³
¹⁷⁵⁻¹⁷⁶ In 2000, Grubbs *et al.* showed that using a harder, more sterically bulk N,O-chelating Ni complex enabled PE synthesis with tolerance for the presence of such additives as trimethylamine and ethyl alcohol (see Figure 3.2 (L)). However, the lifetime and activity of the catalyst was significantly diminished in the presence of these additives.

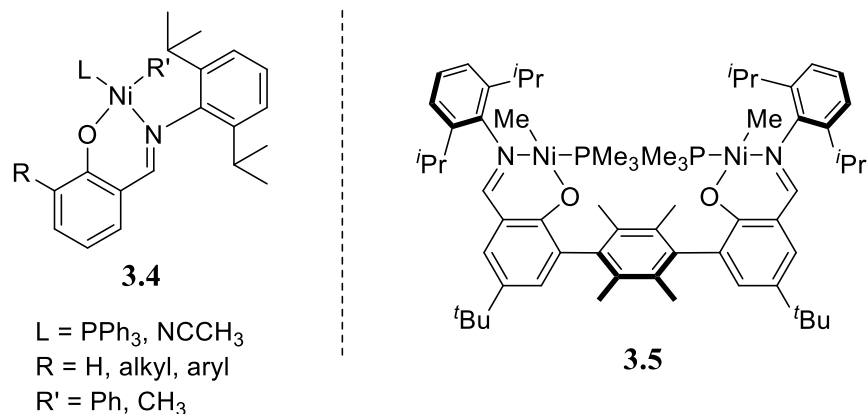


Figure 3.2 Nickel catalysts for PE synthesis (L) Grubbs *et al.*¹⁷³ (R) Agapie *et al.*¹⁴⁴

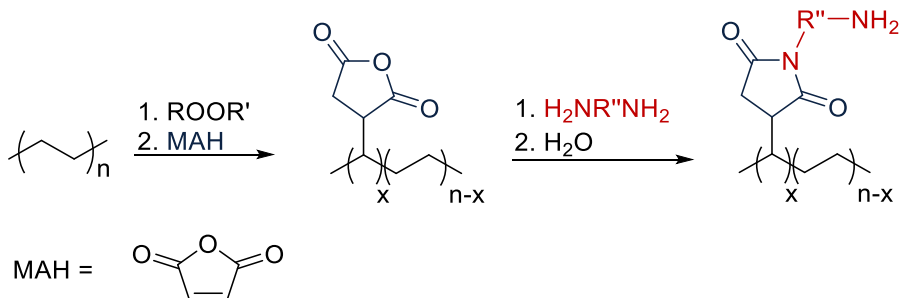
In a more recent example, Agapie *et al.* have reported a bimetallic nickel catalyst that has succeeded in co-polymerizing ethylene with amino-olefins without requiring protection of tertiary amine groups (see Figure 3.2 (R)).¹⁴⁴ In contrast to monometallic systems in which inhibition by amines is more readily observed,¹⁷³ this system avoids deactivation by sterically preventing N-coordination of amine moieties to both metal centers. While one amine can coordinate, the other amino olefin preferentially binds to the Ni center with its olefin, therefore enabling polymerization. The second metal site also increases the tolerance of the system to polar FGs by reducing the overall oxophilicity of the complex. While this report offers a very interesting approach to polymerizing amino olefins, the steric profile of the catalyst and monomer must be precisely matched, limiting the scope of products. The amine incorporation in this system was also limited to 0.1-0.8 mol%.

Altogether, while copolymerization of olefins with amino olefins can be used to directly obtain functionalized polyethylene derivatives, significant catalyst development is required to afford a system that balances monomer reactivity while avoiding deactivation. The requirement of spacers between the functional group and olefin results in a polyolefin with large branches, which can dramatically affect the resulting physical properties. Success has been obtained by the ‘passivation’ of the amine with steric protection, spacers, and protecting groups/MAO.^{144, 151} However, this is circumventing the fundamental challenge of developing a catalyst that shows balanced reactivity profiles by essentially making the characteristics of the functionalized monomer as close to a non-polar olefin as possible. In cases where tolerance has been achieved, the steric parameters of the catalyst have been specifically tuned, limiting the diversity of the scope of functionalized products.

3.1.2 Post-polymerization modification

Post-polymerization modification is currently the most common route to functionalize polyolefins. In principle, any known transformation to functionalize a C-H bond can be applied to polyolefins that are already produced industrially using existing catalytic technologies.¹⁵⁷ Depending on the reaction stoichiometry, the molar incorporation could in theory be tuned to achieve targeted percent functionalization. Unfortunately, the conditions required to activate the aliphatic backbone of PE are sufficiently harsh to produce physical defects *via* chain scission.

The most common post-polymerization technique involves generation of free radicals on the polymer chain, typically using peroxides, followed by anhydride grafting and nucleophilic attack of amine (Scheme 3.3).^{51, 157-158, 177}

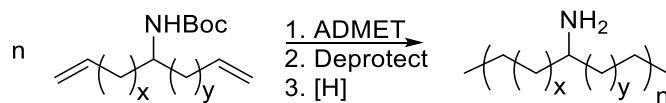


Scheme 3.3 Post-polymerization modification using maleic anhydride (MAH)¹⁷⁷

While this strategy is viable, the generation of free radicals along the polymer backbone often leads to cross-linking or chain scission, thereby compromising its physical properties. The radicals are also randomly generated along the backbone, preventing precise control over functionalization and polymer microstructure. The low inherent solubility of the polymer also proves challenging in both the functionalization and subsequent purification of these materials. While this route can be used, as a general strategy it would greatly benefit from a profound advance in C-H activation chemistry to enable more straightforward functionalization.

3.1.3 Acyclic diene metathesis polycondensation (ADMET)

ADMET utilizes the olefin metathesis reaction followed by reductive hydrogenation as a route to functional polyethylenes (Scheme 3.4). This route requires construction of symmetrical α,ω dienes as functionalized monomers.^{163, 178} As a step-polymerization technique, amine functional groups can be precisely incorporated on a completely linear carbon back-bone. Wagener *et al.*¹⁶² has disclosed a series of protected amine dienes that are amenable to this transformation, that, upon deprotection, give a linear polymer with a pendant free amine with constant methylene run units between amine branches:

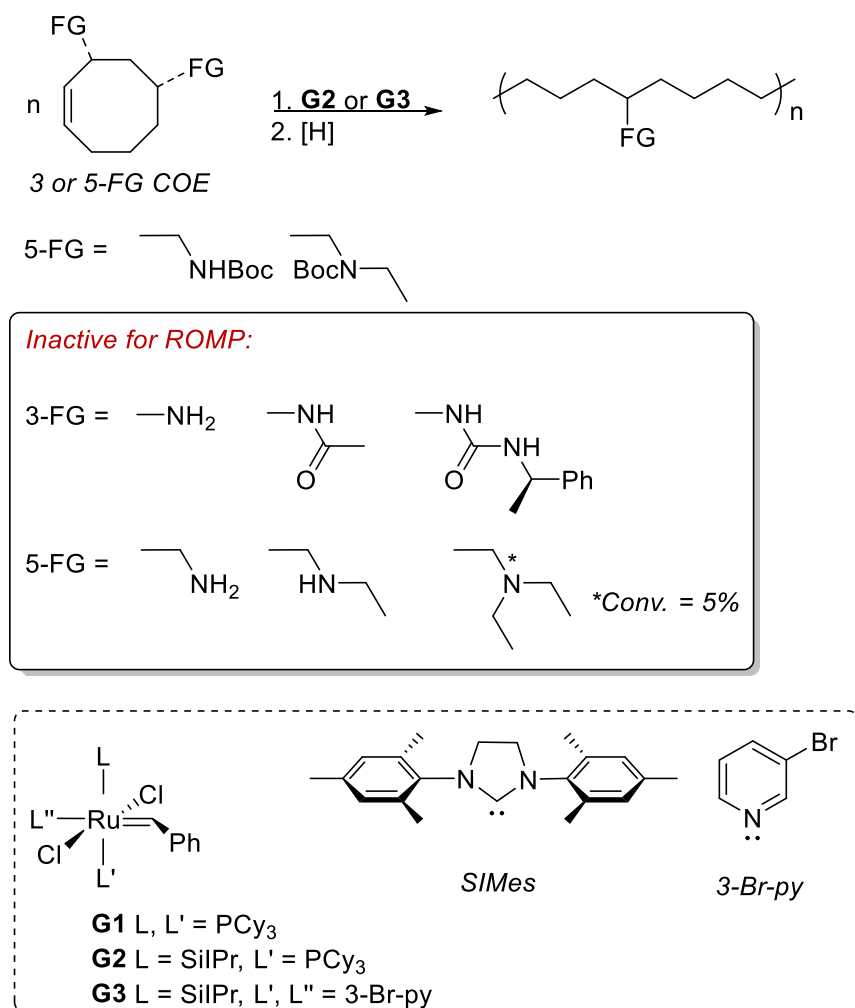


Scheme 3.4 ADMET to obtain polyethylene analogs bearing a pendant amine¹⁶²

However, this strategy still has some drawbacks. The synthesis of the α,ω dienes is challenging for adoption on a large-scale; the above report requires the use of a stoichiometric Grignard reagent. The amine must also be protected, adding steps to the overall path. Attempts to polymerize non-protected substrates were not successful in reports with Ru-based Grubbs catalysts (*vide infra*). As a polycondensation-type reaction, these transformations require very high conversion to obtain high molecular weight material.

3.1.4 Ring-opening metathesis polymerization (ROMP)

A viable alternative to using the above listed methodologies is ROMP followed by hydrogenation (Scheme 3.5). Hillmyer^{168-169, 179} has elegantly achieved success using this route with cyclooctene derivatives. The resulting polymers are analogous to polyethylene and have a functional group on every eighth carbon (by mol, as head-head, head-tail, tail-tail chain linkages are presumably random). As an atom-economic, chain-growth polymerization, this strategy can be used to generate relatively monodisperse polymers with controlled incorporation of functional groups. This strategy is also attractive as the incorporated functional group can potentially be exploited in low mol % *via* copolymerization with non-functionalized cyclic olefins to give block or gradient copolymers.¹⁶⁹



Scheme 3.5 ROMP followed by reductive hydrogenation^{168, 179}

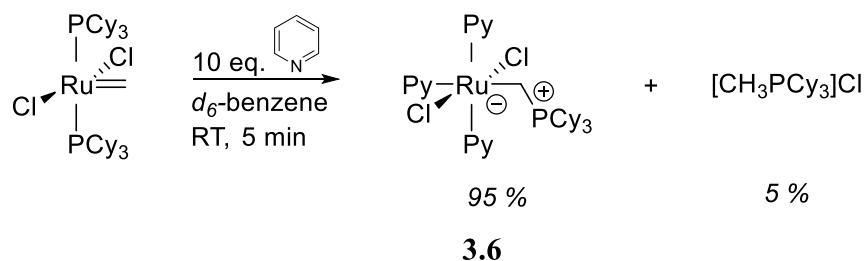
While an attractive platform for generating polyolefins with polar functional groups such as ether, amide and acetoxy derivatives, challenges have been encountered with nitrogen-containing functional groups. Among 3-cyclooctene derivatives, Hillmyer has prepared three different *N*-containing cyclooctene derivatives, including a primary amine, however none were compatible with Grubbs catalyst 2nd or 3rd generation, with evidence for catalyst deactivation in each case.¹⁶⁸ With 5-COE derivatives, **G2** was able to polymerize protected *N*-boc derivatives, including a secondary amine, however unprotected primary and secondary amines were not compatible for ROMP.¹⁷⁹ One tertiary amine example was reported, however, trace conversions

were noted (*ca.* 5%), presumably because of the incompatibilities of this monomer with the ruthenium catalyst.

While marked progress has been made in the last decade regarding functionalized polyolefins, the field remains hindered by inefficient monomer syntheses. Ideally, catalytic, as opposed to stoichiometric, transformations would generate protecting group free substrates in a limited number of high yielding synthetic steps. The 3-substituted cyclooctene derivatives discussed above require multiple stoichiometric transformations.^{168, 180} Indeed, while coupling ROMP and reductive hydrogenation is a feasible pathway to generate functionalized materials, challenges pertaining to monomer synthesis remain unsolved in the field. Furthermore, the associated challenges regarding the compatibility of nucleophilic amine substrates with state-of-the-art ruthenium catalysts prevent their exploitation into polymeric materials. These compatibility issues have been intensely investigated and will be discussed in the following section.

3.1.4.1 Decomposition of Grubbs catalysts in the presence of amines

The observed deactivation of metathesis catalysts has necessitated investigation into the pathways for this phenomenon.¹⁸¹⁻¹⁸⁶ A pathway for the decomposition of Grubbs catalysts has been studied in detail by Fogg and termed ‘donor-induced decomposition’.¹⁸⁴ Their work has shown that Grubbs catalysts bearing methylidene ligands are prone to decomposition in the presence of Lewis donors. After the pre-activation step in which the phosphine ligand dissociates from the metal centre, a Lewis donor such as pyridine can block re-coordination, resulting in nucleophilic attack of the methylidene ligand by the phosphine, thus generating species inactive for metathesis activity (Scheme 3.6).



Scheme 3.6 Donor-induced decomposition of a Ru methylidene¹⁸⁴

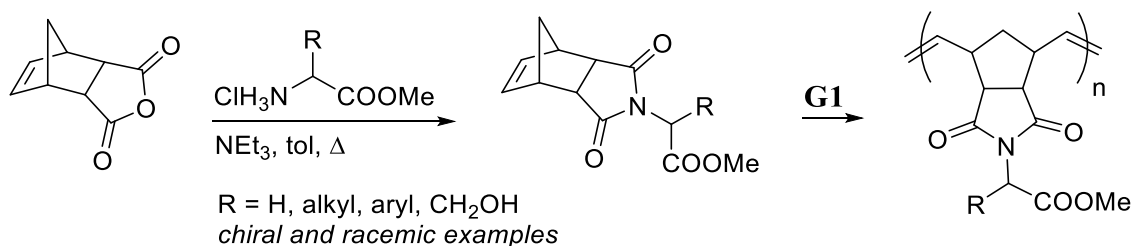
Ru methylidene catalysts, the active species for ring-closing metathesis (RCM), are more prone to decomposition than the Ru benzylidene catalysts used for ROMP.¹⁸⁷⁻¹⁸⁸ While this decomposition should thus be faster in RCM than ROMP reactions, it is possible that liberated phosphine attack may be inhibiting ROMP reactions with monomers containing a Lewis basic functional group such as an amine. In the case where one PCy₃ is replaced with the *N*-heterocyclic carbene SIMes (as in **G1** to **G2**), complete decomposition to a mixture of Ru species and the predominant formation of the [CH₃PCy₃]₂Cl salt was observed at room temperature within five minutes. While these results are more specific to RCM reactions, they provide valuable insight into a pathway by which amines can impede metathesis catalysts.

The Fogg group later reported that deactivation of the second generation Grubbs-Hoveyda catalyst could proceed through metallacyclobutane deprotonation in the absence of phosphine.¹⁸² The presence of amines led to the formation of inactive adducts with the catalyst through this deprotonation. These adducts inhibit metathesis with styrene, following a general trend of increased inhibition with amine basicity. The decomposition of the metathesis catalyst was found to result from the proton abstraction of the metallacyclobutane intermediate after [2+2] cycloaddition. This report demonstrated that basic amines can also deactivate catalysts by C-H activation, in addition to donor-induced decomposition.

3.1.4.2 ROMP of amine-containing norbornenes

While to-date ROMP has not been successful with unprotected amine-containing derivatives of cyclooctene, tolerance has been observed in cases with amine-containing norbornene derivatives.^{46, 55, 189-191} In these cases, overcoming the reported intolerance with the metathesis catalysis may be because of the significantly higher ring strain in norbornene vs. cyclooctene derivatives (ring strain of NBE and COE are 27.2 and 7.4 kcal•mol⁻¹ respectively).¹⁹²

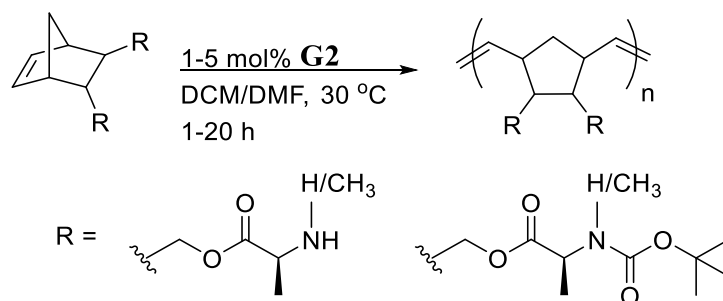
Norbornene monomers bearing pendant amino acid groups have been shown to be amenable to ROMP with Grubbs catalysts. In 1995, Biagini *et al.* reported the synthesis of *N*-norborneyl-amino acids using a one pot procedure starting from norbornene dicarboxylic anhydride and both chiral and racemic amino acids (Scheme 3.7).¹⁹³ The ROMP of this class of monomers was later reported using Grubbs first generation catalyst to give polymers with molecular weights that approximately matched theoretical values predicted by monomer:initiator (M:I) ratios and dispersities that indicate moderate degrees of control ($\mathcal{D} = 1.1$ -1.5).¹⁹⁴



Scheme 3.7 Preparation of *N*-norborneyl- amino acid derivatives and their polymerization with G1¹⁹³⁻¹⁹⁴

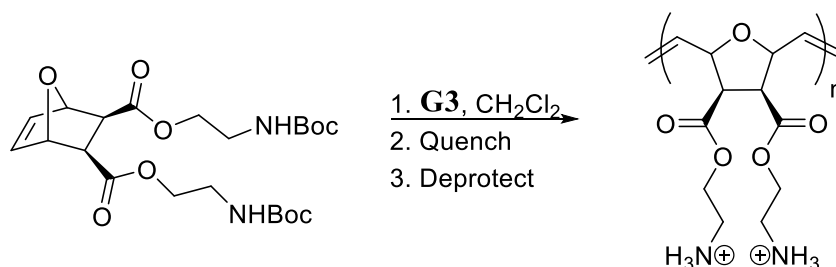
In 2009, Sutthasupa *et al.* reported the polymerization of a different class of norborneyl-amino acids bearing unprotected amine groups using **G2** (Scheme 3.8).¹⁹⁵ Protected amine derivatives could be polymerized in high yields within an hour, however molecular weights were in large excess of the M:I ratio (175-365 Kg•mol⁻¹ vs. *ca.* 50 Kg•mol⁻¹) with high dispersity ($\mathcal{D} = 1.8$ -3.1). The unprotected variant bearing a primary amine did not polymerize, while the secondary

amine variant required longer reaction times (20 h) with catalyst loadings above 2 mol% to polymerize in low to moderate yields (11-83%) with moderate dispersities ($\mathcal{D} = 1.3-1.5$).



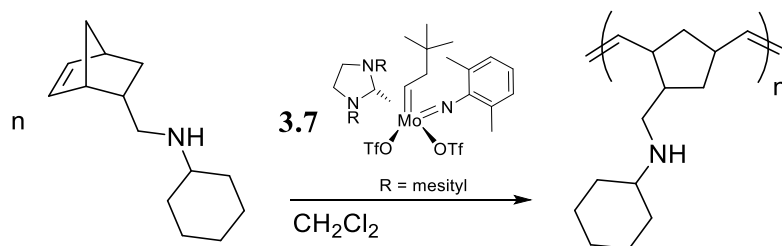
Scheme 3.8 ROMP of *N*-norborneyl- amino acid derivatives with **G2¹⁹⁵**

In 2009, Tew *et al.* reported a poly(oxanorbornene)-based synthetic mimic of an anti-microbial peptide (Scheme 3.9).⁵⁵ The protected diamino oxonorbornene derivative was polymerized in a controlled fashion with **G3**, enabling high yielding formation of polymer from 3-50 Kg•mol⁻¹ with low dispersity ($\mathcal{D} < 1.1$).



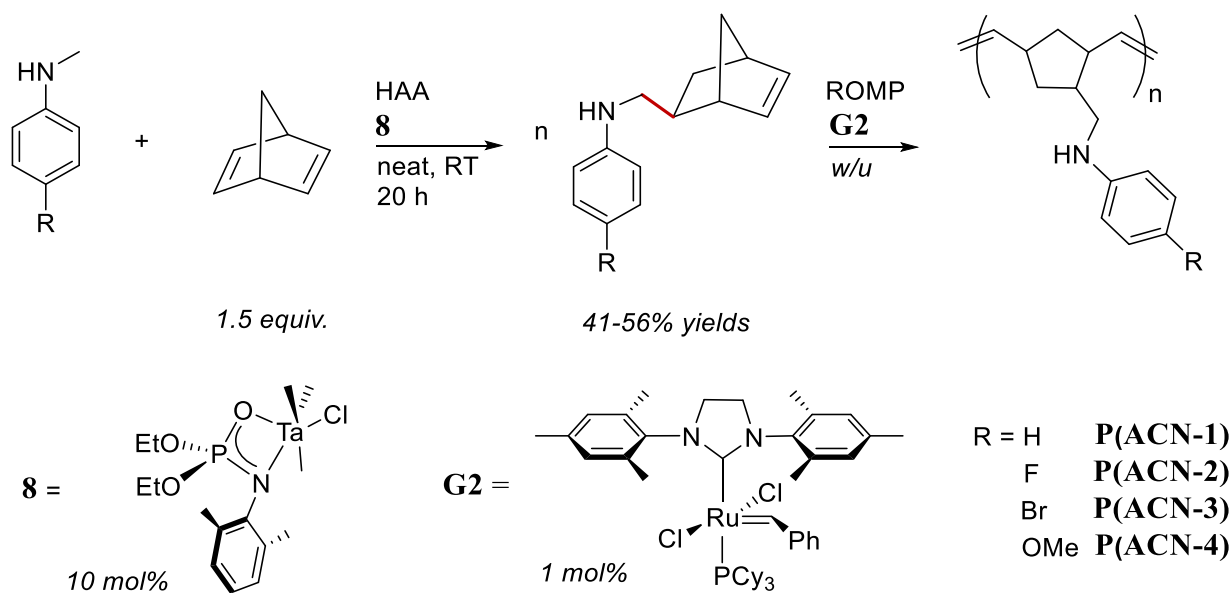
Scheme 3.9 Synthesis of an amine-containing poly(oxanorbornene) using ROMP with **G3⁵⁵**

In 2014, Buchmeiser reported a molybdenum catalyst (**3.7**) that exhibited high activity and functional group tolerance (Scheme 3.10).¹⁹⁶ This catalyst was shown to tolerate hydroxyl and amine groups, with ROMP of a secondary amine-containing monomer generating a polymer (13,100 g•mol⁻¹) with low dispersity ($\mathcal{D} = 1.1$). Impressively, this group 6 system did not require protection of the alkylamine. No rheological characterization of these materials was reported.



Scheme 3.10 ROMP of an unprotected secondary dialkylamine norbornene derivative¹⁹⁶

In 2016, Perry *et al.* in our group reported the synthesis and polymerization of a series of amine-containing norbornene (ACN) derivatives (Scheme 3.11).



Scheme 3.11 ROMP of amine-containing norbornene monomers ACN-1-4⁴⁶

Using **1.8**, hydroaminoalkylation was used for the catalytic mono-alkylation of norbornadiene (NBD) with secondary arylamines. Although yields were only modest (41-56%), this selective reaction operates at room temperature under neat conditions without stoichiometric additives or protecting groups. Halogen and methoxy substituents were tolerated in the *para* position, therefore providing monomers with electronically varied amine groups. After column chromatography, these monomers could undergo living ROMP with **G2**, with precisely controlled molecular weight as predicted by M:I ratio and low dispersity ($\text{Đ} < 1.1$). As the monomers are

functionalized with secondary arylamines, it is proposed that these ACNs are not sufficiently nucleophilic to deactivate **G2**, allowing formation of polymer in high yield.

The rheological properties of these P(ACN) materials was investigated in collaboration with the group of Prof. Savvas Hatzikiriakos in the Department of Chemical and Biological Engineering (UBC). In comparison to poly(norbornene), which exhibits typical shear response for a linear mono-disperse polymer, P(ACN-4) demonstrates shear hardening, in which storage modulus (G') is dominant over loss modulus (G'') over all frequencies of shear rate, and no cross-over point between these moduli is observed. This difference in rheological response can be rationalized by the formation of a transient supramolecular network as a result of hydrogen-bonding between chains. Further rheological analysis of different derivatives P(ACN-1-4) demonstrated that trends in shear response could be correlated to the hydrogen-bond acceptor character of the different R groups, where the strongly accepting fluoro derivative P(ACN-2) demonstrates the highest degree of shear thinning. This result suggested that not only does the amine functional group produce advantageous physical changes in bulk material properties, but that by modulating hydrogen-bond strengths the resultant material properties could also be tuned.

In surveying the development of ROMP of amine-containing monomers, it is apparent that recent breakthroughs in catalyst development have enabled tolerance to functional groups previously thought incompatible in ROMP. While the Lewis basicity of monomers bearing amine functional groups in the absence of protecting groups was once thought to prevent their polymerization, new variations of Grubbs and Schrock catalysts have demonstrated tolerance to this group. These developments have enabled renewed efforts to polymerize amine-containing cyclic olefins possessing lower ring-strain than norbornene derivatives.

3.1.5 Scope of chapter

This chapter explores the synthesis and characterization of poly(olefins) bearing pendant amine functional groups. Previously established work in the Schafer Group utilized the mono-phosphoramidate tantalum catalyst **1.8** for the synthesis of amine-containing norbornene monomers. While this hydroaminoalkylation reaction favorably operates at room temperature, the low robustness of the catalyst limits the scale of reactions to *ca.* 1-3 mmol. In consideration of this challenge, the chapter begins with research completed jointly with Shou-Jen Hsiang, an undergraduate researcher, to provide an alternative synthetic route to these monomers. Using a more readily assembled mono-pyridonate tantalum catalyst **1.11** (Scheme 3.12), this synthesis has been scaled up to *ca.* 50 mmol. The ROMP of monomers generated from either **1.8** or **1.11** has then been compared and key differences in polymerization behavior were noted.

In the following section, the preparation of amine-containing cyclooctene (ACC) monomers has been conducted. By replacing an amido ligand for a chloro group in **1.11** to generate a more electrophilic catalyst **1.9**, these monomers have been prepared on greater scale and generated higher yields than with previously reported catalyst **1.8**. These monomers were tolerated by Grubbs second generation catalyst (**G2**), therefore demonstrating the ROMP of a low-strain cyclooctenes functionalized with unprotected amines.

These novel P(ACC) polymers have been characterized in solution and in bulk using solid-state spectroscopy and melt rheology. The ability of these polymers to participate in extensive hydrogen bonding interactions is apparent in the rheological response of these materials, where non-linear effects have been observed due to the formation of hydrogen-bond networks when materials are subjected to stress-strain. As bulk materials, these interactions in combination with

the low T_g of the polymer give rise to interesting properties, including self-healing and poly(tetrafluoroethylene) adhesion.

To increase the potential of these unique monomers, copolymers have been targeted in which these ACNs/ACCs were paired with inexpensive, unfunctionalized olefin monomers. Attempts to form block or gradient copolymers has resulted in materials that exhibited lower solubility than either respective homopolymer. This has been attributed to phase separation of amine-containing and unfunctionalized segments due to self-assembly. To form a miscible copolymer, alternating addition of monomer feeds has been demonstrated.

As differences between the bulk properties of P(ACN) and P(ACC) polymers has been observed, their combination into copolymers has been conducted. Using different feeds of the respective monomers, the glass transition temperature (T_g) of the resulting copolymers can be tuned. Unexpected differences are noted in the polymerization rates of these monomers when copolymerized, suggesting side-equilibria during ROMP.

To further assess associative interactions in the polymers, an experiment has been designed utilizing variable temperature IR spectroscopy to probe how the material responds to thermal stimuli. In P(ACC) derivatives, thermally sensitive IR modes have been identified and tentatively proposed to arylamine functional groups that are liberated from hydrogen bond interactions.

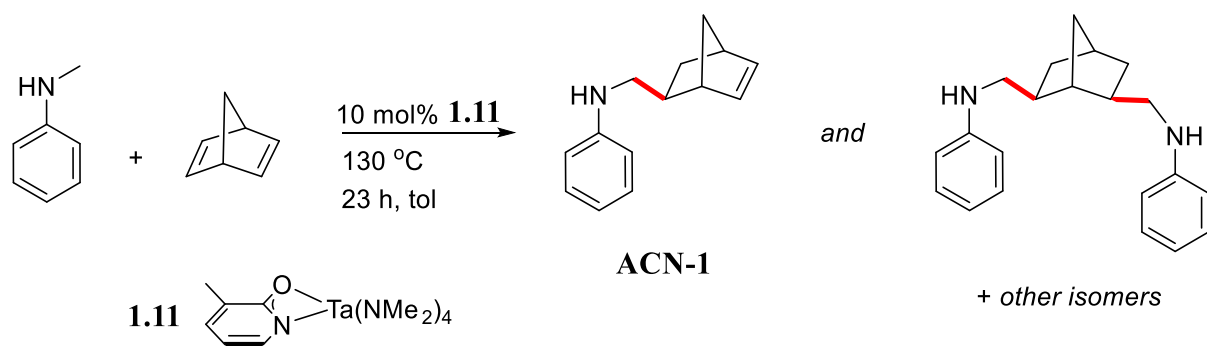
3.2 Results and Discussion

3.2.1 Alternative monomer preparation for gram-scale synthesis

A desirable outcome of fundamental polymer research is the ability to increase the quantity of products to preparative scales. Tantalum catalyst **1.8** has unprecedented room temperature reactivity; however, its activity is diminished upon scaling.⁴⁰ Catalyst **1.8** also requires storage in a freezer in the absence of visible light. The decomposition of this species is related to the kinetic lability of the Ta-C bond, which is susceptible to homolytic cleavage from light and heat. This phosphoramidate complex is also challenging to prepare, requiring a multi-step synthesis of the pyrophoric, air and light sensitive TaMe₃Cl₂ starting material, which itself is derived from pyrophoric ZnMe₂. These challenges in the preparation, storage, and use of catalyst **1.8** encouraged the development of an alternative preparative route to access amine-containing monomers.

3.2.1.1 Preparation of amine-containing norbornenes

In 2014, Chong *et al.* in our group reported that the mono-pyridonate mixed-chloro tantalum system **1.9** was highly active for the HAA of internal alkenes. However, the reactivity with norbornadiene was not reported. While high ring strain activates this alkene for HAA, the propensity for it to polymerize under elevated temperatures in the presence of Lewis acidic ETMs has been reported colloquially within the group. Pleasingly, a screening reaction revealed that a mono-pyridonate tantalum catalyst **1.11** was active for this transformation, with no observed evidence for polymerization (Scheme 3.12).



Scheme 3.12 Hydroaminoalkylation of norbornadiene with *N*-methyl aniline using 11

The conversion of this reaction was assessed by monitoring by ^1H NMR spectroscopy in a sealed NMR tube (Figure 3.3). Consumption of the amine and product formation was determined by the integration of the *ortho* C-H protons (δ 6.34 in the reactant vs. δ 6.44 in the product). As the resonance at δ 6.44 is assigned to both mono- and di-alkylated products, the % of ACN-1 formed was determined by the calculated ratio of the integration of that resonance with that of the product alkene at δ 5.96.

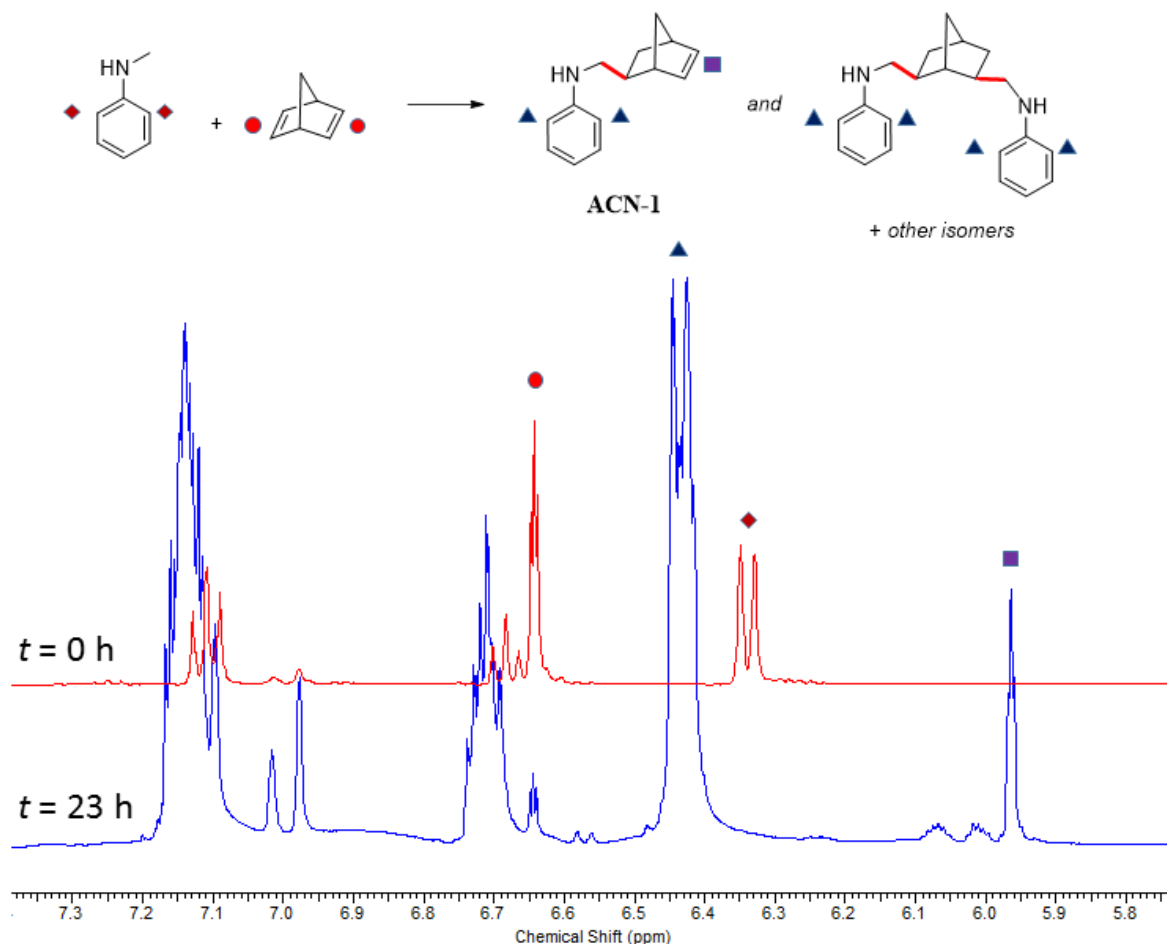
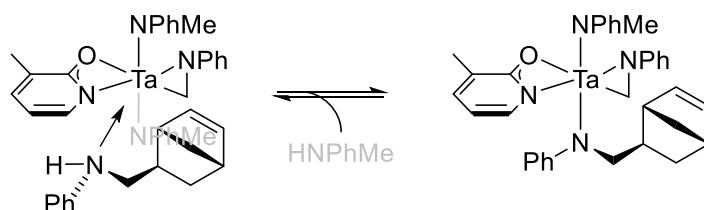


Figure 3.3 ^1H NMR spectrum (300 MHz, 298 K, $d^8\text{-tol}$) from region 7.3-5.8 ppm monitored hydroaminoalkylation conversion. Symbols correlate key diagnostic resonances of the substrate and product to monitor conversion

After 23 hours, the amine starting material was completely consumed, with the desired mono-alkylated ACN-1 formed in 13.5% NMR yield (Table 3.1). The low observed yield of ACN-1 with high conversion of amine suggests that the mono-alkylated product reacts more preferentially as a substrate towards HAA than the starting norbornadiene. Based on the higher ring strain of norbornadiene vs. norbornene (34.7 vs. 27.2 kcal $\cdot$ mol $^{-1}$), the former is predicted to be more activated for HAA.¹⁹² As this is in contrast to what is observed experimentally, it is

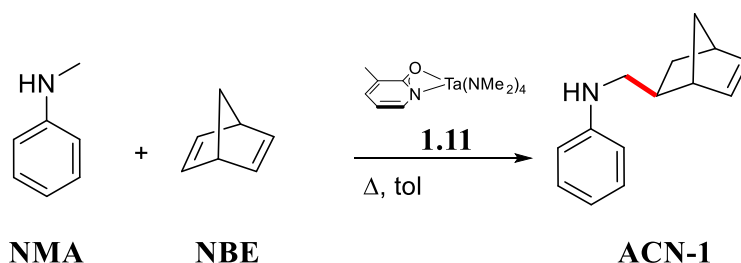
proposed that the amine substituent of ACN-1 may assist alkene insertion through coordination to the tantalum centre (Scheme 3.13). While no conclusive experimental evidence supports these species, they may rationalize the observed preference for ACN-1 over norbornadiene as an HAA substrate.



Scheme 3.13 Proposed coordination-assisted alkene insertion

To optimize the yield of the mono-alkylated product, the reaction time was reduced and the alkene loading was increased to 1.5 equivalents. After 1 hour, the amine was 90% consumed, however the ratio between mono and di-alkylated products was 1:1, for an effective ACN-1 yield of 45%. Reducing the reaction temperature to 120 °C gave a higher proportion of ACN-1, however only 35% of the amine had converted. Based upon these trends, 1 hour at 130 °C was selected as optimum reaction conditions to maximize the yield of the mono-alkylated product before it was further converted to the undesired di-alkylated product.

Table 3.1 Preparation of ACN-1 with *in-situ* generation of catalyst 1.11



Entry	mol ratio: NBD:NMA	% Catalyst	Temp (°C)	Time (h)	% Amine Conversion ^a	% Mono Product ^b	Estimated Yield (%) ^c
1	1 :1	10	130	23	100	13.5	13.5
2	1.5:1	10	130	1	90	50	45
3	1.5:1	10	120	1	35	76	27
4	1.5:1	5	130	1	61	60	37

^aDetermined by the relative integrations of *ortho* C-H proton signals on reacted vs unreacted *N*-methyl aniline.

^bPercent of converted amine that formed the mono-HAA product. Determined by the relative integrations of the *ortho* C-H *N*-methyl aniline signal to the alkene C-H signal of the product. ^cEstimated by multiplying the % amine converted by the % of mono-alkylated product formed.

After optimizing these conditions on small scale, the next goal was to scale up the synthesis to obtain gram-quantities of monomer. A series of reactions with optimized conditions were conducted to probe how this reaction translated to a greater scale.

Table 3.2 Increasing scale of ACN-1 synthesis with *in-situ* generation of catalyst 1.11

Entry	Scale (mmol) ^a	Approx. Total Volume ^b (mL)	Time (h)	Isolated Yield %
1	2.6	5 ^c	0.75	46-56 ^e
2	9.2	20 ^d	1	30
3	9.2	20 ^d	2.3	16
4	9.2	20 ^d	2	35
5	55.5	25 ^d	2	38

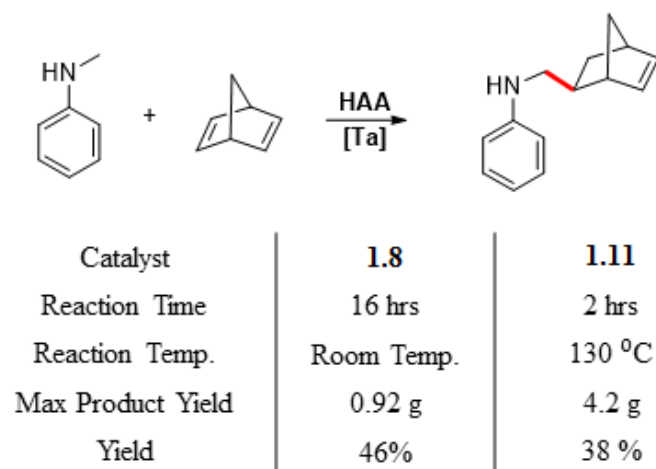
^aBased on *N*-methyl aniline. ^bDue to variations in reaction vessel sizes, absolute concentration was not kept constant. ^cPerformed in a 20 mL scintillation vial. ^dPerformed in a 50 mL Schlenk flask. ^eReported range from triplicate experiments.

The first attempt to scale up the reaction was performed using 2.6 mmol *N*-methyl aniline. After purification with column chromatography, an isolated yield of 46-56% was achieved over 3

repeat experiments. As comparable yields were obtained on this higher scale, the quantities of reactants were further increased to 9.2 mmol. The desired mono-product was isolated in only 30% yield, and analysis by GC-MS revealed a large excess of unreacted amine starting material. To reach higher conversion, the reaction time was increased to 2.3 hours. Unfortunately, this resulted in only 16% of the desired product and significant formation of the di-alkylated product. When reaction time was reduced to 2 hours, a yield of 35% was obtained.

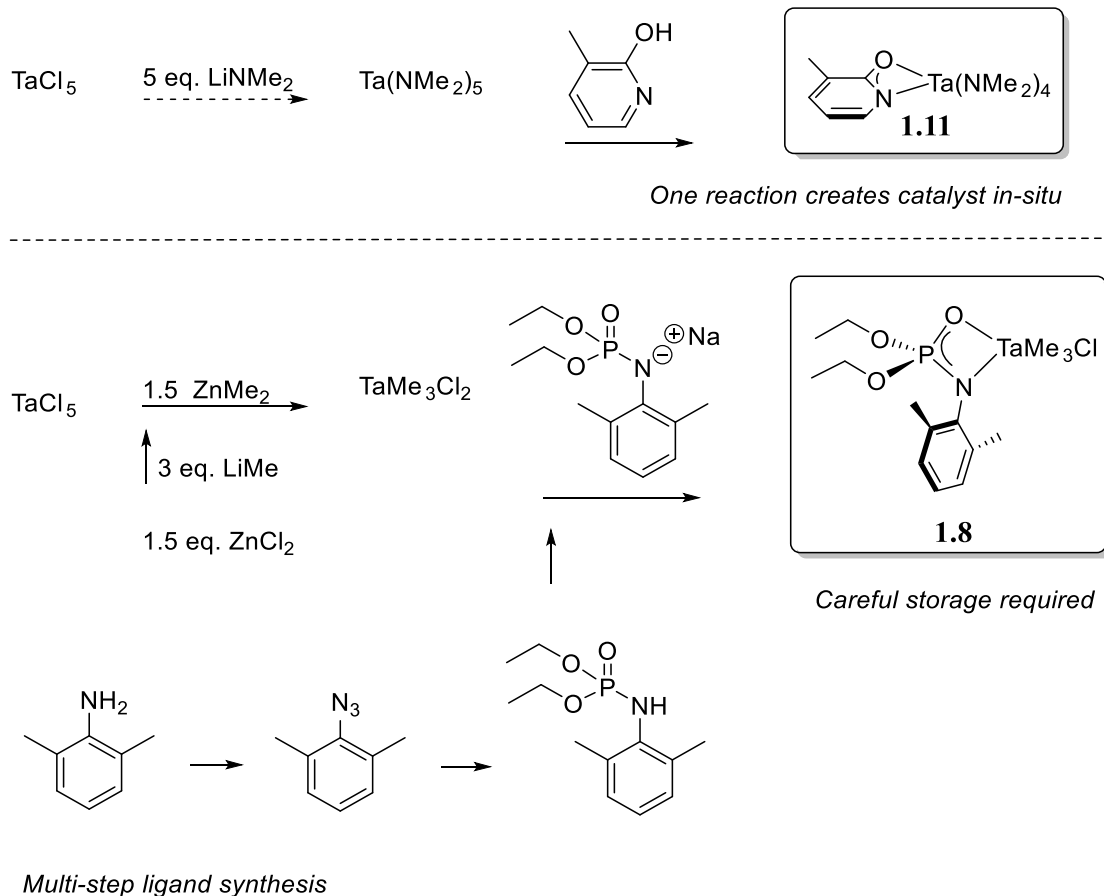
Despite the increased scale of the reaction generating only modest yields, the ability to generate larger quantities of product was gained. As such, a further increase to 55.5 mmol of *N*-methylaniline was performed in order to obtain enough material for subsequent polymerizations and rheological analysis. This scale proved challenging, as the reaction vessel required lowering the ratio of solvent to substrate. While it was thought that longer reaction times would be required, the decreased solvent volume appears to influence reactivity and after a reaction time of 2 hours a 38% yield of the mono-product was obtained. Analysis of the crude reaction mixture by GC-MS revealed the di-alkylated product was present with no traces of amine starting material.

A comparison between monomer synthesis with catalysts **1.8** and **1.11** is shown in Scheme 3.14. While the overall yield with **1.11** is 38%, relative to 46% with **1.8**, this catalyst is able to afford > 4 g of the desired product in a single reaction compared to a maximum of *ca.* 1 g with the latter. This increase in scale enables the rapid preparation of large quantities of amine-containing monomers from inexpensive and simple starting materials.



Scheme 3.14 Comparison between reaction conditions to afford ACN-1 using **1.8 or *in-situ* generation of **1.11****⁴⁰

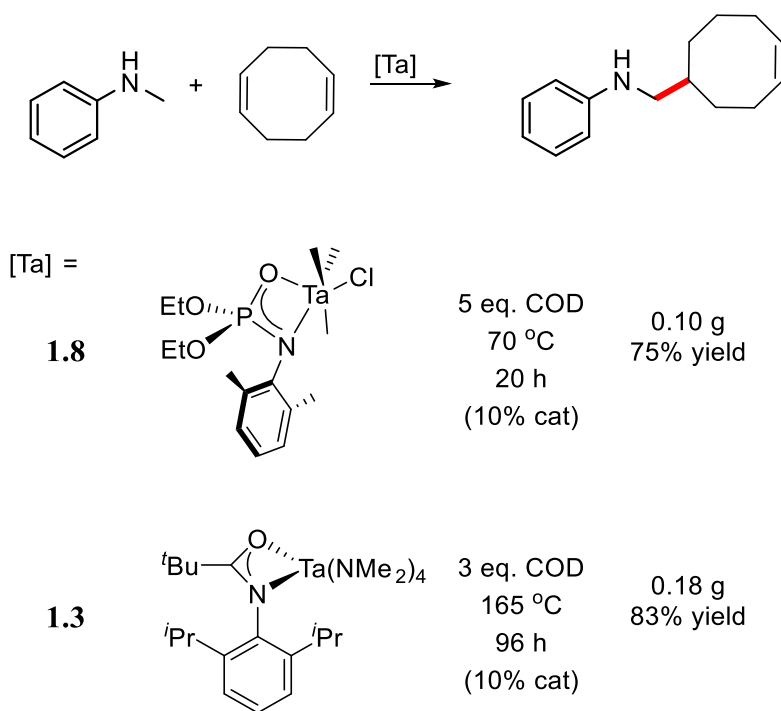
This alternative synthesis also proves highly advantageous with respect to the ease of preparation of **1.11** relative to **1.8** (Scheme 3.15). The phosphoramidate ligand of **1.8** requires several steps of synthesis, and complexation with tantalum *via* salt metathesis requires a filtration step that must be performed in the absence of visible light. Meanwhile, **1.11** is derived *in-situ* from the commercially available reagents 3-methyl-2-hydroxy pyridone and homoleptic Ta(NMe₂)₅. This route therefore represents a less hazardous, more readily assembled system that is scalable.



Scheme 3.15 Comparative synthetic routes to access tantalum hydroaminoalkylation catalysts

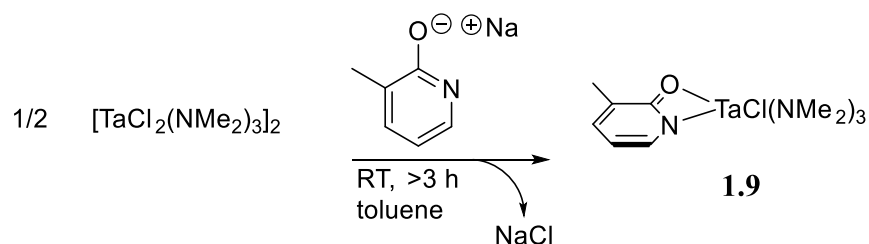
3.2.1.2 Preparation of amine-containing cyclooctenes (ACCs)

Encouraged by the improvements in ACN synthesis with the pyridonate-supported tantalum catalyst **1.11**, the HAA reaction with cyclooctadiene (COD) was explored. There are two previous reports that describe the alkylation of this challenging substrate (Scheme 3.16). In 2009, our group reported that **1.3** could catalyze this transformation in high yield (83%).³⁵ However, very long reaction times and three equivalents of alkene were required. Catalyst **1.8** can also mediate this transformation, however this reaction was limited to small scale and required five equivalents of alkene to reach a maximum yield of 75%.¹⁹⁷



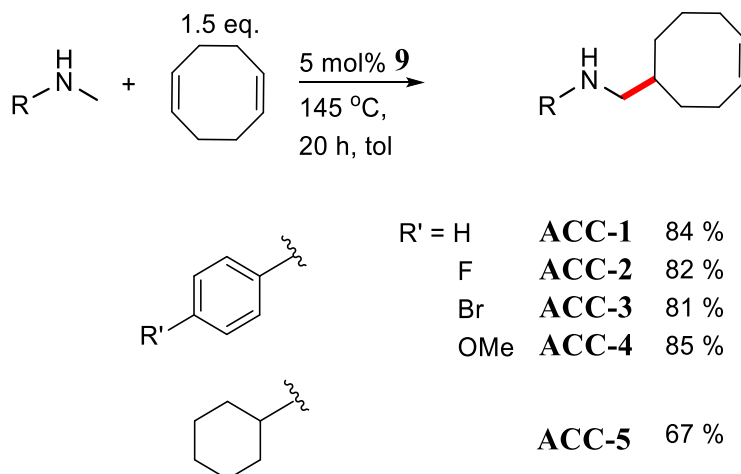
Scheme 3.16 Previously reported hydroaminoalkylations of cyclooctadiene^{35, 197}

This reaction was first screened with **1.11** using analogous conditions to those applied to ACN synthesis (section 3.2.1.1). However, no conversion was observed at 130 °C, even with the reaction time extended to twenty hours. The lack of activation of the olefin substrate is likely because of diminished ring-strain in cyclooctadiene relative to norbornadiene. To prompt reactivity, a reaction screen was conducted with **1.9**, a catalyst with precedent for unactivated internal alkenes.¹⁰⁴ In comparison to **1.11**, the replacement of an amido for a chloro ligand is expected to promote reactivity by forming a more electrophilic metal centre. This catalyst is readily prepared from the salt metathesis of a pyridone ligand salt with a mixed chloro tantalum dimer (Scheme 3.17).¹⁰⁴ After filtration and evaporation of volatiles *in vacuo*, this catalyst was used as a crude orange oil.



Scheme 3.17 Formation of complex 1.9¹⁰⁴

Full conversion of the amine substrate was achieved with this catalyst after twenty hours using 1 equivalent of diene, with 62% of the amine forming the desired mono-alkylated ACC-1. Encouraged by this result, this reaction was scaled to 10 mmol scale using a variety of secondary amines (Scheme 3.18).



Scheme 3.18 Preparation of amine-containing cyclooctene derivatives (ACC-1-5) using catalyst 1.9

The desired mono-alkylated product (ACC-1) was obtained in high yield (1.7 g, 84% yield) using 1.5 equivalents of diene. High selectivity for the mono-alkylated product is rationalized in part by the higher ring strain of cyclooctadiene vs. cyclooctene (13.3 vs. 7.4 kcal•mol⁻¹).^{192, 198} In contrast to ACN synthesis, the difference in ring-strain from the diene to the mono-alkene is more significant, partially rationalizing improved selectivity. The result of amine coordination with an ACC product is also proposed to place the alkene further from the metal

centre than in ACN coordination (Figure 3.4). Less trans-amination may also occur as one coordination site is occupied by a chloride ligand.

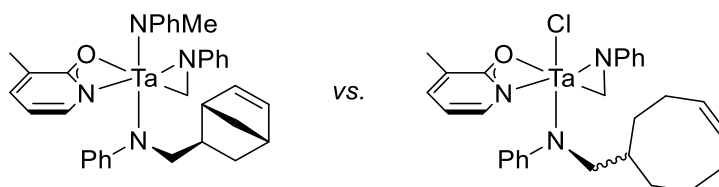


Figure 3.4 Unproductive amine coordination with cyclooctene vs. norbornene amine-containing derivatives

Various groups were tolerated in the *para* position, including halogen and methoxy substituents. The conditions also permitted functionalization with the more challenging dialkylamine substrate (ACC-5). Yield with this product is limited by the isolation by column chromatography, as the analysis of a quenched reaction solution shows no residual amine starting material. This system therefore enabled the gram-scale preparation of amine-containing cyclooctenes (ACCs) within 24 hours.

The isolation of pure ACC monomers was attempted without purification by column chromatography. After quenching the reaction with a small portion of methanol in dichloromethane, the reaction color was observed to gradually turn pale yellow from deep red over several hours. This mixture was filtered through a plug of diatomaceous earth, then reduced to dryness *in vacuo*. The resulting pale yellow residue was checked by GC-MS and ^1H NMR spectroscopy. In the GC-MS chromatogram, only one peak was observed with the corresponding mass ratio of the desired ACC-1 product. In the ^1H NMR spectra, comparison with a pure sample showed no significant differences in the relative integration of peaks. Some minor impurities are present in comparison to a product which has been column purified (Figure 3.5).

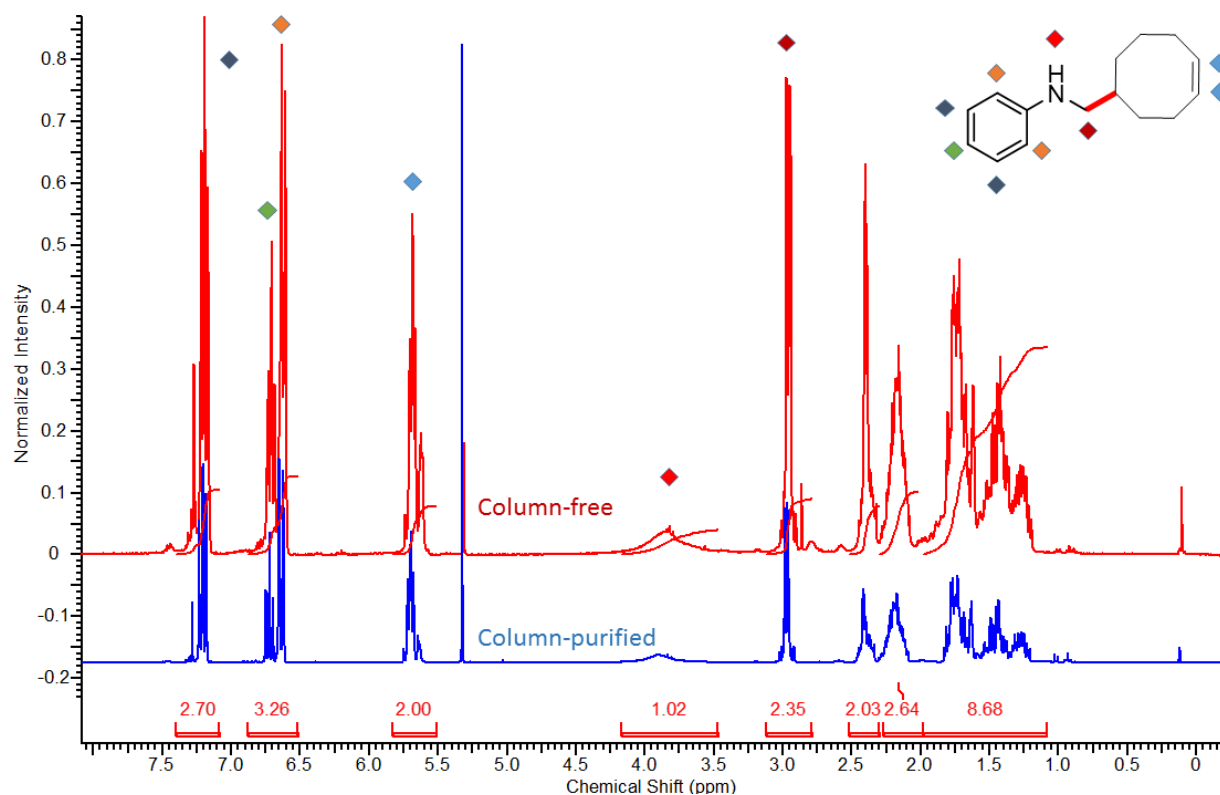
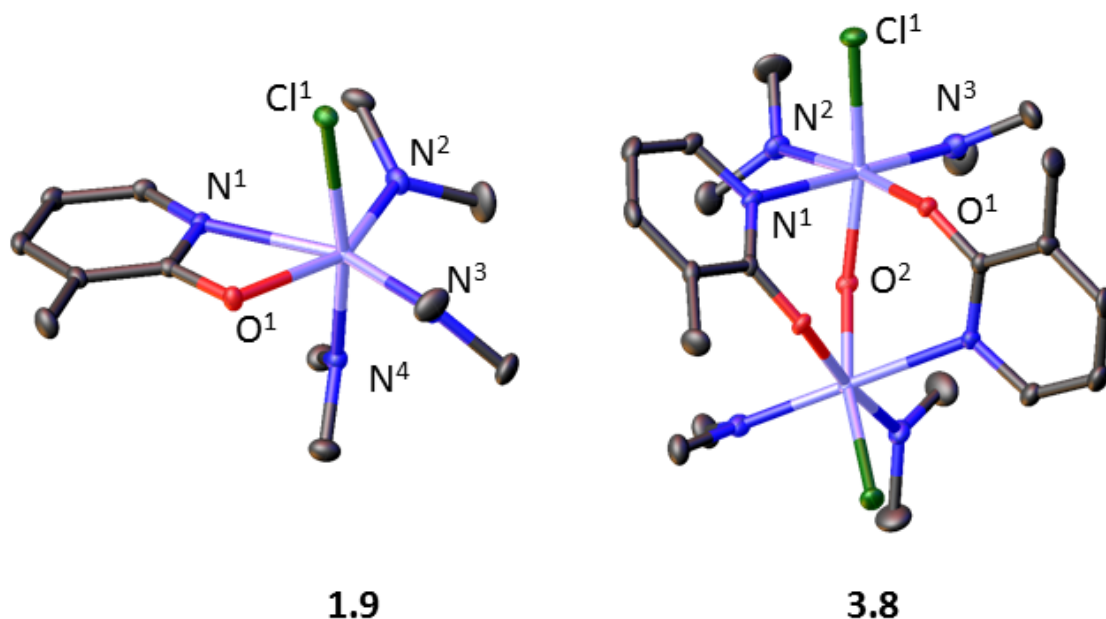


Figure 3.5 ^1H NMR Spectra (300 MHz, 298 K, CDCl_3) of ACC-1 with and without column purification

3.2.1.3 Unexpected formation of oxo-bridged tantalum dimer

A batch of catalyst **1.9** that was used as a crude oil was observed to spontaneously crystallize at room temperature. While the majority of the crystals appear to be yellow-orange, some deep red crystals were also observed in minor amounts. According to the previous report, **1.9** forms yellow crystals.¹⁰⁴ The red crystals were characterized by X-ray diffraction and the solid-state structure is shown in Figure 3.6:



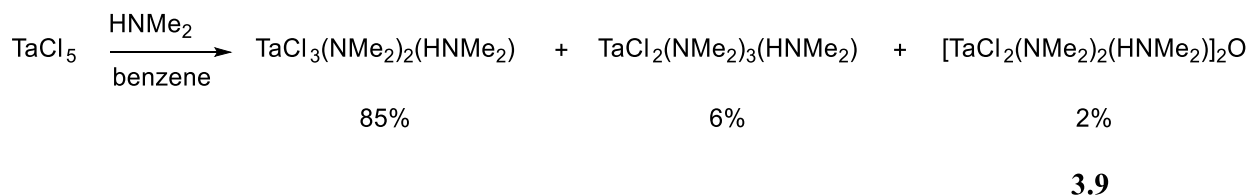
Entry	Ta-O ¹	Ta-N ¹	Ta-O ²	Ta-Cl ¹	Ta-N ²	Ta-N ³	Ta-N ⁴	O ¹ -Ta-N ¹
1.9	2.122(1)	2.307(1)	-	2.4931(5)	1.980(2)	1.961(2)	1.981(2)	59.76(5)
3.8	2.052(2)	2.367(3)	1.921(2)	2.4325(9)	1.997(3)	1.963(3)	-	-

Figure 3.6 Solid-state molecular structure of 1.9¹⁰⁴ and the oxo-bridge tantalum dimer 3.8

The solid-state structure reveals the red crystals are an oxo-bridged tantalum dimer (**3.8**), in which the pyridonate ligand is now in a μ_2 -*N,O* bonding mode. The difference in coordination mode of the *N,O*-chelate does not result in significant changes in M-L bond lengths in comparison to complex **1.9**. The Ta-O contact is slightly shortened (*ca.* 0.07 Å), while the Ta-N is slightly elongated (*ca.* 0.06 Å). As complex **3.8** still has two amido ligands, it was of interest to inspect whether it could catalyze the HAA of COD.

The catalytic performance of an isolated crystal of **3.8** was probed using ¹H NMR spectroscopy in a simple screening reaction using 5 mol% catalyst and 1:1 equivalents of COD:NMA. After 20 hours at 145 °C, the reaction had reached approximately 80% conversion.

This result suggests that **3.8** displays similar reactivity in comparison to **1.9**, and that formation of an oxo-bridge does not preclude catalytic reactivity. While the source of oxygen to form **3.8** is unknown, it is possible that **1.9** is able to form this species in the presence of half an equivalent of oxygen, perhaps from H₂O. Alternatively, **3.8** could be formed directly from contaminated Ta starting material during salt metathesis. In a prior report describing the reaction of TaCl₅ with an excess of dimethylamine, Chisholm reported the formation of a minor product (2%) with an oxo-bridge (**3.9** Scheme 3.19).¹⁹⁹ The authors acknowledge that the origin of the oxygen impurity is unknown, and posit that it may have come from the Ta starting material or by trace hydrolysis. The Ta-O bond length in the bridge of this complex is quite similar to that in **3.8** (1.928(6) Å in **3.9** vs. 1.921(2) Å in **3.8**). As with **3.8**, the authors state that the product “might have gone unnoticed were it not to have had a different crystal morphology.”



Scheme 3.19 Prior report of an oxo-bridged tantalum dimer **3.9**¹⁹⁹

The hemilability of the pyridonate ligand to adopt a bridging coordination mode may enable access to the stabilized oxo-bridged product, preventing full decomposition into unproductive metal species. Although the unknown source of oxygen prevents a clear synthetic strategy to access **3.8**, the oxo-bridge motif may be an interesting ligand framework to generate more robust ETM catalysts in the future.

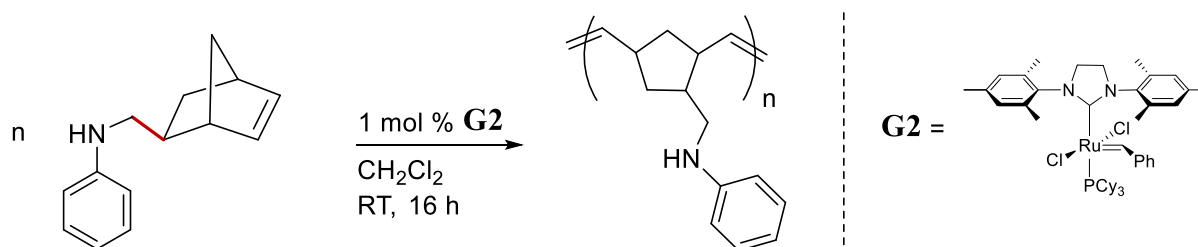
The investigations discussed in this section ultimately led to the desired monomers to be effectively synthesized on multi-gram scales. The following section describes the exploitation of

these substrates in the generation of amine containing polymers and the characterization of such materials.

3.2.2 Polymerization of amine-containing monomers

3.2.2.1 ROMP of ACNs

ACN-1 was first tested as a substrate for ROMP. To begin, the polymerization conditions established by Perry were used; to 100 mg of ACN-1 was added 1 mol% of **G2** in dichloromethane (Scheme 3.20). The reaction was left for 24 hours to ensure full conversion, quenched with ethyl vinyl ether, and isolated *via* precipitation from cold methanol to give stringy, off-white solids (>90% yield). At this time, optimization of ROMP conditions with respect to temperature, pressure, and solvent etc. has not been performed. While the polymer was initially off-white, it was observed to discolor rapidly to a dark purple/black in solution. This observation was noticed for all amine-containing polymers and is attributed to oxidation of the amine group. A reaction that was both precipitated and stored in the glovebox did not show discoloration from the initial off-white color.



Scheme 3.20 Polymerization of amine-containing norbornene derivative ACN-1 with **G2**

Analysis by ^1H NMR spectroscopy showed broadened resonances indicative of polymer formation. Analysis by gel-permeation chromatography (GPC) showed one peak. Surprisingly, the molecular weight ($M_n = 77,350 \text{ g}\cdot\text{mol}^{-1}$) was in large excess of that predicted by monomer to initiator ratio ($[\text{M}]/[\text{I}]$; $M_{n, \text{theo}} = 19,900 \text{ g}\cdot\text{mol}^{-1}$). The dispersity was 1.26, suggesting only

moderate control. Previously, it was shown that ACN monomers polymerize under living conditions in the presence of **G2**, giving experimental molecular weights that match the degree of polymerization based on $[M]/[I]$ ratios with dispersities less than 1.1. Two further repeat experiments likewise showed molecular weights that were in large excess of theoretical values. A different batch of commercial **G2** gave comparable data, ruling out that the discrepancy was because of impurities present from a different lot of catalyst.

The causes for this discrepancy between the polymers that result from the monomers prepared by **1.8** or **1.11** remain unclear. By ^1H NMR spectroscopy and GC-MS, both monomers appear to be identical in composition, with no clear impurity in either. It is proposed that differences in the preparation could result in the differential incorporation of tantalum and/or ligand residues that are not removed by purification and are in low enough amounts to be difficult to detect. Current efforts are underway by Mr. N. Kuanr to understand these differences in reactivity. While somewhat confounding, molecules that appear pure but were prepared *and* react differently is not without precedent. In the chemical synthesis industry, 'scale-up incidents' are known and can result from the small deviations from how the reaction was performed at pilot scale, leading to varying products that can range from 'in-spec' to unusable.²⁰⁰

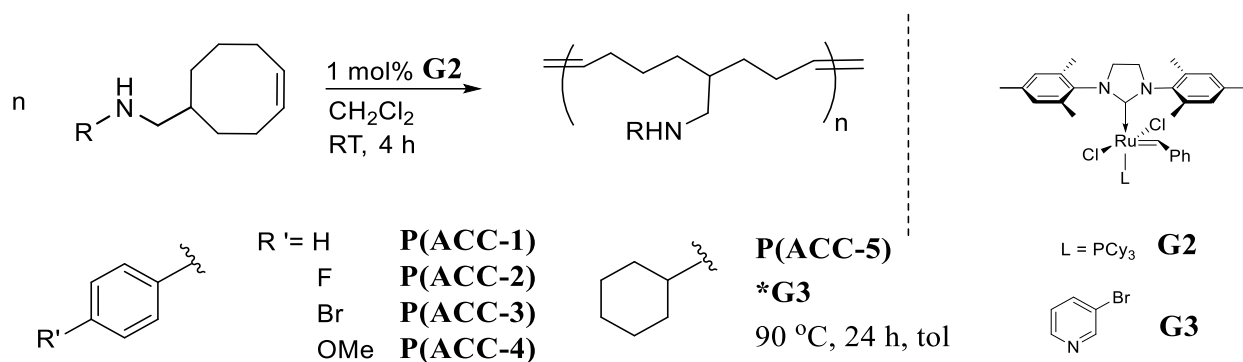
A polymerization was conducted on a 5 mmol scale to obtain gram-scale quantities of P(ACN-1). Using 1 mol% **G2**, P(ACN-1) was isolated in 85% yield after standard purification protocols. By GPC, the experimental molecular weight was $93,660 \text{ g}\cdot\text{mol}^{-1}$, with $\text{Đ} = 1.17$. These values are in reasonable agreement with the small-scale polymerizations, suggesting a ten-fold increase in scale does not dramatically affect the polymerization. The observed tolerance of **G2** to ACN monomers to obtain these polymers in high yield encouraged investigation with the ACC derivatives.

3.2.2.2 ROMP with ACCs

The amine-containing monomers (ACC-1-5) were subjected to ROMP conditions as per P(ACN) synthesis. The arylamine monomers (ACC-1-4) were observed to smoothly polymerize using **G2** to give linear poly(cyclooctene) with pendant secondary amines (Table 3.3). However, ACC-5 did not give any evidence for polymer formation using these conditions. This lack of activity was attributed to the increased nucleophilicity of the alkylamine. When catalyst **G3** was used in place of **G2**, no ROMP was observed at room temperature. However, raising the reaction temperature to 60 °C for 24 hours did result in some polymer formation as determined by ¹H NMR spectroscopy, although conversion did not exceed *ca.* 40%, even with prolonged heating. A new reaction was heated at 90 °C and pleasingly full conversion of the cyclic alkene was observed after heating for 24 hours.

The polymerization of 100 equiv. of ACC-1 could be monitored by NMR spectroscopy in a sealed NMR tube in CDCl₃. After 10 min, approximately 35% of the monomer had been consumed; after 30 minutes the reaction had exceeded 95% completion. In contrast to other amine-functionalized cyclooctene monomers which are incompatible with Grubbs initiators,¹⁶⁸ the rapid conversion of ACC-1 suggests that secondary arylamines in the 5-position do not deactivate ROMP. Reactions were performed on up to gram-scale monomer quantities to access materials for rheological analysis (Table 3.3).

Table 3.3 Homopolymerization of amine-containing cyclooctenes (ACC-1-5)



Entry	ACC-n	Yield ^a	M_n (g•mol ⁻¹) ^b	$M_{n, theo.}$ (g•mol ⁻¹) ^c	$\bar{D}^b$
1	1	81	18,100	21,500	1.40
2	1	84	118,900	21,500	1.23
3	1	87	73,570	21,500	1.34
4	1	83	15,960	21,500	1.70
5 ^d	1	-	-	21,500	-
6 ^e	1	76	29,520	10,750	1.59
7 ^e	1	74	5,269	10,750	1.85
8 ^f	1	86	82,970	43,000	1.32
9	2	88	-	23,400	-
10	3	94	35,080	29,600	1.65
11	4	88	-	-	-
12 ^g	5	42	-	22,100	-

[M]/[I] = 100 ^aIsolated yield. ^bDetermined by GPC. ^c $M_{n, theo.} = [M]/[I] \cdot \text{MW of ACC-n}$ ^dPolymerized using **G1**

^e[M]/[I] = 50 ^f[M]/[I] = 200 ^gPolymerized using **G3** at 90 °C for 24 hrs

Reactions are quenched after completion with ethyl vinyl ether and the polymer is isolated *via* drop-wise addition of the mixture into stirring, cold methanol. An off-white, self-aggregating gum-like solid was obtained, which is notably different in physical appearance to that of non-functionalized poly(cyclooctene), which precipitates as a white, flocculent solid. As was observed in poly(ACN) synthesis, poly(ACC) polymers rapidly discolor to a dark purple/black color in solution. These pendant amine containing polymers are obtained in high yield (>80%) regardless of the amine substituent. Analysis of the ^1H NMR spectra shows broadened signals consistent with polymer formation. For example, P(ACC-4) shows a well resolved singlet arising from the methoxy substituent (δ 3.74). This peak integrates in a 3:2 ratio when compared with the olefinic resonances at δ 5.41, confirming the molar ratio of the pendant amine to the polymer backbone. Attempts to polymerize ACC-1 using Grubbs 1st generation catalyst were unsuccessful, highlighting the importance of more reactive metathesis catalysts to react challenging substrates (Entry 5). The increased temperature required to polymerize ACC-5 also suggests that diminished nucleophilicity of arylamines helps to prevent catalyst deactivation and is a key parameter to access ROMP at room temperature (Entry 12).

In previous work by Perry, P(ACC-4) was synthesized and characterized by ^1H NMR spectroscopy but no GPC data could be obtained because of the low solubility of the polymer after vacuum drying.¹⁹⁷ Here, fully-dried polymers P(ACC-2) and P(ACC-4) were likewise not soluble in tetrahydrofuran, preventing their analysis by GPC (Entries 9 and 11). This is attributed to the formation of enhanced hydrogen bonding interactions with these acceptor groups. However, P(ACC-1) and P(ACC-3) did possess requisite solubility for analysis using GPC. These results indicate polymerization reaches high conversion with moderate control. The first sample of P(ACC-1) has an experimental molecular weight that closely matches that predicted by monomer-

to-initiator ratio ($18,100 \text{ g}\cdot\text{mol}^{-1}$ *exp.* vs. $21,500 \text{ g}\cdot\text{mol}^{-1}$ *theo.*), with a moderate dispersity of $\bar{D} = 1.40$ (Entry 1). However, subsequent repeats to form P(ACC-1) gave variable molecular weights in large excess of M:I ($16\text{--}118 \text{ kg}\cdot\text{mol}^{-1}$ with $\bar{D} 1.23\text{--}1.70$). This data may suggest that rates of propagation exceed rates of initiation in ROMP. This discrepancy in reactivity leads to inconsistent polymer chain lengths and that more rapid initiation is desired for higher levels of control. It is possible that chain exchange processes contribute to this variability. Data for P(ACC-3) likewise confirmed the formation of polymer with only moderate control ($35,080 \text{ g}\cdot\text{mol}^{-1}$ *exp.* vs. $29,600 \text{ g}\cdot\text{mol}^{-1}$ *theo.*, $\bar{D} = 1.65$).

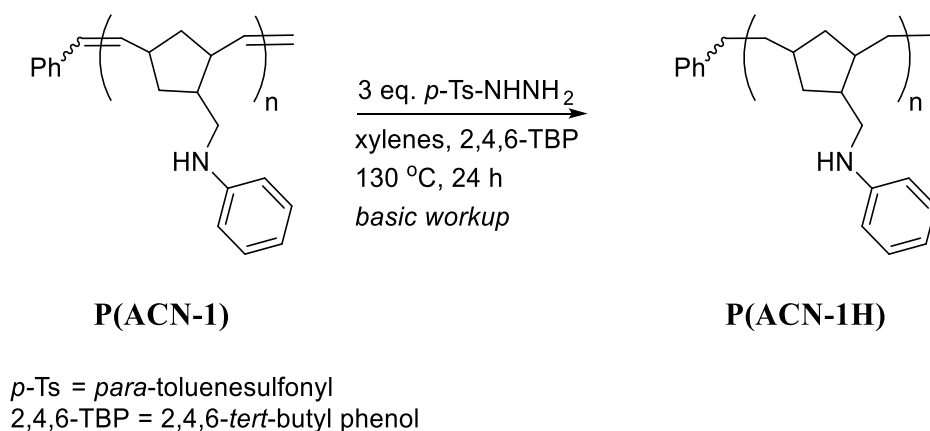
As detailed in section 3.2.1.2, a highly pure sample of monomer ACC-1 could be isolated without column purification. This monomer was subjected to standard polymerization conditions and a typical sample by appearance of P(ACC-1) was obtained (87% yield). This polymer was characterized by ^1H NMR spectroscopy and the expected broadened resonances indicative of P(ACC-1) were obtained. Unfortunately, the polymer was no longer soluble after vacuum drying for analysis by GPC. The low solubility of this polymer was attributed to residual impurities from the HAA reaction, which are likely residual pyridone ligand and the di-alkylated HAA product (see Figure 3.5). While these are only present in small amounts, the ability of these impurities to interact with the pendant amine of the polymer is proposed to cause weak cross-links between the polymer chains, lowering solubility.

The differences in the resulting polymers from monomers derived from catalysts **1.8** vs. **1.9** and **1.11** may provide indirect evidence into the differences between these syntheses. In P(ACN) synthesis, the higher molecular weights obtained with **1.11**-catalyzed monomers could suggest more rapid rates of polymer propagation than in those which are prepared with **1.8**, in which the living polymerization suggests rates of propagation are slow relative to initiation. In

P(ACC) synthesis, polymers lacked solubility when monomers prepared using **1.8** were used. When column purification was not performed, the relatively less pure ACC-1 gave polymer which also lacked solubility after vacuum drying. This was attributed to impurities which cause loose cross-linking between chains. Therefore, it is proposed from these empirical observations that synthesis from **1.8** gives monomers which contain small amounts of impurities which are challenging to detect. These impurities slow down the ROMP of ACNs, giving controlled molecular weights by suppressing rates of polymer propagation. In the ACCs, these impurities are retained in the polymer, lowering solubility for full characterization.

3.2.3 Hydrogenation of amine-containing polymers

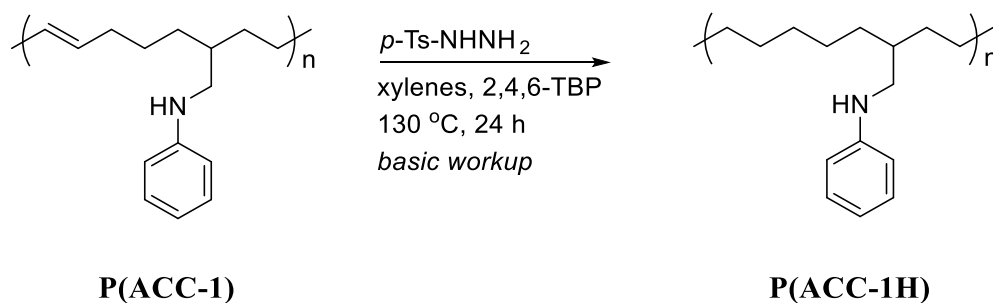
Early investigations focused on making polymers containing unsaturations in the backbone. To further increase the explorations into these novel materials, it was of interest to form saturated polymers and investigate their properties. Hydrogenative reduction of the polymer backbone was conducted using well-known conditions using tosyl hydrazine.²⁰¹⁻²⁰² This method generates diimide *in-situ* to hydrogenate backbone alkenes along the polymer chain (Scheme 3.21).



Scheme 3.21 Hydrogenation of amine-containing poly(norbornene) derivative P(ACN-1)

The reaction was first attempted with isolated P(ACN-1) in a poly(tetrafluoroethylene)-sealed reaction vessel. After the reaction time of 24 hours, a heterogeneous mixture resulted with a large quantity of small brown solids observed in a cloudy orange solution. These solid residues were thought to be hydrogenated polymer and were unfortunately insoluble in common laboratory solvents. After further consideration, it was realized that the mechanism by which tosyl hydrazine generates diimide also forms *p*-toluenesulfonic acid as a by-product. This source of acid could cause protonation of the pendant group, forming cationic species that lower the polymer solubility. Indeed, independent experiments performed in the group have shown that these secondary amino groups are sensitive to acid and can easily become protonated. Therefore, the entire reaction mixture was added to a separatory funnel along with *ca.* 30 mL ethyl acetate and *ca.* 30 mL 3 M NaOH. During a vigorous extraction, all solid pieces slowly dissolved to give a biphasic solution. The aqueous solution was removed and two subsequent washes of the organic layer with 3 M NaOH were conducted. The resulting organic layer was reduced to *ca.* 1 mL on the roto-vap, then the product was isolated by precipitation using 100 mL cold methanol. The resulting off-white polymer P(ACN-1H) was recovered in good yield (93 %) and the absence of alkenyl protons indicative of P(ACN-1) was confirmed by ^1H NMR spectroscopy.

The optimized reduction conditions were also applied to P(ACC) polymers (Scheme 3.22). As previously noted, hydrogenation of functional poly(cyclooctenes) gives functionalized polyethylene analogs in which there is a branch on every eighth carbon (although a precise methylene run length between branches is not obtained because of differences between head-head, head-tail, and tail-tail linkages).



Scheme 3.22 Hydrogenation of an amine-containing poly(cyclooctene) derivative P(ACC-1)

A sample of P(ACC-1) (Table 3.3, entry 3) was reduced under these conditions and isolated in 87% yield after precipitation. Analysis by ^1H NMR spectroscopy corroborates complete hydrogenation of the polymer backbone, with loss of the olefinic resonances at δ 5.40. Analysis of P(ACC-1H) by GPC post-hydrogenation showed no significant difference in molecular weight or dispersity ($71,230 \text{ g}\cdot\text{mol}^{-1}$ with $\text{Đ} = 1.22$ for P(ACC-1H) vs. $73,570 \text{ g}\cdot\text{mol}^{-1}$ with $\text{Đ} = 1.34$).

3.2.4 Thermal properties of P(ACCs)

The thermal properties of the P(ACC) materials was investigated next. It was of interest to explore how the presence of amine functional group branches modifies these properties. While the thermal characterization of P(ACN) materials has previously been investigated, no such analysis has been conducted with P(ACCs). The thermal stabilities of the polymers was first determined by thermogravimetric analysis (TGA) experiments (Figure 3.7).

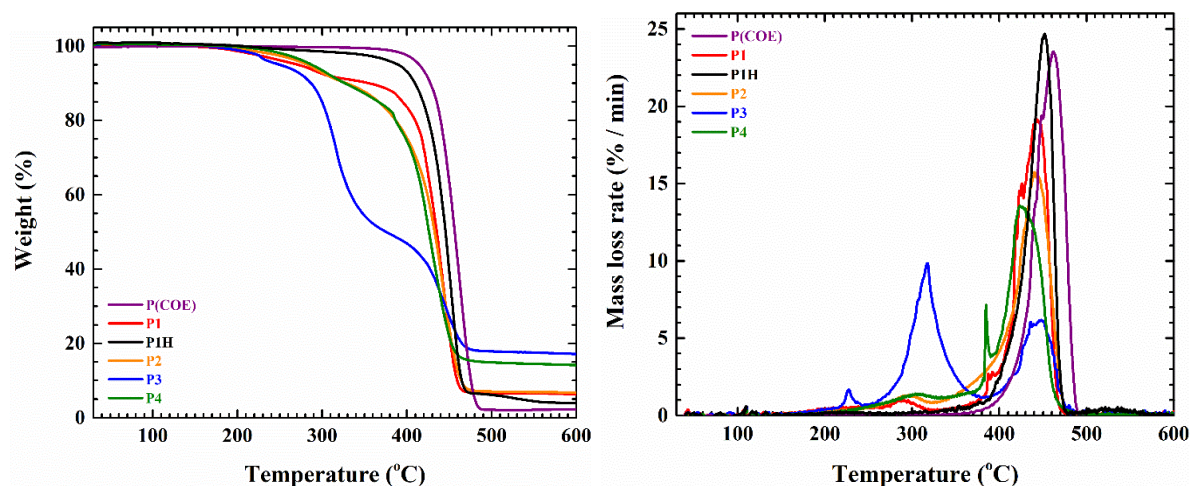


Figure 3.7 Thermogravimetric curves (TGA) of amine-containing poly(cyclooctenes) P(ACC-1-4)

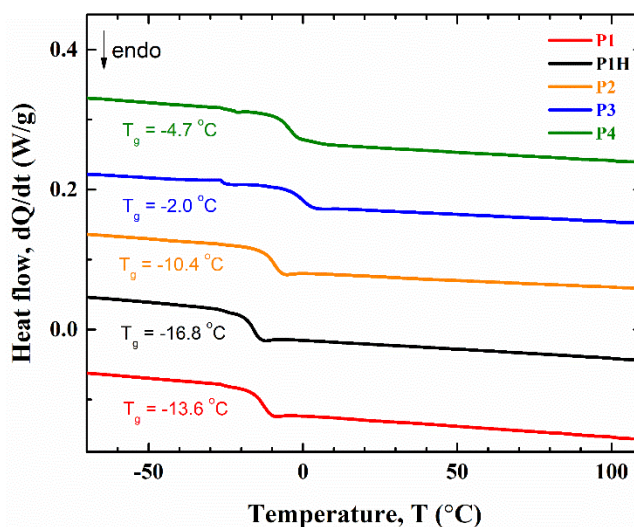
Samples were heated from room temperature to 600 °C at a heating rate of 10 °C/min; their 5% and 50% weight loss temperatures are summarized in Table 3.4. No significant differences in the TGA analysis for samples tested under nitrogen or oxygen atmosphere suggests these polymers demonstrate thermo-oxidative stability. Without functionalization, poly(cyclooctene) is a thermally robust polymer, with only one weight loss step at 415 °C, assigned to the degradation of the polymer chain. P(ACC-1) shows a two-step weight loss; an initial weight loss (300 - 400 °C) was assigned to the loss of the *N*-methyl aniline pendant group, while the second thermal degradation around 420 °C indicates degradation of the main polymer backbone, consistent with poly(cyclooctene). In general, polymers follow free radical degradation mechanisms that are initiated by bond dissociation at the temperature of pyrolysis.²⁰³

Table 3.4 Thermal characterization by differential scanning calorimetry and thermogravimetric analysis

Entry	T_g ($^{\circ}\text{C}$) ^a	$T_{5\%}$ ($^{\circ}\text{C}$) ^b	$T_{50\%}$ ($^{\circ}\text{C}$) ^b
P(COE)	-	415	456
P(ACC-1)	-13.7	275	435
P(ACC-1H)	-16.8	386	450
P(ACC-2)	-10.4	280	432
P(ACC-3)	-2.0	255	378
P(ACC-4)	-4.7	287	426
P(ACC-5)	-28.0	-	-

^aDetermined by differential scanning calorimetry (average of 3 runs) ^bDetermined by thermogravimetric analysis

Differential scanning calorimetry (DSC) experiments were conducted to determine the phase transitions of the polymers. These experiments indicated all polymers are amorphous with no observed melting point (T_m). The glass transition temperature (T_g) of all P(ACC) materials was below ambient conditions (Table 3.4, Figure 3.8).

**Figure 3.8 DSC thermograms of second heating scan (5 °C/min) of amine-containing poly(cyclooctenes)**

The glass transitions range from -28.0 °C for P(ACC-5) to a maximum of -2.0 °C for P(ACC-3). The observed trends in T_g are thought to be related to free volume effects between

polymer chains as well as the nature of associative interactions.²⁰⁴ When the free volume is greater between polymer chains, the T_g is expected to decrease as mobility is increased. Meanwhile, associative interactions such as hydrogen bonding are expected to increase the T_g as chain mobility is decreased. In P(ACC-5), the cyclohexylamine is proposed to be the strongest hydrogen bond donor/acceptor among the polymers evaluated because of its enhanced nucleophilicity as an alkylamine.²⁰⁵ However, it has the lowest T_g (-28.0 °C). The next lowest T_g values are P(ACC-1H) (-16.8 °C) and P(ACC-1) (-13.7 °C). The lower T_g of the saturated polymer may be due to the increase in flexibility of the polymer backbone. Within the *para*-substituted derivatives, an increase in T_g is observed with poorer hydrogen bond acceptors, from F (-10.4 °C), then OMe (-4.7 °C) to Br (-2.0 °C). Across these polymers, the observed trend in T_g appears to *decrease* with the proposed trend of increased associative interactions. As this trend remains unclear, a further understanding of the nature of associative interactions in these polymers and how they affect chain packing will greatly assist interpretation of this data. Nonetheless, the data indicates that all the polymers possess high segmental mobility, allowing chains to flow at ambient conditions. As no melting point T_m was observed, these polymers do not possess crystallinity at the temperature range of -90 to 120 °C.

3.2.5 Rheological analysis of P(ACC) polymers

To further explore the interesting behavior of this novel class of materials, a series of rheological investigations were performed by Ms. T. Tomkovic (Hatzikiriakos lab, UBC Dept. of Chemical and Biological Engineering). At the time of this writing, this study remains on-going, and the full rheological results are to be reported within the thesis of Tomkovic.¹ Linear rheological measurements were conducted using an Anton Paar MCR 702 rotational rheometer, equipped with

a cone-partitioned-plate geometry. Figure 3.9 depicts variation of the linear viscoelastic moduli, indicating liquid-like behavior ($G'' > G'$; P(ACC-2)), gel-like behavior ($G' = G''$ P(ACC-1H)) over a certain range of frequencies to solid-like (P(ACC-1)) behavior ($G' > G''$). Based on this data, the polymers are proposed to form transient networks due to the association of hydrogen-bond interactions as a response to angular shear.

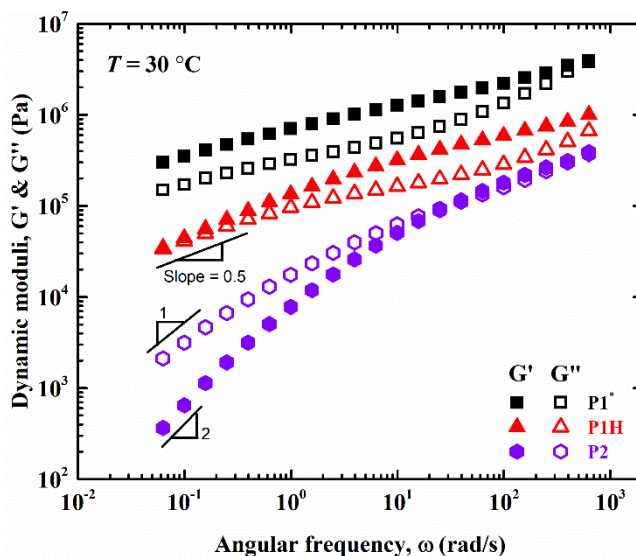


Figure 3.9 Evolution of storage (G') and loss moduli (G''), versus angular frequency for three polymers exhibiting solid-like (P(ACC-1)), gel-like (P(ACC-1H)), and liquid-like (P(ACC-2)) behaviors at 30 °C.¹ Note: (*) represents that the moduli of P(ACC-1) have been multiplied by a factor of 10 for the sake of clarity

Comparing the dynamic moduli of P(ACC-1) and P(ACC-1H) of similar molecular weight reveals stronger network formation in the former, presumably due to higher rigidity in the unsaturated polymer backbone, resulting in a soft-solid material. On the other hand, P(ACC-1H) possesses more flexibility, allowing the further formation of entanglements and resulting in a gel structure. Previously, dramatic effects on viscoelasticity were observed in P(ACN) derivatives due to the introduction of variable hydrogen bonding.⁴⁶ The rheological behavior of these related

polymers is thus strongly dependent upon the saturation of the polymer backbone, molecular weight, and the associative interactions prompted by hydrogen-bonding interactions.

3.2.6 Associative properties of amine-containing polymers

During the course of rheological analysis, dried samples of P(ACC) films were observed to have interesting physical properties. First, self-healing was observed in P(ACC-1) between the surface boundaries of two discrete, vacuum-dried polymer spheres when they are placed into contact at room temperature under ambient conditions. This behavior was observed over 24 hours using time-lapse video. With no externally applied stimuli (neither heat nor pressure) these spheres are observed to become coherent; after 24 hours, no clear boundary between spheres can be found (see Figure 3.10). In addition to healing, an impression in the left-hand polymer sphere that was created with soft contact with the tweezers is observed to ‘fill in’ over the first several hours of the experiment. To minimize their total energy, the polymer films form spherical shapes to minimize the surface area to volume ratio. As in drops of water, minimizing this ratio maximizes hydrogen bond interactions, with surface molecules necessarily possessing fewer interactions than ‘bulk’ molecules.

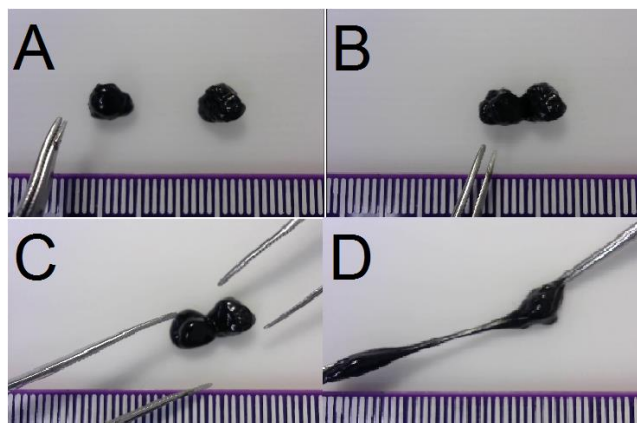


Figure 3.10 Macroscopic self-healing of amine-containing poly(cyclooctene) P(ACC-1) spheres A) Dried spheres resting on poly(tetrafluoroethylene) B) Spheres brought into contact C) After 24 hrs under ambient conditions D) Spheres no longer show discrete boundary when pulled apart

Healing is attributed to the promotion of dynamic chain cross-linking and entanglement by attractive and reversible hydrogen bond interactions between mobile polymer chains present on the surface. As no chemical modification or reaction is taking place, this property is reversible and tearing/healing can be repeated. To the best of my knowledge, this is the first example of self-healing in a polyethylene derivative that does not utilize an external agent such as a microcapsule containing a healing agent, or rely on shape-memory effects.²⁰⁶⁻²¹⁰ Self-healing was also observed with P(ACC-1H), showing that the observed healing phenomenon is not related to alkenes on the polymer backbone of P(ACC-1). Somewhat surprisingly, P(ACC-5) does not exhibit macroscopic self-healing. It is proposed that the stronger hydrogen bond interactions in this sample renders them less reversible, therefore reducing dynamic cross-linking and chain entanglement when two surface boundaries are placed in contact. To further assess self-healing, an extensional stress-strain experiment was conducted (Figure 3.11).

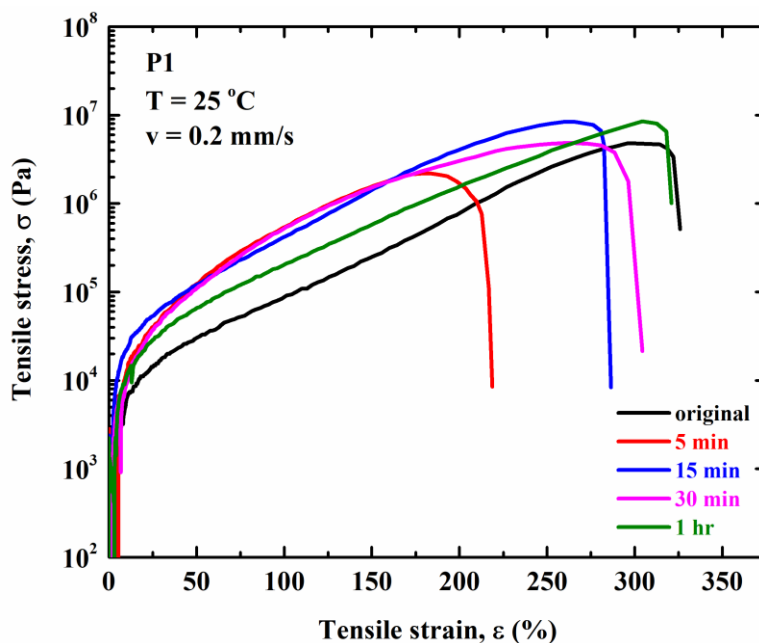


Figure 3.11 Stress-strain curves for amine-containing poly(cyclooctene) P(ACC-1) after variable healing times¹

An original sample of P(ACC-1) (Table 3.3, entry 4) was molded into a tubular shape (*ca.* 1 cm diameter) and subjected to tensional stress. Breakage of this sample was observed at *ca.* 325% elongation after non-linear deformation began at low strain. Qualitatively, this data profile compares favorably with a reported measurement for linear low density polyethylene, which shows a linear deformation over initial 10% of strain, followed by a long period of non-linear deformation and failure at *ca.* 540% elongation.²¹¹ However, unlike typical samples of PE, the experiment could be repeated with P(ACC-1) after 'repairing' the sample. The fragments were placed into contact at the point of breakage, pressed for 5 seconds, then left for a pre-determined healing time. After 5 min of healing, a sample showed breakage at *ca.* 200% elongation, approximately 65% of the original displacement. Subsequent iterations with increasing healing time revealed that 1 hr of healing is sufficient to restore the tensile strength of the original P(ACC-1). These materials also

highly adhesive, with the polymer observed to provide cohesion between two sheets of poly(tetrafluoroethylene) (Figure 3.12).

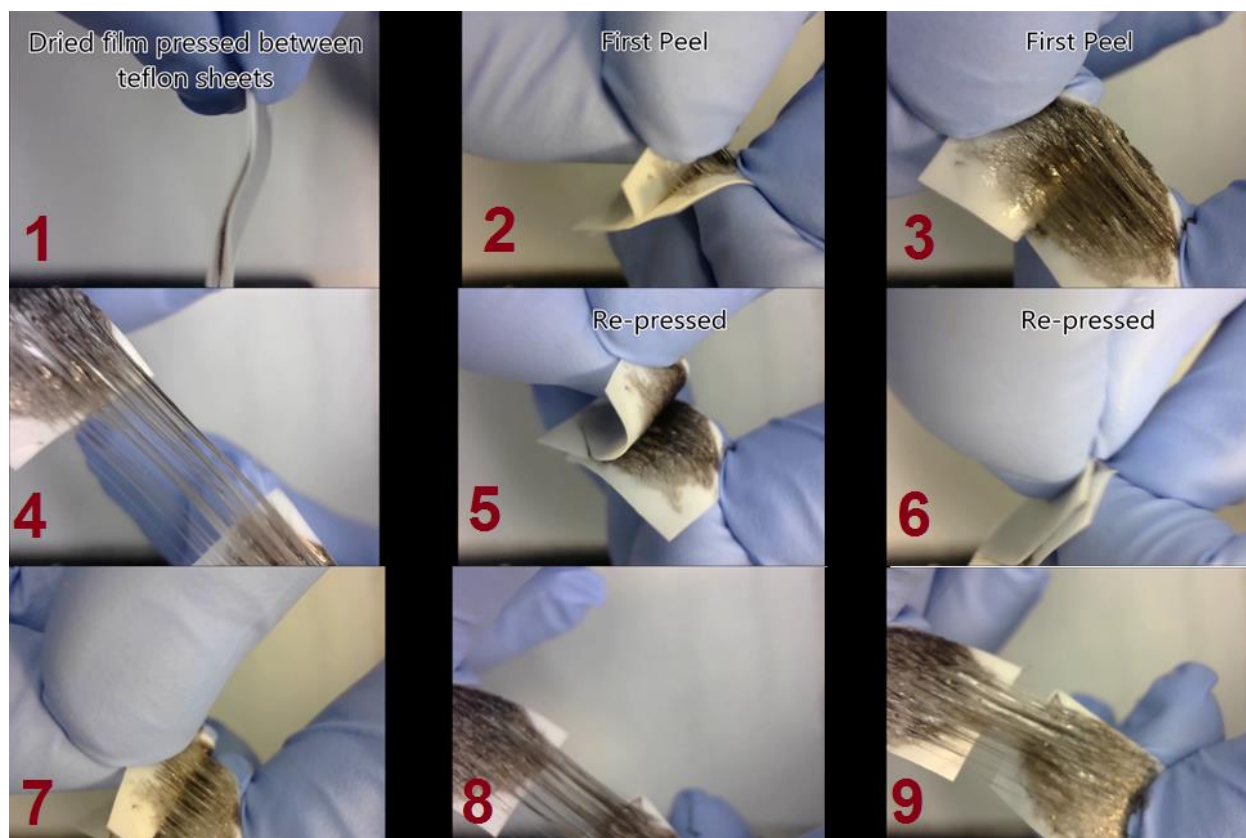


Figure 3.12 Reversible adhesion between poly(tetrafluoroethylene) sheets using amine-containing poly(cyclooctene) P(ACC-1)

The mechanism by which these materials are adhering to poly(tetrafluoroethylene) is unclear. It is proposed that movement of the polymers onto the poly(tetrafluoroethylene) substrate minimizes the surface energy of the polymer film, specifically the chains oriented on the surface. While this comes at a cost of a decrease in the surface area to volume ratio, this is presumably offset by the generation of very weak but numerous hydrogen-bond interactions between the polymer and poly(tetrafluoroethylene). These behaviors are not observed in poly(cyclooctene), which shows no adherence to poly(tetrafluoroethylene) under the same conditions. While this

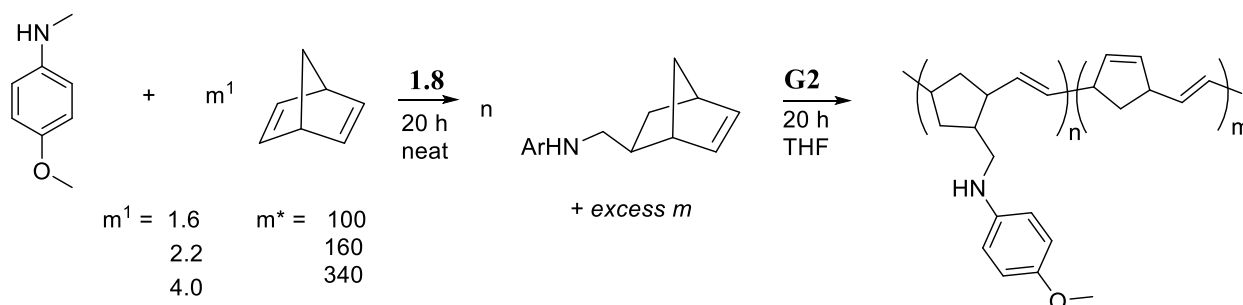
phenomenon is unclear, it provides an exciting example of the manner in which amine functionalization dramatically modifies conventional material properties. Research is currently underway to quantitate and further understand these associative properties.

3.2.7 Preparation of copolymers

3.2.7.1 Polyolefin copolymers to lower amine incorporation

The interesting and variable properties observed in P(ACN) and P(ACC) materials has validated our motivation for incorporating amine pendant branches onto polyolefins. It was of interest to explore the extent to which these properties could be retained with lower incorporations of amine in the polymer. The ultimate goal is to maintain the desirable properties imparted by the amine functional group while lowering its incorporation in more inexpensive unfunctionalized polyolefins.

A direct, one-pot approach using sequential HAA/ROMP to lower the percent of amine in the final polymer was first attempted. Based on previously obtained yields, the HAA of norbornadiene with *p*-methoxy *N*-methyl aniline using catalyst **1.8** reaches 60% conversion. To decrease the amine incorporation in the final polymer, excess equivalents of norbornadiene were added to the HAA reaction. Based upon a theoretical conversion of 60%, excess alkene was added to give 50, 40, and 23% theoretical functionalization of all units (Scheme 3.23). After the reaction time of 20 hr was complete, a solution of **G2** in THF was directly added into the reaction mixture.



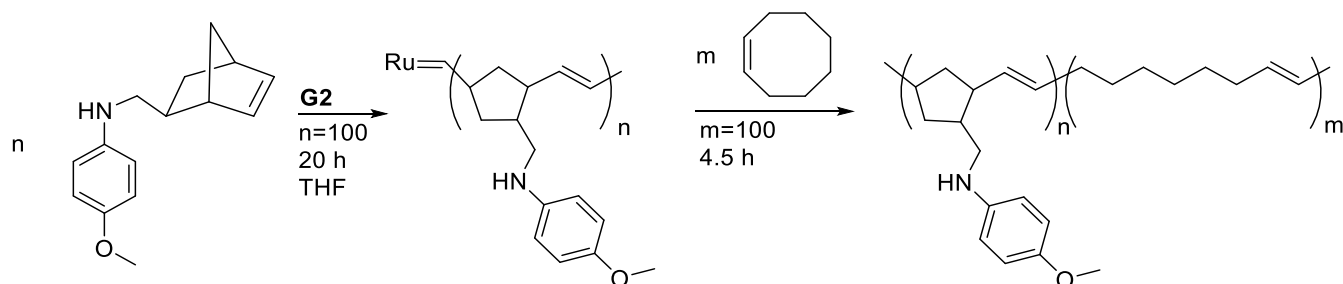
Scheme 3.23 One-pot sequential transformation of hydroaminoalkylation followed by ROMP with excess norbornadiene substrate

After these reactions were quenched with ethyl vinyl ether, dark black gels were formed in reaction vials. These gels unfortunately proved insoluble in a variety of solvents, instead taking up solvent and swelling. To attempt to gain some characterization data, the gel with 50% theoretical functionalization was soaked in an excess of deuterated chloroform and gently heated. A slightly discolored, light purple supernatant was analyzed by ^1H NMR spectroscopy. The appearance of a peak at δ 3.75 that is indicative of the methoxy group suggests the amine was incorporated into the polymer. No resonances from 6.4-5.9 ppm as would be expected for the alkene protons of monomeric ACN-2 were seen. In the region from 5.7 to 5.0 ppm where alkene protons are expected to resonate, several ill-defined multiplets are evident, however none can be clearly assigned to the P(ACN) fragment. No resonance in this region precisely matches the reported chemical shift of P(ACN-2) (δ 5.42-5.20)⁴⁶ nor does one integrate in a 2:3 ratio with the methoxy group resonance. Overall, the resonances observed in this spectrum were sharper than expected for a polymeric sample, potentially suggesting that the soluble portion of this sample consisted of short-chain oligomers.

It is proposed that the internal cyclopentenyl double bond that is retained after HAA of norbornadiene is also able to participate in ROMP. As this internal double bond is not highly

strained, its rate of metathesis should be much slower than that of the highly strained double bonds of norbornadiene and ACN-2. Nonetheless, any reactivity at this bond will effectively make a cross-link, which is expected to dramatically diminish the solubility of the resulting material. Although these materials pose challenges in their solubility, they may have potential application as rubber-like materials reinforced by hydrogen bonding interactions.

Next, a block copolymer was attempted through the sequential addition of amine-containing monomers and cyclooctene (Scheme 3.24). Generally, block copolymers from ROMP are prepared by adding the faster reacting of the two monomers second to prevent randomization *via* cross-metathesis; thus, the slower ACN monomer was first polymerized. After reacting 100 equivalents of ACN-4, a small aliquot (10% by volume) was removed for analysis, followed by the addition of 90 equivalents of cyclooctene (1:1 equivalents with ACN-4).



Scheme 3.24 Attempted block copolymers with cyclooctene and an amine-containing norbornene derivative (ACN-4)

After five hours, the reaction was quenched and analyzed by ^1H NMR spectroscopy and GPC. Over two duplicate runs, the molecular weight of the first block is in excess of the theoretical molecular weight (29,000 and 39,130 $\text{g}\cdot\text{mol}^{-1}$ relative to theoretical 22,900). The addition of 100 equivalents of cyclooctene should theoretically raise the molecular weight by 100 units of COE (*ca.* 11,000 $\text{g}\cdot\text{mol}^{-1}$), however the molecular weights of the copolymers show only slight increases

(+4,920 and +2,450 g•mol⁻¹ respectively). By ¹H NMR spectroscopy, the approximate percentage of amine-units in the precipitated mixtures is 54 and 64% respectively (Figure 3.13). This result suggests that the cyclooctene monomers are not fully incorporated into the pendant poly(ACN) chain. This could be because of the associative interactions of the amine-containing polymer, which could cause it to aggregate around the metal center and hamper coordination of cyclooctenes. To determine that a copolymer between blocks had formed, rather than two homopolymers, a crude portion of the sample was investigated by DOSY NMR spectroscopy.²¹² Using this method, it was determined that the diagnostic NMR signals had consistent coefficients of diffusion, which does not indicate two separate polymers (see Appendix). However, without distinct, non-overlapping NMR signals that can be assigned to each respective block, the accuracy of this method is limited.²¹²

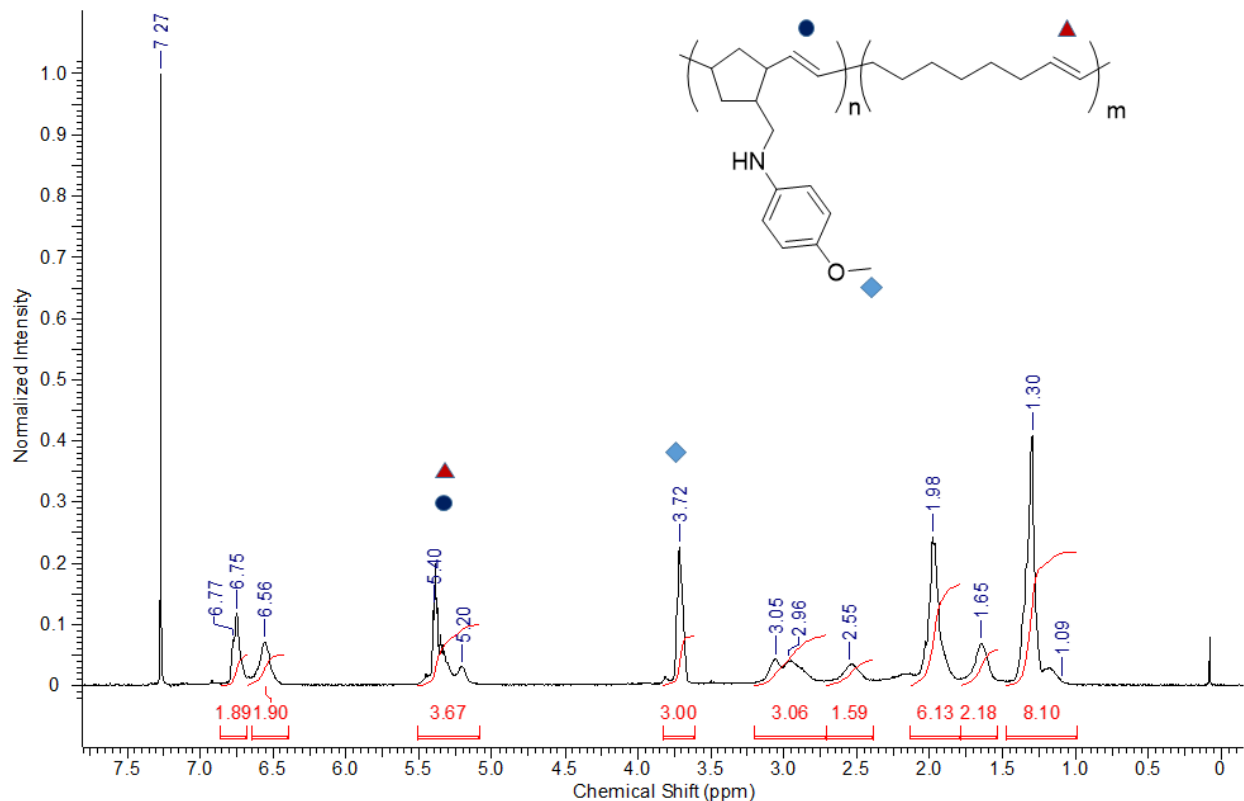
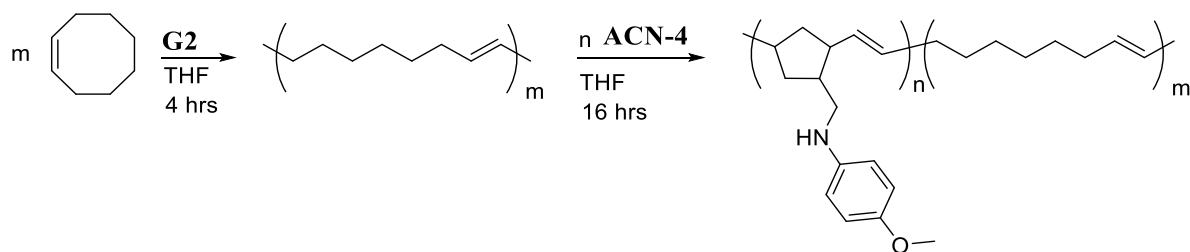


Figure 3.13 ^1H NMR spectrum (300 MHz, 298 K, CDCl_3) of attempted block copolymer with cyclooctene and ACN-4. Symbols correlate key diagnostic resonances of the respective blocks to calculate their molar ratio

An alternative order of addition was attempted to evenly incorporate both monomers. First, cyclooctene was polymerized, followed by an equimolar portion of ACN-4 (Scheme 3.25).



Scheme 3.25 Alternative order of addition for an attempted block copolymer between cyclooctene and amine-containing poly(norbornene) ACN-4

After the addition of both monomers, the reaction was quenched and a black solid was collected in 90% yield, suggesting both monomers were polymerized. Unfortunately, once dried

the polymer lacked solubility in all common lab solvents, preventing analysis by ^1H NMR spectroscopy. This poor solubility is proposed to originate from the phase separation of the two polymer domains, in which the disparate electronic features of the amine-containing and non-polar olefinic segments cause these blocks to organize apart from each other.

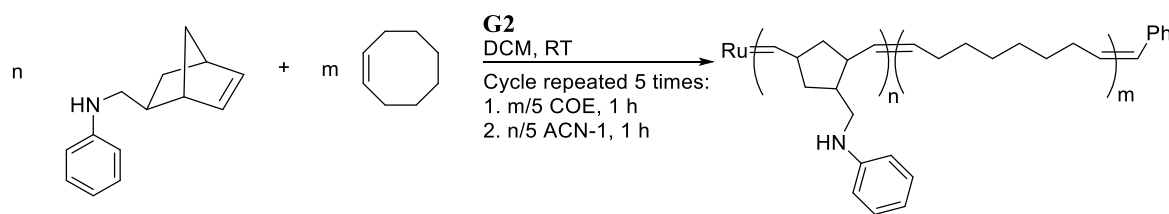
A series of smaller oligomers were prepared with the goal to obtain solubility for full characterization. First, 5, 10, and 50 equivalents of cyclooctene were homopolymerized, followed by the addition of 5 equivalents of ACN-4. After isolation by precipitation, these materials only possessed solubility for ^1H NMR spectroscopy if they were not fully dried from solvent. By ^1H NMR spectroscopy, the molar incorporation approximately matches the ratio of the monomers provided to the reaction (Table 3.5). In the 5:5 ratio, a slight over-incorporation of the amine-containing monomer was observed (60 and 57 % by mol in two repeat experiments). When the feed of cyclooctene was increased to 10:5, the % of amine segment in the product shows reasonable agreement (37 and 39 % relative to 33 % theoretical). With cyclooctene increased to 50:5, the ratio obtained in the product matches the monomer feed (10% amine units). Unfortunately, these materials did not possess solubility once vacuum dried for analysis by GPC. Elemental analysis was employed on the materials to corroborate the desired incorporation of the amine segment. Investigating these values, the %N found in the materials matches trends in the feed ratio, with reasonable agreement between found values and those calculated for the theoretical block oligomers.

Table 3.5 Formation of cyclooctene-(amine-containing norbornene) oligomers

Entry	m	n	% Yield ^a	m/n ratio ^b	Calculated EA ^c			Found EA ^d		
					%N	%C	%H	%N	%C	%H
1	5	5	80	40/60	3.92	82.76	9.32	4.38	71.69	8.58
2	5	5	56	43/57	3.92	82.76	9.32	4.08	76.19	9.15
3	10	5	>95	63/37	3.00	83.85	10.14	3.31	76.69	9.50
4	10	5	>95	61/39	3.00	83.85	10.14	3.67	77.26	10.01
5	50	5	66	90/10	1.04	86.14	11.90	1.36	83.95	12.04

^aGravimetric yield. ^bRatio determined by ¹H NMR spectroscopy. ^cCalculated based on theoretical m/n ratio^dFound values from elemental analysis.

The low solubility of these copolymers has thus far been proposed to originate because of the separation of the electronically distinct blocks. To test this hypothesis, a copolymer was attempted in which short blocks of either segment alternated along the polymer chain. To accomplish this, alternating portions of the respective monomers were fed to the reaction vessel (Scheme 3.26).

**Scheme 3.26 Preparation of an alternating-short block copolymer between cyclooctene and amine-containing norbornene ACN-1**

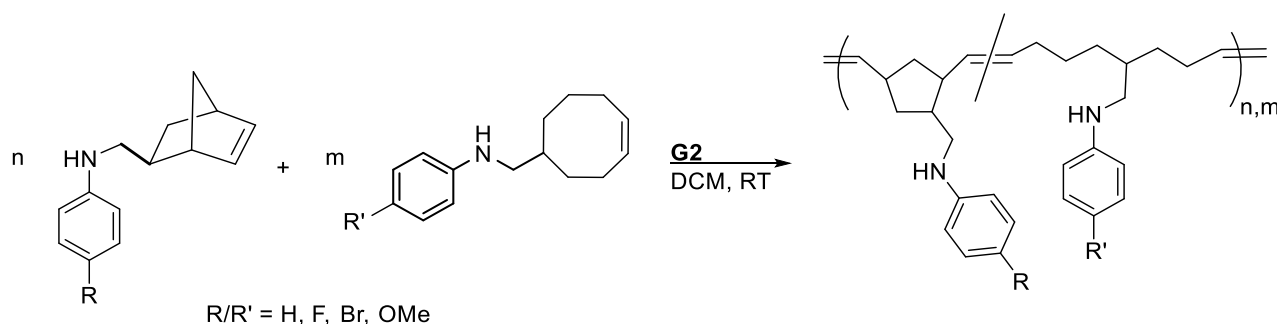
In total, 100 equivalents of each monomer were added in five portions each, with one hour between each addition, for a total of ten additions to the starting **G2** in solution. After all monomers were added, the reaction was stirred for 24 hours to ensure all monomers were reacted. After quenching and isolation by precipitation, a material with a favorable solubility profile was obtained. By ¹H NMR spectroscopy, 55% of the units were amine-containing, providing good agreement with an equimolar monomer feed. This material possessed the requisite solubility for

GPC after vacuum drying ($106,700 \text{ g}\cdot\text{mol}^{-1}$, $\bar{M}_w = 1.19$). The molecular weight is far greater than theoretically predicted ($30,900 \text{ g}\cdot\text{mol}^{-1}$), however this is not unusual as this was observed in ACN-1 homopolymerization. The improved solubility of this material provides some validation for the hypothesis that the low solubility of the block copolymers is due to self-assembly.

3.2.7.2 Copolymers between ACN and ACC monomers

Another targeted material was a combination of the ACN and ACC monomers into a copolymer. The exploration of this class of materials was conducted in collaboration with a visiting student, Mr. Hans Gildenast. As determined by differential scanning calorimetry, the glass transition temperatures of the polymers derived from these monomers are distinct; cyclooctene derivatives have T_g below room temperature (*eg.* $P(\text{ACC-1}) = -13.7^\circ\text{C}$) while norbornene derivatives cross this transition above room temperature ($P(\text{ACN-1}) = 58.4^\circ\text{C}$). In $P(\text{ACCs})$, the observation of self-healing is related to the ability of these polymers to possess chain mobility as amorphous materials. In contrast, $P(\text{ACNs})$ do not show self-healing behaviour. It was of interest to combine these materials to explore whether this behavior could be tuned, allowing the preparation of materials with variable physical properties.

A simultaneous addition of monomers was employed in the attempted formation of an $P(\text{ACN-ACC})$ copolymer (Scheme 3.27).



Scheme 3.27 Copolymer synthesis with amine-containing norbornene and amine-containing cyclooctene monomers

A series of different combinations of monomers with varying *para* R/R' substituents were co-polymerized *via* ROMP (50 equivalents of each monomer). Isolation of quenched reaction solutions by precipitation gave a material with physical properties that are intermediate to the respective homopolymers. Where P(ACN)s are stiff threads and P(ACC)s are sticky and tough gums, the copolymers aggregate and are tacky as in the latter, however with more pronounced stiffness. By ^1H NMR spectroscopy, it was found that the resultant polymers had higher incorporations of the given ACN (52-74 %). ACN-1 (R = H) and ACC-2 (R' = F) was chosen as a model system as both monomers were evenly incorporated (52:48 ACN:ACC). To ensure that a copolymer was formed, rather than two homopolymers, GPC analysis was performed on this sample; one peak was observed with reasonable agreement to the theoretical value ($M_{n, \text{exp}} = 18,130 \text{ g}\cdot\text{mol}^{-1}$, $\text{Đ} = 1.61$, $M_{n, \text{theo.}} = 21,630 \text{ g}\cdot\text{mol}^{-1}$). Notably, most monomer combinations gave copolymers which did not possess the requisite solubility for GPC analysis. In contrast to homopolymerizations, which typically give experimental weights that exceed the theoretical value predicted by $[\text{M}]/[\text{I}]$, the copolymers which could be analyzed by GPC gave values that were less than theoretical values.

In the prior kinetic study, it was found that ROMP of ACC-1 was complete within an hour, exceeding the rates of ACN polymerization. As this is not the trend that would be expected by relative ring strain values, it has been proposed that ACN monomers may inhibit polymerization rates by participating in non-productive equilibria with the ruthenium catalyst. As the copolymeric mixtures gave higher incorporations of the ACN monomer, a simple kinetic experiment was conducted with both monomer derivatives. Unexpectedly, it was found that when both monomers are copolymerized, the rate of ACN polymerization is faster than the rate of ACC polymerization. As previously mentioned, the trend in rates in homopolymerizations suggests that ACN monomers inhibit polymerization. This result suggests that when ACN monomers are present in copolymer synthesis, their inhibitory effect is greater in the ROMP of ACCs than ACNs. A full and detailed kinetic study is currently underway by Mr. N. Kuanr.

To explore whether the thermal properties can be tuned based on the relative incorporation of monomers, three different ratios of the chosen ACN-1/ACC-2 model system were prepared. The experimental ratios determined by ^1H NMR spectroscopy and glass transition temperatures as determined by DSC are shown in Figure 3.14.

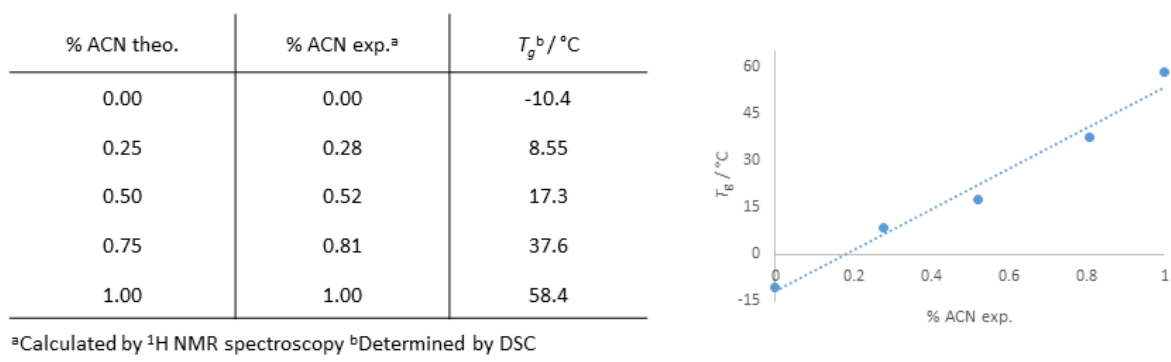


Figure 3.14 Effect of ACN/ACC ratio in copolymer on observed glass transition temperature

It was found that the glass transition could be tuned by adjusting the feed ratio of both monomers. The observation of a single glass transition in each sample is also indicative of copolymer synthesis in which both blocks possess miscibility.²¹³

Next, the effects of these varied ratios on viscoelasticity was probed. Melt rheology was conducted on the model copolymer with equal incorporation of P(ACN):P(ACC) segments (Figure 3.15).

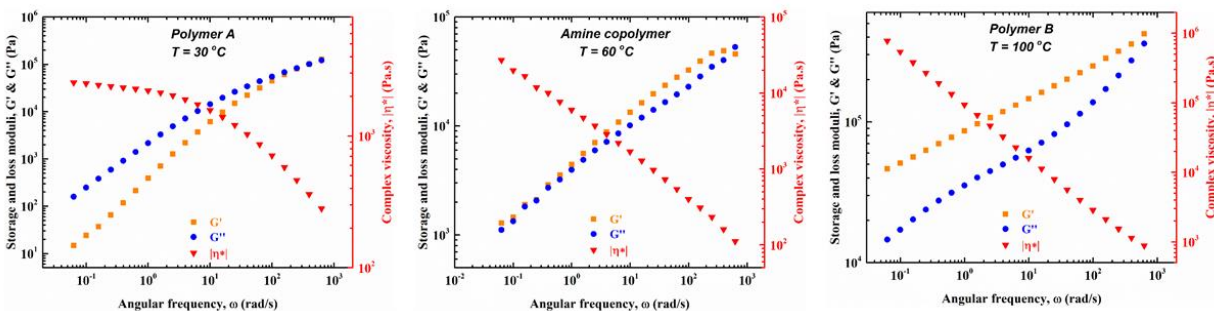


Figure 3.15 Melt rheology of (L) P(ACC-2) (C) P(ACC-2-co-ACN-1) (R) P(ACN-1)¹

The P(ACC-2-co-ACN-1) copolymer demonstrates rheological characteristics that are intermediate to the two pure homopolymers. P(ACC-2) shows that loss modulus is dominant over the entire frequency range, suggesting liquid-like behavior. Storage modulus predominates in P(ACN-1) as a soft-solid material. In the copolymer, storage and loss moduli are roughly equivalent at low frequency; at higher frequencies storage modulus is dominant, with a cross-over point at the terminal zone. This observed rheological behavior is supportive of the proposed copolymer with miscible domains.

Qualitative healing tests were performed to explore the effect of varying the glass transition temperature (T_g). It was hypothesized that all samples that had a glass transition below room temperature would demonstrate self-healing. Of the three copolymers, only the sample with 3:1 ACC:ACN ratio ($T_g = 8.6$ °C) demonstrated healing within 24 hours. The sample with 1:1

ACC:ACN ($T_g = 17.3\text{ }^{\circ}\text{C}$) did not demonstrate healing at the ambient conditions. This sample is likely too close to its glass transition temperature to show healing within 24 hours. These results suggest that tuning the thermal behavior may allow tuning of healing time depending on the needs of the material.

3.2.8 VT-IR spectroscopy

As currently understood, the two main criteria for the self-healing behavior observed in P(ACC) polymers is their amorphous phase at room temperature (*ie.* above T_g) and the dynamic, associative interactions between chains to promote entanglement. While the former can be determined by DSC, associative interactions can be challenging to directly detect experimentally. All macroscopic features of a bulk material are a superimposition of all molecular forces, therefore obscuring relatively weak interactions such as hydrogen-bonding and π - π stacking.

A well-known technique for determining the presence of hydrogen bonds that has been reported in the literature is VT-IR spectroscopy.^{139, 214-216} As thermal energy is provided to the sample, hydrogen bonds will rupture, thus changing the bond character of groups participating in such bonding and causing a shift in wavenumber (Figure 3.16). For a bending mode, such as in $\text{R}_2\text{N-H}$, hydrogen-bond interactions cause an increase in wavenumber by narrowing the bending motion. For stretching modes, hydrogen bond interactions cause a decrease in wavenumber as bond order is reduced.

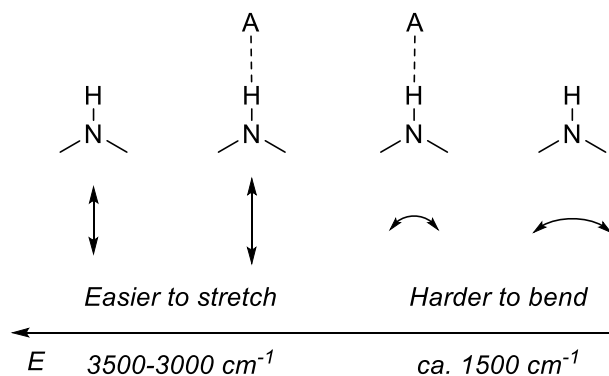


Figure 3.16 General trends in stretching and bending vibrational modes with hydrogen bonding

VT-IR spectroscopy was modified to analyze solid P(ACC) derivatives. Typically, these measurements are performed using an ATR-IR spectrometer equipped with a heating cell. As no heating accessory was available, the experimental set-up was modified based on equipment available. A piece of dry polymer film was adhered to the end of a ReactIR probe using the inherent adhesion of the material. The probe was then placed in a temperature-controlled bed of steel beads. Starting from room temperature (*ca.* 20 °C), a given P(ACC) sample was heated to 100 °C (upper limit of the equipment) at a rate of 4 °C•min⁻¹. Spectra were collected every 30 seconds from 3000-600 cm⁻¹. The challenge in modifying this experiment for P(ACC) derivatives is that the secondary amine groups that are theoretically participating in hydrogen bond interactions limit primary modes of interest to relatively weak N-H stretches and bends. Typically, modes of interest are strong and very diagnostic vibrational modes, such as C=O carbonyl stretches in polyurethanes or polyamides.^{139, 214-216} A further challenge is that the detection range is limited by the instrument probe, preventing analysis above 3000 cm⁻¹ in the region expected for N-H stretching modes (3500-3300 cm⁻¹). This limits the key region of interest to the region between 1600-1400 cm⁻¹ where N-H bending modes may be observed. However, these may also be obscured by C=C

aromatic stretches which are expected in the same region. The IR spectra of P(ACC-2) under ambient conditions and at 100 °C are shown in Figure 3.17.

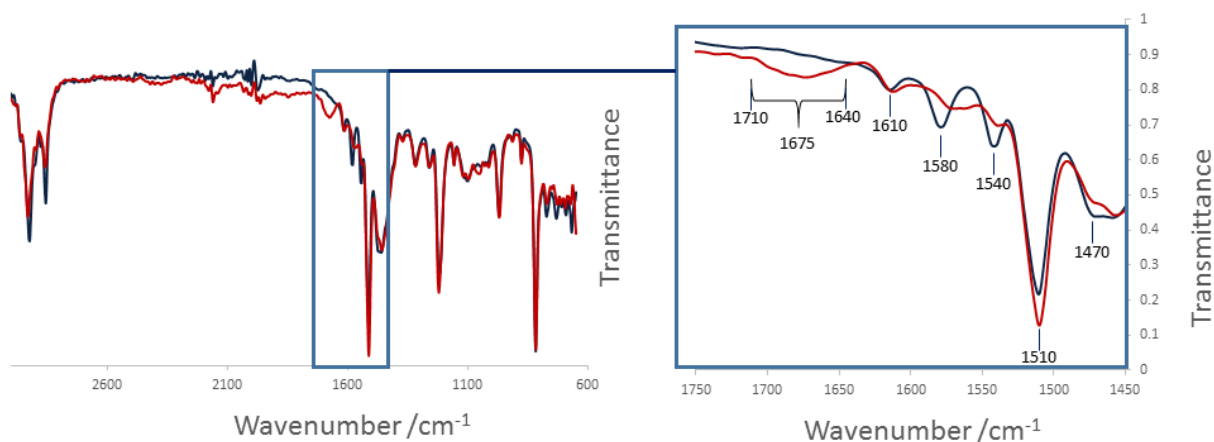


Figure 3.17 IR spectra of P(ACC-2) and zoom of the region from 1750-1450 cm^{-1} . Spectrum acquired at 100 °C shown in red (also can be identified by broad peak from 1710-1640 cm^{-1}); the spectrum acquired at room temperature spectrum is in blue

Prior to heating, the region of interest contains a major peak at 1510 cm^{-1} , a branch at 1470 cm^{-1} , and three weak peaks at 1540, 1580, and 1610 cm^{-1} . Upon heating, a new mode is observed as a broad peak centered at 1675 cm^{-1} . The emergence of this peak suggests that the bond providing this mode of vibration is thermally responsive. As the room temperature spectrum contains no apparent modes between 1800-1650 cm^{-1} , this is not considered a bending mode that has relaxed to a lower wavenumber. However, the weaker absorbance peaks at 1540 and 1580 cm^{-1} in the spectrum acquired at elevated temperature appear to have become notably less sharp.

This bonding mode demonstrates reversibility upon cooling. As shown in Figure 3.18, the measured absorbance at 1680 cm^{-1} increases with heating. After reaching 100 °C, the peak reaches maximum absorbance after a lag of approximately 5-10 minutes. Cooling causes the peak to immediately decrease in absorbance; after reaching 20 °C, the absorbance of the peak is slightly

higher than before heating. This suggests that after cooling the functional group may be in a slightly different conformation than before heating. This correlation between heating and peak absorbance is indicative of a reversible thermally-dependent vibrational mode, and not a mode that has resulted from a chemical reaction from heating the polymer.

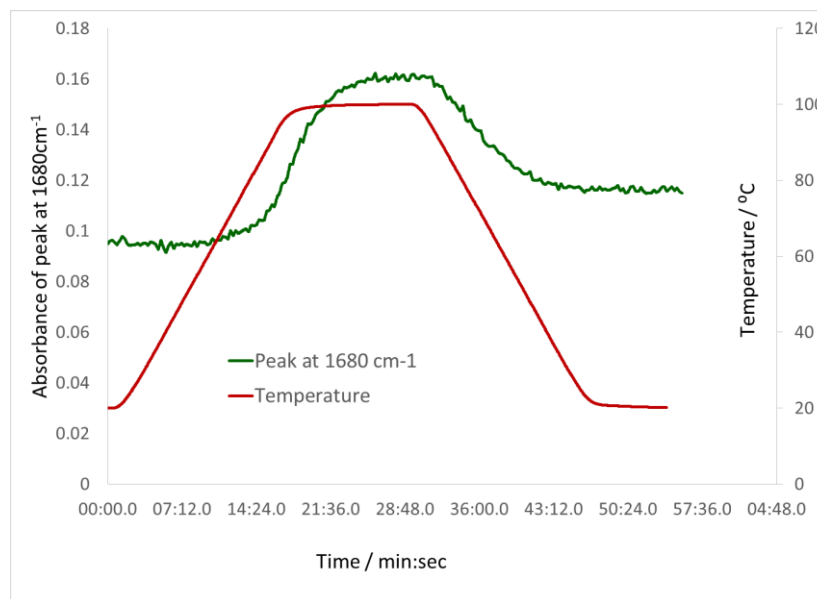


Figure 3.18 Peak reversibility with heating and cooling in amine-containing poly(cyclooctene) P(ACC-2)

A DFT calculation was performed on the ACC-2 monomer to investigate the theoretically predicted IR modes. This calculation was performed in the gas phase and thus does not include any hydrogen-bonding effects, thus making it a reasonable model for the heated spectrum in which hydrogen bond effects are diminished. The theoretical spectrum is shown in the zoomed region of interest (Figure 3.19).

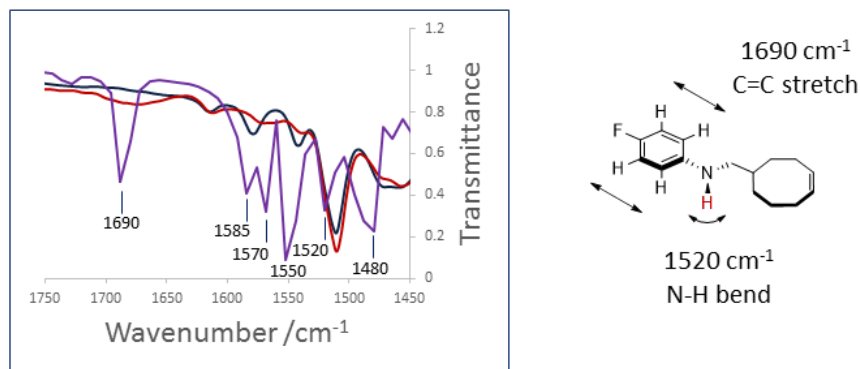


Figure 3.19 Computed IR spectra of ACC-2 and associated vibrational modes (indicated by sharp peak at 1690 cm^{-1}). B3LYP/svp

Theoretically, a major peak is predicted at 1690 cm^{-1} . Visualization of this stretching mode shows a symmetric C=C stretch through the aromatic ring. A weak N-H bending mode with a small amplitude of displacement is synchronous to this stretch and appears coupled. Another mode at 1520 cm^{-1} shows the same coupled motion of atoms, however this mode is predominantly the N-H bending mode as its amplitude has increased while the amplitude of the C=C stretch has diminished. While this is only an approximate calculation, these modes can qualitatively rationalize the new IR-active modes observed when heating P(ACC-2). At room temperature, spectra are dominated by hydrogen-bond interactions, limiting their vibrational displacement. However, when these H-bond interactions are diminished with heating these peaks become detectable above the baseline again.

This experiment was also conducted with other P(ACC) derivatives. Experimental runs with P(ACC-1H), P(ACC-3), and P(ACC-4) all showed the emergence of a broad peak between 1700 and 1650 cm^{-1} (Figure 3.20).

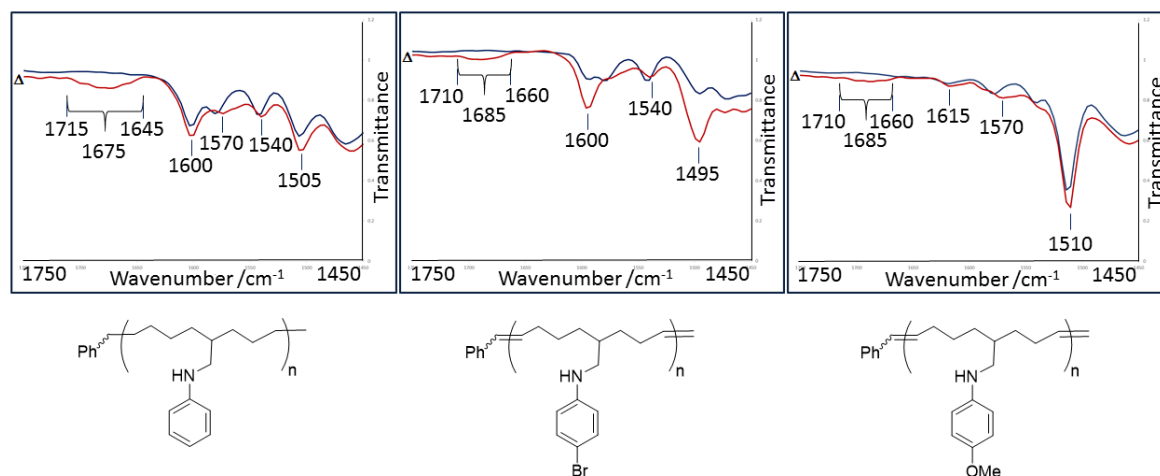


Figure 3.20 VT-IR spectra in the region of 1750-1450 cm^{-1} for (L) P(ACC-1H) (M) P(ACC-3) (R) P(ACC-4).

Heated spectra indicated with (Δ)

If the peak at *ca.* 1500 cm^{-1} is tentatively assigned to the N-H bending mode, a trend can be observed between the four derivatives. As hydrogen-bonding is known to increase the wavenumber of bending modes,²¹⁵ the position of P(ACC-2) ($\text{R}=\text{F}$, ν N-H bend = 1515 cm^{-1}) and P(ACC-4) ($\text{R}=\text{OMe}$, ν N-H bend = 1510 cm^{-1}) at higher wavenumbers than P(ACC-1H) ($\text{R}=\text{H}$, ν N-H bend = 1505 cm^{-1}) and P(ACC-3) ($\text{R}=\text{Br}$, ν N-H bend = 1495 cm^{-1}) matches the trend in which fluorine and methoxy groups are considered the strongest acceptors.

While these experiments do not conclusively identify the nature of the associative interactions in P(ACC) derivatives, the detection of thermally reversible vibrational modes does corroborate that these materials respond to external stimuli. These experiments do not confirm loss of H-bonding at 100 $^{\circ}\text{C}$, which is the limit of the IR probe. However, the use of a heating cell that can allow detection of the full spectral window and higher temperature may allow for visualization of all modes through the complete rupture of hydrogen bonds, thereby enabling more straightforward analysis in future experiments.

3.3 Conclusions

The hydroaminoalkylation reaction is a powerful synthetic tool for the catalytic assembly of amine-containing monomers for ROMP. The development of reactive tantalum-based catalysts has enabled the mono-alkylation of the cyclic dienes norbornene and cyclooctadiene, thus giving amine-containing norbornene (ACN) and amine-containing cyclooctene (ACC) derivatives in a single, atom-economic step. Using optimized methodology with alternative catalysts, these derivatives were obtained on gram-scale. These monomers are amenable for ROMP without the use of protecting groups, giving polyolefins bearing pendant amine branches. Hydrogenation was successfully performed to give fully saturated backbones; in the class of P(ACCs) the products can be recognized as polyethylene derivatives bearing an amine group on 12.5 mol% of the backbone carbons.

The physical properties of these materials were investigated and novel features were observed with amine incorporation. Melt rheology was an effective technique to elucidate dramatic differences in response to shear-strain in polymers with amine-containing groups. In comparison to unfunctionalized poly(cyclooctene) and poly(norbornene), the presence of amine branches prompts associative interactions between polymer chains, causing the formation of transient supramolecular networks. Macroscopically, P(ACCs) were observed to be capable of responding to external stimuli, including self-healing and adhesion to a poly(tetrafluoroethylene) substrate. Key criteria for these observed effects are proposed to be chain mobility (glass transition temperature below ambient conditions) and associative interactions to encourage chain entanglement.

Various copolymers were also prepared to change the physical properties from that observed in homopolymeric P(ACN) and P(ACC). Amine incorporation was lowered by the

preparation of copolymers with unfunctionalized cyclic alkenes, ultimately leading to low cost, value-added materials. However, it was found that amine-functionalized segments are sufficiently distinct from unfunctionalized segments to cause phase separation by self-assembly. To tune the physical properties of the respective amine-containing homopolymers, copolymers were prepared between their monomers. Varying the respective feed ratio was found to enable the controlled modification of the T_g . These copolymers verified chain flow as a criteria for self-healing, as a copolymer demonstrated self-healing only when ambient conditions are clearly above the T_g . Unexpected trends in the reactivity of ACN and ACC monomers for ROMP were observed when these monomers were copolymerized, suggesting off-pathway equilibria that interfere with catalysis and polymer propagation.

A VT-IR study was also performed to probe the associative interactions present in P(ACC) derivatives. The detection of a thermally responsive vibrational mode was observed and assigned to the functional group, in which an aromatic stretching mode is coupled to an amine bending mode. These modes are reversibly observed with heating, which is proposed to break hydrogen-bonding interactions that are present under ambient conditions.

Ultimately, this chapter presented results of investigations into novel amine-containing monomers and their respective polymers. Preliminary rheological analysis suggests the promising potential of the incorporation of amine groups into polyolefins to improve and add functionality. The associative interactions of these groups produce interesting macroscopic effects in the bulk material, including improved adhesion characteristics and the ability to self-heal. The synthesis of these materials is also highly controlled, allowing for the variable incorporation of different amine-containing monomers to tune physical properties, for example in the glass transition temperature.

In particular, this route harnesses sustainable catalysis to circumvent the long-standing challenges in the amine functionalization of polyethylene.

3.4 Experimental

3.4.1 Materials and Methods

General Details All air-sensitive reactions were performed under an inert atmosphere using a double manifold Schlenk line equipped with N₂ and high vacuum (10⁻³ mbar) or a glovebox filled with N₂. All glassware used was heated above 160 °C for a minimum of 12 hours in an oven prior to use. Reactions were performed in threaded 20 mL scintillation vials equipped with a poly(tetrafluoroethylene)-coated magnetic stir bar and a poly(tetrafluoroethylene)-lined polypropylene screw-cap. Toluene and hexane were purified by passing over activated alumina columns prior to collection and storage in the glovebox. Thin layer chromatography (TLC) was performed on EMD Silica gel 60 F254 plates and visualized under a 254 nm UV light. Flash chromatography was performed using an automated Biotage purification system using SilicaFlash F60 silica gel (230-400 mesh) (Silicycle) as a stationary phase and ACS grade hexanes/ethyl acetate as a mobile phase.

Reagents All reagents were purchased from commercial sources unless otherwise stated. 3-methyl 2-pyridone (Combi-blocks) was purified by sublimation. Cyclooctadiene (Aldrich), *N*-methyl aniline (Aldrich), 4-fluoro-*N*-methyl aniline (Aldrich), and 4-bromo-*N*-methyl aniline (Oakwood) were stirred over CaH₂ for a minimum of 2 h, separated by distillation, then manipulated using standard Schlenk techniques. 4-methoxy-*N*-methyl aniline was prepared as according to literature and purified via sublimation. [TaCl₂(NMe₂)₃]₂¹⁹⁹ and catalyst **1.8**⁴⁰ was prepared as per literature precedent. Grubbs Catalyst TM 2nd Generation (**G2**) (Sigma-Aldrich) was purchased and used without further purification. Grubbs Catalyst 3rd Generation (**G3**) was prepared as according to the literature.²¹⁷ Toluene and hexane were purified by passing over activated alumina columns prior

to collection and storage in the glovebox. Common solvents and work-up reagents were used as received.

Instrumentation

NMR spectroscopy NMR spectra were collected using a Bruker Avance instrument operating at 300 or 400 MHz. Chemical shifts, δ , are reported in parts per million (ppm) and coupling constants (J) are given in Hertz (Hz). Abbreviations for NMR assignments are as follows: s = singlet; d = doublet; dd = doublet of doublets; t = triplet; q = quartet; m = multiplet; br = broad; appt = apparent.

IR spectroscopy Spectra were recorded at room temperature on a Perkin Elmer FTIR equipped with an ATR accessory for direct measurement on oils and polymeric materials. Bands are reported in wavenumbers (cm^{-1}) and assigned with the abbreviations s = strong, m = medium, w = weak, sh = shoulder, br = broad. VT-IR monitoring was conducted with a Mettler–Toledo ReactIR 15 equipped with a DiComp (Diamond) ATR probe connected using a AgX (silver halide) 6 mm x 1.5 m fiber optic cable. Reaction temperatures were monitored using an internal thermistor in the IR probe. Sampling was carried out over 2000–800 cm^{-1} at 4 wavenumber resolution with 1x gain.

Gel Permeation Chromatography Polymer M_n , M_w and dispersity ($\mathcal{D}$) were obtained using triple detection gel permeation chromatography (GPC) using a Waters liquid chromatograph equipped with an Agilent 1200 series isocratic pump and autosampler, Phenomenex Phenogel 5 μm narrow bore columns, Wyatt OptilabEx differential refractometer, Wyatt tristar miniDAWN (laser light scattering detector) and a Wyatt ViscoStar viscometer. A flow rate of 0.5 $\text{ml} \cdot \text{min}^{-1}$ was used and samples were dissolved in THF ($\sim 1\text{--}2 \text{ mg} \cdot \text{ml}^{-1}$). The measurements were carried out at a laser wavelength of 690 nm, at 25 °C. The data was analyzed using the Astra® processing program

provided by Wyatt Technology Corp. The dn/dc values were calculated using a 100% mass recovery method. For P(ACC-1), the average dn/dc was 0.116 ± 0.011 . For P(ACC-3), the dn/dc value was calculated to be 0.1179.

Differential Scanning Calorimetry DSC was performed on a TA Instruments DSC Q2000 equipped with a TA Instruments Refrigerated Cooling System 90. A heating/cooling rate of 5 °C/min was used for each run in the range of -90 °C to 120 °C. Duplicate runs were measured after the completion of one heating/cooling cycle to remove thermal history.

Thermogravimetric Analysis The thermal stability of the polymers was determined by using a Shimadzu TGA-50 thermogravimetric analyser. Experiments were carried out on a small amount of sample (2-5mg) by continuously passing a high purity nitrogen stream (99.5% N₂) into the furnace at a flow rate of 50 mL/min at atmospheric pressure and room temperature. Weight loss as a function of time was continuously monitored in the temperature range from 25 to 600 °C at a heating rate of 10 °C/min.

Rheological Measurements Polymers were prepared as films for rheological testing.¹ The precipitated polymer (0.5-1 g) was fully dissolved in THF (ca. 10-20 mL) and solution cast in a custom fabricated poly(tetrafluoroethylene) mould. Solvent was allowed to evaporate at room temperature/pressure overnight, followed by drying in a vacuum oven (45 °C). Films could then be carefully removed from the mould and used for analysis. During film-casting, polymers were noted to become darker in color, presumably due to oxidation of amine or residual ruthenium residue.

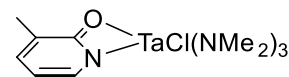
Viscoelastic measurements were conducted using the Anton Paar MCR 702 rotational rheometer, equipped with a cone-partitioned-plate geometry. The top part of this type of geometry contains an 8 mm in diameter plate attached to the transducer (centre plate), and a coaxial stationary ring (partitioned plate, 25 mm in diameter), which acts as a shield and prevents edge fracture of the sample. The bottom plate is 25 mm in diameter with an angle of 0.07 radians. The experiments were performed at distance gap of 51 μm .

The thermal stability of the samples was studied isothermally using dynamic time sweep tests by applying the frequency of 0.1 Hz and shear strain of 0.01 radians for 2 hrs. An initial strain sweep test at the frequency of 0.1 Hz was used to detect the limits of the linear viscoelasticity. Frequency sweep experiments (0.01-100 Hz) at a fixed shear strain of 0.01 radians, which is within the linear viscoelastic region, were performed at different temperatures. Obtained experimental results are presented at the temperature of 30 $^{\circ}\text{C}$.

3.4.2 Synthesis and Characterization

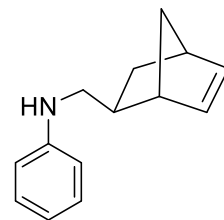
Chlorotris(dimethylamido)(κ^2 -N,O-3-methyl-2-pyridonato)

tantalum(V) (1.9).¹⁰⁴ To a suspension of $[\text{TaCl}_2(\text{NMe}_2)_3]_2$ (0.23 g, 0.3



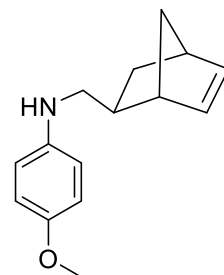
mmol) in toluene (~ 2 mL) was added a suspension of sodium 3-methyl-2-pyridonate (0.075 g, 0.6 mmol) in toluene (~ 2 mL) at room temperature. Upon stirring overnight, the initially yellow, cloudy mixture became an orange, clear solution. Volatiles were removed *in vacuo* to give 0.250 g orange-brown oil (90 %). The crude residue was dissolved in 1.0 g toluene solvent (0.25 w/w%) and used for hydroaminoalkylation (HAA). **^1H NMR** (400 MHz, d_8 -tol): δ 8.23 (d of d, 1H, ArH), δ 6.83 (d, 1H, ArH), δ 6.20 (t, 1H, ArH), δ 3.75-3.53 (br s, 18H, $(\text{NCH}_3)_2$) δ 2.10 (s, 3H, CH_3). Characterization was consistent with previously reported values.

ACN-1.⁴⁶ Generated using the *in-situ* preparation of catalyst **1.11**; small-scale reactions were conducted in 20 mL scintillation vials while large-scale synthesis was conducted in a poly(tetrafluoroethylene)-capped reaction vessel.



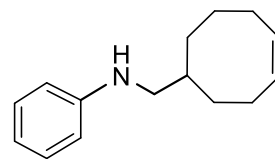
For a small-scale reaction, Ta(NMe₂)₅ (0.190 g, 0.5 mmol), 3-methyl-2-pyridone (0.050 g, 0.5 mmol), *N*-methyl aniline (0.50 g, 5 mmol), and norbornadiene (0.64 g, 7 mmol) were combined along with toluene (~3 mL) and a poly(tetrafluoroethylene) coated stir bar. The initially orange, cloudy solution was capped, removed from the glovebox, and heated to 130 °C in an oil-bath. Upon reaching temperature the reaction mixture goes dark red and was then heated for a pre-determined period (2 hrs for this scale). After this time, the reaction was quenched with exposure to ambient atmosphere and the addition of ~1 mL methanol. Purification was completed *via* automated column chromatography (0 to 20% gradient of ethyl acetate/hexanes) to afford 0.37 g of orange oil (40 %). ¹H NMR (300 MHz, CDCl₃): δ 7.21 (d of d, ³J_{HH} = 7.40 Hz, ³J_{HH} = 8.55 Hz, 2H, 2 × ArH), δ 6.72 (t, ³J_{HH} = 7.40 Hz, 1H, ArH), δ 6.64 (d, ³J_{HH} = 8.55 Hz, 2H, 2 × ArH), δ 6.12 (m, 2H, RHC=CHR), δ 3.15 (m, 2H, CH₂), δ 2.88 (m, 1H, CH), δ 2.75 (m, 1H, CH), δ 1.71 (m, 1H, CH), δ 1.41 (m, 2H, CH₂), δ 1.37 (m, 1H, CH), δ 1.25 (s, 1H, CH). Characterization was consistent with previously reported values.

ACN-4⁴⁶ May be synthesized using catalyst **1.8** or optimized synthesis by the *in-situ* generation of catalyst **1.11**. Using the latter, this monomer can be prepared on gram-scale with comparable yields to ACN-1 (conducted by N. Kuanr). Using catalyst **1.8**, ACN-4 was prepared according to literature precedent. To a 20 mL scintillation vial, norbornadiene (0.5 g, 5 mmol), 4-methoxy aniline (0.5 g, 3.6 mmol), and **1.8** (0.2 g, 0.36 mmol) were added along with a



poly(tetrafluoroethylene)-coated stir bar. The resulting deep red, neat solution was stirred for 20 hrs in a glovebox. After the reaction was completed, the vial was removed from the box, uncapped, and quenched with the addition of *ca.* 1 mL methanol, causing an immediate loss in color. Purification was completed *via* automated column chromatography (0 to 20% gradient of ethyl acetate/hexanes) to afford 0.47 g of dark brown oil (55%). **¹H NMR** (400 MHz, CDCl₃): δ 6.80 (d, ³J_{HH} = 8.86 Hz, 2H, ArH), δ 6.62 (d, ³J_{HH} = 9.13 Hz, 2H, 2 x ArH), δ 6.10 (m, 2H, RHC=CHR), δ 3.76 (s, 3H, OCH₃) δ 3.10 (m, 2H, CH₂), δ 2.86 (s, 1H, CH), δ 2.73 (s, 1H, CH), δ 1.68 (s, 1H, CH), δ 1.36 (s, 2H, CH₂), δ 1.35 (m, 1H, CH₂), δ 1.33 (s, 1H, CH₂), δ 1.22 (s, 1H, CH). Characterization was consistent with previously reported values.

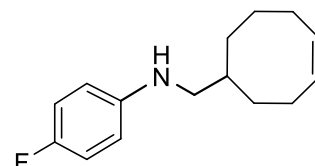
ACC-1. To a solution of catalyst **1.9** (0.2 g, 5 mol %) in toluene (~3 mL) was added *N*-methyl aniline (1.0 g, 9.34 mmol) followed by cyclooctadiene (1.5 g, 14 mmol). The initially orange, cloudy solution was



equipped with a stirring bar, capped, removed from the glovebox, and heated to 145 °C in an oil-bath. Upon reaching temperature the reaction mixture goes dark red and was then heated with stirring for 20 h. After this time, the reaction was quenched with exposure to ambient atmosphere and the addition of ~1 mL methanol. Purification was completed *via* automated column chromatography (0 to 20% gradient of ethyl acetate/hexanes) to afford 1.7 g of pale-yellow oil (84 %). **¹H NMR** (300 MHz, CDCl₃): δ 7.20 (dd, ³J_{HH} = 7.35 Hz, ³J_{HH} = 8.53 Hz, 2H, 2 x ArH), δ 6.72 (t, ³J_{HH} = 7.39 Hz, 1H, ArH), δ 6.64 (d, ³J_{HH} = 8.79 Hz, 2H, 2 x ArH), δ 5.68 (m, 2H, RHC=CHR), δ 4.09 (br s, 1H, NH), δ 2.96 (m, 2H, CH₂), δ 2.38 (m, 1H, CH), δ 2.16 (m, 3H, CH₂), δ 1.81-1.19 (m, 7H, CH₂). **¹³C{¹H} NMR** (75 MHz, CDCl₃): δ 148.7 (C), δ 130.2 (CH), δ 130.1 (CH), δ 129.3 (CH), δ 117.0 (CH), δ 112.7 (CH), δ 51.7 (CH₂), δ 37.8 (CH₂), δ 33.5 (CH₂), δ 31.2 (CH₂), δ 28.3

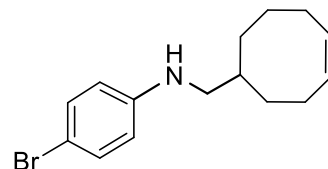
(CH), δ 26.0 (CH), δ 24.9 (CH). **IR** (neat oil, cm^{-1} , int): 3428br, 3019w, 2924s, 2856sh, 1600s, 1506s, 1314m, 1252w, 1125br, 994br, 749s, 689s. **HRMS-ESI** (m/z) Calcd: 216.1752; found: 216.1748.

ACC-2. Prepared as per ACC-1 using 4-fluoro-*N*-methylaniline as the amine substrate to afford 1.5 g of pale-yellow oil (82 %). **^1H NMR** (300



MHz, CDCl_3): δ 6.90 (t, 2H, $2 \times \text{ArH}$), δ 6.72 (m, 2H, $2 \times \text{ArH}$), δ 5.69 (m, 2H, $\text{RHC}=\text{CHR}$), δ 3.50 (br s, 1H, NH), δ 2.91 (m, 2H, CH_2), δ 2.38 (m, 1H, CH), δ 2.17 (m, 3H, CH_2), δ 1.79-1.19 (m, 7H, CH_2). **$^{13}\text{C}\{^1\text{H}\}$ NMR** (75 MHz, CDCl_3): δ 157.2 (C), δ 154.1 (CH), δ 145.0 (CH), δ 130.1 (CH), δ 115.4 (CH), δ 113.5 (CH), δ 52.4 (CH_2), δ 37.7 (CH_2), δ 33.4 (CH_2), δ 31.2 (CH_2), δ 28.2 (CH), δ 25.9 (CH), δ 24.8 (CH). **$^{19}\text{F}\{^1\text{H}\}$ NMR** (282 MHz, CDCl_3): δ -128.6. **IR** (neat oil, cm^{-1} , int): 3428br, 3010w, 2909m, 2856sh, 1615w, 1513s, 1470sh, 1320w, 1221s, 814s, 720m. **HRMS-EI** (m/z) Calcd: 233.15798; found: 233.15817.

ACC-3. Prepared as per ACC-1 using 4-bromo-*N*-methyl aniline as the amine substrate to afford 1.3 g of pale-yellow oil (81 %). **^1H NMR**

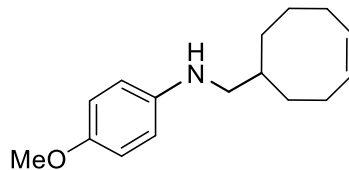


(300 MHz, CDCl_3): δ 7.25 (d, $^3J_{\text{HH}} = 8.77$ Hz, 2H, $2 \times \text{ArH}$), δ 6.48 (d, $^3J_{\text{HH}} = 8.77$ Hz, 2H, $2 \times \text{ArH}$), δ 5.68 (m, 2H, $\text{RHC}=\text{CHR}$), δ 3.78 (br s, 1H, NH), δ 2.91 (m, 2H, CH_2), δ 2.36 (m, 1H, CH), δ 2.17 (m, 3H, CH_2), δ 1.78-1.18 (m, 7H, CH_2). **$^{13}\text{C}\{^1\text{H}\}$ NMR** (75 MHz, CDCl_3): δ 147.5 (C), δ 131.9 (CH), δ 130.1 (CH), δ 114.3 (CH), δ 108.5 (CH), δ 51.7 (CH_2), δ 37.6 (CH_2), δ 33.4 (CH_2), δ 31.1 (CH_2), δ 28.2 (CH), δ 26.0 (CH), δ 24.8 (CH). **IR** (neat oil, cm^{-1} , int): 3422br, 3015w, 2922s, 2854sh, 1593s, 1497s, 1313m, 1249m, 1175w, 1073w, 999w, 808s, 723m. **HRMS-ESI** (m/z) Calcd: 293.07791; found: 293.07770.

ACC-4. Prepared as per ACC-1 using 4-methoxy *N*-methyl aniline

as the amine substrate to afford 1.5 g of yellow oil (85 %). **¹H NMR**

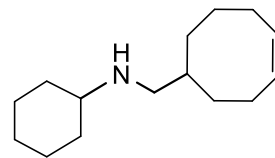
(300 MHz, CDCl₃): δ 6.81 (d, ³J_{HH} = 8.79 Hz, 2H, 2 × ArH), δ 6.60



(d, ³J_{HH} = 8.79 Hz, 2H, 2 × ArH), δ 5.68 (m, 2H, RHC=CHR), δ 3.77 (s, 3H, OCH₃), δ 3.38 (br s, 1H, NH), δ 2.91 (m, 2H, CH₂), δ 2.38 (m, 1H, CH), δ 2.18 (m, 3H, CH₂), δ 1.81-1.19 (m, 7H, CH₂). **¹³C{¹H} NMR** (75 MHz, CDCl₃): δ 152.0 (C), δ 142.7 (CH), δ 130.2 (CH), δ 115.0 (CH), δ 114.1 (CH), δ 55.9 (CH₃), 52.9 (CH₂) δ 37.7 (CH₂), δ 33.5 (CH₂), δ 31.2 (CH₂), δ 28.2 (CH), δ 26.0 (CH), δ 24.9 (CH). **IR** (neat oil, cm⁻¹): 3415br, 3014w, 2919s, 2854sh, 1620w, 1506s, 1463m, 1228s, 1125w, 1035m, 818s, 724w. **HRMS-EI** (m/z) Calcd: 245.17796; found: 245.17794.

ACC-5. To a solution of **1.9** (60 mg, 3.8 mol %) in toluene (~3 mL) was

added *N*-methylcyclohexylamine (450 mg, 4 mmol) followed by



cyclooctadiene (650 mg, 6 mmol). The initially yellow, clear solution was

equipped with a stirring bar, sealed with a cap, removed from the glovebox, and heated to 145 °C in an oil-bath. Upon reaching temperature the reaction mixture slowly becomes orange and was then heated with stirring for 20 h. After this time, the reaction was quenched with exposure to ambient atmosphere and the addition of ~1 mL methanol. The solvent was removed under reduced pressure and the residue was applied to a plug of silica gel. Excess cyclooctadiene was washed away with hexanes and the product was subsequently eluted with a mixture of triethylamine and hexanes (1:14). The solvent was removed under reduced pressure and 0.61 mg of product was obtained as a colourless oil (53 %). **¹H NMR** (300 MHz, CDCl₃): δ 5.64 (m, 2H, RHC=CHR), δ 2.44 (m, 2H, CH₂), δ 2.34 (m, 1H, CH), δ 2.12 (m, 3H, CH), δ 1.88-1.00 (m, 18H). **¹³C{¹H} NMR**

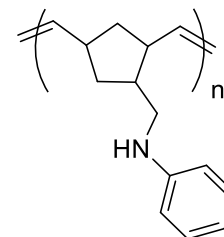
(75 MHz, CDCl₃): δ 130.2 (CH), δ 129.9 (CH), δ 56.9 (CH), δ 54.9 (CH₂), δ 38.1 (CH), δ 33.7 (CH₂), δ 33.6 (CH₂), δ 31.6 (CH₂), δ 28.2 (CH), δ 26.2 (CH₂), δ 25.9 (CH₂), δ 25.1 (CH₂), δ 24.9 (CH₂). **IR** (neat oil, cm⁻¹): 3014w, 2923vs, 2851s, 1651m, 1612w, 1570w, 1463s, 1449s, 1374w, 1348w, 1258w, 1228w, 1131m, 1028w, 989w, 972w, 941w, 886m, 844w, 775m, 754m, 721vs. **HRMS-ESI** (m/z) Calcd: 222.2222; found: 222.2228.

General Polymer Synthesis

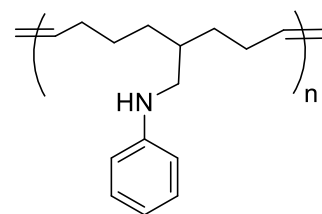
Preparation of P(ACN) and P(ACC) homopolymers Polymerization of monomers was completed using ring-opening metathesis polymerization (ROMP) using Grubbs Catalyst™ 2nd Generation (**G2**) unless otherwise stated. To a stirring solution of the monomer in CH₂Cl₂ was added a solution of catalyst in CH₂Cl₂. Reactions were capped and reacted at room temperature while stirring for a given time period (minimum 16 hours to ensure full conversion with ACN monomers, minimum 4 hours with ACC monomers). As the reaction proceeds there is a general observation that solutions slowly turn light amber-yellow/green from the originally dark amber solution. Reactions are also noticed to increase in viscosity, however stirring is maintained throughout the reaction despite this change. Reactions were quenched *via* exposure to ambient atmosphere and drop-wise addition of an excess of ethyl vinyl ether (min. of 2 drops per mg of [Ru] catalyst) and left to stir for a minimum of thirty minutes, after which the solution slowly changes color to dark amber/black. The polymer was isolated with precipitation *via* drop-wise addition to a stirring vortex of methanol (-35 °C, minimum of 1 mL per mg polymer). Isolation was completed by decanting the supernatant and drying overnight of the collected material under high vacuum. All characterization was thereafter completed with the exception of GPC analysis, for which further purification was completed *via* two additional precipitations (using addition of a

CH₂Cl₂ solution of the polymer into a large excess of methanol) followed by drying in a vacuum oven at 40 °C.

P(ACN-1). Prepared as above on gram-scale to afford 0.85 g of an off-white gum-like solid (85 %). ¹H NMR (300 MHz, CDCl₃): δ 7.16 (s, 2H, 2 × ArH), δ 6.75 (m, 3H, 3 × ArH), δ 5.27 (m, 2H, RHC=CHR), δ 3.05 (d, 2H, CH₂), δ 2.90 (s, 1H, CH), δ 2.53 (s, 1H, CH), δ 1.95 (s, 2H, CH₂), δ 1.65 (s, 2H, CH₂), δ 1.19 (s, 1H, CH).

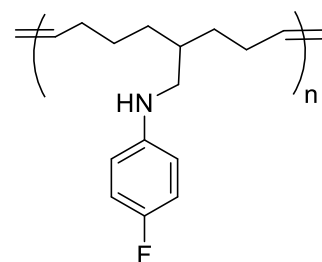


P(ACC-1). Prepared as above to afford 0.84 g of an off-white gum-like solid (84 %). ¹H NMR (300 MHz, CDCl₃): δ 7.17 (m, 2H, 2 × ArH), δ 6.73 (br s, 3H, 3 × ArH), δ 5.40 (m, 2H, RHC=CHR), δ 3.03



(d, 2H, CH₂), δ 2.00 (m, 4H, CH₂), δ 1.68 (br s, 1H, CH), δ 1.49-1.26 (m, 6H, CH₂). **IR** (neat oil, cm⁻¹,int): 3425br, 2924s, 2847sh, 1602 s, 1505s, 1430sh, 1320m, 1258m, 1180w, 1023w, 964m, 862w, 743s, 691s.

P(ACC-2). Prepared as above to afford 0.69 g of gummy, off-white solid (88 %). ¹H NMR (300 MHz, CDCl₃): δ 6.87 (m, 2H, 2 × ArH), δ 6.55 (br s, 2H, 2 × ArH), δ 5.39 (m, 2H, RHC=CHR), δ 2.97 (d, 2H, CH₂), δ 2.00 (m, 4H, CH₂), δ 1.63 (br s, 1H, CH), δ 1.36 (br s, 6H, CH₂).



¹⁹F{¹H} NMR (282 MHz, CDCl₃): δ -127.7. **IR** (neat oil, cm⁻¹, int): 3419br, 2919m, 2850sh, 1614w, 1510s, 1473sh, 1316w, 1214s, 1101w, 816s

P(ACC-3). Prepared as above to afford 0.59 g of gummy, off-white

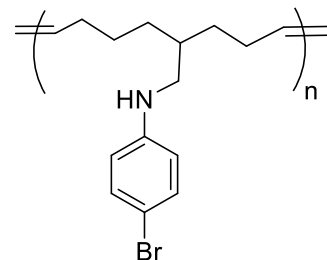
solid (94 %). $^1\text{H NMR}$ (400 MHz, CDCl_3): δ 7.27 (m, 2H, $2 \times \text{ArH}$),

δ 6.52 (br s, 2H, $2 \times \text{ArH}$), δ 5.42 (m, 2H, $\text{RHC}=\text{CHR}$), δ 3.00 (d, 2H,

CH_2), δ 2.01 (br s, 4H, CH_2), δ 1.66 (br s, 1H, CH_2), δ 1.38 (br s, 6H,

CH_2). **IR** (neat oil, cm^{-1} , int): 3422br, 2922s, 2854sh, 1593s, 1497s, 1313m, 1249m, 1175m,

1073m, 964m, 808s.



P(ACC-4). Prepared as above to afford 0.54 g of gummy, off-white

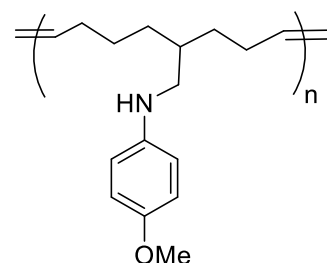
solid (88 %). $^1\text{H NMR}$ (400 MHz, CDCl_3): δ 6.78 (d, 2H, $2 \times \text{ArH}$),

δ 6.59 (br s, 2H, $2 \times \text{ArH}$), δ 5.39 (m, 2H, $\text{RHC}=\text{CHR}$), δ 3.74 (s, 3H,

OCH_3), δ 2.98 (d, 2H, CH_2), δ 2.01 (br s, 4H, CH_2), δ 1.63 (br s, 1H,

CH_2), δ 1.37 (br s, 6H, CH_2). **IR** (neat oil, cm^{-1} , int): 3394br, 2923s, 2848sh, 1655br, 1510s,

1464sh, 1233s, 1017s, 816s, 668m.



P(ACC-5) Prepared using Grubbs 3rd generation catalyst (**G3**) with

heating to 90 °C in an oil-bath for 24 h. The solution became brown

and the reaction was quenched with ethyl vinyl ether and stirred for another 30 min before the

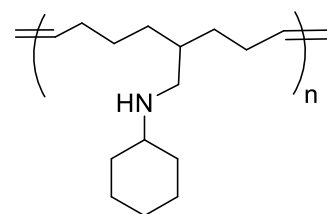
solvent volume was reduced to about 0.5 mL under reduced pressure. The residue was precipitated

in cold MeOH to afford 55 mg of a dark orange solid (42 %). After isolation, the sample is insoluble

in common solvents. $^1\text{H NMR}$ (300 MHz, C_7D_8 , recorded *in-situ* in reaction solution after

polymerization complete): δ 5.53 (br s, 2H, $\text{RHC}=\text{CHR}$), δ 2.55 (br s, 2H, CH_2), δ 2.37 (m, 1H,

CH), δ 2.11 (br s, 4H, CH_2), δ 1.86-1.07 (m, 17H, CH , CH_2). **IR** (neat oil, cm^{-1}): 2921vs, 2851s,

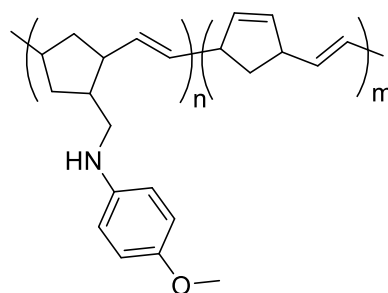


1670w, 1449s, 1365w, 1347w, 1259w, 1241w, 1130m, 966vs, 922w, 888m, 845m, 845w, 786w, 723s.

Preparation of Copolymers

One pot sequential transformation of HAA/ROMP with excess norbornadiene

P(ACN-4-co-norbornadiene) A theoretical 1:1 by mol copolymer was attempted to be synthesized as follows: To a 20 mL scintillation vial was added **1.8** (38 mg, 0.07 mmol), 4-methoxy *N*-methyl aniline (100 mg, 0.7 mmol) and norbornadiene (147 mg, 1.1 mol). Assuming HAA proceeds to

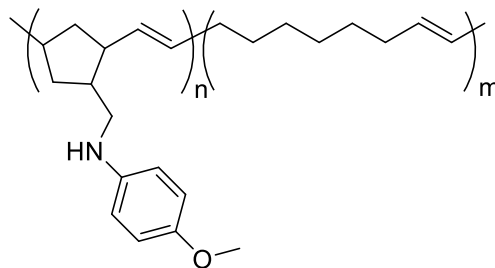


typical 60% completion, 0.7 mol norbornadiene reacts with 0.7 mol amine to give 0.4 mol ACN-4, with $1.1 - 0.7 = 0.4$ mol norbornadiene remaining; this gives a theoretical 1:1 mol ratio for ROMP. To this neat mixture was added a stir bar and reacted while stirring at room temperature for 24 hrs. After 24 hours, to the deep red solution was added a solution of **G2** (3.7 mg, 0.004 mmol, 1 mol%) in THF (*ca.* 1 mL); effervescence was observed. After stirring at room temperature for 24 hours, the reaction was quenched with *ca.* 5 drops ethyl vinyl ether. A dark black solid is obtained that is insoluble to common solvents. An ^1H NMR spectrum was recorded by heating the gel and collected a spectra of the soluble portion in CDCl_3 . ^1H NMR (300 MHz, CDCl_3): δ 7.04 (s, 1H, unassigned), δ 6.78 (m, 2H, 2 x ArH), δ 6.59 (m, 2H, 2 x ArH), δ 5.56 (m, 1H, unassigned), δ 5.27 (m, 1H, RHC=CHR), δ 5.08 (m, unassigned), δ 3.75 (s, 3H, OCH_3), δ 2.87 (d, 2H, CH_2), δ 2.59 (s, 1H, unassigned), δ 2.41 (s, 2H, unassigned), δ 2.19 (s, 1H, unassigned), δ 1.8-1.00 (many signals, 6H, unassigned).

Sequential addition of ACN with cyclooctene

P(ACN-4-co-cyclooctene)

General preparation for a 1:1 by mol copolymer was prepared as follows: To a 20 mL scintillation vial was added the first monomer, *eg.* ACN-4 (100 mg, 0.4 mmol) and a solution of G2 (3.7 mg, 0.004

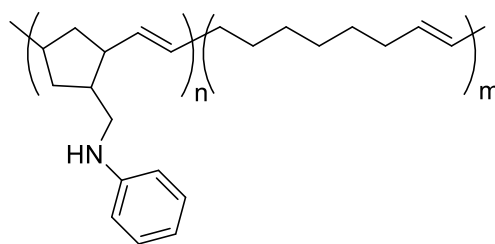


mmol) in THF (1 mL) with a stir bar. After reacting the first monomer at room temperature for the time required (*eg.* 20 hrs for ACN-4), the reaction was sampled by removing *ca.* 10 % of the reaction mixture by withdrawing 100 μ L with an auto-pipettor (not every reaction was sampled after the first block). To the reaction was added the second monomer, *eg.* cyclooctene (48 mg, 0.4 mmol, 1:1 mol ratio with 0.9 • ACN-4). No apparent observations upon the addition of the second monomer. After time required to react second monomer, the entire reaction was quenched and polymer isolated using standard practice with addition of ethyl vinyl ether and precipitation into methanol. Typical yields are 60-90%, with low yields reflected by challenges in isolating very sticky, insoluble polymer from the flask. ¹H NMR (300 MHz, CDCl₃): δ 6.76 (s, 2H, 2 $\times$ ArH), δ 6.56 (s, 2H, 2 $\times$ ArH), δ 5.40-5.20 (m, 4H, 2 $\times$ RHC=CHR), δ 3.72 (s, 3H, OCH₃), δ 3.05-2.95 (m, 3H), δ 2.55 (s, 1H, CH), δ 1.95 (m, 6H), δ 1.65 (s, 2H, CH₂), δ 1.30-1.10 (m, 9H).

Alternating addition of ACN with cyclooctene

P(ACN-1-co-cyclooctene)

Prepared as per sequential addition with different manner of addition. The reaction was set-up in the box beginning with the addition of cyclooctene (10 μ L, 8.5 mg, 0.08 mmol) to a solution of



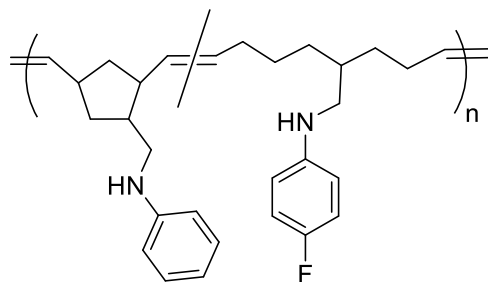
G2 (4.3 mg, 0.004 mmol) in CH₂Cl₂ (*ca.* 1 mL). After 1 hr, ACN-1 was added (100 μ L of a *ca.* 20% solution by volume, 0.1 mmol) and left to stir for 2 hrs. This was repeated until 100

equivalents of each monomer (with respect to G2) was added. Typical work-up isolated the copolymer in quantitative yield. . **¹H NMR** (300 MHz, CDCl₃): δ 7.17 (s, 2H, 2 × ArH), δ 6.72 (s, 1H, 1 × ArH), δ 6.60 (s, 2H, 2 x ArH), δ 5.40-5.21 (m, 4H, 2 x RHC=CHR), δ 3.11-2.90 (m, 3H), δ 2.56 (s, 1H, CH), δ 1.99 (m, 6H), δ 1.66 (s, 3H, CH₂), δ 1.30-1.12 (m, 7H).

Copolymers between ACN and ACC monomers

Copolymers were prepared as in P(ACC)/P(ACN) homopolymers using various stoichiometric amounts of ACN and ACC monomers to give theoretical ratio in polymer product. A typical procedure is as follows:

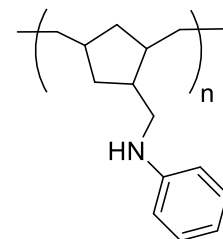
P(ACN-1-co-ACC-2) To a 20 mL scintillation vial was added ACN-1 (50 mg, 0.25 mmol) and ACC-2 (58 mg, 0.25 mmol) with *ca.* 1 mL CH₂Cl₂. To this solution was added a solution of G2 (4.2 mg, 0.005 mmol) in *ca.* 1 mL CH₂Cl₂. The reaction was stirred for 20 h at room



temperature, during which the solution slowly goes brown-green from the initial amber color. The polymer was isolated using standard practice with addition of ethyl vinyl ether and precipitation into methanol; yields are quantitative with losses due to collection from precipitation. **¹H NMR** (300 MHz, CDCl₃): δ 7.16 (s, 2H, 2 × ArH), δ 6.87 (m, 2H, 2 × ArH), δ 6.75 (m, 3H, 3 ArH), δ 6.55 (br s, 2H, 2 x ArH), δ 5.39-5.27 (m, 4H, 2 x RHC=CHR), δ 3.05-2.97 (d, 4H, CH₂), δ 2.90 (s, 1H, CH), δ 2.53 (s, 1H, CH), δ 2.00-1.95 (m, 6H, CH₂), δ 1.65-1.63 (br s, 3H), δ 1.36 (br s, 6H, CH₂), δ 1.19 (s, 1H, CH).

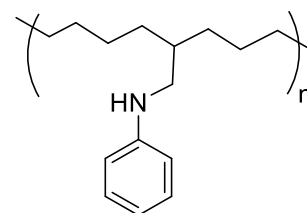
Polymer Hydrogenation

P(ACN-1H) As per literature procedure.⁴⁻⁵ To a 100 mL reaction vessel, equipped with a poly(tetrafluoroethylene)-coated stir bar and a poly(tetrafluoroethylene) capped-valve and side-arm, was added P(ACN-1) (100 mg, 0.5 mmol alkene) and *p*-toluenesulfonyl hydrazide (0.3 g, 1.6 mmol)



in xylenes (7 mL). Approximately 3 mgs of 2,4,6-tri-*tert*-butyl phenol added as a radical trap. The resulting heterogeneous mixture was degassed using three freeze-pump-thaw cycles under an N₂ atmosphere. The N₂ filled vessel was sealed and heated to 130 °C in an oil-bath for a minimum of 8 hours. After the reaction, a pale-yellow, clear solution was obtained. The vessel was opened and the mixture transferred to a separatory funnel, using ethyl acetate (50 mL) to quantitatively transfer the solution. The organic layer was washed three times with 3 M NaOH, then once with brine, then reduced to ~ 3 mL *via* rotary evaporation under reduced pressure. This residue was then added drop-wise to a large excess of stirring methanol (-35 °C, 100 mL) to afford the product as a brown, gummy solid (0.090 g, 90 %). **¹H NMR** (300 MHz, CDCl₃): δ 7.18 (m, 2H, 2 × ArH), δ 6.72 (m, 3H, ArH), δ 3.14 (s, 1H, CH₂), δ 2.86 (s, 1H, CH₂), δ 2.10-1.0 (br m, 11H), δ 0.70 (m, 2H)

P(ACC-1H) Prepared as above with **P(ACC-1)** (480 mg, 2 mmol alkene) and *p*-toluenesulfonyl hydrazide (1.5 g, 8 mmol) in xylene (15 mL). After work-up, 0.350 g of material was obtained (73 %). **¹H NMR** (300 MHz, CDCl₃): δ 7.17 (m, 2H, 2 × ArH), δ 6.69 (t, 1H, ArH), δ 6.63



(d, 2H, ArH), δ 3.01 (d, 2H, CH₂), δ 1.61 (br s, 1H, CH), δ 1.28 (m, 14H, CH₂). **IR** (neat oil, cm⁻¹, int): 3420br, 3045w, 2922s, 2849sh, 1601s, 1504s, 1466sh, 1316m, 1261m, 1095br, 1030br, 804s, 746s, 689s.

Chapter 4: Metal complexes for the ring-opening of cyclic esters

4.1 Introduction: Sustainable plastics

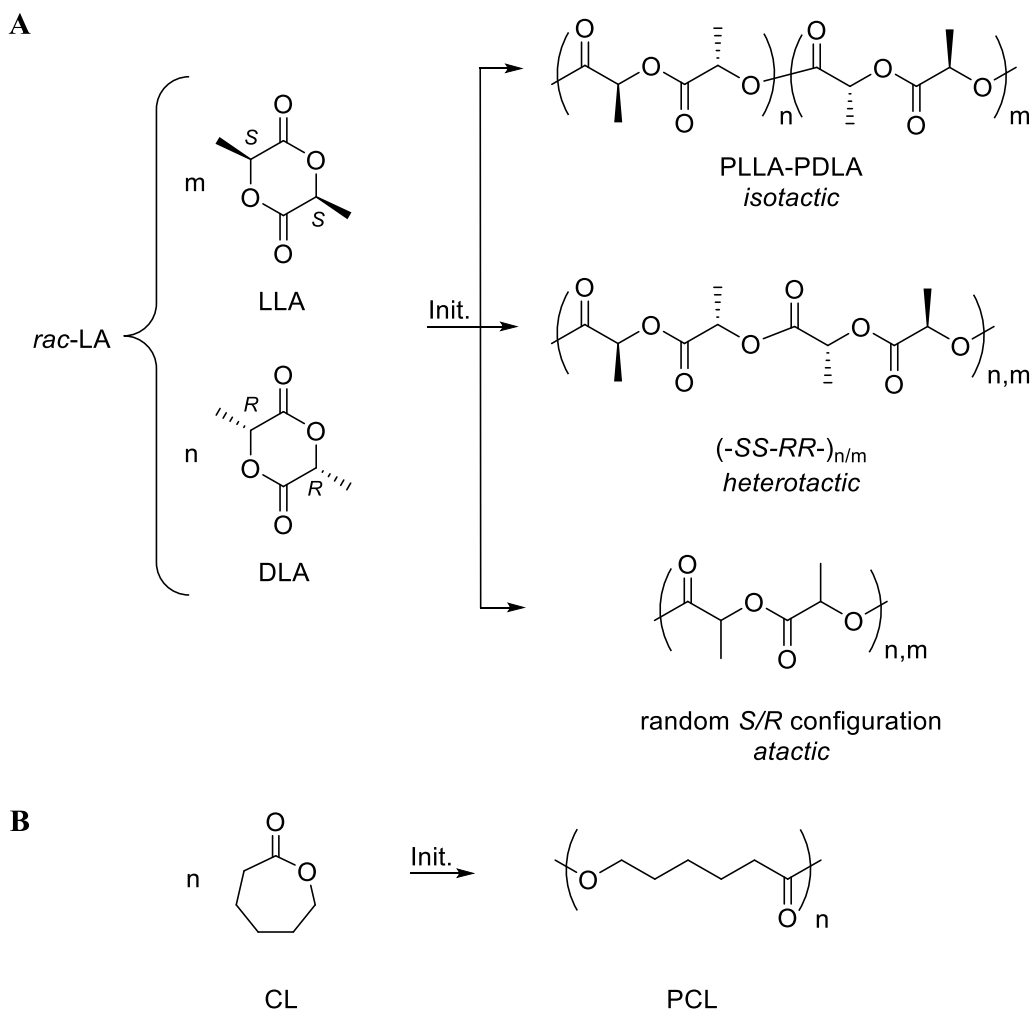
The disturbing prevalence of plastic pollution in the biosphere is an enormous and ever-growing crisis. Plastics have been produced in abundance since the beginning of the twentieth century and have become indispensable to human life, with today's production being over 300 million tonnes annually.²¹⁸ While the scope and usefulness of these materials have grown, so too has their rise as an environmental pollutant. It has been estimated that approximately 75% of all virgin plastic that has been produced has now been discarded, and that 80% of this waste has now accumulated in landfills or the natural environment.²¹⁹ If current trends continue, this accumulation will have reached an estimated 10^{10} tonnes by the year 2050.²¹⁹

To prevent such accumulation will require alternative technologies to the current standards of plastic production, application, and disposal/remediation. One such strategy is to replace traditional plastics with those that degrade in shorter lifetimes, thus not persisting in the environment as waste. The field of biodegradable polymer research has thus experienced a marked increase in intensity in pursuit of new materials with options for renewable production and/or recycling.²²⁰ Ideally, these materials can physically perform as competent alternatives to traditional polyolefinic polymers while possessing the biodegradability to allow for their facile disposal.

4.1.1 Biodegradable polyesters derived from lactide and caprolactone

The field of biodegradable polymer research has experienced a marked increase in attention in recent years.²²⁰ Investigations into the polymerization of lactide (LA) and ϵ -caprolactone (CL), to generate poly(lactic acid) (PLA) and poly(ϵ -caprolactone) (PCL) respectively, are largely driven by their potential applicability as substitutes for commodity plastics derived from polyolefins

(Scheme 4.1). The most commonly utilized mechanism to conduct well-controlled polymerizations is the ring-opening of cyclic esters by an initiator, often a metal complex.⁶²⁻⁶³ These polyesters have practical merit in many traditional applications as well as specialized utility in fields such as biomedicine as oral implants, sutures, and microspheres for drug delivery purposes.²²¹⁻²²²



Scheme 4.1 Ring-opening polymerization of the cyclic esters (A) *rac*-lactide (B) ϵ -caprolactone, including possible microstructures from *rac*-LA⁵⁹

As homopolymers, poly(lactic acid) and caprolactone possess unique physical properties that are of interest to combine into a copolymeric material. Lactide contains two stereocentres and

therefore exists as DD- (D-LA), LL- (L-LA), and DL- (*meso*) stereoisomers. The D-LA and L-LA isomers are commercially available in their enantiomerically pure form or as a racemic mixture (*rac*-lactide). Thus, some initiators have been investigated for their potential to form stereoregular poly(lactic acid) from *rac*-lactide (see Scheme 4.1).⁵⁹ Rheological investigations have revealed that changes to the tacticity of the polymer microstructure gives rise to different bulk polymer properties.²²³ For example, while PLLA forms a crystalline polymer, PDLLA is amorphous.²²⁴ As a homopolymer, poly(ϵ -caprolactone) is tough material that demonstrates high max strain.²²⁴ Aside from the homopolymerization of lactide and caprolactone, these monomers can be used to prepare copolymers which, depending on their composition and polymer microstructure, allow for a range of physical and mechanical properties.²²⁴ Two common microstructures are block and random copolymers (Figure 4.1).

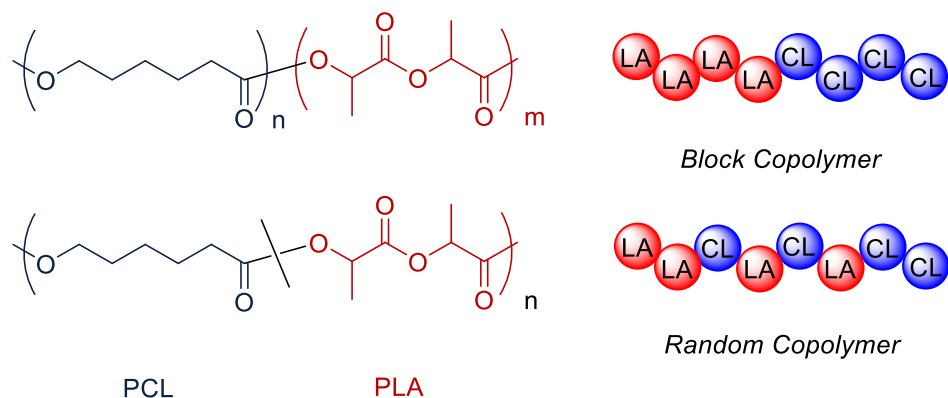
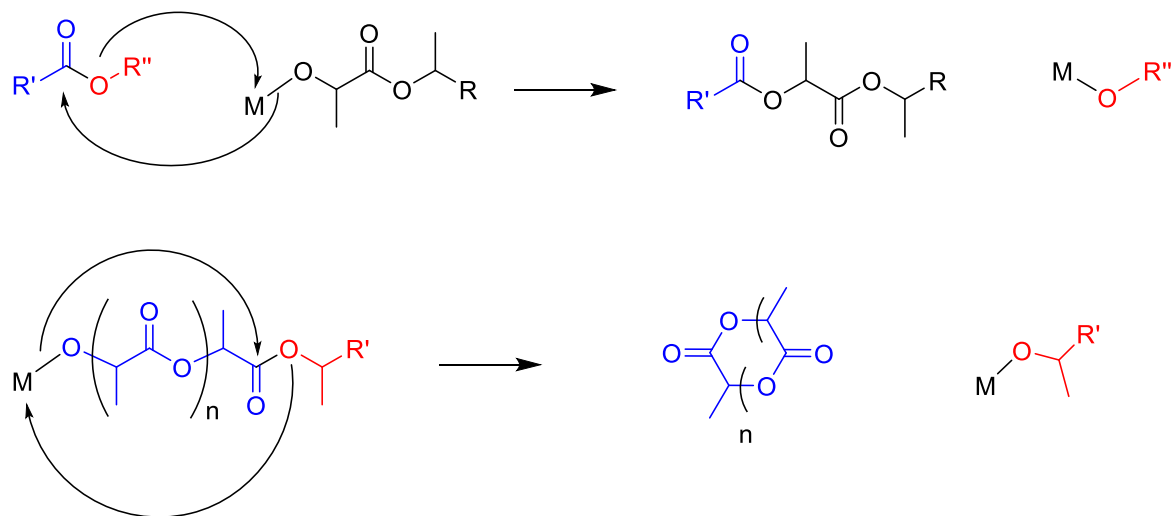


Figure 4.1 Random and block copolymers of poly(ϵ -caprolactone) (PCL) and poly(lactic acid) (PLA)

Ideally, controlled preparation of block or random copolymers can provide access to materials with intermediate or complementary properties to their respective homopolymers.²²⁴ A significant synthetic challenge in random copolymer formation is balancing differences in monomer reactivity and relative polymerization rates. In block copolymer formation, the challenge is to maintain ‘pure’ di-blocks without incorporation of, for example, the B monomer into the A

block. In the ring-opening of cyclic esters, this unwanted cross-incorporation can result from a well-known side reaction called transesterification (Scheme 4.2).²²⁵ This reaction may enable ‘back-biting’ of chains as well as result in the formation of cyclic fragments.



Scheme 4.2 *Inter- and intra-molecular transesterification*²²⁵

A variety of metal complexes, enzymes, and organic molecules have demonstrated the ability to initiate the ring-opening of these cyclic esters to afford the desired polymers.⁶²⁻⁶³ Industrially, the most commonly used initiators are highly active tin octoate systems that can furnish these polyesters in high yield with large molecular weight.²²⁶ In comparison between systems, initiators are evaluated on their activity (reaction time) and their ability to afford polymers with large molecular mass (M_n) in high control (assessed in part by dispersity $\mathcal{D}$). The ability to control the stereochemistry when polymerizing various isomers of lactide is also highly desired.⁵⁹ Due to the widespread interest in biodegradable polymer research, the investigation of titanium complexes as initiators has attracted significant attention from the research community. While titanium complexes have displayed activities and control that is reduced when compared with other leading initiators, the low cost, high abundance, and low toxicity of titanium has motivated

vigorous research into initiators designed around this metal centre.^{2, 59, 64-85, 92, 227-235} Low toxicity is an especially advantageous property as these polymers are bio-compatible and may be used for specialized applications in the medical field where residual metal residues could be problematic.⁸⁶

While titanium initiators are as yet less competitive than the leading initiator systems, their practical advantages have motivated vigorous research interest into a variety of ligand scaffolds. High molecular weight polymers with control of dispersity, co-monomer incorporation and tacticity are all desired features.⁵⁹ Selected titanium examples include species ligated with tetradentate amino-phenolates,⁸⁷ salen ligands,⁸⁸ catecholates,⁸⁹ aminodiols,⁶⁶ thio-etherphenolates,⁸⁵ sulfur or tellurium bridged bimetallic species,⁸³ and sulfonamide supported complexes.⁷⁵ Typically, these complexes range from tetra- to hexa-coordinate species with bulky ancillary ligands to vary the steric and electronic environment about the metal center. Select examples of titanium complexes bearing bulky, *N,O*-chelating ancillary ligands are shown in Figure 4.2.

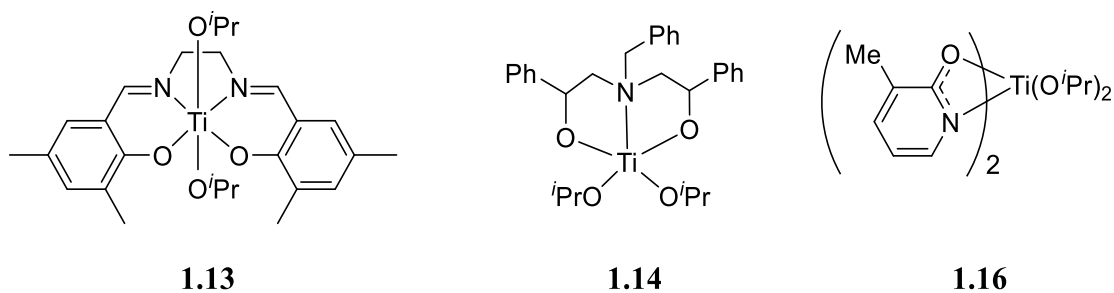
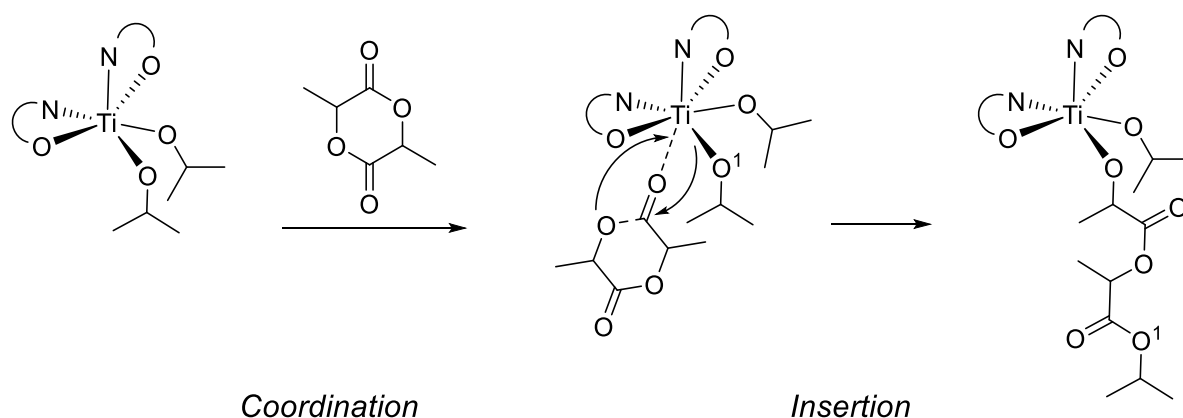


Figure 4.2 Selected examples of titanium initiators for ROP of cyclic esters^{2, 66, 88}

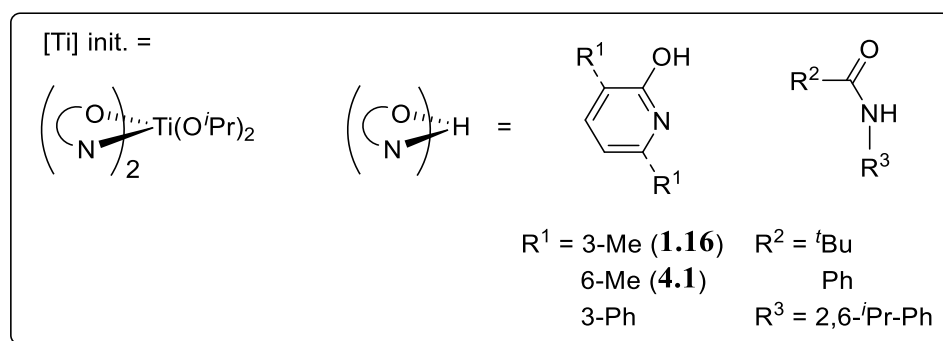
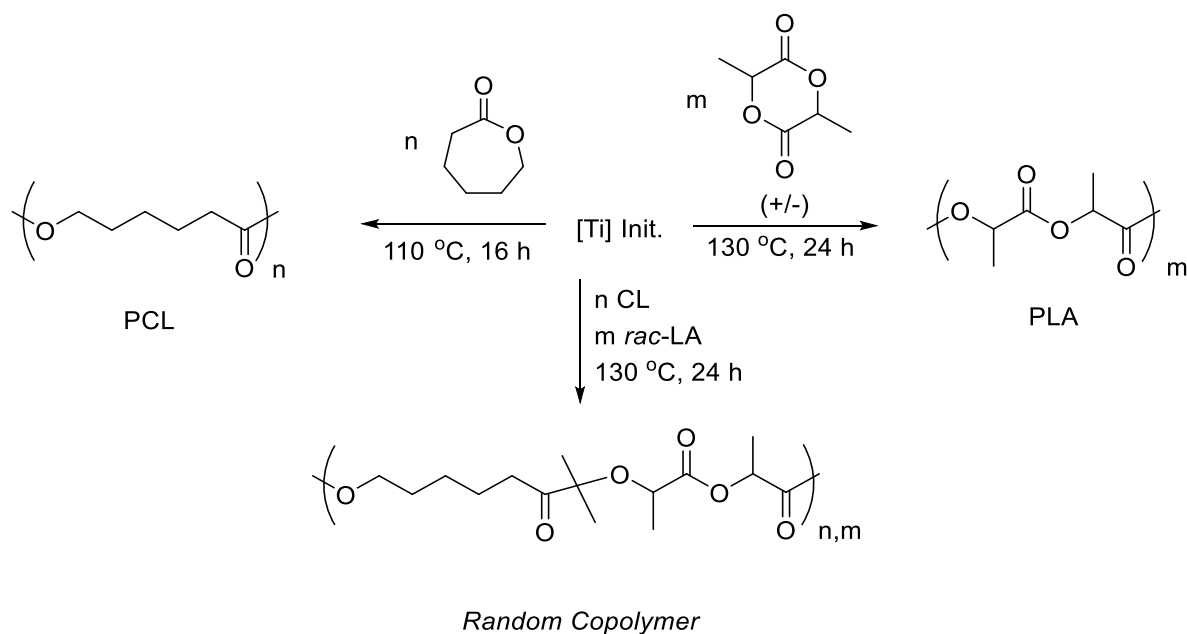
In addition to such supporting ancillary ligands, initiator complexes also possess one or more ‘reactive’ ligands (alkoxide, aryloxy, and halogen initiating ligands^{78, 90-91}) that function as the nucleophilic species for polymerization initiation under a coordination-insertion mechanism (Scheme 4.3). Most commonly, initiators with two reactive ligands are proposed to propagate two

polymer chains for each metal center.^{64, 66, 74} However, in some cases it has been suggested that only one of the two reactive ligands initiates if the metal center is sterically crowded.⁶⁷



Scheme 4.3 Coordination-insertion mechanism for initiation of *rac*-lactide with a generic *N,O*-chelated titanium complex

In 2013, the Schafer group reported the ability of pyridonate and amidate titanium alkoxides to initiate the ROP of *rac*-lactide and ϵ -caprolactone to form their respective homopolymers (Scheme 4.4).² These complexes could also be used to prepare random copolymers through the simultaneous addition of both monomers.



Scheme 4.4 Titanium pyridonates and amidates for ROP of cyclic esters²

As initiators for ROP, these complexes demonstrated reasonable activity (reactions complete within 16-24 h) and control ($\bar{D}$ as low as 1.17), with molecular weights suggesting that initiators grew one or two chains per metal centre. Amidate-supported initiators were effective for homopolymerization but could not be used to prepare copolymers with predictable composition. In contrast, pyridonate-supported catalysts (*eg.* **1.16**) could be used to prepare random copolymers containing an equal incorporation of the two monomers. Further analysis of the copolymers by ¹H NMR spectroscopy also revealed an equivalent number of hetero-junctions (*ie.* LA-CL) to homo-

junctions (*ie.* LA-LA, CL-CL) as expected for a random sequencing of monomers. This result inspired further investigation into the structure of the pyridonate-supported catalysts, strategic variations to their design, and a more thorough analysis of their structure-activity relationships in ROP.

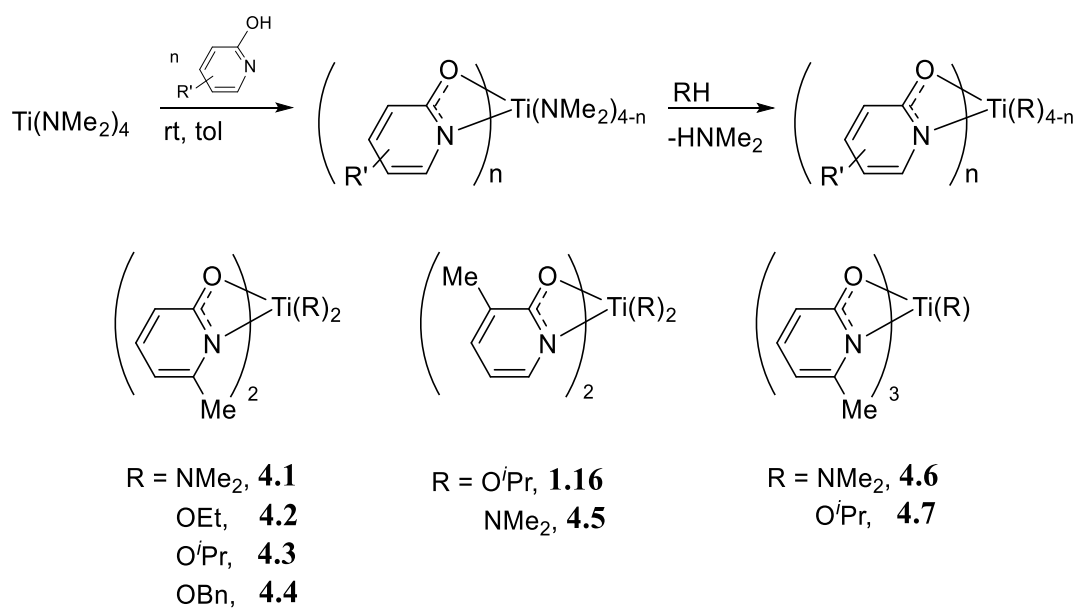
4.1.2 Scope of chapter

This chapter begins with a full investigation into titanium pyridonates as initiators for the ring-opening polymerization of *rac*-lactide and ϵ -caprolactone. Earlier, bis-pyridonate titanium dialkoxides have shown promising reactivity for homopolymerization of these monomers as well as copolymer synthesis. In search of an initiator with improved reactivity and/or control for this transformation, different structural modifications have been made to this class of titanium complexes and the resulting complexes evaluated for their utility in ROP. To increase steric bulk, tris-pyridonate titanium complexes have been explored that contain only one nucleophilic ligand for insertion. Among *N,O*-chelated complexes, the effect of various nucleophilic ligands on ROP has also been explored. These complexes have also been screened for their ability to mediate the formation of copolymers between LA and CL. By varying the order of addition, block and random copolymers can be prepared.

4.2 Results and Discussion

4.2.1 Synthesis of initiators

Earlier work reported in our group in 2013 by Dr Ruth Webster established that pyridonate-supported titanium complexes showed superior reactivity in forming copolymers than related amidate-supported catalysts.² In the continuation of this project, Dr Webster next sought to prepare a broader class of titanium pyridonate initiators. With bis-pyridonate complexes bearing two reactive isopropoxide ligands, the obtained molecular weights (*vide infra*) in the homopolymerization of *rac*-lactide and ϵ -caprolactone do not clearly suggest that either one or two polymer chains are propagating from the metal centre. For example, initiator **4.3** gave PLA with a $M_n = 13,800 \text{ g}\cdot\text{mol}^{-1}$, suggesting two chains per Ti centre ($M_{n,theo} = 19,030 \text{ g}\cdot\text{mol}^{-1}$ for 300:1 M:I with two chains per equivalent of Ti complex, 88% polymer yield). However, for PCL synthesis the determined M_n of $39,400 \text{ g}\cdot\text{mol}^{-1}$ suggests one chain per Ti centre ($M_{n,theo} = 33,560 \text{ g}\cdot\text{mol}^{-1}$ for 300:1 M:I with one chain per I, 98% polymer yield). It was also typical to obtain experimental molecular weights that are between the theoretical values for one or two propagating chains per metal centre. Therefore, the work of Dr Webster expanded the structural diversity of titanium-pyridonate complexes for their application in ROP. To address the uncertain number of propagating species, tris-pyridonate complexes with only one nucleophilic ligand were prepared. The nucleophilic ligand was also varied to explore its effect on polymer initiation. The complexes were readily formed in high yield at room temperature by combining the homoleptic starting material $\text{Ti}(\text{NMe}_2)_4$ with the desired pro-ligand (Scheme 4.5).

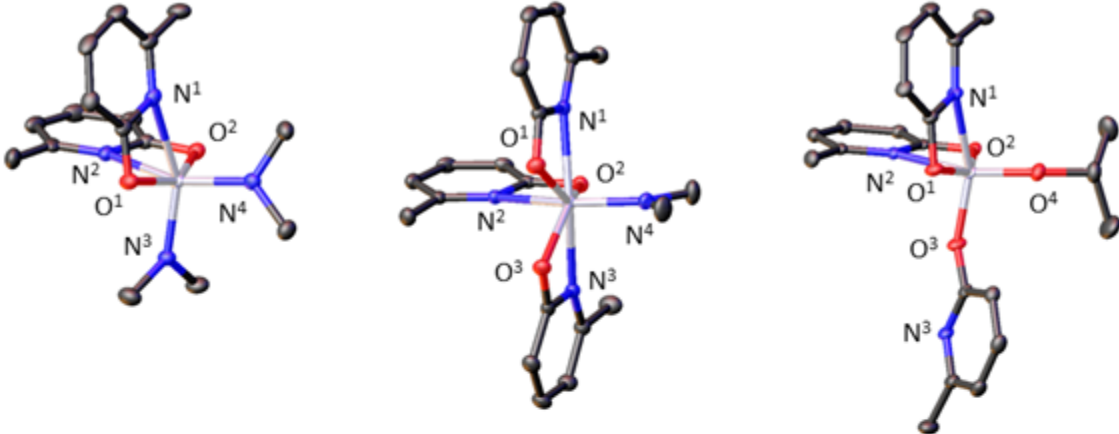


Scheme 4.5 Preparation of titanium pyridonate complexes

Transformation of the dimethylamido species (for example **4.1**, **4.5**, and **4.6**) into the related alkoxide is readily achieved within minutes at room temperature by the addition of a stoichiometric amount of alcohol.^{2, 236} A range of sterically varied alkoxides can be used without adversely affecting the yield (compare **4.2**, **4.3** and **4.4**). It was of interest to compare the differences in reactivity of **4.3**, **4.5**, **4.2**, and **4.4** to investigate whether a change in the reactive ligand systematically influences polymerization. Variable substitution patterns on the pyridonate ring at the 3- and 6- position were also tolerated (compare **1.16** and **4.3**). Crystals were grown by slow evaporation of a hexane solution; the solid-state molecular structures of the complexes were obtained by Dr Webster (**4.1** shown in Figure 4.3).

Bis(ligated) complexes are typically anticipated to furnish systems that initiate twice to grow two polymer chains per metal simultaneously. In an effort to appreciate the steric environment about the metal center, the preparation of tris-pyridonate complexes (**4.6-4.7**) was pursued, as this system would be expected to afford only one growing polymer chain per metal.

These targeted complexes could be readily prepared by simply changing the ligand stoichiometry and it was found that both the mono(dimethylamido), **4.6**, and mono(isopropoxide) species, **4.7**, could be synthesized in high yield. Analysis of the crystal structure reveals that **4.6** maintains a highly unusual 7-coordinate ligation mode, displaying a distorted pseudo tetrahedral geometry around the metal center (Figure 4.3), with each *N,O*-chelate being assigned a coordination number of 1. Similar to the bis-coordinated analogues, an unsymmetrical binding of the *N,O*-chelate is observed, in which the Ti-O contact (2.009(2)-2.059(2) Å) is shorter than the Ti-N contact (2.169(2)-2.270(1) Å) in all three chelates. It is also interesting to note that all three pyridonate ligands are relatively symmetrical, with only a slight lengthening of the N³-Ti and O³-Ti bond lengths and marginal widening of the N³-Ti-O³ bond angle in complex **4.6** (see Figure 4.3).



	4.1	4.6	4.7
Ti-O ¹	2.035(1)	2.009(2)	2.001(2)
Ti-N ¹	2.284(2)	2.270(1)	2.200(2)
Ti-O ²	2.016(2)	2.059(2)	1.983(1)
Ti-N ²	2.267(3)	2.169(2)	2.229(1)
Ti-O ³	-	2.018(2)	1.846(1)
Ti-N ³	1.884(2)	2.267(1)	
Ti-O ⁴	-	-	1.752(1)
Ti-N ⁴	1.910(3)	1.873(2)	
O ¹ -Ti-N ¹	61.58(8)	61.13(6)	62.34(5)
O ² -Ti-N ²	62.11(8)	62.56(6)	62.98(5)
O ³ -Ti-N ³		61.17(6)	

Figure 4.3 Solid-state molecular structures of **4.1**, **4.6**, and **4.7** obtained by Dr Webster. Bond lengths reported in Å, bond angles in (°). Ellipsoids are shown at 50% probability and hydrogen atoms omitted for clarity

In the isopropoxide complex **4.7**, one of the pyridonates is bound κ^1 in the solid-state (Figure 4.3). However, analysis of these complexes by ^1H NMR spectroscopy shows one set of resonances that can be assigned to the pyridonate ring. Therefore, fluxional behaviour is occurring at a rate faster than the NMR timescale. Presumably, all three pyridonate ligands show hemilability and fluctuate between these κ^2 and κ^1 coordination modes in solution. In complex **4.7**, the introduction of an alkoxide ligand and a concomitant increase in π -donation to the metal center does result in a slight lengthening of the *trans* Ti-N² bond (compare Ti-N² = 2.169(2) Å in **4.6** to

Ti-N² 2.229(1) Å in **4.7**). With this family of titanium complexes in hand, exploration of initiating ligand, pyridonate substituent effects and number of growing polymer chains per metal was explored.

4.2.1.1 Homopolymerization of *rac*-lactide and ϵ -caprolactone

Initially, different reaction conditions were screened for the synthesis of PLA. However, it soon became clear that polymerization is favored in the melt phase. Solution phase reactions gave greatly reduced yields and with it far inferior M_n values. Therefore, the polymerization was conducted in the melt using a 300:1 M:I ratio for 24 hours at 130 °C.

Table 4.1 Homopolymerization of *rac*-lactide with titanium pyridonate complexes

Entry	Initiator	Yield (%) ^a	M_n (g•mol ⁻¹) ^b	$M_{n, \text{theo.}}$ (g•mol ⁻¹) ^c	$\bar{D}^b$	P_m^d
1	4.1	91	17,500	19,670	1.22	0.49
2	4.2	91	21,210	19,670	1.28	0.51
3	4.3	88	13,800	19,030	1.17	0.49
4	4.4	93	14,380	20,110	1.19	0.49
5	4.5	92	23,070	19,890	1.44	0.49
6	1.16	90	14,120	19,460	1.21	0.46
7	4.6	96	15,260	41,510 ^e	1.18	0.51
8	4.7	82	16,410	35,460 ^e	1.16	0.50

[M]/[Ti] = 300. ^aIsolated yield. ^bDetermined by GPC. ^c $M_{n, \text{theo.}} = ([LA]/2[Ti] \cdot \%Yield \cdot 144.13 \text{ g} \cdot \text{mol}^{-1})$. ^d¹H{¹H} NMR spectrum. ^e $M_{n, \text{theo.}} = ([LA]/[Ti] \cdot \%Yield \cdot 144.13 \text{ g} \cdot \text{mol}^{-1})$.

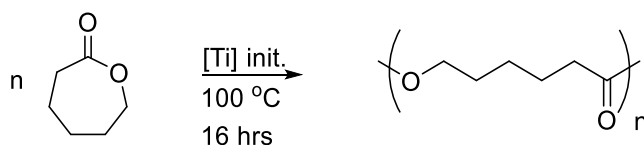
The reactions were performed in duplicate with the experimental molecular weights varying by *ca.* 10%. Therefore, the molecular weights across the initiators tested do not vary significantly. Comparing initiators **4.1**, **4.3**, and **4.4**, the determined molecular weights agree reasonably well with theoretical molecular weights calculated with the assumption that each initiator forms two polymer chains. Control, assessed by the dispersity ($\bar{D}$) of the samples, is moderate, ranging from 1.16 to 1.44. No meaningful difference is observed in comparison between pyridonates with methyl substitution at the 3- vs. the 6-position (**1.16**, **4.5** vs. **4.1**, **4.3**), suggesting the relative position of the methyl group does not dramatically impact the steric environment about the metal center. To determine the degree of stereoregularity, the probability of *meso* enchainment (P_m) can be calculated from homonuclear decoupled $^1\text{H}\{^1\text{H}\}$ NMR spectra.⁵⁹ In this spectrum, the methine region shows five tetrad sequences that result from different connectivity patterns. Using Bernoullian statistics based on the assignments of Coates, the relative ratios of these dyads are reflective of the initiators ability to control the stereochemistry of monomer addition (See Appendix). As all P_m values are close to 0.50, it does not appear in the isolated polymers that these initiators demonstrate stereo-preference when polymerizing *rac*-lactide; however, to ensure this is the case the polymer structure should be characterized at lower conversion to rule out that one isomer is reacted first followed by transesterification.

Interestingly, the experimental M_n values for the tris-pyridonate complexes do not provide a good match to the theoretical value, presuming that only one polymer chain can propagate per metal center. Analysis by ^1H NMR spectroscopy of the isolated polymers can identify dimethylamino (**4.6**) or isopropoxide (**4.7**) end-groups; no aryl signals could be observed in the NMR spectrum that could be assigned to the pyridonate ligand. This rules out initiation by the pyridonate ligand *via* a coordination-insertion mechanism. These results may be rationalized by

transesterification, which is observed in random copolymer synthesis² and can result in chain scission and ultimately diminished molecular weight values.

Next, the use of these metal initiators for PCL synthesis was evaluated. Solvent-free reaction conditions were adopted as in PLA synthesis (Table 4.2 Homopolymerization of ϵ -caprolactone with titanium pyridonate complexes).

Table 4.2 Homopolymerization of ϵ -caprolactone with titanium pyridonate complexes



Entry	Catalyst	Yield (%) ^a	M_n ($\text{g}\cdot\text{mol}^{-1}$) ^b	$M_{n, \text{theo.}}$ ($\text{g}\cdot\text{mol}^{-1}$) ^c	$\bar{D}^b$
1	4.1	89	20,670	15,240	1.32
2	4.2	85	31,790	14,450	1.34
3	4.3	98	39,400	16,780	1.29
4	4.4	92	19,720	15,750	1.22
5	4.5	92	22,470	15,750	1.35
6	1.16	89	23,570	15,240	1.32
7 ^d	4.6	79	30,600	27,050	1.25
8 ^d	4.7	84	33,500	28,760	1.16

$[\text{M}]/[\text{Ti}] = 300$ ^aIsolated yield. ^bDetermined by GPC. ^c $M_{n, \text{theo.}} = ([\text{CL}]/2[\text{Ti}] \cdot \% \text{Yield} \cdot 114.14 \text{ g}\cdot\text{mol}^{-1})$. ^d $M_{n, \text{theo.}} = ([\text{CL}]/[\text{Ti}] \cdot \% \text{Yield} \cdot 114.14 \text{ g}\cdot\text{mol}^{-1})$.

The lowered reaction times and temperatures to reach completion suggest these initiators are more reactive toward ϵ -caprolactone than *rac*-lactide. This is corroborated in consideration of the ring strain of the respective monomers ($-28.8 \text{ KJ}\cdot\text{mol}^{-1}$ vs. $-22.9 \text{ KJ}\cdot\text{mol}^{-1}$ for L-lactide),²³⁷ which is considered the driving force of polymerization. In the case of the bis-pyridonate

complexes, the obtained molecular weight values are in excess of the molecular weight proposed for an initiator propagating two chains. This may be rationalized by considering relative rates of initiation and propagation. If propagation is strongly favoured after initiation, insertion of subsequent monomers into the growing polymer chain would occur to a greater extent than insertion into the reactive ligand (thereby initiating the second polymer chain). Thus some initiators could be conceivably operating as a mono-initiation and propagation site. This would lead to molecular weights that more closely align with theoretical values predicted for a mono-propagating initiator. Based on the data presented, it is proposed that a mixture of mono- and bis-propagating initiators could be present, giving molecular weights between predicted values. Another possibility that could rationalize higher than expected molecular weights that cannot be ruled out is that not all of the initiators are active, either by undesired deactivation by side reactions or by denied access to the monomer because of limited diffusion as the viscosity of the reaction mixture increases. As in PLA synthesis, there is no evidence to suggest incorporation of pyridonate groups into the chain ends, as evidenced by the lack of aromatic signals in the ^1H NMR spectrum.

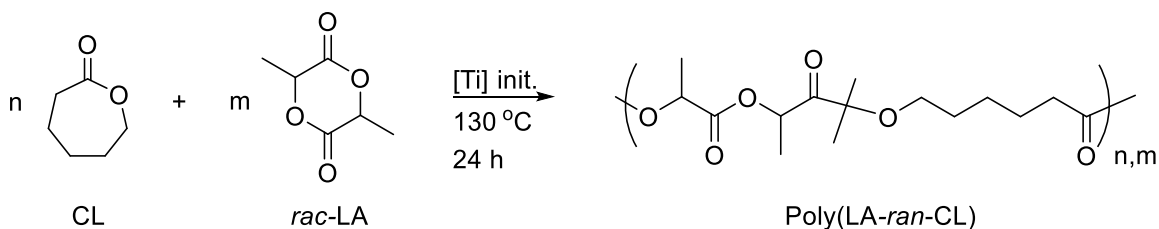
Overall, the differences in the obtained polymeric materials only vary slightly with the nucleophilic initiator chosen, suggesting that varying the nature of the pyridonate substitution or nucleophilic ligand has only slight effects on ROP. Although ϵ -caprolactone can be considered more reactive based on milder experimental conditions, molecular weight data does not suggest that it propagates from both reactive ligands in the bis-pyridonate complexes. Meanwhile, the generally lower experimental molecular weights obtained in the polymerization of *rac*-lactide relative to theoretically predicted values suggest it is more prone to transesterification reactions.

The trends observed in the reactivity of the respective monomers was next explored when they were combined into a copolymer.

4.2.2 Random copolymers of PLA and PCL

Given the capacity of the initiators to form homopolymers in high yield, their ability to form a random copolymer by simultaneously reacting them with an equimolar mixture of *rac*-lactide and ϵ -caprolactone was attempted (Table 4.3). Previously, it was reported by our group that the titanium pyridonate complexes **1.16** and **4.3** were able to form random copolymers of poly(lactide-*co*-caprolactone) with equal incorporation of both monomers.² Equal incorporation of both monomers is a significant synthetic challenge because of the inherent reactivity differences between the cyclic esters. For example, other reported examples of titanium-based random copolymer formation show a deficit of caprolactone incorporation when copolymer synthesis is attempted.^{66, 76, 85, 227-228, 232} As these pyridonates are a rare class of titanium initiator capable of this balance in monomer reactivity, the synthesis of random copolymers was explored with the expanded library of complexes.

Table 4.3 Random copolymerization of *rac*-lactide and ϵ -caprolactone with titanium pyridonate complexes



Entry	Cat.	Yield (%) ^a	CL/ LA ^b	L _{CL} /L _{LL} ^c	Hetero Diads (%) ^d	M_n (g•mol ⁻¹) ^e	$M_{n, theo.}$ (g•mol ⁻¹) ^f	$\bar{D}^e$
1	4.1	72	50/50	1.9/3.4	48	20,660	28,930	1.37
2	4.2	81	51/49	2.0/4.9	49	54,065	31,154	1.79
3	4.3	82	45/55	1.8/3.4	51	18,750	33,390	1.41
4	4.4	82	48/52	-	44	56,170	31,734	1.64
5	4.5	70	44/56	1.7/5.2	53	27,920	26,379	1.39
6	1.16	83	52/48	1.9/2.9	46	19,070	33,190	1.29
7	4.6	75	48/52	1.9/3.0	44	19,370	58,050 ^g	1.35
8	4.7	56	23/77	-	73	18,610	43,344 ^g	1.32

Total [monomers]/[Ti] = 600. ^aIsolated yield. ^bDetermined by ¹H NMR spectroscopy. ^cDetermined by ¹³C{¹H} NMR spectroscopy. ^dRatio of CL homo vs. hetero signals in ¹H NMR spectrum. ^eDetermined by GPC. ^f $M_{n, theo.} = [([CL]/2[Ti] \cdot 114.14 \text{ g}\cdot\text{mol}^{-1}) + ([LA]/2[Ti] \cdot 144.13 \text{ g}\cdot\text{mol}^{-1})] \cdot \%Yield$. ^g $M_{n, theo.} = [([CL]/[Ti] \cdot \%_{conv}CL \cdot 114.14 \text{ g}\cdot\text{mol}^{-1}) + ([LA]/[Ti] \cdot \%_{conv}LA \cdot 144.13 \text{ g}\cdot\text{mol}^{-1})] \cdot \%Yield$.

With the exception of initiator **4.7** (entry 8), all initiators are able to produce a copolymer in reasonable yield with near equal incorporation of both monomers. The ratio of the monomers was determined by taking the ratio of the signals assigned to the methine protons of poly(lactic acid) (δ 5.16) to the methylene protons of poly(ϵ -caprolactone) (δ 4.20-4.00) in the ¹H NMR spectrum. Inspection of the resonance assigned to the poly(ϵ -caprolactone) methylene protons shows two distinct peaks (δ 4.16 and 4.06) which differentiate CL-LA heterojunctions (heterojunction resonances are slightly downfield to homojunction resonances because of greater

deshielding by the adjacent poly(lactic acid) segment) and CL-CL homojunctions (4.06 ppm; assigned from PCL synthesis) (see Figure 4.4).

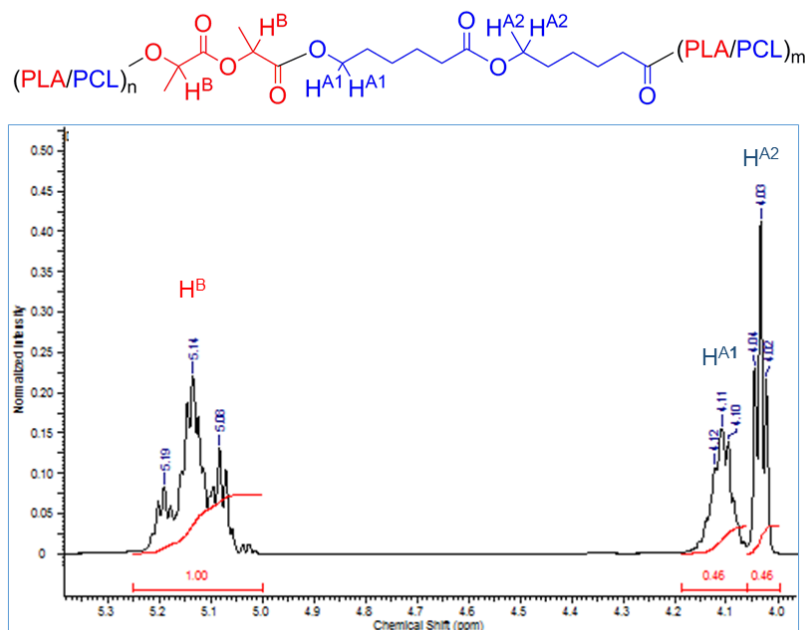


Figure 4.4 Zoom-in of the region of 5.3–4.0 ppm in the ¹H NMR spectrum (300 MHz, CDCl₃, 298 K) of a random copolymer (Table 4.3 entry 4)

With the exception of entry 8, all obtained polymers give close to the desired 50% heterojunctions for a random copolymer. Average sequence lengths (L_{CL}/L_{LL}) of the respective poly(ϵ -caprolactone) and poly(lactic acid) segments were calculated using the carbonyl region (δ 174–169) in the ¹³C{¹H} NMR spectrum according to assignments made by Bero and Kasperczyk²³⁸ from within Dr Webster’s previous disclosure.² Calculated values show close to two for poly(ϵ -caprolactone) segments while poly(lactic acid) units were slightly longer, with average lengths between 3.5 and 5. The signal at δ 171.1 can be assigned to a ‘CLC’ sequence (where C and L refer to caprolactone and lactide respectively). Since the lactide monomer is a dimer, a sequence with a single lactide ester resonance can only originate from a chain transfer

event such as transesterification. While the mechanism of copolymerization is poorly understood, these transesterification processes are believed to contribute to the randomization of the polymer backbone.⁶³ The samples described in entries 2 and 4 have noticeably large molecular weight, this indicates that initiation with the ethoxide and benzyl alkoxide reactive ligands may be sluggish relative to the dimethylamido or isopropoxide ligands, or that mono-propagating species may be more prevalent. As described in PCL synthesis, poor initiation is believed to result in increased molecular weights when using the bis-pyridonate initiators due to a mixture of mono- and bis-propagating species. With the exception of entries 2 and 4, the obtained molecular weights are less than the predicted theoretical values (with exception of 5, which shows good agreement). This suggests transesterification side reactions are occurring, producing shorter chains because of chain scission events while randomizing the monomers along the polymer backbone.²²⁵ These initiators are rare examples of titanium complexes that are able to afford equal monomer incorporation given an equimolar monomer feed.^{66, 232} While these results show random copolymers can be generated with reasonable control, the ability to further understand transesterification reactions in these titanium initiated polymerizations is highly desired.

4.2.3 Block copolymers of PLA and PCL

Beyond the ability to form random copolymers, the initiators' ability to form block copolymers was explored. Block copolymers are comprised of two subunits, in this case a segment of poly(lactic acid) with ideally a single heterojunction to a block or segment of poly(ϵ -caprolactone). The attempted synthesis of these copolymers with titanium pyridonate initiators was performed using sequential addition of the monomers, thereby forming polymer chains of one monomer followed by addition and polymerization of the second monomer.

In the case of these initiators, it was found that attempts to polymerize *rac*-lactide first followed by addition of ϵ -caprolactone resulted in a polymer that features a low incorporation of caprolactone. However, when the order was reversed and poly(ϵ -caprolactone) was polymerized first, followed by addition of *rac*-lactide, the desired copolymer was obtained (Table 4.4).

Table 4.4 Block copolymerization of *rac*-lactide and ϵ -caprolactone with titanium pyridonate complexes

Poly(LA- <i>b</i> -CL)						
Entry	Catalyst	Yield (%) ^a	CL/LA ^b	M_n (g•mol ⁻¹) ^c	$M_{n, \text{theo.}}$ (g•mol ⁻¹) ^d	$\bar{D}$ ^e
1	4.1	80	55/45	21,450	31,382	1.41
2	4.2	81	55/45	61,660	31,774	1.25
3	4.3	86	51/49	23,770	33,230	1.28
4	4.4	82	55/45	40,000	32,087	1.24
5	4.5	83	56/44	26,185	32,559	1.37
6	1.16	77	56/44	20,720	29,430	1.31
7	4.6	68	57/43	46,280	52,632 ^f	1.53
8	4.7	66	59/41	44,440	51,858 ^f	1.37

Total [monomers]/[Ti] = 600. ^aIsolated yield. ^bDetermined by ¹H NMR spectroscopy. ^cDetermined by GPC. ^d $M_{n, \text{theo.}} = [([CL]/2[Ti]) \cdot \%_{\text{conv}}CL \cdot 114.14 \text{ g} \cdot \text{mol}^{-1}) + ([LA]/2[Ti]) \cdot \%_{\text{conv}}LA \cdot 144.13 \text{ g} \cdot \text{mol}^{-1})] \cdot \%Yield$ ^e $M_{n, \text{theo.}} = [([CL]/[Ti]) \cdot \%_{\text{conv}}CL \cdot 114.14 \text{ g} \cdot \text{mol}^{-1}) + ([LA]/[Ti]) \cdot \%_{\text{conv}}LA \cdot 144.13 \text{ g} \cdot \text{mol}^{-1})] \cdot \%Yield$.

While the yields obtained were generally lower than those obtained for the homopolymerizations, block copolymers were obtained in reasonably good yields with moderate levels of control. Inspection of the downfield poly(ϵ -caprolactone) methylene signal in the ¹H

NMR spectrum shows a triplet at δ 4.06 with no detectable resonance at δ 4.16 that could be assigned to a CL-LA heterojunction (Figure 4.5). This indicates that segments of ring-opened ϵ -caprolactone appear to be homo-coupled to one another, suggesting that the desired block segment of poly(ϵ -caprolactone) is present in the obtained polymer and there has been little to no transesterification into this block. The ratio of the monomers incorporated was determined by comparison of this signal to the methine protons of poly(lactic acid) at δ 5.16 and in all cases showed only a slight over incorporation of poly(ϵ -caprolactone).

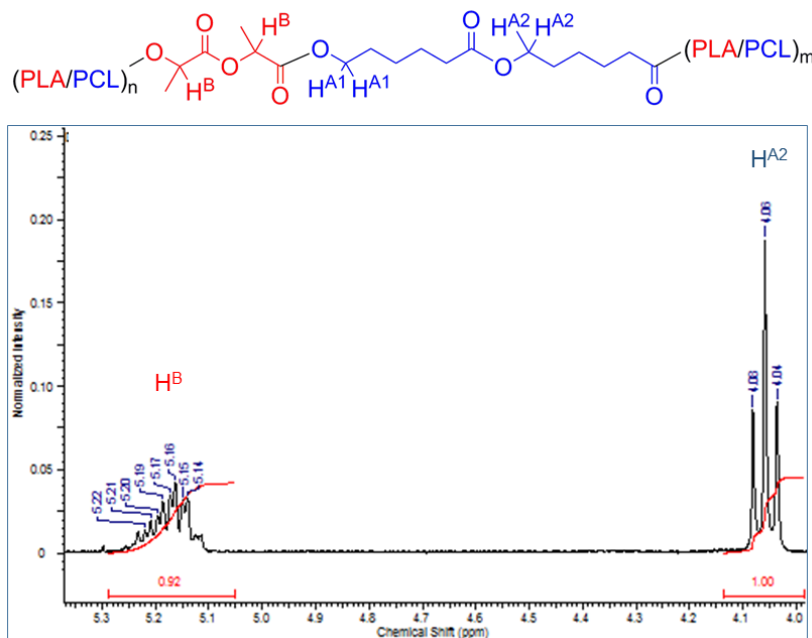


Figure 4.5 Zoom-in of the region of 4.0-5.3 ppm in the ^1H NMR spectrum of a block copolymer (Table 4.4 entry 4)

When analyzing the polymers formed with bis-pyridonate initiators, molecular weight values were found to be lower than theoretically predicted, with the exception of the complexes with the ethoxide and benzoxide reactive ligands (entries 2 and 4). It is speculated that these reactive ligands may contribute to sluggish rates of initiation compared to the dimethylamido or

isopropoxide ligands, once again resulting in larger molecular weights than predicted. In the case of the tris-pyridonate initiators, which are expected to propagate a single chain, the obtained molecular weights are in good agreement with theoretical values, albeit with diminished yields. Interestingly, the results obtained here do not provide evidence for transesterification. If chain transfer was occurring to a large extent, CL-LA heterojunctions would be expected to be present in the ^1H NMR spectrum of these polymers. Furthermore, diminished molecular weight was not observed to the same extent as was observed in random copolymer synthesis. These differences highlight the effect of simultaneous vs. sequential addition in attempts to form random or block copolymers respectively.

A critical mechanistic question that has surrounded polymerizations with the bis-pyridonate complexes is whether they are able to initiate and propagate two polymer chains per metal center. The results explored here generally suggest mono-initiation and propagation with the tris-pyridonate initiators; however, they do not differ as dramatically as anticipated from the results obtained with the bis-pyridonate initiators. From the results obtained with the bis-pyridonate initiators, it is speculated that a combination of mono- and bis-propagation could be occurring in the polymerization of poly(ϵ -caprolactone). While the number of propagating chains cannot be inferred from molecular weight data in the case of poly(lactic acid) synthesis, the lower than predicted experimental molecular weights suggest that transesterification plays a significant role when attempting to polymerize this monomer.

Analysis of the copolymers is therefore complicated by chain transfer processes that cause scrambling of polymer chain lengths, thus layering complexity into direct structure activity relationships between initiators and their respective polymers. Furthermore, it was observed that

in the formation of block copolymers, attempts to form a poly(lactic acid) block first, followed by ϵ -caprolactone addition, resulted in very low incorporation of poly(ϵ -caprolactone). However, the inverse addition of ϵ -caprolactone followed by *rac*-lactide was successful. This observation suggests that while *rac*-lactide is able to insert into either a pendant poly(lactic acid) or poly(ϵ -caprolactone) chain, the ϵ -caprolactone monomer is only able to appreciably insert into ring-opened poly(ϵ -caprolactone). This could rationalize the random copolymer synthesis in part, as it was stated earlier that despite the seemingly higher reactivity of ϵ -caprolactone, as based on reaction temperature and ring strain, it is frequently reported to be the more challenging monomer to incorporate in the copolymer.^{66, 85} It appears that while ϵ -caprolactone is inherently more reactive, the *rac*-lactide monomer, whether for steric or electronic reasons, is more predominantly involved in insertion and transesterification. This may rationalize the apparent contradiction between the difference in monomer reactivity and equivalent incorporation in the formation of copolymers.

4.3 Conclusions

Dimethylamido and alkoxide complexes of titanium bearing pyridonate ligands have demonstrated their utility in the ROP of *rac*-lactide and ϵ -caprolactone to afford homopolymers as well as block and random copolymers. While not possessing the high activity and control demonstrated by leading initiators,²²⁶ these complexes are competitive with other reported titanium initiators.^{66-67, 71-72, 74, 92} Notably, the ability to form random copolymers with close to equal monomer incorporation makes these complexes distinguished amongst titanium complexes. Furthermore, the ability to form block copolymers comprised of equimolar monomer incorporation by using sequential monomer addition highlights the versatility of these initiators. Investigations into homo- and co-polymerization suggest that lactide is more susceptible to transesterification

and chain scission events than caprolactone. While the variations of initiator design explored herein do not dramatically affect the resulting polymer properties, the overall scope of reactivity suggests the pyridonate ligand class indeed provides a favorable steric and electronic environment about the metal center for unique trends in ROP.

4.4 Experimental

4.4.1 Materials and Methods

General Details All air-sensitive reactions were performed under an inert atmosphere using a double manifold Schlenk line equipped with N₂ and high vacuum (10^{-3} mbar) or a glovebox filled with N₂. All glassware used was heated above 160 °C for a minimum of 12 hours in an oven prior to use. Reactions were performed in threaded 20 mL scintillation vials equipped with a poly(tetrafluoroethylene)-coated magnetic stir bar and a poly(tetrafluoroethylene)-lined polypropylene screw-cap. Toluene and hexane were purified by passing over activated alumina columns prior to collection and storage in the glovebox.

Reagents All reagents were purchased from commercial sources unless otherwise stated. Proligands were purified by sublimation then stored and manipulated in a nitrogen filled glovebox. Alcohols were stirred over 3 Å molecular sieves for 18 h then distilled and degassed using three freeze-pump-thaw cycles. All synthetic steps were carried out in a nitrogen filled glovebox. *rac*-Lactide (Aldrich) was sublimed once then stored in a freezer (-30 °C) in a nitrogen-filled glovebox. ϵ -Caprolactone (Aldrich) was stirred over CaH₂ for a minimum of 2 h, separated by distillation, then manipulated using standard Schlenk techniques. Titanium initiators **1.16**, **4.3-4.7** were prepared as per literature reference.²³⁶

Instrumentation

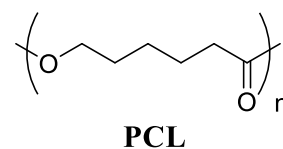
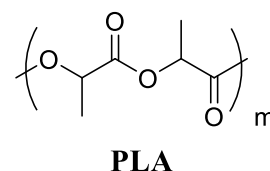
NMR spectroscopy ¹H NMR spectra were collected using a Bruker Avance instrument operating at 300 or 400 MHz. Chemical shifts, δ , are reported in parts per million (ppm). Abbreviations for NMR assignments are as follows: s = singlet; d = doublet; dd = doublet of doublets; t = triplet; q = quartet; m = multiplet; br = broad; appt = apparent. P_m (probability of *meso* enchainment) values were calculated from ¹H{¹H} NMR spectroscopy using the Bruker Avance 400 instrument.

Random copolymer sequence lengths were calculated from $^{13}\text{C}\{^1\text{H}\}$ NMR spectroscopy using the Bruker Avance 400 or 600 instrument. Please see Appendix E for sample calculation of P_m in the ROP of *rac*-lactide using $^1\text{H}\{^1\text{H}\}$ NMR spectrum. Please see Appendix E for sample calculation for average sequence lengths in random copolymers using ^{13}C NMR Spectrum.

Gel Permeation Chromatography Polymer M_n , M_w and dispersity ($\mathcal{D}$) were obtained using triple detection gel permeation chromatography (GPC) using a Waters liquid chromatograph equipped with an Agilent 1200 series isocratic pump and autosampler, Phenomenex Phenogel 5 μm narrow bore columns, Wyatt OptilabEx differential refractometer, Wyatt tristar miniDAWN (laser light scattering detector) and a Wyatt ViscoStar viscometer. A flow rate of $0.5\text{ ml}\cdot\text{min}^{-1}$ was used and samples were dissolved in THF ($\sim 1\text{-}2\text{ mg}\cdot\text{ml}^{-1}$). The measurements were carried out at a laser wavelength of 690 nm, at 25 °C. The data was analyzed using the Astra® processing program provided by Wyatt Technology Corp. The dn/dc values were calculated using a 100% mass recovery method.

4.4.2 Synthesis and Characterization

General procedure for the homopolymerization of LA or CL. In a nitrogen filled glovebox, a Kontes®-valve reaction tube was charged with a stirrer bar, the appropriate quantity of catalyst was added from a standard solution in toluene, the solvent removed *in vacuo*, then followed by addition of CL (300 eq., 0.396 g) or *rac*-LA (300 eq., 0.500 g). The tube was sealed and subsequently placed in a pre-heated oil bath. PLA



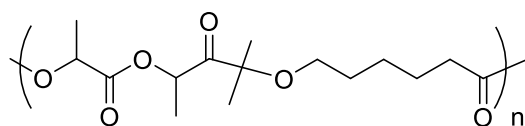
synthesis was carried out at 130 °C for 24 h, the reaction was then quenched with 10 mL of dichloromethane and allowed to dissolve. The resulting viscous solution was precipitated directly into cold methanol ($-20\text{ }^{\circ}\text{C}$), filtered, and washed with small amounts of methanol. It was then

dried under vacuum for minimum 8 hours to obtain the isolated polymer (off-white/light brown solid). PCL synthesis was carried out at 100 °C for 16 h, and worked-up as above to obtain the isolated polymer (white solid).

Poly(lactic acid) (PLA) ^1H NMR (300 MHz; CDCl_3): δ 5.24-5.11 (m, $\text{C(O)CH}(\text{CH}_3)$, 2H), 1.59-1.52 (br. m, $\text{C(O)CH}(\text{CH}_3)$ 6H).

Poly(ϵ -caprolactone) (PCL) ^1H NMR (300 MHz; CDCl_3): δ 4.06 (br t, $\text{CH}_2\text{CH}_2\text{OC(O)CH}_2\text{CH}_2\text{CH}_2$, 2H) 2.31 (t, $\text{CH}_2\text{CH}_2\text{OC(O)CH}_2\text{CH}_2\text{CH}_2$, 2H), 1.67-1.32 (br m, $\text{CH}_2\text{CH}_2\text{OC(O)CH}_2\text{CH}_2\text{CH}_2$, 6H).

General procedure for the random copolymerization of LA and CL. In a nitrogen filled glovebox, a Kontes®-valve reaction tube was charged with a stirrer bar and the appropriate quantity of catalyst was added from a standard



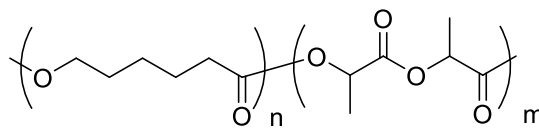
Poly(LA-*ran*-CL)

solution in toluene, the solvent was then removed *in vacuo*. Random copolymerizations were carried out with simultaneous addition of CL (300 eq., 0.396 g) and *rac*-LA (300 eq., 0.500 g) followed by heating at 130 °C using a preheated oil bath for 24 h. The reaction was then worked-up as with the homopolymerizations to obtain the isolated polymer (brown, sticky solid).

Poly(lactide-*ran*-caprolactone) ^1H NMR (300 MHz; CDCl_3 , 298 K) δ 5.22-5.11 (m, $\text{C(O)CH}(\text{CH}_3)\text{O}$ 2H), 4.13 (br s, $\text{CH}_2\text{CH}_2\text{OC(O)CH}(\text{CH}_3)$ 1H), 4.06 (t, $\text{CH}_2\text{CH}_2\text{OC(O)CH}_2\text{CH}_2$, 1H), 2.39 (br s, $\text{CH}(\text{CH}_3)\text{OC(O)CH}_2\text{CH}_2\text{CH}_2$, 1H), 2.31 (t, $\text{CH}_2\text{CH}_2\text{OC(O)CH}_2\text{CH}_2\text{CH}_2$, 1H), 1.67-1.36 (br m, $\text{CH}(\text{CH}_3)$, $\text{C(O)CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{O}$ 12H).

General procedure for the block copolymerization of LA and CL. In a nitrogen filled glovebox,

a Kontes®-valve reaction tube was charged with a stirrer bar and the appropriate quantity of catalyst was



added from a standard solution in toluene, the solvent

Poly(LA-*b*-CL)

was then removed *in vacuo*. Block copolymerizations began with the addition of CL (300 eq., 0.396 g). This was followed by heating at 100 °C using a preheated oil bath for 16 h. The reaction tube was then returned to the glovebox and *rac*-LA (300 eq., 0.500 g) was added, followed by heating at 130 °C for 24 h. The reaction was then worked-up as with the above polymerizations to obtain the isolated polymer (off-white, solid).

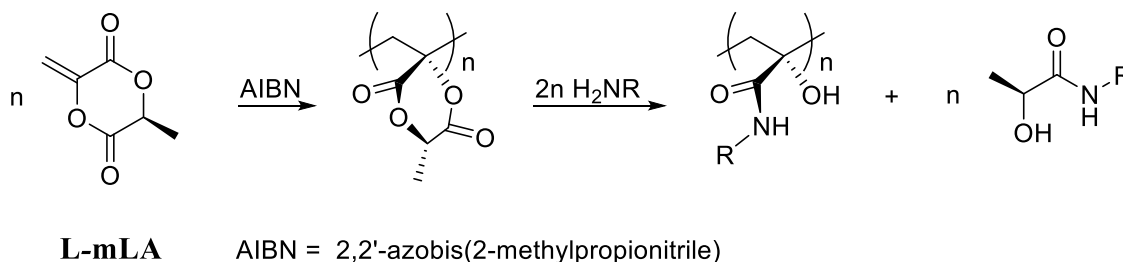
Poly(lactide-*co*-caprolactone) PLA-*co*-PCL ^1H NMR (300 MHz; CDCl_3): δ 5.22-5.14 (m, $\text{C}(\text{O})\text{CH}(\text{CH}_3)\text{O}$ 2H), 4.06 (t, $\text{CH}_2\text{CH}_2\text{OC}(\text{O})\text{CH}_2\text{CH}_2\text{CH}_2$, 2H), 2.32 (br t, $\text{CH}_2\text{CH}_2\text{OC}(\text{O})\text{CH}_2\text{CH}_2\text{CH}_2$ 2H), 1.67-1.52 (br m, $\text{CH}(\text{CH}_3)$, $\text{C}(\text{O})\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{O}$ 12H).

Chapter 5: Probing reactivity with methylene lactide

5.1 Introduction

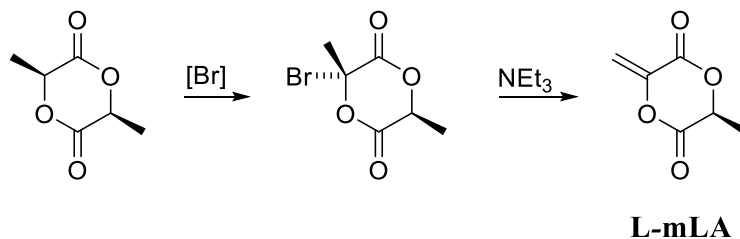
Chapter 4 of this thesis detailed the modification of poly(lactic acid) *via* its incorporation into random and block copolymers with poly(ϵ -caprolactone). An alternative route to modifying the properties of PLA that has received less investigation is the direct modification of the lactide monomer prior to polymerization. However, such modifications are challenging without undesired ring-opening because of the ring strain and high reactivity of the diesters present. Thus, there have been only select reports on monomers derived from lactide.²³⁹⁻²⁴³

A report by Ritter in 2015 sparked my interest in an unsaturated derivative of lactide, methylene lactide (mLA).²⁴⁰⁻²⁴¹ Their group reported the radical polymerization of this monomer using AIBN as an initiator, giving polymer of moderate molecular weight and broad dispersity (M_n up to 100 Kg•mol⁻¹ and $\mathcal{D}$ = 2.5). The resulting poly(mLA) contains activated esters which readily react with amine nucleophiles to provide variable branched amide groups; however, stoichiometric by-products are produced (Scheme 5.1).



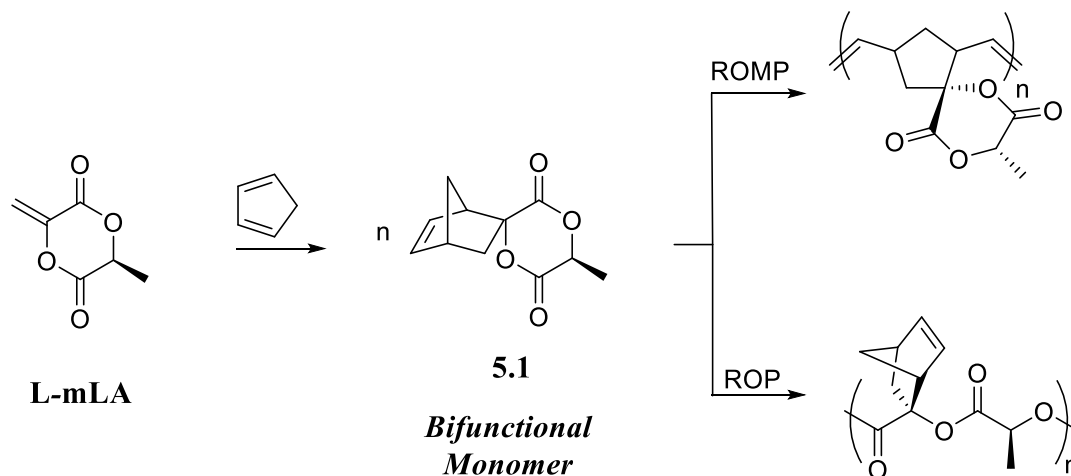
Scheme 5.1 Radical polymerization and post-polymerization modification of methylene lactide²⁴¹

This molecule was first prepared in 1969, when Scheibelhoffer *et al.* reported its synthesis using a two-step photobromination/elimination reaction sequence starting from L-lactide (Scheme 5.2).²⁴³ The radical polymerization was initially reported to give low molecular weight polymer (degree of polymerization = 6) and could be polymerized with styrene.



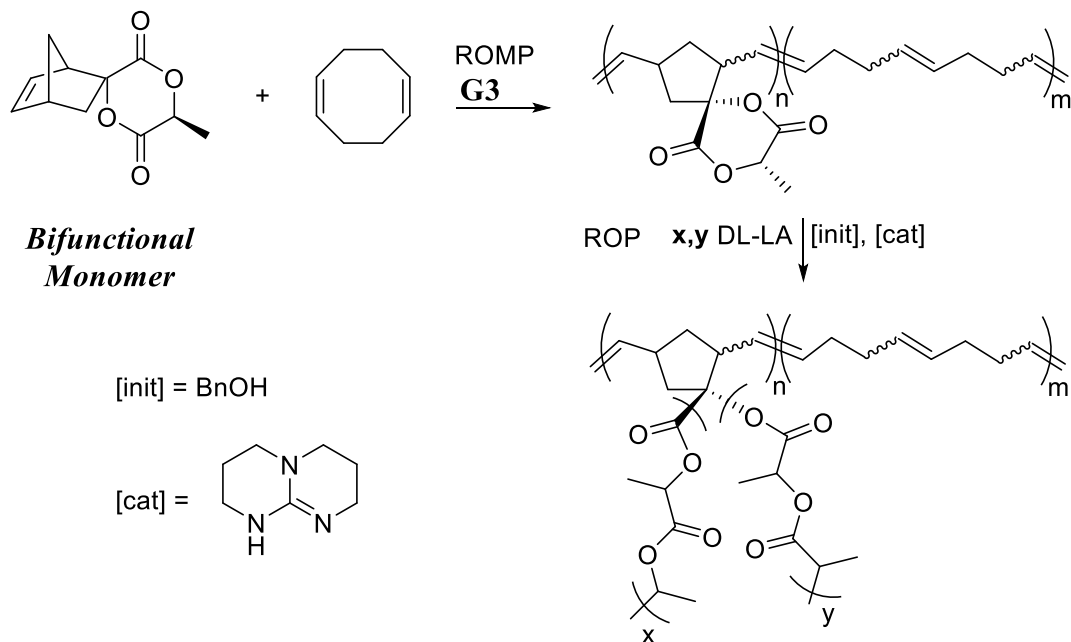
Scheme 5.2 Preparation of L-methylene lactide²⁴³

This report was dormant until 2008, when it was revisited by Hillmyer. They reported the practical synthesis of mLA which was further used to prepare a bifunctional monomer from a Diels-Alder reaction (Scheme 5.3).²⁴² This bifunctional monomer could be polymerized through two different methods: opening of the cyclic ester using ROP or the norbornene moiety using ROMP.



Scheme 5.3 Preparation and reactivity of bifunctional monomer 5.1²⁴²

This reactivity was harnessed to prepare novel polymeric derivatives of PLA through a reactive grafting approach. First, the bifunctional monomer was randomly copolymerized with cyclooctadiene using ROMP to give a copolymer with pendant cyclic esters (3 mol% bifunctional monomer with respect to cyclooctadiene). These pendant groups were then grafted with DL-lactide using ROP (Scheme 5.4).

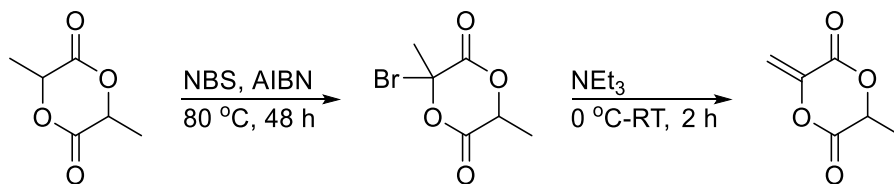


Scheme 5.4 Preparation of a composite material using sequential ROMP and ROP²⁴²

Compared to PLA homopolymer, this composite material exhibited improved physical properties with respect to elongation at breakage and tensile strength and toughness. Improved miscibility was also obtained as compared to a composite blend of poly(cyclooctadiene) and PLA homopolymers, which display typically-observed macrophase separation.²⁴²

5.2 Results and Discussion

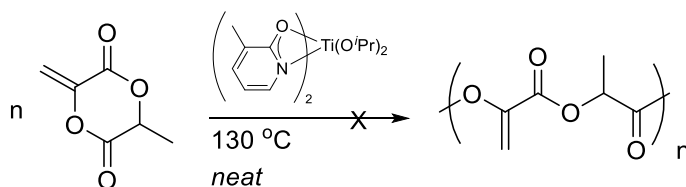
These select reports motivated interest in exploring this molecule with our catalytic systems. First, mLA was prepared as per literature reference;²⁴² however, *rac*-lactide was used in place of L-lactide (Scheme 5.5). After work-up, crude mLA was obtained as an off-white solid that was observed to rapidly hydrolyze if not promptly sublimed and stored under an inert atmosphere.



NBS = *N*-bromosuccinimide

Scheme 5.5 Preparation of mLA from *rac*-lactide

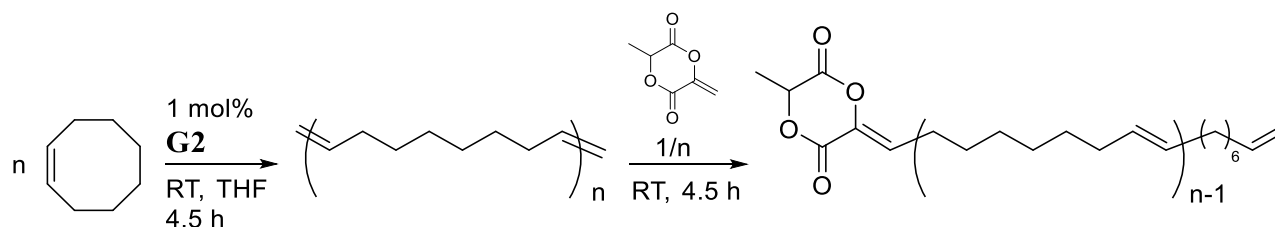
This monomer was tested as a substrate for ROP using a titanium pyridonate initiator under similar conditions to PLA synthesis with a 100:1 M:I ratio (Scheme 5.6). After 24 hrs, the reaction mixture appeared to be an orange, clear liquid. Unlike PLA synthesis, no change in viscosity of the reaction melt was observed during heating at 130 °C. After the reaction, analysis of a reaction aliquot by ^1H NMR spectroscopy showed no broadened peaks indicative of polymer formation, nor peaks that could be assigned to unreacted mLA. It is proposed that these reaction conditions led to decomposition of the monomer.



Scheme 5.6 Attempted ring-opening polymerization of mLA

To probe whether mLA is incompatible with titanium initiators, a stoichiometric 1:1 experiment was conducted with homoleptic dimethylamido titanium, $\text{Ti}(\text{NMe}_2)_4$. These reagents were combined in the glovebox at room temperature; upon addition of mLA to the initially yellow solution of $\text{Ti}(\text{NMe}_2)_4$ an immediate color change to dark brown is observed along with formation of precipitate. It is proposed that the high reactivity of the ester groups, in combination with the high oxophilicity of titanium, leads to decomposition.

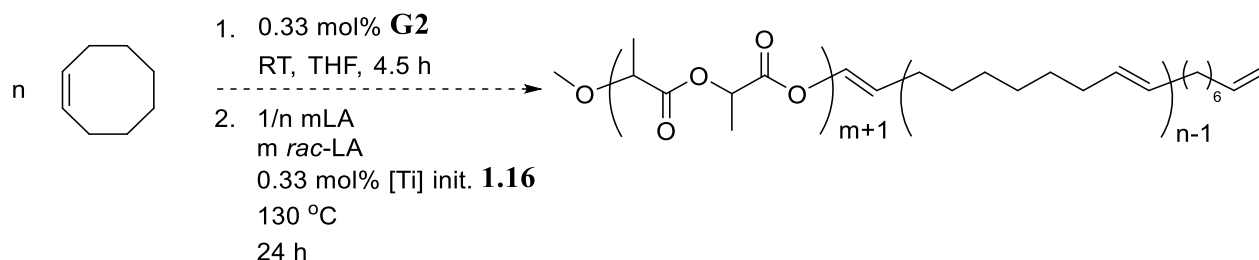
The observed decomposition of mLA in the presence of titanium led to the exploration of its reactivity with late transition metals. A key reaction of interest was exploring its compatibility with Grubbs catalysts, with an eye towards olefin metathesis. It was envisioned that the product of cross-metathesis (CM) between polyCOE and mLA could result in a polymer with a terminal cyclic ester from which ROP could be performed. Therefore, the first attempted reaction was to conduct CM after conducting ROMP on COE (Scheme 5.7).



Scheme 5.7 Attempted cross-metathesis of poly(cyclooctene) with methylene lactide

After performing ROMP with cyclooctene using **G2**, mLA was added and no changes were observed. The polymer was isolated and analyzed by ^1H NMR spectroscopy; however, only peaks assigned to P(COE) could be made. No diagnostic peaks were observed for an mLA end-unit. It was unclear from this experiment whether any of the desired reactivity with mLA was obtained.

Although it was unclear whether cross-metathesis was operative with mLA, the synthesis of a copolymer was attempted (Scheme 5.8). It was hoped that characterization of the attempted copolymer may indirectly demonstrate reactivity with mLA was incorporated. After the ROMP of cyclooctene, mLA was added along with 300 equiv. of *rac*-lactide and [Ti] initiator **1.16**.



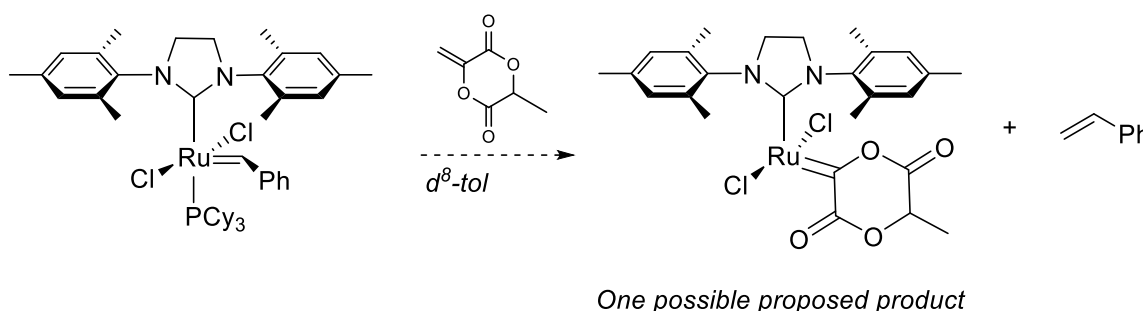
Scheme 5.8 Attempted copolymer using cyclooctene and *rac*-lactide

An off-white solid was obtained after precipitation in 61% yield. By ^1H NMR spectroscopy, the solid contains COE:LA in a 52:48 ratio as determined by comparison of the alkene protons of PCOE to the methine protons of PLA. The sample retained the requisite solubility for GPC; one peak was observed with $M_n = 56,330 \text{ g}\cdot\text{mol}^{-1}$ and $\text{Đ} = 1.53$. This experimental molecular weight is in large excess of theoretical PCOE with a 300:1 M:I ratio ($M_{n, \text{theo}} = 33,000 \text{ g}\cdot\text{mol}^{-1}$). For a PLA homopolymer, the observed molecular weight using initiator **1.16** was $14,120 \text{ g}\cdot\text{mol}^{-1}$. While the greater molecular weight obtained relative to what would be expected for the homopolymers is promising, this is not sufficient to conclude a copolymer was indeed formed. In the ^1H NMR spectrum, no peak was identified that could be reasonably assigned to a heterojunction between the separate units. Also, this sample was analyzed by TGA-FTIR, a method that enables the collection of IR spectroscopic data of the released gases during thermal treatment of the sample. A two-step mass loss was observed; an event began at 350 °C resulting in 35% mass loss. An extracted IR spectrum at this temperature was characterized using comparison to a reference library. Based on agreement with the peak profiles of acetaldehyde, carbon monoxide, and carbon dioxide, this mass-loss event was assigned to the degradation of PLA. A second event beginning at 472 °C showed loss of the remaining 65% mass. The IR spectrum extracted at this temperature compared favorably with a reference sample of PE decomposition. Thus, the second mass-loss event was assigned to decomposition of the P(COE)

portion of the sample. Further characterization of this material is required to conclude whether a copolymer was indeed formed or whether two homopolymers have been blended. Due to emerging advances in other projects, this work was discontinued.

5.2.1 Stoichiometric reactions with ruthenium starting materials

Stoichiometric experiments were conducted with mLA and **G2** in an attempt to probe whether mLA undergoes metathesis. A 1:1 reaction was prepared in deuterated toluene and monitored *in-situ* by ^1H and $^{31}\text{P}\{^1\text{H}\}$ NMR spectroscopy (Scheme 5.9).



Scheme 5.9 Stoichiometric experiment between methylene lactide and **G2**

A key diagnostic signal that was monitored in the ^1H NMR spectrum is the alkylidene $\text{Ru}=\text{CHPh}$ proton, which is observed at 19.56 ppm in d^8 -toluene. After adding mLA, a new, minor peak in the far downfield region ($\delta > 15$ ppm) is observed at 18.31 ppm. This peak slowly gains intensity but remains minor; after 24 hours it integrates in an approximately 1:8 ratio with respect to the peak at 19.56 ppm. In the $^{31}\text{P}\{^1\text{H}\}$ NMR spectrum, one peak was initially observed in **G2** at 29.85 ppm, after 24 hours another minor peak was observed at 32.69 ppm. These observations tentatively suggested some transformation was occurring to the **G2** starting material. The ^1H NMR resonances assigned to the alkene of methylene lactide (δ 5.42 and 4.77) are also observed to diminish in integration as the reaction is monitored. The ^1H NMR spectrum was compared to that of styrene in the same solvent. The detection of styrene as the product of the starting benzylidene

would be indicative of the desired cross-metathesis reactivity. Minor resonances (δ 6.54, 5.57, 5.06) that compared favourably to the peak profile of styrene were observed in the ^1H NMR spectrum. These results suggest minor reactivity may be occurring at room temperature. The reaction was heated to 70 °C in an attempt to prompt further reactivity. The relative integration of the new peak at 18.31 ppm is observed to increase with respect to the alkylidene peak of the starting material; however, complete consumption of the latter signal was not observed after 24 hours of heating. The reaction was further heated to 110 °C and checked by ^1H NMR spectroscopy and no peaks were observed in the downfield region > 15 ppm. This observation suggested that this increase in heat may have led to decomposition of the (unknown) mystery product(s). The crystallization of the reaction mixture was attempted several times using a variety of solvents and conditions. Unfortunately, only poor quality crystals were obtained. These were sufficient for establishing connectivity using X-ray diffraction and were identified as a protonated *N*-heterocyclic carbene. As this ligand is not expected to readily dissociate from **G2**, this result further suggests the decomposition of **G2** at 110 °C. The stoichiometric experiments with **G2** and mLA indicate a reaction takes place; however, the products remain unclear.

Another stoichiometric experiment with mLA was performed with a different ruthenium starting material. $\text{RuCl}_2(\text{PPh}_3)_3$ is widely used as a precursor to a variety of ruthenium complexes, including Grubbs metathesis catalysts.²⁴⁴ This reaction investigates whether reactivity with mLA is obtained in the presence of a ruthenium complex with chloro and phosphine ligands. A 1:1 reaction stoichiometry was combined in dichloromethane at room temperature. After 24 hours the reaction solution was observed to turn color to dark, brick red. The reaction was concentrated *in vacuo* to give a dark, brick red solid. Analysis of the ^1H NMR spectrum did not show any clear resonances aside from those from residual solvent. Another ^1H NMR spectrum was acquired using

parameters for analysis of paramagnetic compounds. However, no resonances were observed with this experiment as well. No significant resonances were observed in the ^{31}P NMR spectrum either. These observations were unexpected as the red solid was well-dissolved in the NMR sample. Fortunately, recrystallization of the reaction residue from toluene/dichloromethane gave dark red crystals that were sufficient for X-ray diffraction. The solid-state molecular structure is shown in Figure 5.1.

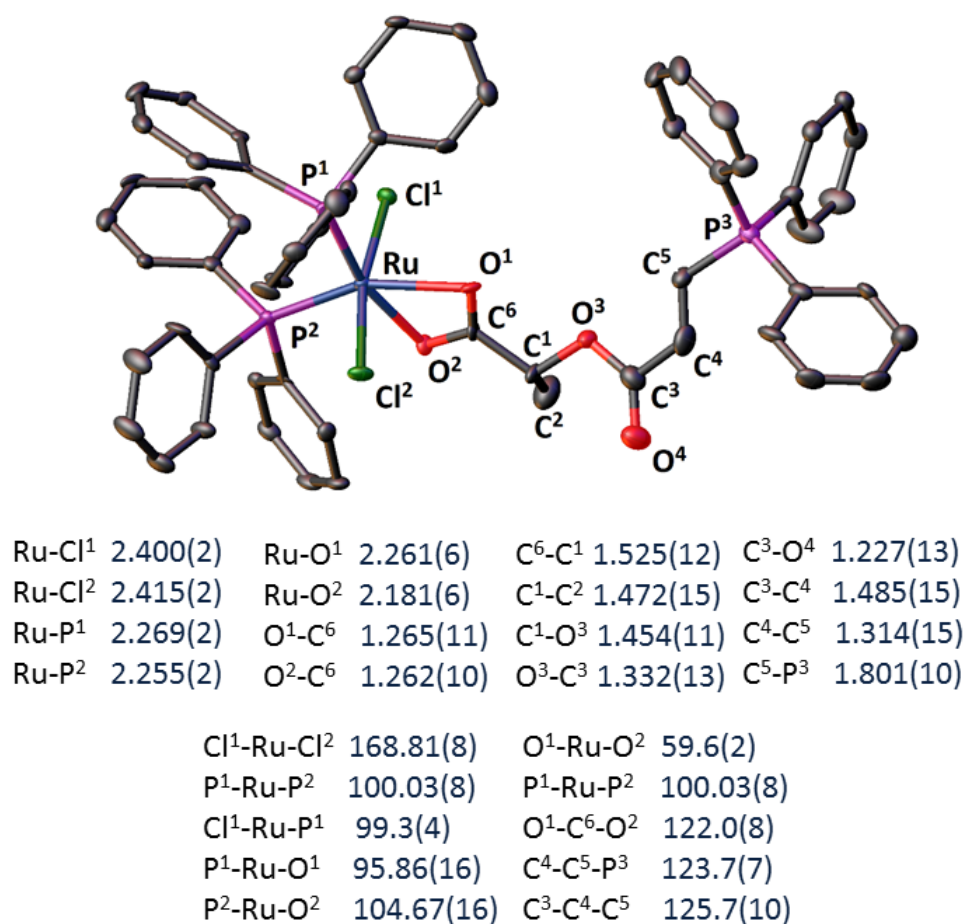
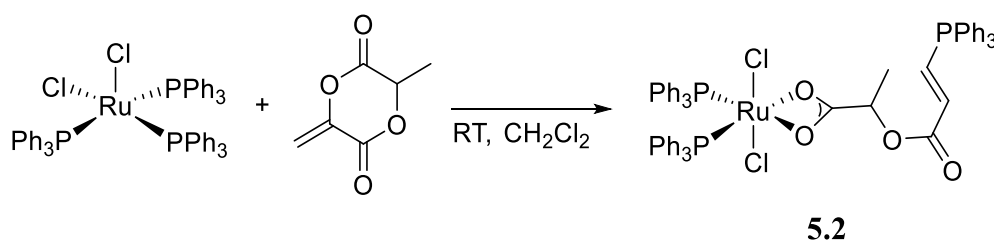


Figure 5.1 Solid-state molecular structure of complex 5.2 and corresponding bond lengths (Å) and angles (°)

The solid-state molecular structure reveals 5.2 is a ruthenium complex in an octahedral geometry with a carboxylate ligand that is presumed to originate from the ring-opening of mLA.

The carboxylate is bound κ^2 -O₂ to ruthenium *trans* to two triphenylphosphine ligands. While one Ru-O contact is slightly shorter (2.261(6) and 2.181(6) Å), the negligible difference between the C-O bonds of the carboxylate suggest delocalized binding (O¹-C⁶ = 1.265(11) and O²-C⁶ = 1.262(10) Å). The terminus of this carboxylate bears an alkene which is coupled to a triphenylphosphine group. The bond lengths of the alkene (C⁴-C⁵ = 1.314(15) Å) and the carbon-phosphorous bond (1.801(10) Å) are typical for a C=C double bond and C-P single bond respectively.



Scheme 5.10 Preparation of ruthenium carboxylate complex 5.2

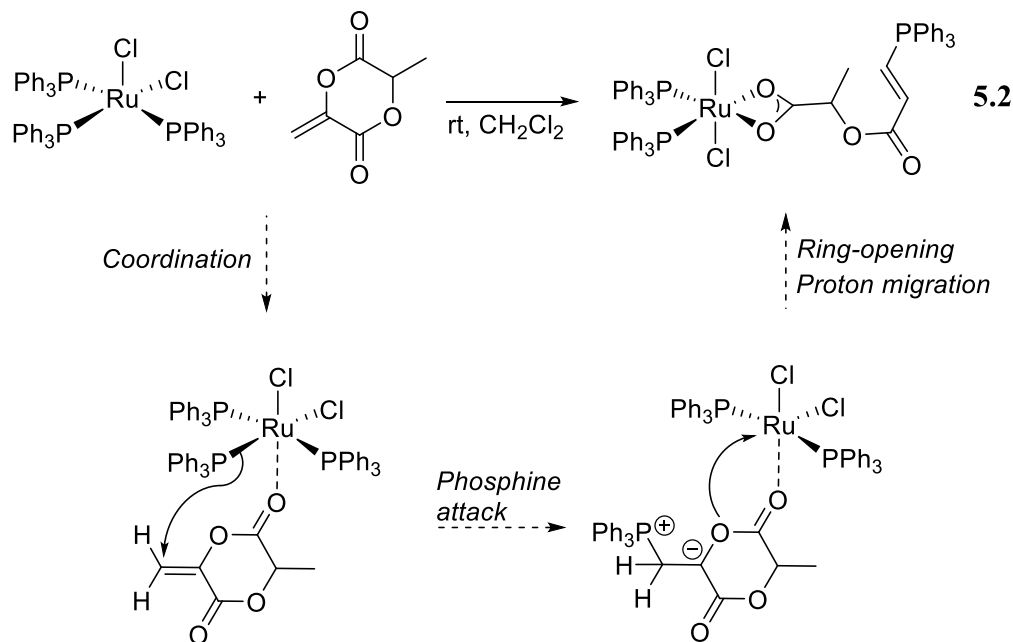
Accounting for the atoms of the product and 1:1 stoichiometry of reactants, this reaction maintains 100 % atom economy (Scheme 5.10). Along with the quantitative gravimetric yield of the crude product, it is proposed that this reaction proceeds to completion. Furthermore, resonances from unreacted starting materials were not present in the ¹H NMR spectrum. Elemental analysis indicates the product is pure (calculated 65.46 % C, 4.67 % H; determined 64.69 % C, 4.82 % H). Analysis by ESI-MS does not show the expected product peak at 1100 m/z. However, a significant peak at 838.2 m/z is detected that corresponds to the product minus a triphenylphosphine group. In the full window, the highest intensity peak is 405.2 m/z, corresponding to the mass of the ring-opened carboxylate with a terminal triphenylphosphine.

The oxidation state of complex **5.2** is challenging to assign in consideration of the solid and solution state characterization. If the carboxylate is considered a monoanionic LX-type ligand,

the complex should be classified as Ru^{3+} . However, the phosphorous bound to the alkene formally carries a positive charge, therefore the carboxylate overall could be classified as a neutral ligand. This classification would suggest that the complex should be Ru^{2+} , but an octahedral Ru^{2+} complex would be expected to be a low-spin, diamagnetic species. As a paramagnetic complex, this implies the system is high-spin if Ru^{2+} , however reports of high-spin, Ru^{2+} complexes are extremely rare. Evans method is a well-known experimental method to quantitate the number of unpaired electrons experimentally.²⁴⁵⁻²⁴⁶ Using this technique, the magnetic moment μ_{exp} was $1.95 \text{ J}\cdot\text{T}^{-1}$, corresponding approximately to one unpaired electron. One unpaired electron suggests a $d^5 \text{Ru}^{3+}$ species, rather than a high-spin Ru^{2+} in which there are two unpaired electrons.

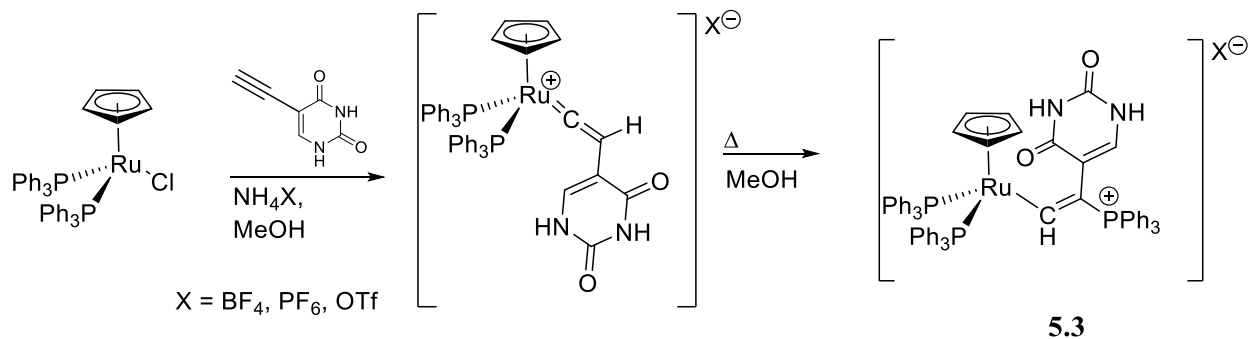
The lack of any detected resonances in the $^{31}\text{P}\{^1\text{H}\}$ NMR spectrum is also somewhat unexpected. As a paramagnetic complex, it is unsurprising that there are no observed resonances for the two triphenylphosphine groups coordinated to the metal. However, the terminal phosphine is eight atoms away from ruthenium and is also not detected by any resonances in the $^{31}\text{P}\{^1\text{H}\}$ NMR spectrum.

The mechanism for the formation of complex **5.2** remains unclear. It is reasonable to propose the reaction begins with coordination of mL A to ruthenium (Scheme 5.11). This coordination could be followed by the nucleophilic attack on the unsubstituted carbon of the alkene by a triphenylphosphine. Subsequently, the nature and order of the next steps is unclear. Proton transfer presumably occurs to form the *trans* alkene from the formerly geminal disubstituted alkene. The ring-opening of mL A between the alkene and ester is evident from the final product and is proposed to provide a thermodynamic driving force for the reaction. This ring-opening likely also makes the reaction irreversible. However, to date a logical mechanism to account for the formation of this complex has not been envisioned, much less elucidated.



Scheme 5.11 Proposed mechanistic steps to form complex 5.2

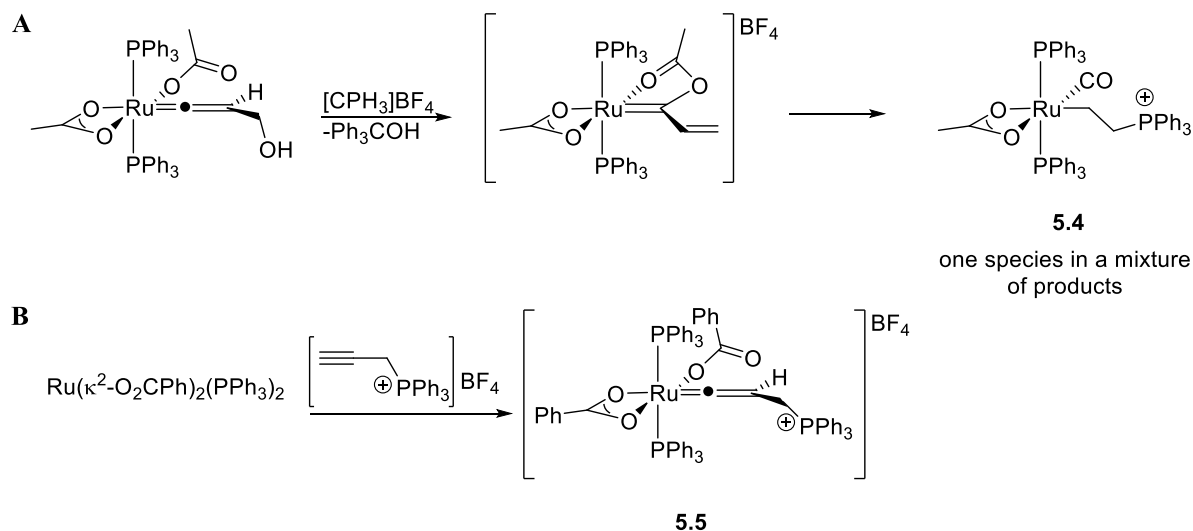
There are prior reports of products that have seemingly arisen from the nucleophilic attack of a liberated phosphine onto a coordinated unsaturated species to ruthenium.²⁴⁷⁻²⁴⁹ In 2009, an alkenyl phosphonio complex was serendipitously discovered as a minor byproduct upon refluxing a ruthenium vinylidene complex in methanol (Scheme 5.12).²⁴⁹



Scheme 5.12 Formation of alkenyl phosphonio ruthenium complex 5.3²⁴⁹

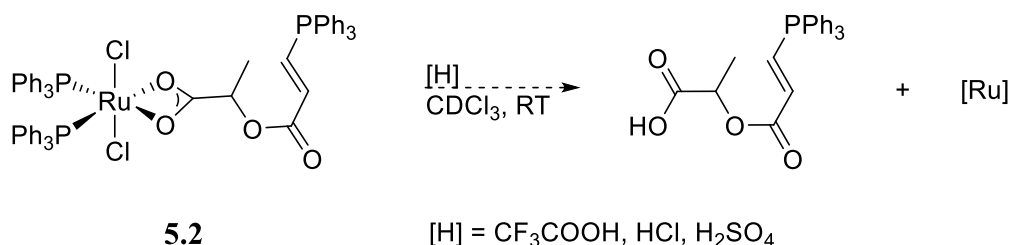
This byproduct was formed in sufficient amounts for characterization in the solid-state by X-ray diffraction. In complex 5.3, the relevant bond lengths of the phosphonio-alkene are 1.531(7) Å for the alkene and 1.790(6) Å for the carbon-phosphorous bond. In comparison, complex 5.2

has a slightly shorter alkene (1.314(15) Å) and a very similar carbon-phosphorous length (1.801(10) Å). Another example of an unexpected phosphorous substitution of an unsaturated fragment was observed in the attempted synthesis of a ruthenium carbene derivative (Scheme 5.13).²⁴⁷ Upon storage at room temperature, the formed ruthenium carbene proved unstable and transformed to a range of compounds, including a species appearing to arise from addition of triphenylphosphine (5.4). The detection of species 5.4 inspired the authors to directly access the vinylidene species 5.5 and characterize it in the solid-state. In complex 5.5, the $\kappa^2\text{-O}_2$ is less delocalized than what was observed in 5.2, with Ru-O bond lengths of 2.342(3) and 2.112(3) Å. The Ru-O bond of the carboxylate that is bound κ^1 to Ru is shorter as expected (2.095(5) Å). The carbon-phosphorous single bond (1.797(4) Å) is of similar length to what was observed in complex 5.2.



Scheme 5.13 A) Formation of species 5.4 as a product of the decomposition of a ruthenium carbene B) Direct synthesis of ruthenium vinylidene complex 5.5²⁴⁷

It was next of interest to explore the reactivity of complex **5.2**. First, it was tested whether the carboxylate group was labile under acidic conditions. A sample of complex **5.2** was dissolved in CDCl_3 followed by the drop-wise addition of trifluoroacetic acid (Scheme 5.14).

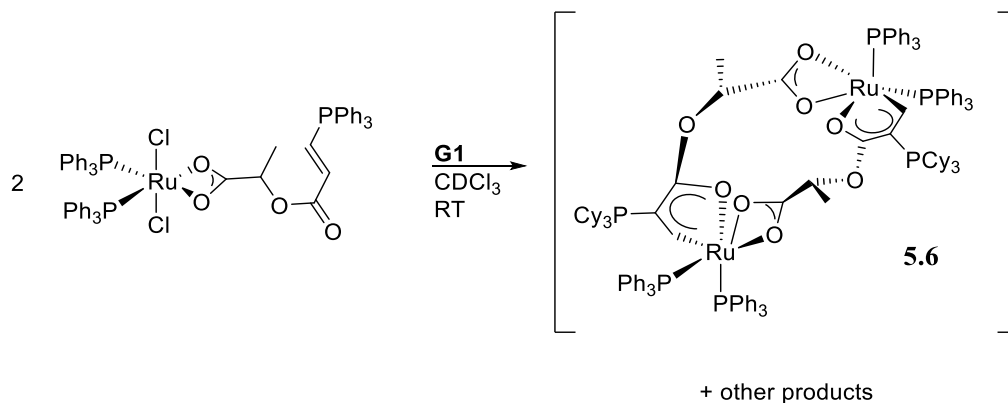


Scheme 5.14 Attempted cleavage of the carboxylate group of complex 5.2 under acidic conditions

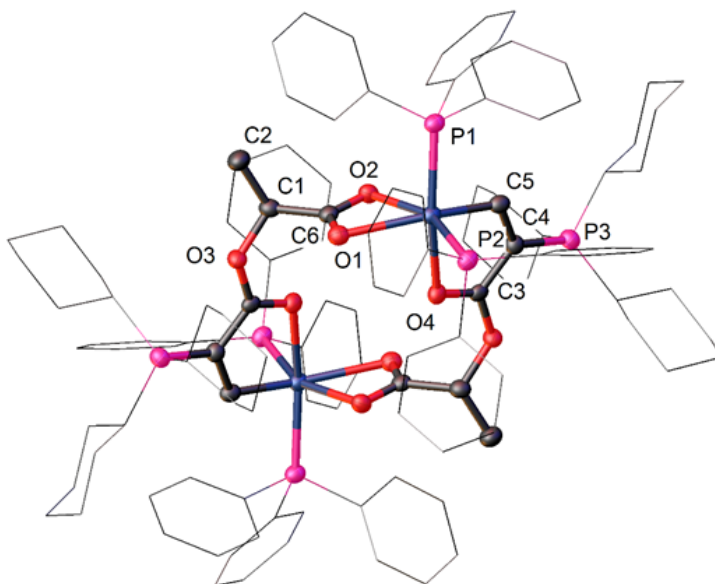
After addition, the solution was transferred to an NMR tube and evaluated by NMR spectroscopy. No new peaks were observed in the ^1H or $^{31}\text{P}\{^1\text{H}\}$ NMR spectra that could indicate the carboxylate ligand being freed from the metal. Using sulfuric or hydrochloric acid as the acid source similarly did not lead to any detection of the free carboxylate. This experiment suggests the carboxylate ligand is strongly bound to ruthenium. Further stoichiometric experiments with complex **5.2** in the presence of cyclic alkenes, alkynes, cyclic esters, and alcohols were evaluated by NMR spectroscopy and showed no reactivity. In all cases, the only resonances observed in the ^1H NMR spectra originate from the unreacted added reagent.

While complex **5.2** appears to be rather stable under inert atmosphere, it was of interest to explore whether the terminal alkene could participate in metathesis. A 1:1 stoichiometric reaction between **5.2** and **G1** was conducted in CDCl_3 at room temperature (Scheme 5.15). After 24 hours, a clear, dark amber solution was observed from the initially cloudy purple/red solution. The reaction mixture was evaluated by ^1H and $^{31}\text{P}\{^1\text{H}\}$ NMR spectroscopy. In the ^1H NMR spectra, two peaks were observed in the far downfield region; a singlet at δ 19.99 is assigned to **G1** starting material.²⁵⁰ A doublet is also observed at δ 20.20 that integrates in a 1:5 ratio with respect to the

singlet. In the $^{31}\text{P}\{^1\text{H}\}$ NMR spectra, one peak is observed at δ 36.32 that is also assigned to **G1**.²⁵⁰ No new peaks were apparent that were clearly assignable to a species other than **G1**. Fortunately, crystals were grown from the reaction mixture that were suitable for X-ray diffraction. The solid-state molecular structure is shown in Figure 5.2.



Scheme 5.15 Formation of ruthenafuran complex 5.6



Ru-P ¹	2.2682(12)	Ru-O ⁴	2.187(3)	C ⁴ -C ³	1.423(6)	C ¹ -C ²	1.507(7)
Ru-P ²	2.3234(12)	Ru-C ⁵	1.923(5)	C ³ -O ⁴	1.252(6)	C ¹ -C ⁶	1.510(6)
Ru-O ¹	2.295(3)	C ⁵ -C ⁴	1.401(6)	C ³ -O ³	1.339(5)	C ⁶ -O ¹	1.267(6)
Ru-O ²	2.158(3)	C ⁴ -P ³	1.780(5)	O ³ -C ¹	1.461(6)	C ⁶ -O ²	1.278(6)
O ¹ -Ru-O ²				O ¹ -C ⁶ -O ²			
P ¹ -Ru-P ²				C ⁵ -Ru-O ⁴			
59.39(12)				120.5(4)			
102.59(4)				78.39(16)			

Figure 5.2 Solid-state molecular structure of complex 5.6. Ellipsoids shown at 30% probability, H-atoms omitted for clarity, phosphine substituents shown as wire-frames

The solid-state molecular structure of complex **5.6** appears to be the product of a dimerization of complex **5.2** with the elimination of chloride ligands. Apart from dimerization, the structure does also indicate there was a transformation of the terminal phosphine-alkene. In complex **5.2**, there was a triphenylphosphine on C⁵, whereas in complex **5.6** this fragment is cyclometallated with a tricyclohexylphosphine (P³) instead bound to C⁴. This PCy₃ group originates from **G1**; however, its incorporation does not imply there must have been a reaction between the two complexes, as **G1** readily dissociates PCy₃ in an equilibrium process.⁴⁷

No substantial changes are noted in the bonding metrics of the carboxylate ligand. In complex **5.6**, the Ru-O¹ contact is now *trans* to C⁵ of the metallacycle. However, only subtle changes are noted in bond lengths and angles of the Ru-O contacts in **5.6** (Ru-O¹ = 2.295(3) Å, Ru-O² = 2.158(3) Å, O¹-Ru-O² = 59.39(12)°) compared to **5.2** (Ru-O¹ = 2.261(6) Å, Ru-O² = 2.181(6) Å, O¹-Ru-O² = 59.6(2)°).

The bonding features of the 5-membered metallacycle indicate this group is aromatic and may be classified as a ruthenafuran.²⁵¹ The planarity of the metallacycle in **5.6** is depicted in Figure 5.3. Two resonance structures are depicted; the fragment may be described as an alkoxy-carbene as well as a carbonyl-coordinated vinyl group. The Ru-C⁵ bond length of 1.923(5) Å is intermediate between the typical values for ruthenium-carbon single and double bonds.²⁴⁴ Within the metallacycle, the two carbon-carbon bond lengths are of similar length (C⁵-C⁴ = 1.401(6) Å, C⁴-C³ = 1.423(6) Å).

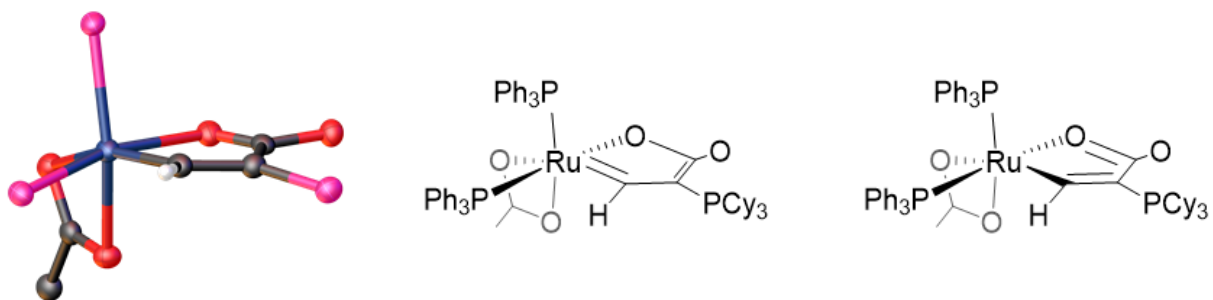
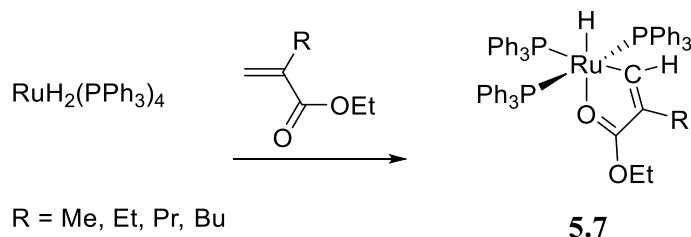


Figure 5.3 (L) Truncated solid-state molecular structure of 5.6 showing planarity of metallacycle (M-R) Two dominant ruthenafuran resonance forms

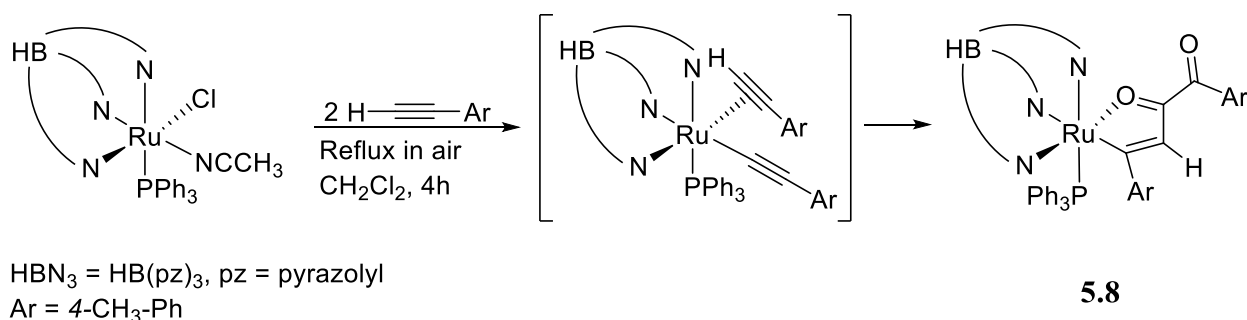
Metallafurans as a general class of organometallic complexes have been known since the 1960's.²⁵¹ In 1976, Ibers reported the synthesis of a structurally similar ruthenafuran to complex **5.6** through the oxidative addition of α,β -unsaturated ester (Scheme 5.16).²⁵² NMR spectra showed these to be diamagnetic complexes.



Scheme 5.16 Synthesis of ruthenafuran **5.7** through C-H activation of an alkenoate²⁵²

In comparison to **5.6**, the bond lengths of this complex (R = Me) indicate that the carbonyl-coordinated vinyl resonance form is more dominant. In this complex the Ru-C bond is longer (2.061(10) Å) while the differences between the C¹-C² (1.368(15) Å) and C²-C³ (1.442(15) Å) bonds lengths within the ring suggest less delocalization than in complex **5.6**. The Ru-O of the carbonyl is also slightly longer (2.246(7) Å) than as in **5.6** (Ru-O⁴ = 2.187(3) Å).

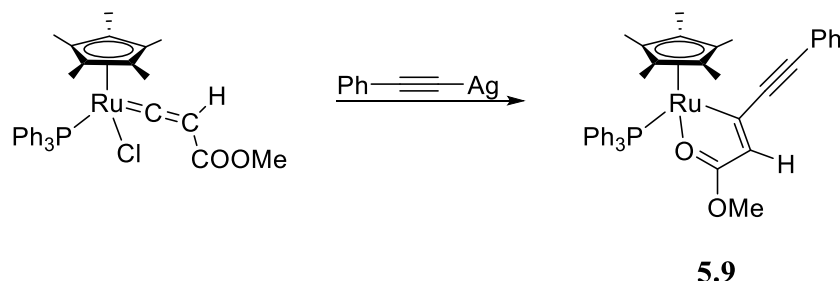
There has also been the reported formation of a ruthenafuran *via* the oxidation of *in-situ* generated vinyl diketone complexes. Hu *et al.* has described the synthesis of such a complex through the oxidation of a enyne intermediate in air (Scheme 5.17).²⁵³ This complex is diamagnetic and was characterized by NMR spectroscopy.



Scheme 5.17 Synthesis of ruthenafuran complex **5.8** through oxidation by air²⁵³

In comparison to complex **5.6**, this complex has a longer Ru-C bond (1.999(3) Å); however, the Ru-O bond (2.086(3) Å) is slightly shorter. Compared to **5.6**, there exists greater delocalization, with carbon-carbon bond lengths of 1.404(5) and 1.397(5) Å in **5.8**.

Another reported ruthenafuran has been prepared starting from a ruthenium vinylidene. A reaction of this starting complex with silver acetylide gives an intermediate that transforms to a ruthenafuran through migratory insertion followed by carbonyl coordination (Scheme 5.18).²⁵⁴ In this diamagnetic complex, **5.9**, the Ru-C and Ru-O bond distances were 2.032(8) and 2.156(5) Å respectively.



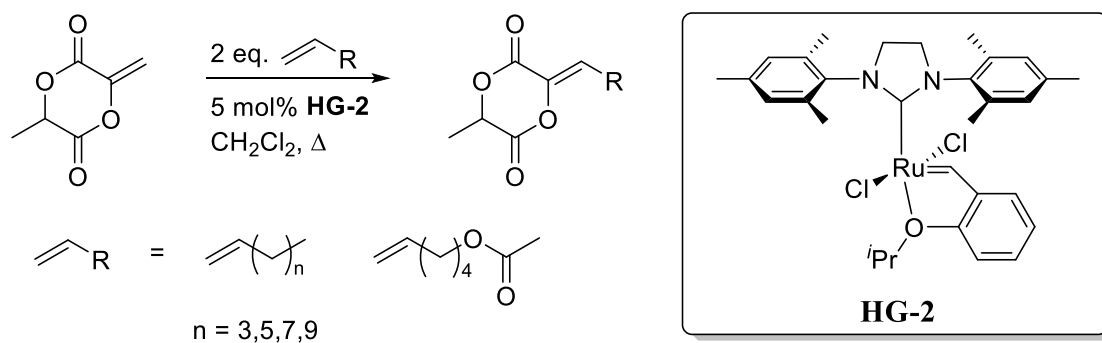
Scheme 5.18 Preparation of ruthenafuran complex 5.9²⁵⁴

The metallacycles of these ruthenafuran complexes exhibit similar bonding parameters to complex **5.6**. Furthermore, none of these reported ruthenafuran complexes are reported to be paramagnetic.

It was next of interest to explore whether a similar compound to **5.6** could be prepared without using **G1**. In comparing complex **5.2** to **5.6**, it was hypothesized that dimerization of the former may be possible through the abstraction of the chloride ligands. Thus, a reaction was performed in which complex **5.2** was treated with 2 equivalents of AgBF₄. Upon combination of these reactants, the initial red, clear solution of complex **5.2** promptly turns cloudy orange with a large amount of precipitation being observed. The reaction mixture was filtered through diatomaceous earth, giving a clear orange solution. The residue was evaporated to dryness and analyzed by NMR spectroscopy. In the ¹H NMR spectrum, some peaks were observed in the aromatic region δ 7.8-7.2; however, these may be because of impurities as no other signals are observed. In the ³¹P{¹H} NMR spectrum, 4 peaks of similar intensity are observed at δ 25.65,

23.68, 23.40, and 20.35. Crystallization of this reaction mixture was attempted; however to-date crystals of sufficient quality for X-ray diffraction have not been obtained. However, some poor quality orange crystals have been isolated. Qualitatively, the orange color of these crystals more closely matches the orange of complex **5.6** than the brick red of complex **5.2**, giving some indication that dimerization of may have occurred. Efforts to grow and characterize crystals in the solid-state by X-ray diffraction are in progress.

Since the initiation of this project, the cross-metathesis of mLA with the Hoveyda-Grubbs 2nd generation catalyst (**HG-2**) was reported.²³⁹ In this disclosure, cross-metathesis of mLA was achieved using terminal alkenes with 5 mol% catalyst in refluxing dichloromethane (Scheme 5.19). To undergo ROP, these CM products first required hydrogenation to prevent decomposition from non-productive ring-opening *via* alcoholysis.



Scheme 5.19 Cross-metathesis of methylene lactide²³⁹

This is the only report in which olefin cross metathesis is used to further functionalize a lactide derivative prior to ROP. In comparing this reaction to the attempted cross-metathesis described earlier, the choice of metathesis catalyst is likely crucial. In the reaction described in Scheme 5.2, **G2** was used as the metathesis catalyst. However, the reaction with $\text{RuCl}_2(\text{PPh}_3)_3$ suggested that nucleophilic attack by liberated phosphine groups may be occurring during attempted CM with **G2**. In the above report, **HG-2** does not contain labile phosphine groups; this

could suggest that CM of mLA is possible in the absence of any nucleophiles that may prompt ring-opening. Interestingly, the authors do not state that any other metathesis catalyst other than **HG-2** was used. It is proposed that attempts to form the CM product of mLA with **G1** or **G2** may be challenged by unproductive ring-opening from attack by free phosphine groups.

While the use of methylene lactide to prepare copolymers between lactide and olefins was not successful, the isolation of complex **5.2** may assist further efforts to derive polymeric materials from mLA. From the perspective of coordination chemistry, the observation of the ring-opened ester fragments and their interactions with the metal and other ligands is intriguing. Complex **5.2** is reminiscent of the Fogg intermediate complex **3.6** that highlighted the limited compatibility of phosphine-stabilized metathesis catalysts in RCM reactions in the presence of Lewis donors. As in their case, the isolation of complex **5.2** demonstrates that phosphine groups can stabilize organometallic complexes as ligands but also provide pathways for their decomposition when liberated.

5.3 Conclusions

Investigations into the rarely-reported methylene lactide monomer revealed interesting reactivity with ruthenium starting materials. While stoichiometric reactions between mLA and titanium complexes did not lead to controlled reactivity, reactions of the former with ruthenium starting materials demonstrated interesting reactivity profiles. Initial forays with **G1** and mLA suggested a reaction at room temperature was occurring; however, the product was challenging to characterize in solution. Fortunately, a reaction with the structurally less elaborate $\text{RuCl}_2(\text{PPh}_3)_3$ starting molecule produced meaningful quantities of product which was successfully recrystallized for solid-state characterization by X-ray diffraction. The resulting solid-state molecular structure suggested reaction of mLA with this ruthenium starting material results in ring-opening and

concomitant phosphine-alkene coupling. While this observed reactivity with methylene lactide is without precedent, this is another example of the side reactivity that can be accessed using phosphine-stabilized complexes. Further reactivity was also obtained to transform this complex further into a novel ruthenafuran complex. While the solid-state bonding features of this molecule compared favorably to other reported molecules of this class, the paramagnetic nature of complex **5.6** is much less common and challenging to interpret. While mLA was not incorporated into a copolymer as initially intended, these isolated complexes provide fundamental understanding of the reactivity of this rarely-reported molecule.

5.4 Experimental

5.4.1 Materials and Methods

General Details All air-sensitive reactions were performed under an inert atmosphere using a double manifold Schlenk line equipped with N₂ and high vacuum (10^{-3} mbar) or a glovebox filled with N₂. All glassware used was heated above 160 °C for a minimum of 12 hours in an oven prior to use. Reactions were performed in threaded 20 mL scintillation vials equipped with a poly(tetrafluoroethylene)-coated magnetic stir bar and a poly(tetrafluoroethylene)-lined polypropylene screw-cap. Toluene and hexane were purified by passing over activated alumina columns prior to collection and storage in the glovebox. Dichloromethane and deuterated chloroform were dried over CaH₂ followed by distillation *in vacuo* prior to storage in the glovebox.

Reagents All reagents were purchased from commercial sources unless otherwise stated. All synthetic steps were carried out in a nitrogen filled glovebox. Grubbs Catalyst™ 1st Generation (Sigma-Aldrich) and RuCl₂(PPh₃)₃ (Aldrich) were purchased and used without further purification. Methylene lactide was prepared as per literature reference.²⁴¹

Instrumentation

NMR spectroscopy ¹H NMR spectra were collected using a Bruker Avance instrument operating at 300 or 400 MHz. Chemical shifts, δ , are reported in parts per million (ppm). Abbreviations for NMR assignments are as follows: s = singlet; d = doublet; dd = doublet of doublets; t = triplet; q = quartet; m = multiplet; br = broad; appt = apparent. P_m (probability of *meso* enchainment) values were calculated from ¹H{¹H} NMR spectroscopy using the Bruker Avance 400 instrument. Random copolymer sequence lengths were calculated from ¹³C{¹H} NMR spectroscopy using the Bruker Avance 400 or 600 instrument. Evans method²⁴⁵⁻²⁴⁶ experiments were measured using coaxial capillary tubes containing 1% cyclooctane in CDCl₃.

Gel Permeation Chromatography Polymer M_n , M_w and dispersity ($\bar{D}$) were obtained using triple detection gel permeation chromatography (GPC) using a Waters liquid chromatograph equipped with an Agilent 1200 series isocratic pump and autosampler, Phenomenex Phenogel 5 μ m narrow bore columns, Wyatt OptilabEx differential refractometer, Wyatt tristar miniDAWN (laser light scattering detector) and a Wyatt ViscoStar viscometer. A flow rate of 0.5 ml $\cdot$ min $^{-1}$ was used and samples were dissolved in THF ($\sim$ 1-2 mg $\cdot$ ml $^{-1}$). The measurements were carried out at a laser wavelength of 690 nm, at 25 $^{\circ}$ C. The data was analyzed using the Astra $^{\circ}$ processing program provided by Wyatt Technology Corp. The dn/dc values were calculated using a 100% mass recovery method.

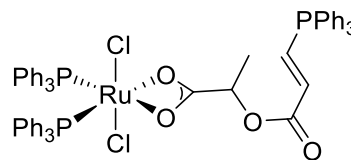
5.4.2 Synthesis and Characterization

Attempted homopolymerization of mL A. In a nitrogen filled glovebox, a Kontes $^{\circ}$ -valve reaction tube was charged with a stirrer bar, the appropriate quantity of catalyst **1.16** (0.042 g, 1 mol%) was added from a standard solution in toluene, the solvent removed *in vacuo*, then followed by addition of mL A (100 equivalents, 0.100 g). The resulting heterogeneous mixture was heated at 130 $^{\circ}$ C for 24 h, after which no change in viscosity was observed as in PLA synthesis. A portion of the reaction mixture was dissolved in CDCl $_3$ and investigated by 1 H NMR spectroscopy.

Attempted copolymer between COE and LA using mL A. In a nitrogen filled glovebox, to a 20 mL scintillation vial was added cyclooctene (300 eq., 0.600 g) and **G2** (0.33 mol%, 0.016 g) in THF (4 mL). After stirring for four hours, the reaction changed to a lighter color and an increase in viscosity was observed. To this mixture was added mL A (1 eq., 0.004 g), *rac*-lactide (300 eq., 0.780 g) and the appropriate quantity of catalyst **1.16** (0.33 mol%, 0.007 g), followed by heating to 130 $^{\circ}$ C for 24 hours. After the reaction time, the reaction was quenched through the addition of excess ethyl vinyl ether (*ca.* 10 drops) and diluted with 10 mL dichloromethane. After quenching,

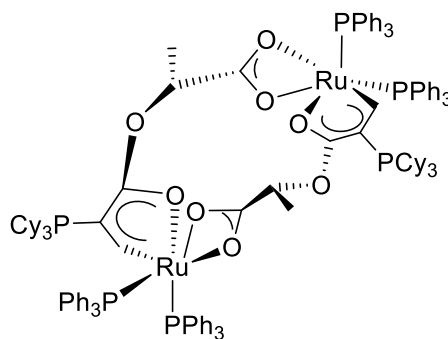
the resulting mixture was biphasic, with a clear amber liquid above a viscous white liquid. The entire mixture was precipitated directly into cold methanol (-20 °C), filtered, and washed with small amounts of methanol; 0.73 g of an off-white solid was obtained (61% yield). **¹H NMR (300 MHz; CDCl₃):** δ 5.39 (m, RCH=CHR, 2H), 5.17 (m, C(O)CH(CH₃), 2H), 1.98 (m, RCH₂CH=CHCH₂R, 4H) 1.59-1.52 (br m, C(O)CH(CH₃) 6H) 1.35-1.29 (br m, -CH₂CH₂CH₂CH=CHCH₂CH₂CH₂-, 8 H).

Synthesis of ruthenium carboxylate complex 5.2. In a nitrogen-filled glovebox, RuCl₂(PPh₃)₃ (0.150 g, 0.15 mmol) and methylene lactide (0.022 g, 0.15 mmol) in dichloromethane (*ca.* 2-3 mL). The



reaction was left to stir at room temperature; after 24 hours the reaction solution had turned slightly darker/brownish clear red ('brick-red') from the initially dark red clear solution. The reaction mixture was evaporated to dryness, giving 0.170 g of a dark brick-red solid (> 95 % yield). Recrystallization was conducted in a mixture of dichloromethane and toluene at -20 °C.

Synthesis of ruthenafuran complex 5.6. In a nitrogen-filled glovebox, complex 5.2 (0.020 g, 0.02 mmol) and **G1** (0.015 g, 0.02 mmol) were combined in deuterated chloroform (*ca.* 1 mL). The reaction was left to stir at room temperature; after 24 hours the reaction solution had



turned clear, dark amber from the initially heterogeneous dark purple/red solution. The reaction mixture was characterized *in-situ* by NMR spectroscopy using a sealed tube, then returned to the glovebox. Storage of this solution in a vial in the freezer gave orange crystals suitable for X-ray diffraction.

Chapter 6: Conclusions and Future Work

6.1 Summary

A central theme in this thesis has been the investigation and utility of two central reactions catalyzed by *N,O*-chelated early transition-metal complexes, hydroaminoalkylation and the ring-opening polymerization of cyclic esters. These reactions have both been applied toward the synthesis of functional polymeric materials. The predominant focus was on the hydroaminoalkylation reaction, a novel connection strategy to prepare diverse amine molecules from simple amine and alkene starting materials. To better understand the key features to access improved catalytic reactivity, the reaction mechanism was studied computationally with structurally varied tantalum complexes using DFT. This insight was then leveraged for the efficient, gram-scale synthesis of amino-alkenes for the preparation of amine-containing polyolefins *via* ring-opening metathesis polymerization. The second key reaction featuring *N,O*-chelated early transition metal complexes was the ring-opening polymerization of cyclic esters using titanium pyridonate initiators to produce biodegradable polyesters. While these initiators demonstrated reactivity with only moderate control, the pyridonate ligand was shown to provide a favorable steric and electronic environment about the metal centre for the formation of homopolymers as well as block and random copolymers.

Chapter 2 was focused on the mechanistic elucidation of the hydroaminoalkylation reaction catalyzed by *N,O*-chelated tantalum complexes. While this reaction was first described in the early 1980's and has experienced a surge in research attention over the last decade, a clear understanding of the reaction mechanism has remained elusive. To uncover key features of reactivity, DFT was used to model the mechanism of intermolecular hydroaminoalkylation catalyzed by a known *N,O*-chelating mono-amidate tantalum complex **1.3**. Modelling was also completed on a system

analogous to the previously reported catalyst $[\text{Cl}_3\text{Ta}(\text{NEt}_2)_2]_2$ (**1.2**). The trends in the computed energy profiles between these catalysts were compared to understand the effect of varying the steric and electronic properties of the metal. It was quickly established that ligands that promote the formation of highly electrophilic metal centres was critical for efficient catalysis. The amidate ligand was found to confer important steric and electronic properties. With the mono-amidate catalyst **I**, various C-H activation steps to form the catalytically active tantallaziridine were modelled. It was found that the plane of the *N,O*-chelating amidate ligand provides a favorable plane of reactivity for the formation of this species. Furthermore, the bulk of this ligand favors the sterically driven release of an amine product to promote the formation of a tantallaziridine species which is stabilized relative to the starting pre-catalyst. In contrast, the computed cycles for sterically less-bulky complexes **II** and **III** predict that amine-release to form a tantallaziridine is turnover-limiting. While the amidate ligand in **I** provides a more facile entry into the catalytic cycle, the steric bulk proves detrimental to protonolysis of the 5-membered metallacycle, which is the theoretically predicted turnover-limiting step. Ligand hemilability and electron delocalization throughout the amidate backbone were also shown to contribute to improved catalysis. These results point toward attractive features of *N,O*-chelated catalysts that are bidentate to promote catalyst stability while maintaining a highly electrophilic character. This study is the first reported theoretical model for Group 5 catalyzed hydroaminoalkylation and has contributed insight to ongoing catalyst development.

This theoretical model was corroborated with experimentally observed trends in reactivity. While protonolysis was theoretically predicted to be turnover-limiting, previous KIE studies by Lauzon have shown only a small KIE when investigating the initial rates of deuterated *N*-methyl aniline.¹² However, a complicating factor in interpreting these kinetic experiments is the fact that

because of various reversible equilibria including *ortho*-metallation and transamination it is anticipated that the *N*-deuterium label is “diluted” over the course of the reaction. Thus, a kinetic study was undertaken using analysis by GC-FID with a novel deuterated amine substrate that could not undergo unproductive side-equilibria. While this method reliably enabled the accurate detection of reaction analytes, attempts to monitor the reaction were challenged by the observation of a variable induction time. Although heated to the reaction temperature simultaneously, the onset of catalysis in an individual reaction was highly variable and on the same order of time as the period typically required for 20% amine consumption. Nonetheless, a preliminary KIE was observed that could be rationalized in consideration of the predicted energies of the theoretical catalytic cycle.

The investigation of hydroaminoalkylation shifted to its application in Chapter 3 for the synthesis of amine-containing monomers for application in ROMP. Earlier work by Perry showed that this reaction could selectively produce strained amino-alkenes in a single, atom-economic step at room temperature using tantalum phosphoramidate catalyst **1.8**.⁴⁶ Due to the limitations in scaling the reaction with this sensitive organometallic catalyst, an alternative route was developed using the *in-situ* generation of catalyst **1.11**. Controlling the selective mono-alkylation was challenging using this catalyst; however, this route nonetheless permitted the gram-scale formation of amine-containing norbornene derivatives in under 3 hours. As with the previous report, these monomers are unexpectedly tolerated in ROMP with Grubbs metathesis catalyst **G2**.

Chapter 3 also explored the optimized synthesis and subsequent polymerization of amine-containing cyclooctene derivatives. Using catalyst **1.9**, the selective mono-aminoalkylation of cyclooctadiene was achieved in high yield (> 80%) to produce gram-scale quantities of product with a variety of secondary arylamines. Using catalyst **1.9**, the substrate scope in amine was also

extended to a more challenging dialkylamine, methyl cyclohexylamine (ACC-5). While possessing less ring-strain than the analogous norbornene derivatives, these monomers were found to undergo ROMP using **G2**. Polymerizations with ACC-1-4 reach high yields but are not completely controlled, as assessed by the dispersity of the determined molecular weights. Due to the low solubility of the polymers, only P(ACC-1) and P(ACC-3) could be characterized by GPC, which determined that polymers possess moderate dispersity (1.2-1.8) with molecular weights that do not consistently align with that predicted by monomer-to-initiator ratio. Interestingly, less-strained cyclooctene derivatives polymerize to full conversion in less time than the analogous norbornene derivatives as determined by ^1H NMR spectroscopy. This may suggest non-productive side-equilibria with the latter monomers. Polymerization of the alkylamine substrate (ACC-5) was achieved using the more reactive **G3** metathesis catalyst with elevated temperature. To fully saturate the polymer backbone, well-known hydrogenative reduction conditions were adopted.²⁰² In the case of amine-containing cyclooctenes, saturation results in a polymer that is a polyethylene analog in which every eighth carbon possesses an amine branch.

The observed reactivity with these amine-containing monomers constitutes a rare report of the use of Grubbs metathesis catalysts with unprotected amines. This tolerance is attributed to several factors. An attempt to polymerize the monomer ACC-1 with **G1** was not successful, suggesting the use of the more reactive metathesis catalyst supported by an *N*-heterocyclic carbene ligand is necessary. A second key factor is related to the nucleophilicity of the amine group, which may result in the generation of unproductive amine-coordinated resting states. As the monomers ACC-1-4 are arylamines, they have a lowered nucleophilicity than alkylamines, such as ACC-5. Polymerization with ACC-5 requires elevated temperature and a more reactive metathesis catalyst than with arylamines ACC-1-4. A third factor is the proximity of the amine group to the alkene

moiety. In the cyclooctene derivatives, the placement of the functional group in the 5-position of the ring is proposed to spatially prevent its interaction with the metal centre while productive metathesis is occurring. Indeed, this is reflected in the rapid conversion of monomer to polymer. This spatial effect is also indirectly apparent from the differences in reactivity between cyclooctene and norbornene derivatives, where the latter possesses more ring-strain although they display more sluggish reactivity. As this trend is non-intuitive, it is proposed that the proximity of the amine in the norbornene derivatives enables its interaction with the metal centre while metathesis is occurring, thereby slowing down the rates of ROMP. Thus, we show that ROMP can be performed with amine-containing monomers given, careful consideration to the metathesis catalyst selected and the design of the monomer.

The viscoelasticity of the materials was also assessed by melt rheology in collaboration with Ms. Tanja Tomkovic. The presence of the amine branches was found to have significant effects on viscoelasticity in comparison to the typical behavior exhibited by an unfunctionalized polyolefin such as polyethylene. Depending on the amine substituent and polymer molecular weight, a range of behaviors from liquid-like ($G' < G''$) to solid-like ($G' > G''$) was observed. Comparing P(ACC-1) and P(ACC-1H) of similar molecular weight revealed the latter was relatively more 'liquid-like', which is proposed to be because of the enhanced flexibility in the fully saturated backbone. In all polymers tested, the ability of the amine group to participate in hydrogen-bonding interactions is proposed to promote chain association, resulting in the formation of supramolecular networks that are dynamically responsive to stress and strain.

The P(ACC) polymers were also macroscopically observed to have interesting bulk properties. When dried polymer samples were placed into contact, self-healing between the boundaries was spontaneous. This observation was noted for P(ACC-1-4), which is proposed to

be related to two key factors. First, these polymers are above their glass-transition temperature under ambient conditions, thereby existing as amorphous materials with chain mobility. Second, the associative interactions of the amine groups to hydrogen-bond promotes chain entanglement, such that two boundaries coalesce when brought into contact. Notably, self-healing is not observed in P(ACC-5). While not clearly understood, it is proposed that the hydrogen-bonds formed in this polymer are stronger and thus less-reversible than as in the other polymers, preventing rapid re-entanglement at a 'healing point'. The self-healing was measured quantitatively in a stress-strain experiment. For P(ACC-1), it was found that one hour of healing time could completely return the tensile strength of a sample to the same elongation as prior to the first break. This observed behavior demonstrates the differences that are conferred in a polyolefin upon the installation of amine branches that possess associative properties. In addition to self-healing, a sample of P(ACC-1) was also observed to adhere to poly(tetrafluoroethylene). While the mechanism of this behavior remains unclear, it is to the best of my knowledge without precedent for synthetic materials.

Chapter 3 also explored the incorporation of amine-containing monomers into copolymeric materials. It was of interest to lower the incorporation of amine functionalization in the materials by combining with other non-functionalized cyclic olefins. However, balancing the disparate reactivity between polar and non-polar monomers proved challenging. In an attempt to form copolymers in a one-pot sequential transformation, an excess of norbornadiene was used in the hydroaminoalkylation reaction to ensure a defined amount was in place for ROMP. However, attempts to form copolymers resulted in insoluble materials that were challenging to characterize. Analysis of a soluble residue of this material by ^1H NMR spectroscopy did indicate some amine was incorporated into the product. Attempts to form copolymers by sequential addition of monomers was likewise challenged by differences in monomer reactivity. A copolymer could be

obtained between cyclooctene and an amine-containing norbornene (ACN-4); however, the solubility of the material prevented its complete characterization, which is observed even in the deliberate preparation of oligomers. This solubility is lower than what is observed in the respective homopolymers, suggesting that differences between the properties of the respective polymer segments results in their self-assembly. This hypothesis was partially validated by the synthesis of a copolymer that was prepared through multiple iterative monomer addition steps. This copolymer is not proposed to self-assemble because of the periodic nature of the respective segments and it is observed to possess significantly improved solubility than the aforementioned block copolymers.

It was also of interest to target copolymers comprised of amine-containing cyclooctene and norbornene monomers. Surprisingly, ACN and ACC monomers were found to have different rates of polymerization when combined than in their respective homopolymerizations. While ACCs homopolymerize faster than ACNs, they react more slowly when polymerized in the presence of ACN monomers, and are also the slower of the two monomers to convert in the copolymerization. While these differences in rate were not investigated in detail, it would be consistent with non-productive side equilibria being present between the metathesis catalyst and ACNs. Nonetheless, it was found that ACN and ACC monomers could be combined to give a copolymer of predictable composition of both monomers given that the reaction was given sufficient time to react fully. A series of copolymers with variable relative incorporation were prepared (P(ACN-1-*co*-ACC-2)). A linear relationship was found between the relative composition and the glass-transition temperature, with increasing T_g with increasing relative incorporation of the ACN derivative. Thus, these monomers can be combined into a miscible material with predictably tuned thermal properties. Of these copolymers, only the copolymer with a glass transition temperature

significantly below the temperature of ambient conditions exhibited self-healing characteristics. This corroborates the T_g of the amine-containing material as a key parameter for this observed behavior.

In Chapter 4, reactions involving the ring-opening of cyclic esters were investigated. Using titanium pyridonate initiators, the ring-opening polymerization of *rac*-lactide and ϵ -caprolactone to synthesize copolymers as well as their respective homopolymers was explored. A series of bis- and tris-pyridonate titanium complexes were prepared with various reactive ligands to initiate polymerization. Bis- and tris-pyridonate initiators were prepared with the expectation that they would propagate two or one polymer chains per metal, respectively. However, analysis of the resulting polymers from these initiators did not demonstrate significant differences in molecular weights. Variation of the reactive ligand likewise did not lead to dramatic differences in the metrics of the isolated polymers, suggesting that within the class of titanium pyridonates studied the polymerization is somewhat insensitive to these changes of design.

In addition to homopolymers of *rac*-lactide and ϵ -caprolactone, these titanium initiators were also used for the preparation of random and block copolymers. In random copolymer synthesis, most initiators could furnish polymers bearing equivalent incorporation of both monomers from the simultaneous addition of both to the reaction. When instead the sequential addition of ϵ -caprolactone followed by *rac*-lactide was employed, a block copolymer could be obtained with equal incorporation of both monomers. Using ^1H NMR spectroscopy, resonances assigned to poly(caprolactone) were used to calculate the ratio of *homo* vs. *hetero* (ie. adjacent to a lactide segment) junctions; in which the random copolymers possessed an equivalent ratio of both while in block copolymers only the desired homojunctions are observed. As in homopolymer synthesis, dramatic differences were not observed in the polymers obtained across the initiators

evaluated. Nonetheless, the results of these polymerizations demonstrate that the pyridonate ligand provides a favorable steric and electronic environment for titanium complexes for ROP.

Chapter 4 also investigated the ring-opening of methylene lactide, a derivative of lactide of which the reactivity has rarely been reported in the literature. While the incorporation of this molecule into a polymeric material was not obtained as desired, intriguing reactivity was observed in stoichiometric experiments with a ruthenium starting material. The 1:1 addition of methylene lactide with $\text{RuCl}_2(\text{PPh}_3)_3$ was observed to form a complex (**5.2**) bearing an adduct that was the product of the ring-opened ester. This paramagnetic compound was structurally characterized in the solid-state by X-ray diffraction. Although the mechanism to form this product is unclear, it appears to partially result from the nucleophilic attack of a phosphine group. This complex is largely inert to further transformation; however, reactivity was obtained in a stoichiometric experiment with Grubbs metathesis catalyst **G1**. Crystals obtained from this reaction mixture were characterized in the solid-state to be dimeric ruthenafuran complex **5.6**. Although complexes **5.2** and **5.6** did not ultimately lead to the formation of polymeric materials, their characterization contributes to the underexplored reactivity profile of mLA.

In all chapters, the twelve principles of green chemistry were used as a guide for experimental design. Within these methods, some respects have satisfied these principals while others necessitate further improvement. From the perspective of waste generation, hydroaminoalkylation coupled with ring-opening metathesis polymerization constitutes an atom-economic strategy for the formation of amine-pendant polyolefins, obviating the generation of waste from substrate. However, this does not include the catalyst or the solvents required for the reaction; the development of a method that could avoid the use of solvents would represent a more sustainable path to these materials. Furthermore, while tantalum catalysts have demonstrated

superior reactivity for the hydroaminoalkylation reaction in contrast to other metals, the use of alternative, more abundant transition-metals such as titanium would further increase the sustainability of this pathway. Nonetheless, the cognition of green chemistry throughout this work has influenced reaction design towards green chemistry goals, with the acknowledgement that this influence could and should extend further within the development of any chemical process.

6.2 Future Directions

6.2.1 Continued theoretical investigations

Chapter 2 detailed efforts to understand the mechanism of hydroaminoalkylation catalyzed by mono-amidate tantalum catalysts using theoretical calculation. Results from that study showed that the amidate ligand scaffold provides both beneficial and detrimental steric effects depending on the particular step in the catalytic cycle. While steric effects promoted amine release to form the catalytically active tantallaziridine, they also contribute to sluggish protonolysis, in which an amine must enter the coordination sphere. The ability of the amidate ligand to possess hemilability to access κ^1 modes to alleviate steric congestion was also considered an attractive feature for catalysis.

A future direction for this investigation would seek to leverage this insight for future catalyst development. While catalyst **1.3** was discovered from the empirical investigation of various amidate ligands, the development of a theoretical mechanism provides a modular framework for guiding catalyst design. Moving forward, it would be of interest to make structural modifications to the ligand and calculate the difference in energetics relative to the mono-amidate in **I**. A key goal would be to identify structural modifications to the amidate ligand that tunes the steric environment such that protonolysis is more facile without raising the energy to form the

tantallaziridine. It is believed that a more sophisticated understanding of hemilability may enable the design of ligand features that allow this behavior to be controllably harnessed.

The computational model explored in this thesis was also limited to amidates as *N,O*-chelating ligands. However, on-going efforts in catalyst development have led to the identification of pyridonates and ureates as supporting ligands for tantalum as well.^{41, 43, 45, 104} In particular, the ureate ligand is able to form a tantalum species *in-situ* with a number of attractive features in hydroaminoalkylation, including low catalyst loading, high turnover number/frequency, and large substrate scope.⁴³ In the future, expanding modelling efforts to understand how these ligands result in changes in the energy profile of the catalytic cycle may provide clues to the origin of improved reactivity with these systems. As most catalysts are known to be effective for a particular class of substrates, the comparison between these ligated systems may reveal key characteristics that are necessary for efficient catalysis and an expanded scope of products. Ideally, the goal is to have constant feedback between theoretical and experimental approaches to guide catalyst development.

6.2.2 *In-situ* catalyst monitoring

In Chapter 2, the experimental monitoring of a hydroaminoalkylation reaction was developed using GC-FID. Unfortunately, attempts to monitor the initial rates of catalysis were challenged by a variable induction period when using catalyst **1.3**. While this method was not useful for the reaction catalyzed by **1.3**, it may provide a foundation for future efforts in reaction development.

The detection of reaction analytes using GC-FID could potentially be coupled *in-situ* with a hydroaminoalkylation reaction. Traditionally, reaction screening in hydroaminoalkylation is performed by preparing a reaction in a sealed NMR tube followed by checking by NMR spectroscopy at given time points. For each combination of substrates, a characteristic resonance

for the reactant and product must be determined to calculate conversion. If reactions are in refluxing solvent, they must be cooled below their reflux temperature before measuring by NMR spectroscopy, preventing detection while the reaction is occurring. In contrast, a method using detection by GC-FID can potentially overcome several of these challenges. As a reaction is proceeding, an aliquot could be removed using syringe techniques and directly injected into a GC for quantification. This could be particularly advantageous in an automated process, where multiple different reactions are set up and sampled using robotic techniques. There is also no instrumental limitation in the sampling of a refluxing sample. As GC first separates all analytes prior to detection, identifying product(s) from reactants is much more straightforward than the superimposition of an NMR spectrum. In theory, such a method could be used to rapidly screen different reaction variables in catalyst, solvent etc. The interplay of this data collection along with theoretical insight may provide a synergistic path to catalyst discovery in the future.

6.2.3 Towards efficient and tunable amine incorporation

In Chapter 3, the synthesis and characterization of amine-containing polyolefins was developed. These materials were found to have significant differences in physical properties in comparison to non-functionalized polyolefins. The presence of the amine branch and its propensity to undergo associative interactions such as hydrogen-bonding resulted in interesting features to be observed in both rheological measurements and bulk properties. It was of interest to lower the percentage of amine groups to investigate the extent of change in physical properties; however, attempts to form copolymers led to highly insoluble materials due to proposed self-assembly. When the monomers were copolymerized using an iterative, step-wise addition, the material demonstrated solubility for characterization after complete drying. This improved solubility is thought to result from the periodic placement of amine branches along the chain, preventing their

self-assembly which in turn challenges their characterization. In the future, it would be of interest to investigate the properties materials with variable amine incorporation; however this will require a more straightforward means of their preparation.

Although this step-wise addition was not practical, monomer addition can be automated. Instead of manually adding the monomers sequentially, a syringe pump could be used to slowly deliver one of the two monomers to the reaction solution. By taking into account the rates of polymerization of each respective monomer, the rate of addition could be tuned to ensure that the concentration of each monomer in the reaction mixture remained constant (or whatever desired ratio for a targeted microstructure). Using variable feeds of each monomer, this in principle could enable the formation of polyolefins with control over not only the amount of amine group, but the placement of them along the polymer chain as well.

In section 3.2.1.2, a crude sample of ACC-1 was obtained without purification by column chromatography. While possessing some impurities, this sample was able to form polymer in high yield using ROMP. The solubility of the material was lower than typically observed in polymers derived from column-purified monomer, which is proposed to be because of the likely impurities (liberated pyridone ligand and di-alkylated products) forming weak cross-links between the polymer chains. This result provides a few opportunities for future investigation. First, while this sample of ACC-1 is not completely pure, it could still be useful to combine it with the syringe techniques described above. After hydroaminoalkylation, a solution of Grubbs catalyst can be directly added to form polymers in a one-pot sequential transformation. Alternatively, the hydroaminoalkylation could be quenched, followed by cannula transfer into a reaction vessel for ROMP that also has an inlet for a second monomer. This route could represent a more convenient

method for the assembly of polymeric materials than those described in Chapter 3. While the 'less-pure' P(ACC-1) is not highly soluble, this does not preclude it from being a useful material.

A second opportunity for investigation that has been inspired by the column-free purification is to prepare cross-linked materials. If the proposal that polymeric materials prepared from crude monomers are less soluble due to cross-linking impurities is valid, it would also be interesting to deliberately prepare cross-linked materials and investigate their properties. These materials may have interesting differences with respect to thermal behavior and/or viscoelasticity, where it would be anticipated that the addition of cross-links would further increase the strength and toughness of the material.

6.2.4 Specialized applications of amine-containing polymers

An exciting future direction of the research presented in Chapter 3 is to explore these materials within specialized applications. As stated previously, amines have been utilized in materials designed for metal-scavenging,¹³⁰ CO₂ uptake,¹³¹⁻¹³² water-treatment,¹³³ drug-delivery,¹³⁴ and anti-microbial activity.^{53, 55, 135} With the synthesis of gram-scale quantities of polymer established in Chapter 3, it is now practical to produce sufficient amounts to test the viability of these materials for these specialized roles. Additionally, the observation of dramatic adhesive forces and self-healing in these materials suggests that applications that can take advantage of these properties should be targeted.

An interesting application that could capitalize on the associative interactions of the amine-containing polymer would be its incorporation into a membrane for the treatment of liquids. This membrane could be designed for an application such as metal-scavenging or water-treatment by harnessing interactions with incorporated amine groups. In these applications, the membrane would serve as a permeable layer that could purify solutions from metal residues or organic

impurities as they pass through. This method of purification could potentially offer significant advantages to traditional purification methods such as chromatography and crystallization with respect to convenience, cost, and time and energy demand.

The powerful adhesive and cohesive forces that are observed in these amine-containing materials could also allow them to be investigated as tie polymers. Tie polymers refer to a class of adhesive polymer resins which are used to improve the lamination within multi-layer films of dissimilar materials. While the layering of films can improve mechanical properties and modify the characteristics of a film, for instance its gas permeability, these layers can de-laminate when the chemical nature of the layers to be combined are too dissimilar. A commonly used tie polymer is anhydride modified polyethylene.²⁵⁵ As discussed in Section 3.1.2, the process of forming this polymer is energetically intensive and can result in finished materials with physical defects because of the grafting process. Thus, it would be interesting to explore the ability of the amine-containing polymers to be used as tie polymers between different combinations of polymers that show poor cohesion, for example polyethylene and nylon. This study also need not be limited to polymers; these materials could also be investigated as tie polymers between any number of substrates, such as wood, glass, metal etc. As these materials most intriguingly show rare adhesion to poly(tetrafluoroethylene), the investigation of this substrate specifically is of interest.

6.2.5 Incorporation of amine-containing polymers in blends

An area for future investigation is to combine the polymers developed in Chapters 3 and 4. In Chapter 4, titanium pyridonate initiators were used to prepare random and block copolymers between *rac*-lactide and ϵ -caprolactone. One targeted goal in the copolymer synthesis was to modify the properties of poly(lactic acid), which is a strong but brittle material. Another way to modify the properties of PLA would be to combine it with an amine-containing polymer. As the

esters of PLA should render it a good hydrogen-bond acceptor, the combination with the amine group's role as a hydrogen bond donor might result in useful physical properties. Ultimately, the goal would be to use a small amount of amine-containing polymer to allow PLA to maintain its high strength while improving its ductility and toughness. While the observed properties of the amine-containing polymers makes them highly interesting as stand-alone materials, their ability to participate in beneficial associative interactions suggests that they may also be highly useful when combined in formulations with PLA.

Beyond PLA, all classes of polymer bearing groups that are capable of hydrogen-bonding could be explored in combination with amine-containing polymers in pursuit of new and advanced composite materials. A particularly aspiring target would be using the amine-containing polymer to compatibilize the incorporation of waste plastic into virgin materials to produce new classes of post-consumer recycled materials. The significance of the amine-containing polymer would be to enable the combination of the disparate components of waste feed into a physically useful material. While composite materials generated from plastic waste typically display poor physical properties,²⁵⁶ the targeted goal would be the utilization of the associative interactions of the amine-containing polymers as an additive to create a robust composite material. An exciting aspect of this project is the positive social impact of using advances in polymer science to provide a partial solution to the catastrophic problem of plastic pollution.

6.3 Concluding remarks

The findings within this thesis have highlighted the utility of early-transition metal complexes towards the preparation of functional polymeric materials. In Chapter 2, a theoretical investigation into the hydroaminoalkylation reaction revealed that *N,O*-chelating ligands improve catalyst efficiency by promoting the formation of electrophilic metal centres that possess dynamic

steric effects as a result of flexible ligand binding. The advances of this ligand-modified reactivity enable this reaction to be used for the formation of amine-functionalized pre-cursors that can then be polymerized by ROMP. Critically, this combination of atom-economic catalytic transformations represents a far more straightforward route for the preparation of amine-functionalized polyolefins in comparison to traditional routes. Through the combination of a robust non-polar backbone with a polar functional group that possesses profound hydrogen-bonding interactions, these materials exhibit advanced properties and novel functions. The work in this thesis will serve to guide others in the future who apply and build upon these reactions to prepare diverse amine-containing materials with novel features.

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Appendices

Appendix A Tabulated raw energies from computational calculations with I-III

Table A.1 Tabulated raw energies from computational calculations with I

	E(B3PW91-D3/SVP)	E(B3PW91-D3/def2-qzvpp)	E(B3PW91-D3/def2-qzvpp) SMD	G(363)	$\Delta G(\text{B3PW91-D3/SVP})$ (kcal•mol ⁻¹)	G(363) (kcal•mol ⁻¹)
Propene	-117.787754	-117.9249259	-117.9281644	0.047643		
NIMePI	-326.588388	-326.9561141	-326.9661842	0.1049		
Product	-444.4248	-444.9235843	-444.9362179	0.181251		
TS-A1-A2ircf	-1770.87	-1772.801424	-1772.826627	0.728973	0.00	0.00
TS-A1-A2	-1770.83	-1772.758488	-1772.784021	0.726091	25.12	24.93
TS-A1-A2-ircr	-1770.86	-1772.788565	-1772.814978	0.73075	9.66	8.42
TS-ortho-ircr	-1770.87		-1772.825765	0.723891	-1.29	-2.65
TS-ortho	-1770.81527		-1772.770473	0.726708	33.88	33.82
TS-ortho-ircf	-1770.84		-1772.801024	0.729613	17.62	16.47
A2						
B1	-1444.24	-1445.807826	-1445.831127	0.590716	6.65	-2.54
TS-B1-B2ircf	-1562.04	-1563.739912	-1563.761158	0.667783	18.81	14.76
TS-B1-B2	-1562.03	-1563.735209	-1563.756315	0.672677	24.40	20.87
TS-B1-B2ircf	-1562.06	-1563.754821	-1563.779127	0.667349	6.61	3.21
C1						
TS-C1-C2ircf	-1888.67	-1890.731113	-1890.757874	0.817694	17.97	23.84
TS-C1-C2	-1888.64	-1890.696308	-1890.721446	0.808143	33.65	40.71
TS-C1-C2ircr	-1888.70	-1890.765336	-1890.791378	0.806657	-9.42	-4.11
C2						
TS-C2-C3	-1888.69	-1890.7548	-1890.787968	0.804229	-2.78	-3.49
	-1888.64	-1890.702186	-1890.735451	0.800315	27.69	27.01
	-1888.66	-1890.724917	-1890.757874	0.800695	14.49	13.18
	-1888.71		-1890.798598	0.80713	-13.91	-8.34
	-1888.62		-1890.70977	0.801107	40.88	43.62
	-1888.64		-1890.738451	0.804994	26.83	28.06
D1	-1444.23	-1445.79719	-1445.821044	0.59013	1.44	-4.84
	-1444.23	-1445.797189	-1445.821042	0.590081	1.41	-4.86
	-1444.24	-1445.807826	-1445.831127	0.590716	6.65	-10.80

Table A.2 Tabulated raw energies from computational calculations with II

	E(B3PW91-D3/SVP)	E(B3PW91-D3/def2-qzvpp) SMD	G(363)	$\Delta G(\text{B3PW91-D3/SVP})$ (kcal•mol ⁻¹)	G(363) (kcal•mol ⁻¹)
Propene	-117.787754	-117.9281644	0.047643		
NHMePh	-326.588388	-326.9661842	0.1049		
Product	-444.424800	-444.9362179	0.181251		
TS-A1-A2trans-ircf	-2089.399222	-2090.67152	0.202466	0.00	0.00
TS-A1-A2trans-	-2089.347034	-2090.618312	0.201939	32.42	33.06
TS-A1-A2trans-ircr	-2089.390686	-2090.662875	0.203418	5.95	6.02
TS-A1-A2trans-ircr-N	-1762.758934	-1763.661999	0.067655	13.80	8.42
TS-B1-B2trans-ircf-ene	-1762.758934	-1763.661998	0.067662	13.80	8.43
TS-B1-B2trans-ircf	-1880.562277	-1881.601966	0.143083	21.45	18.45
TS-B1-B2trans-	-1880.560957	-1881.599667	0.148458	25.65	23.27
TS-B1-B2trans-ircr	-1880.589743	-1881.62821	0.149703	8.37	6.14
TS-C1-C2trans-ircr-N	-1880.602645	-1881.636084	0.146018	-2.04	-1.11
TS-C1-C2trans-ircr	-2207.223721	-2208.623196	0.284184	-1.68	6.63
TS-C1-C2trans-	-2207.179365	-2208.57797	0.275447	20.68	29.53
TS-C1-C2trans-ircf	-2207.240316	-2208.642466	0.278304	-15.78	-9.15
TS-C2-C3trans-ircr	-2207.244378	-2208.643937	0.282542	-15.67	-7.42
TS-C2-C3trans-	-2207.181611	-2208.583915	0.277688	20.67	27.20
TS-C2-C3trans-ircf	-2207.238559	-2208.638015	0.285421	-10.21	-1.89
TS-C2-C3trans-ircf-N	-1762.758934	-1763.661999	0.067655	1.28	0.17
	-1762.758934	-1763.661999	0.067655	1.28	0.17

Table A.3 Tabulated raw energies from computational calculations with III

	E(B3PW91-D3/SVP)	E(B3PW91-D3/def2-qzvpp) SMD	G(363)	ΔG (B3PW91-D3)/SVP (kcal•mol ⁻¹)	G(363) (kcal•mol ⁻¹)
Propene	-117.787754	-117.9281644	0.047643		
NHMePh	-326.588388	-326.9661842	0.1049		
Product	-444.424800	-444.9362179	0.181251		
TS-A1-A2trans-ircf	-1669.194561	-1670.341397	0.233331	0.00	0.00
TS-A1-A2trans-	-1669.127268	-1670.274898	0.230702	39.94	40.08
TS-A1-A2trans-ircr	-1669.171318	-1670.31709	0.243043	20.28	21.35
TS-A1-A2trans-ircr-N	-1342.547637	-1343.327106	0.102449	15.81	13.88
TS-B1-B2trans-ircf-ene	-1342.547637	-1343.327099	0.102445	15.81	13.89
TS-B1-B2trans-ircf	-1460.347913	-1461.261783	0.17629	26.37	26.24
TS-B1-B2trans-	-1460.338220	-1461.253868	0.180395	35.22	33.78
TS-B1-B2trans-ircr	-1460.378035	-1461.292596	0.182696	13.74	10.92
TS-C1-C2trans-ircr-N	-1460.392137	-1461.302061	0.183625	6.16	5.56
TS-C1-C2trans-ircr	-1787.001998	-1788.279386	0.317511	15.31	16.76
TS-C1-C2trans-	-1786.963445	-1788.239526	0.311636	36.22	38.09
TS-C1-C2trans-ircf	-1787.031886	-1788.308126	0.314498	-5.31	-3.16
TS-C2-C3trans-ircr	-1787.040316	-1788.318652	0.312938	-12.04	-10.75
TS-C2-C3trans-	-1786.964959	-1788.243493	0.309882	32.38	34.50
TS-C2-C3trans-ircf	-1787.018066	-1788.292559	0.316611	4.32	7.93
TS-C2-C3trans-ircf-N	-1342.547637	-1343.3271	0.102444	7.13	5.63
	-1342.547637	-1343.327106	0.102449	7.13	5.62

Appendix B GC-FID kinetic method analysis: representative data from entry 249

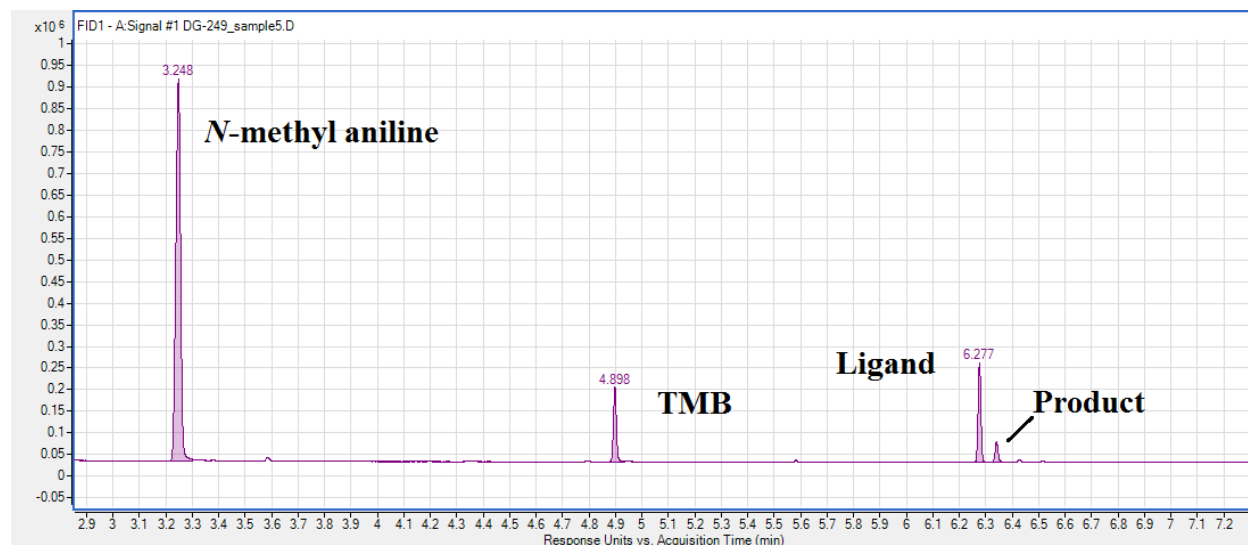


Figure B.1 Sample chromatogram from Figure 2.13, entry 249, sample 5

Table B.1 Reaction stoichiometry from Figure 2.13, entry 249

						'Master rxn'		Split Rxns		Quench Conc t ₀
	MW	d	moles	mass /g	vol /mL	conc /M	ppm /mg/L	conc /M	ppm /mg/L	ppm /mg/L
[Ta]	617.66		2.2E-05	0.0135		0.0347	21448	0.00694	4290	107
TMB	168.19		5.6E-05	0.0095		0.090	15093	0.01795	3019	75.5
Octene d7-	112.21	0.715	0.00064	0.0715	0.100	1.012	11359	0.20246	22719	568
NMA	107.15	0.989	0.00044	0.0475	0.048	0.704	75419	0.14077	15084	377
d8-tol	100.19	0.943		0.454	0.481					
Total Volum e /mL					0.629					

Table B.2 Raw Data from Figure 2.13, entry 249

Sample0

Peak	RT	Area	Area %	Height
1	3.211	795823.18	100	375230.19
2	4.159	35099.46	4.41	33011.62
3	4.856	101861.12	12.8	123337.52
4	6.235	114191.19	14.35	158923.74

Sample 1

1	3.211	253296.78	100	120559.36
2	4.159	12044.75	4.76	11847.75
3	4.856	32675.44	12.9	38850.32
4	6.235	36085.83	14.25	48765.63
1	6.235	36085.83	100	48765.63
2	6.3	672.94	1.86	950.81

Sample 2

1	3.212	688584.48	100	319992.09
2	4.16	30636.73	4.45	28387.41
3	4.856	88595.34	12.87	106913.91
4	6.235	99281.35	14.42	134702.42
1	6.235	99281.35	100	134702.42
2	6.3	3701.51	3.73	4885.9

Sample 3

1	3.21	770809.52	100	365955.12
2	4.158	36221.94	4.7	34007.63
3	4.856	99566.36	12.92	123123.27
4	6.235	111817.67	14.51	150934.97
5	6.299	10320.19	1.34	13697.5

Sample 4

1	3.212	530844.7	100	246160.72
2	4.159	23608.34	4.45	22474.97
3	4.857	69202.85	13.04	84514.28
4	6.235	77216.54	14.55	105572.68
5	6.299	10960.16	2.06	14223.33

Sample 5

1	3.213	548393.91	100	255722.16
2	4.159	24321.81	4.44	22424.06
3	4.857	71617.06	13.06	87396.68
4	6.235	80192.28	14.62	110756.02
5	6.299	18366.34	3.35	24425.86

Sample 6

1	3.214	697526.41	100	319963.44
2	4.159	26008.67	3.73	23959.64
3	4.857	93249.39	13.37	113442.1
4	6.235	104546.16	14.99	144626.29
5	6.3	35698.2	5.12	45518.16

Table B.3 Analyzed data for entry 249 to calculate plots in Figure 2.13

Name	rxn time /h	R NMA /TMB	PPM	mM in vial	mM in rxn	R Prod /TMB	PPM	mM in vial	mM in rxn
DG- 249_0	0	8.172462	460.1309	4.030579	161.2232	0	0.283697	0.001804	0.072142
DG- 249_1	0.5	8.171165	460.0588	4.029948	161.1979	0.0185	1.130199	0.007185	0.2874
DG- 249_2	1	8.183893	460.7664	4.036146	161.4458	0.038851	2.061413	0.013105	0.524199
DG- 249_3	1.5	8.262687	465.1471	4.074519	162.9808	0.101696	4.937047	0.031386	1.255447
DG- 249_4	2	8.133241	457.9504	4.011478	160.4591	0.155279	7.388901	0.046973	1.878932
DG- 249_4ii	2	8.033095	452.3826	3.962707	158.5083	0.158063	7.516286	0.047783	1.911325
DG- 249_5	3	7.977682	449.3018	3.93572	157.4288	0.264713	12.39634	0.078807	3.15228
DG- 249_6	4.5	7.793907	439.0846	3.846221	153.8488	0.392038	18.22239	0.115845	4.633792

Appendix C X-Ray Crystallographic Data

Structure refinement and analysis were performed using Olex2 software.¹²¹

Table C.1 Crystallographic parameters for complex 2.4

	2.4
Empirical formula	C ₁₈ H ₃₆ N ₅ OTa
Formula weight	519.47
Temperature/K	90
Crystal system	monoclinic
Space group	P2 ₁ /n
a/Å	8.8312(7)
b/Å	20.7066(18)
c/Å	12.1066(10)
α /°	90
β /°	99.140(2)
γ /°	90
Volume/Å ³	2185.8(3)
Z	4
ρ_{calc} /cm ³	1.579
μ /mm ⁻¹	5.044
F(000)	1040.0
Crystal size/mm ³	0.408 × 0.401 × 0.341
Radiation	MoK α (λ = 0.71073)
2 θ range for data collection/°	3.934 to 60.2
Index ranges	-12 ≤ h ≤ 12, -26 ≤ k ≤ 29, -17 ≤ l ≤ 17
Reflections collected	46262
Independent reflections	6425 [R_{int} = 0.0249, R_{sigma} = 0.0146]
Data/restraints/parameters	6425/0/236
Goodness-of-fit on F ²	1.227
Final R indexes [$I \geq 2\sigma(I)$]	R_1 = 0.0154, wR_2 = 0.0334
Final R indexes [all data]	R_1 = 0.0168, wR_2 = 0.0337
Largest diff. peak/hole / e Å ⁻³	0.87/-1.37

Table C.2 Crystallographic parameters for complex 2.5

	2.5
Empirical formula	C ₁₄ H ₃₆ N ₅ OTa
Formula weight	471.42
Temperature/K	90
Crystal system	triclinic
Space group	P-1
a/Å	8.4228(6)
b/Å	9.9793(7)
c/Å	11.5424(8)
$\alpha/^\circ$	91.612(2)
$\beta/^\circ$	92.761(2)
$\gamma/^\circ$	92.452(2)
Volume/Å ³	967.72(12)
Z	2
$\rho_{\text{calc}}/\text{g}/\text{cm}^3$	1.831
μ/mm^{-1}	5.698
F(000)	536.0
Crystal size/mm ³	0.09 × 0.082 × 0.051
Radiation	MoK α (λ = 0.71073)
2 Θ range for data collection/ $^\circ$	3.534 to 58.342
Index ranges	-11 ≤ h ≤ 11, -13 ≤ k ≤ 11, -15 ≤ l ≤ 15
Reflections collected	19435
Independent reflections	5209 [R_{int} = 0.0457, R_{sigma} = 0.0450]
Data/restraints/parameters	5209/0/180
Goodness-of-fit on F ²	1.361
Final R indexes [$I \geq 2\sigma(I)$]	R_1 = 0.0509, wR_2 = 0.1279
Final R indexes [all data]	R_1 = 0.0551, wR_2 = 0.1294
Largest diff. peak/hole / e Å ⁻³	5.56/-4.39

Table C.3 Crystallographic parameters for complex 2.7

	2.7
Empirical formula	C ₂₄ H ₇₂ N ₁₂ O ₄ Ta ₄
Formula weight	1316.73
Temperature/K	90
Crystal system	cubic
Space group	I-43d
a/Å	26.4748(14)
b/Å	26.4748(14)
c/Å	26.4748(14)
$\alpha/^\circ$	90
$\beta/^\circ$	90
$\gamma/^\circ$	90
Volume/Å ³	18557(3)
Z	16
$\rho_{\text{calc}}/\text{g}/\text{cm}^3$	1.885
μ/mm^{-1}	9.440
F(000)	9984.0
Crystal size/mm ³	0.182 × 0.178 × 0.108
Radiation	MoK α (λ = 0.71073)
2 Θ range for data collection/ $^\circ$	3.768 to 86.672
Index ranges	-31 ≤ h ≤ 36, -51 ≤ k ≤ 44, -31 ≤ l ≤ 30
Reflections collected	32329
Independent reflections	6842 [R_{int} = 0.6457, R_{sigma} = 0.2493]
Data/restraints/parameters	6842/0/141
Goodness-of-fit on F ²	1.704
Final R indexes [$I \geq 2\sigma(I)$]	R_1 = 0.4990, wR_2 = 0.8104
Final R indexes [all data]	R_1 = 0.5170, wR_2 = 0.8257
Largest diff. peak/hole / e Å ⁻³	16.72/-19.03
Flack parameter	0.5(3)

Table C.4 Crystallographic parameters for complex 3.8

	3.8
Empirical formula	C ₂₀ H ₃₆ Cl ₂ N ₄ O ₃ Ta ₂
Formula weight	424.67
Temperature/K	90
Crystal system	monoclinic
Space group	P2 ₁ /c
a/Å	18.6109(18)
b/Å	10.6878(10)
c/Å	28.071(3)
α/°	90
β/°	93.311(5)
γ/°	90
Volume/Å ³	5574.3(9)
Z	15
ρ _{calc} /g/cm ³	1.898
μ/mm ⁻¹	7.403
F(000)	3107.0
Crystal size/mm ³	0.512 × 0.386 × 0.377
Radiation	MoKα (λ = 0.71073)
2θ range for data collection/°	2.906 to 61.176
Index ranges	-26 ≤ h ≤ 23, -14 ≤ k ≤ 15, -37 ≤ l ≤ 40
Reflections collected	65640
Independent reflections	17051 [R _{int} = 0.0498, R _{sigma} = 0.0468]
Data/restraints/parameters	17051/0/615
Goodness-of-fit on F ²	1.044
Final R indexes [I ≥ 2σ (I)]	R ₁ = 0.0292, wR ₂ = 0.0573
Final R indexes [all data]	R ₁ = 0.0360, wR ₂ = 0.0592
Largest diff. peak/hole / e Å ⁻³	1.95/-1.22

Table C.5 Crystallographic parameters for complex 5.2

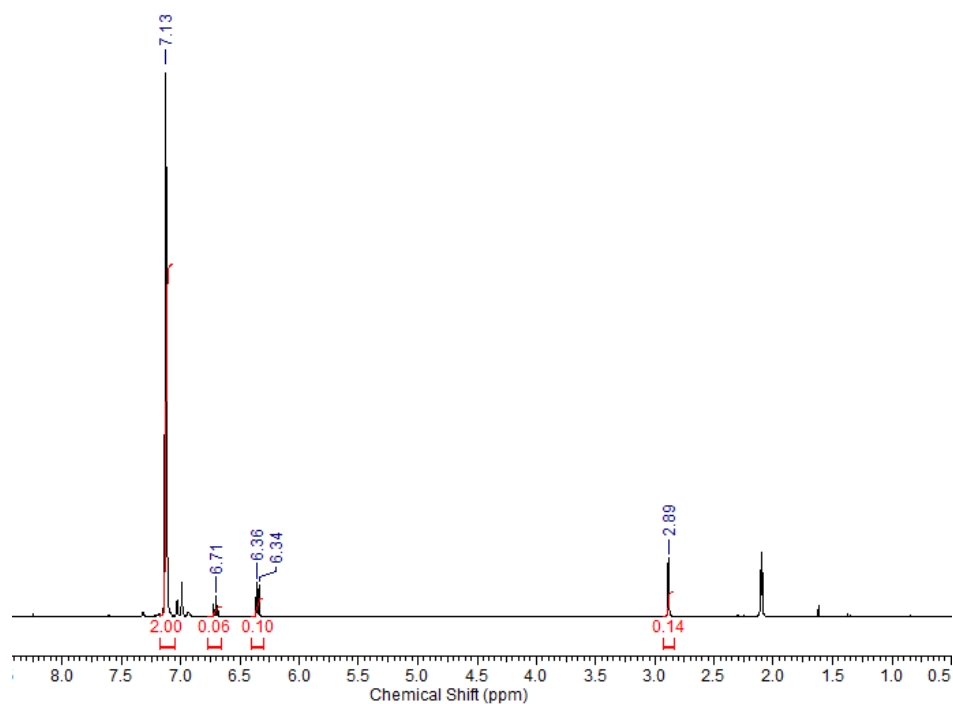
	5.2
Empirical formula	C ₆₀ H ₅₀ Cl ₂ O ₄ P ₃ Ru
Formula weight	1099.88
Temperature/K	90
Crystal system	monoclinic
Space group	C2/c
a/Å	21.104(5)
b/Å	16.623(4)
c/Å	37.445(9)
$\alpha/^\circ$	90
$\beta/^\circ$	98.500(5)
$\gamma/^\circ$	90
Volume/Å ³	12991(6)
Z	8
$\rho_{\text{calc}}/\text{g}/\text{cm}^3$	1.125
μ/mm^{-1}	0.436
F(000)	4520.0
Crystal size/mm ³	0.331 × 0.294 × 0.201
Radiation	MoK α (λ = 0.71073)
2 Θ range for data collection/ $^\circ$	3.132 to 50.99
Index ranges	-25 ≤ h ≤ 25, -20 ≤ k ≤ 20, -45 ≤ l ≤ 45
Reflections collected	81622
Independent reflections	12020 [R_{int} = 0.0693, R_{sigma} = 0.0483]
Data/restraints/parameters	12020/0/727
Goodness-of-fit on F ²	1.140
Final R indexes [$I \geq 2\sigma(I)$]	R_1 = 0.1196, wR_2 = 0.2984
Final R indexes [all data]	R_1 = 0.1369, wR_2 = 0.3094
Largest diff. peak/hole / e Å ⁻³	5.76/-1.86

Table C.6 Crystallographic parameters for complex 5.6

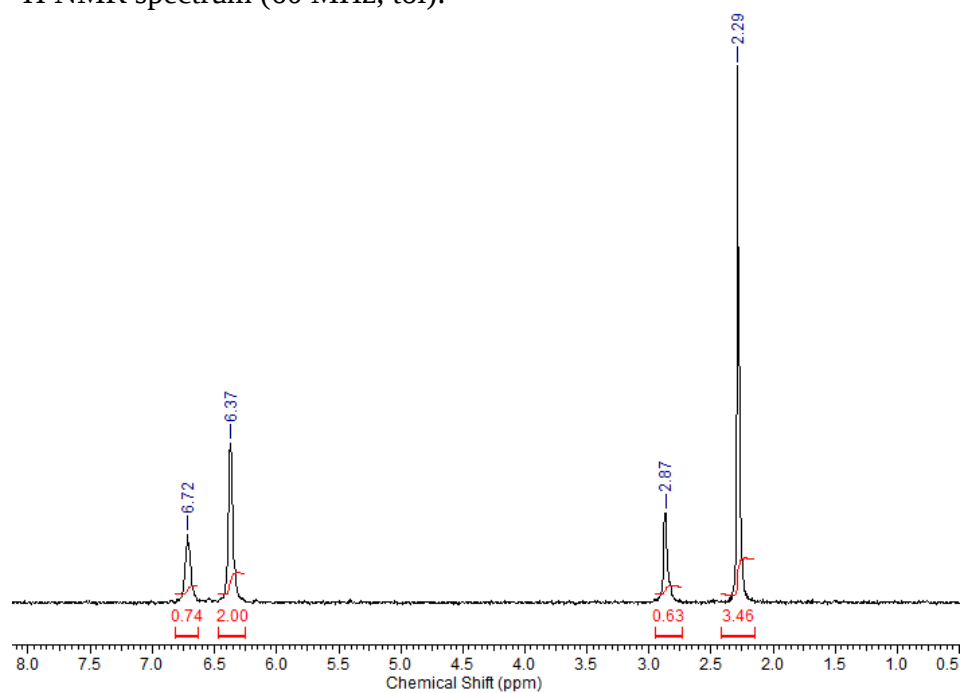
5.6	
Empirical formula	C ₆₇ H _{0.5} Cl ₁₃ O ₈ P ₃ Ru
Formula weight	1588.00
Temperature/K	90
Crystal system	triclinic
Space group	P-1
a/Å	14.3139(9)
b/Å	16.8758(9)
c/Å	18.4122(10)
α /°	96.854(3)
β /°	112.106(2)
γ /°	104.769(2)
Volume/Å ³	3867.8(4)
Z	2
ρ_{calc} /g/cm ³	1.364
μ /mm ⁻¹	0.761
F(000)	1553.0
Crystal size/mm ³	0.222 × 0.218 × 0.122
Radiation	MoK α (λ = 0.71073)
2 Θ range for data collection/°	2.572 to 54.34
Index ranges	-18 ≤ h ≤ 18, -17 ≤ k ≤ 21, -23 ≤ l ≤ 22
Reflections collected	62824
Independent reflections	16949 [R _{int} = 0.0251, R _{sigma} = 0.0269]
Data/restraints/parameters	16949/0/803
Goodness-of-fit on F ²	1.558
Final R indexes [I ≥ 2 σ (I)]	R ₁ = 0.0981, wR ₂ = 0.3244
Final R indexes [all data]	R ₁ = 0.1098, wR ₂ = 0.3466
Largest diff. peak/hole / e Å ⁻³	5.39/-2.24

Appendix D Selected NMR Spectra

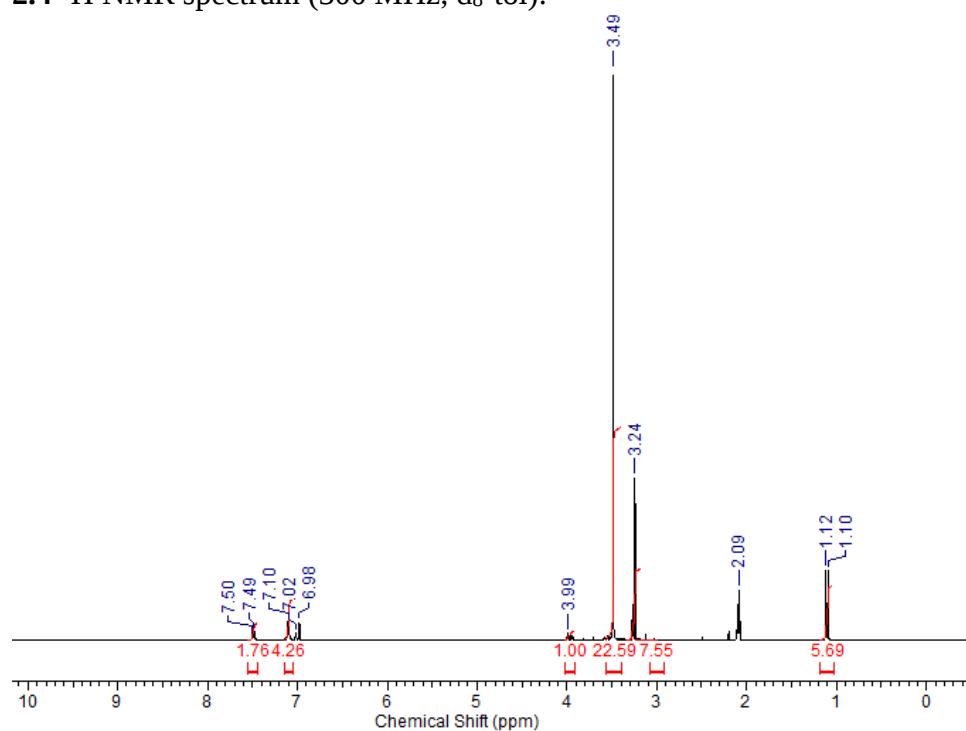
2.1 ^1H NMR spectrum (300 MHz, $\text{d}_8\text{-tol}$):



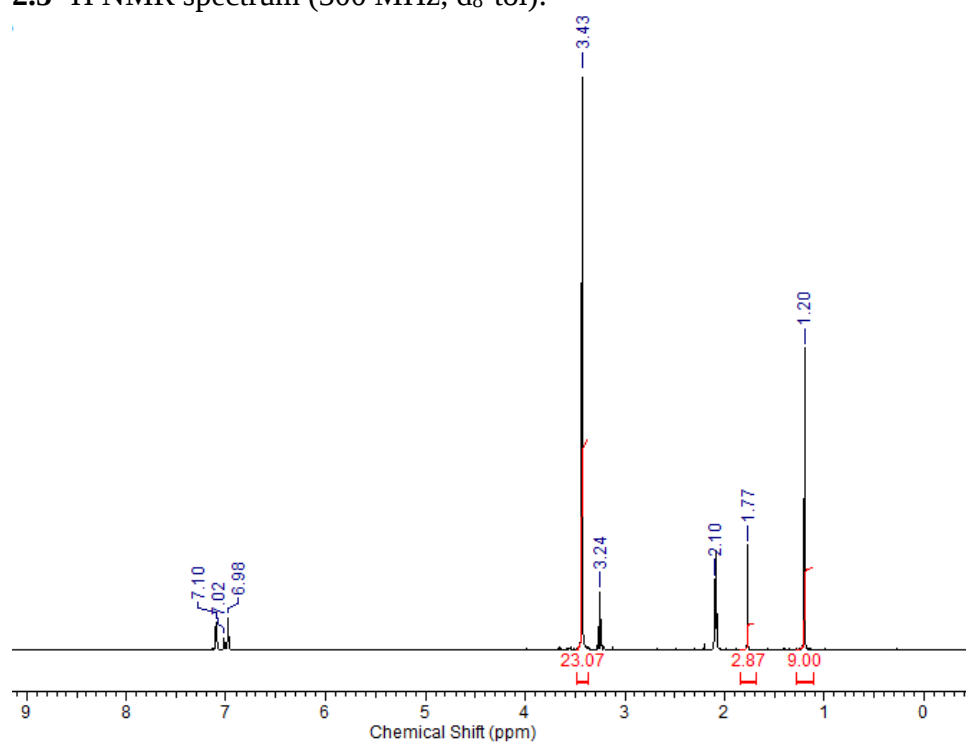
^2H NMR spectrum (60 MHz, tol):



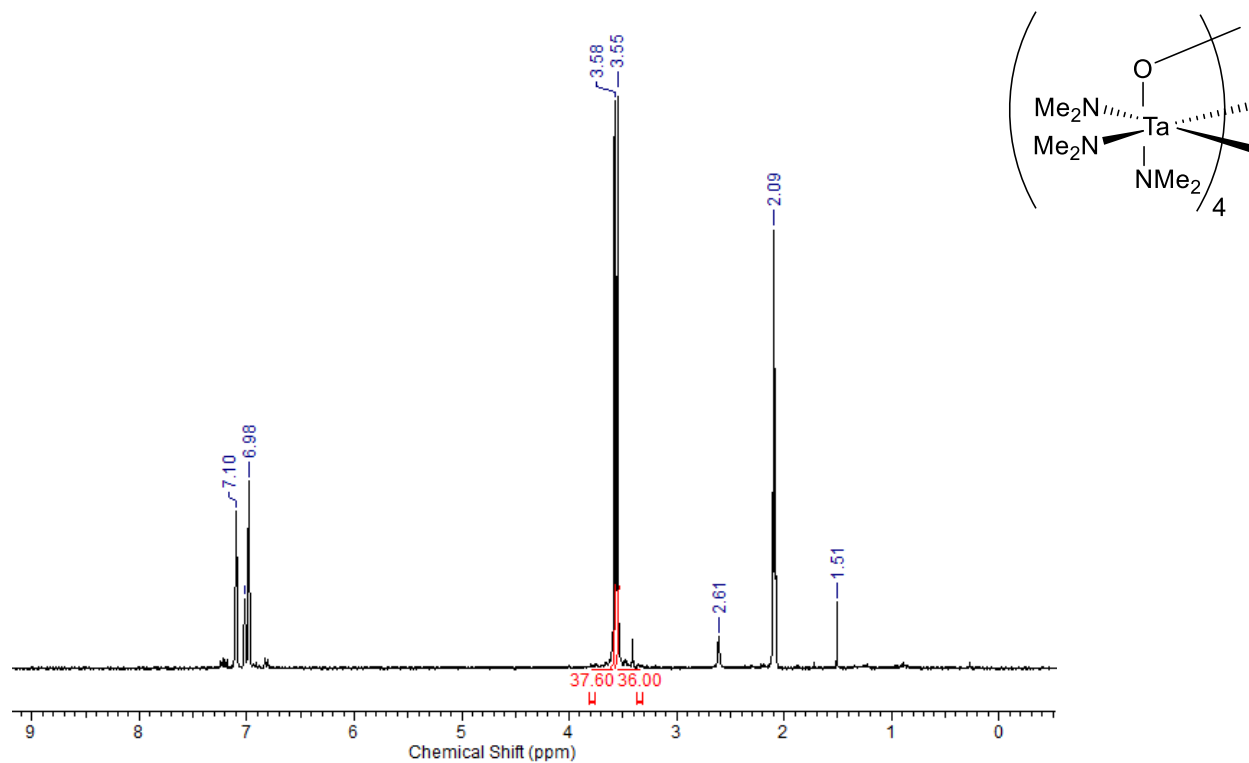
2.4 ^1H NMR spectrum (300 MHz, $\text{d}_8\text{-tol}$):



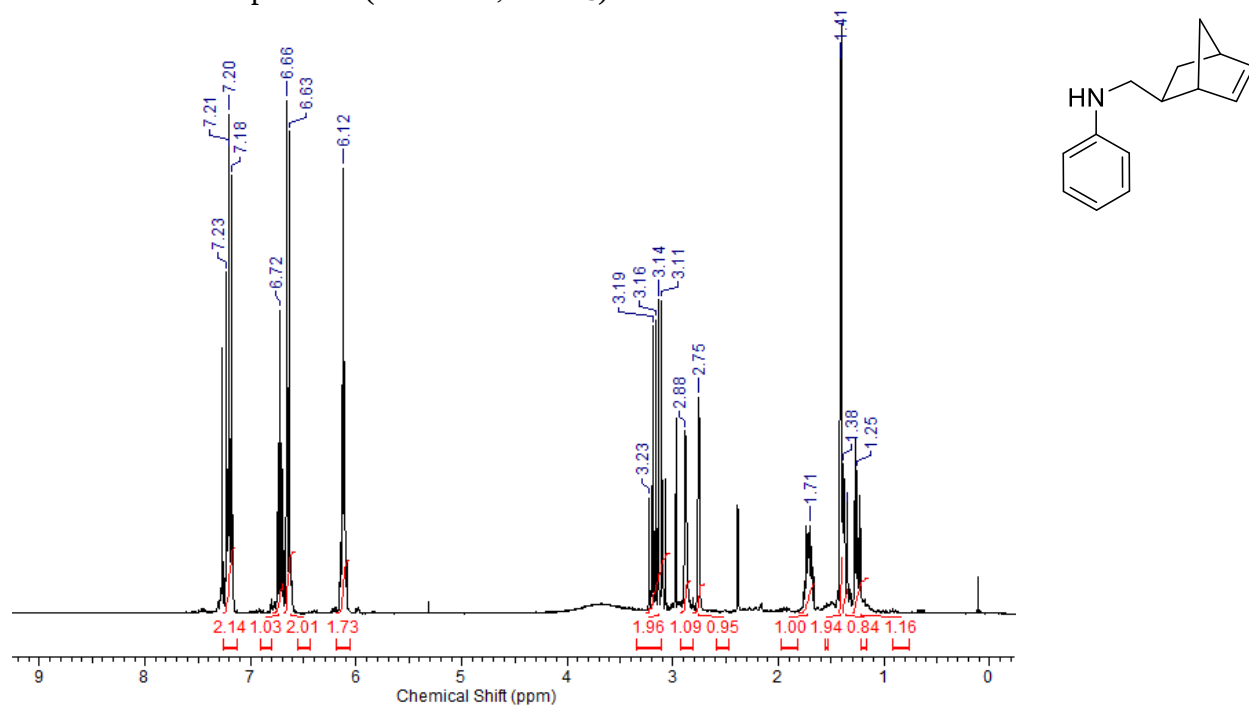
2.5 ^1H NMR spectrum (300 MHz, $\text{d}_8\text{-tol}$):



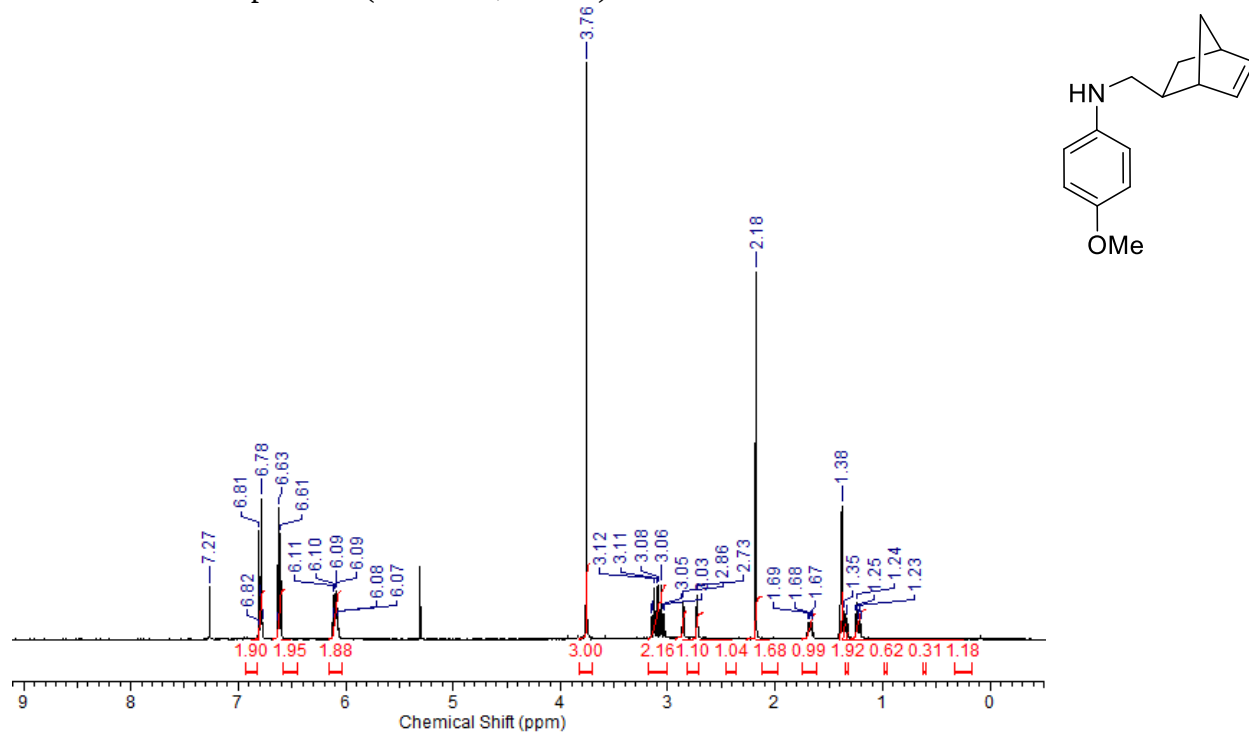
2.7 ^1H NMR spectrum (300 MHz, $\text{d}_8\text{-tol}$):



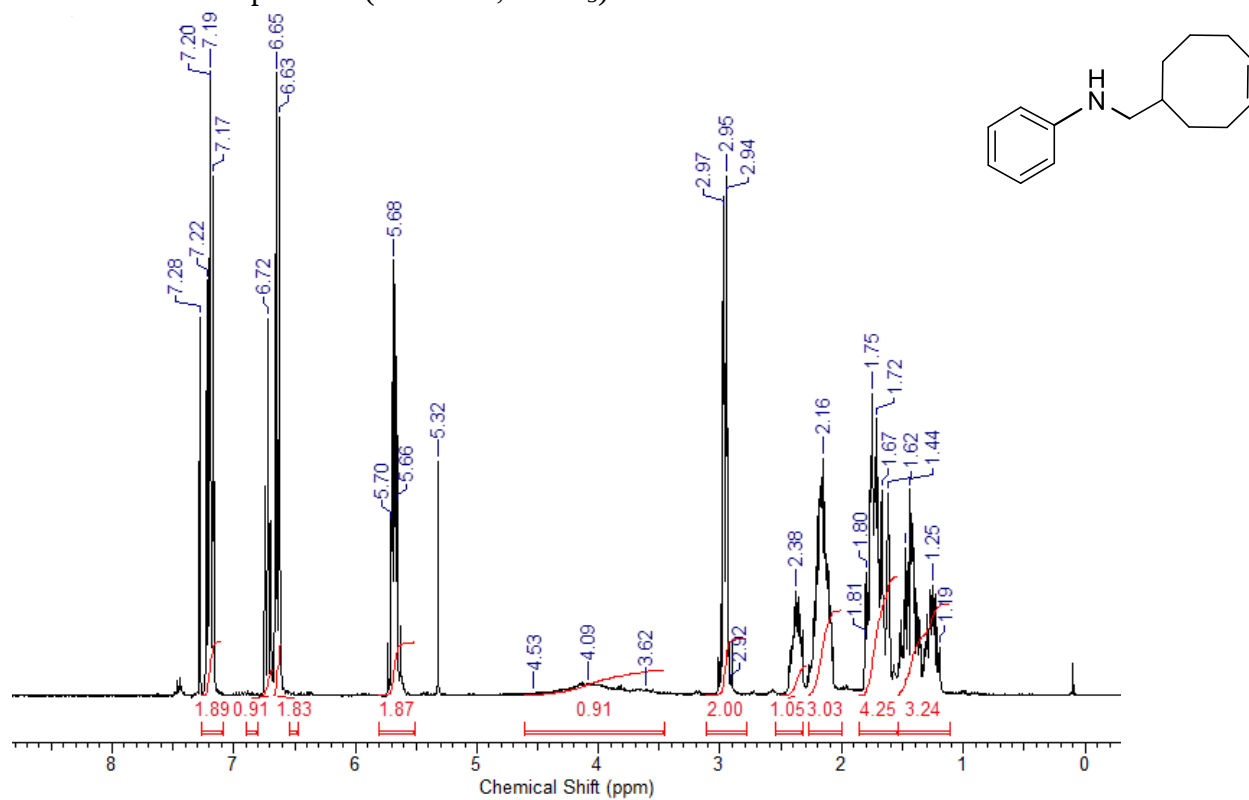
ACN-1 ^1H NMR spectrum (300 MHz, CDCl_3):



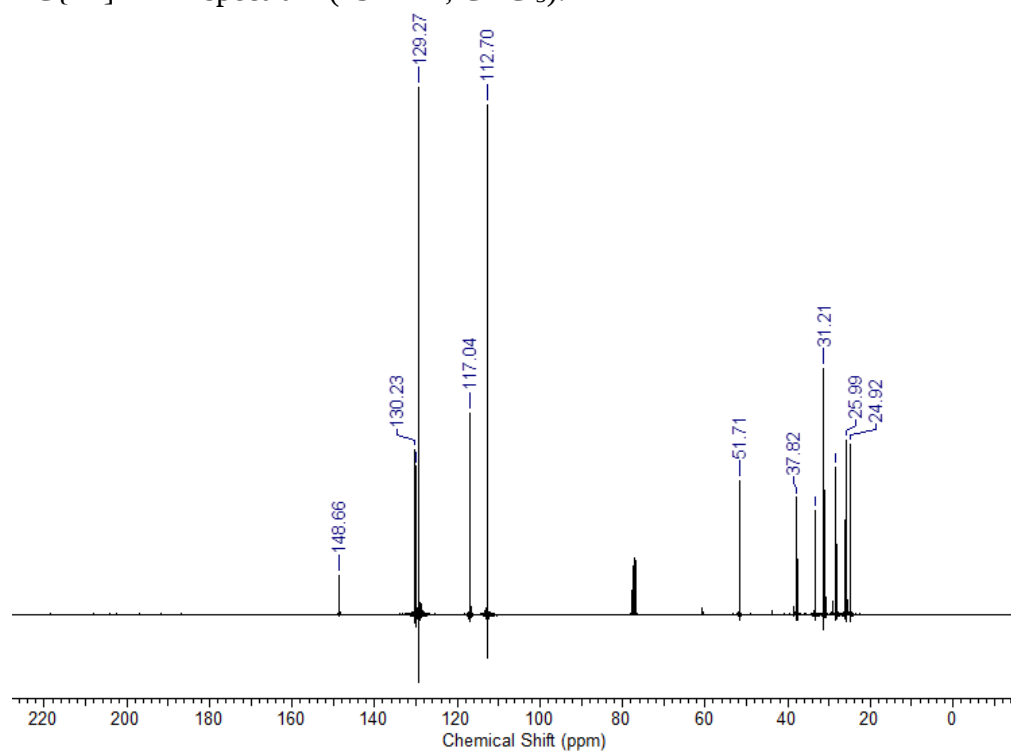
ACN-4 ^1H NMR spectrum (400 MHz, CDCl_3):



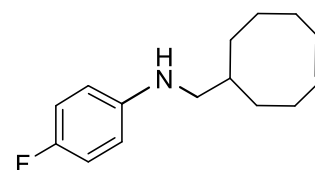
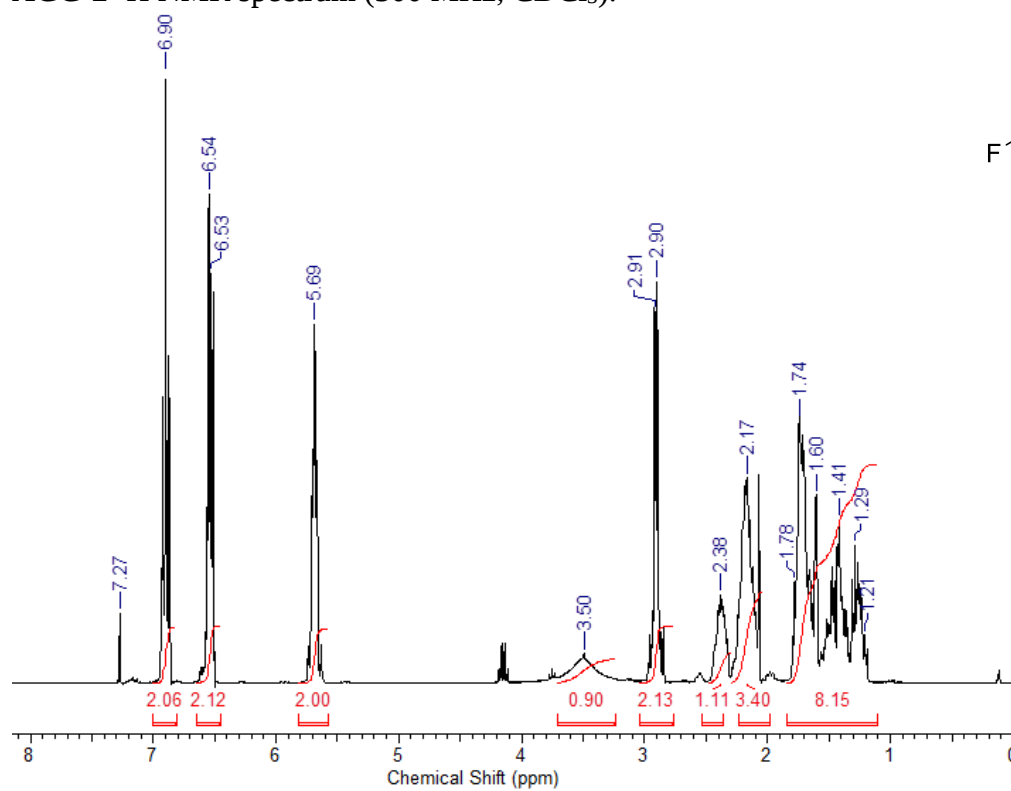
ACC-1 ^1H NMR spectrum (400 MHz, CDCl_3):



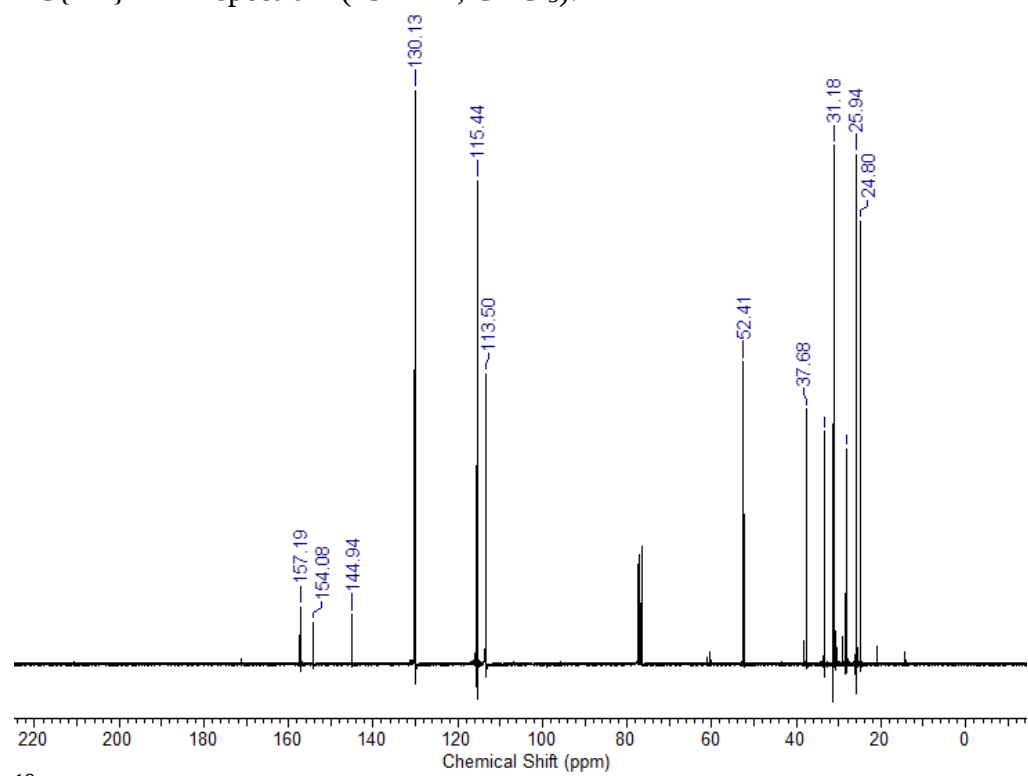
$^{13}\text{C}\{^1\text{H}\}$ NMR spectrum (75 MHz, CDCl_3):



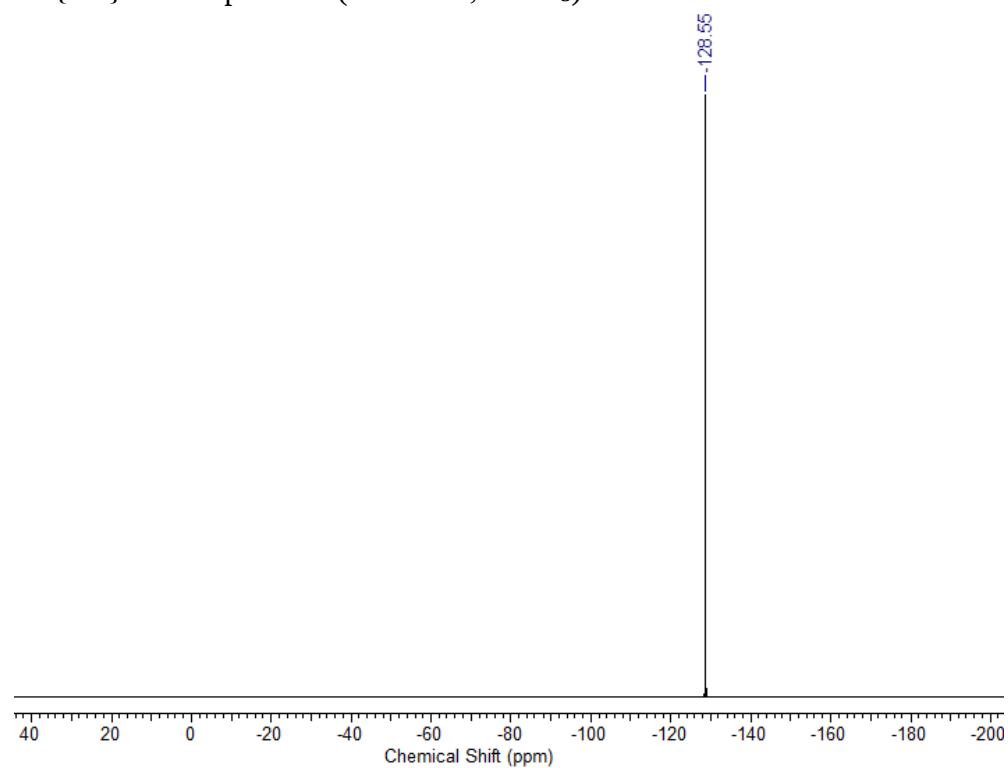
ACC-2 ^1H NMR spectrum (300 MHz, CDCl_3):



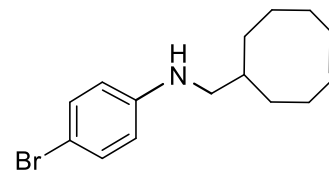
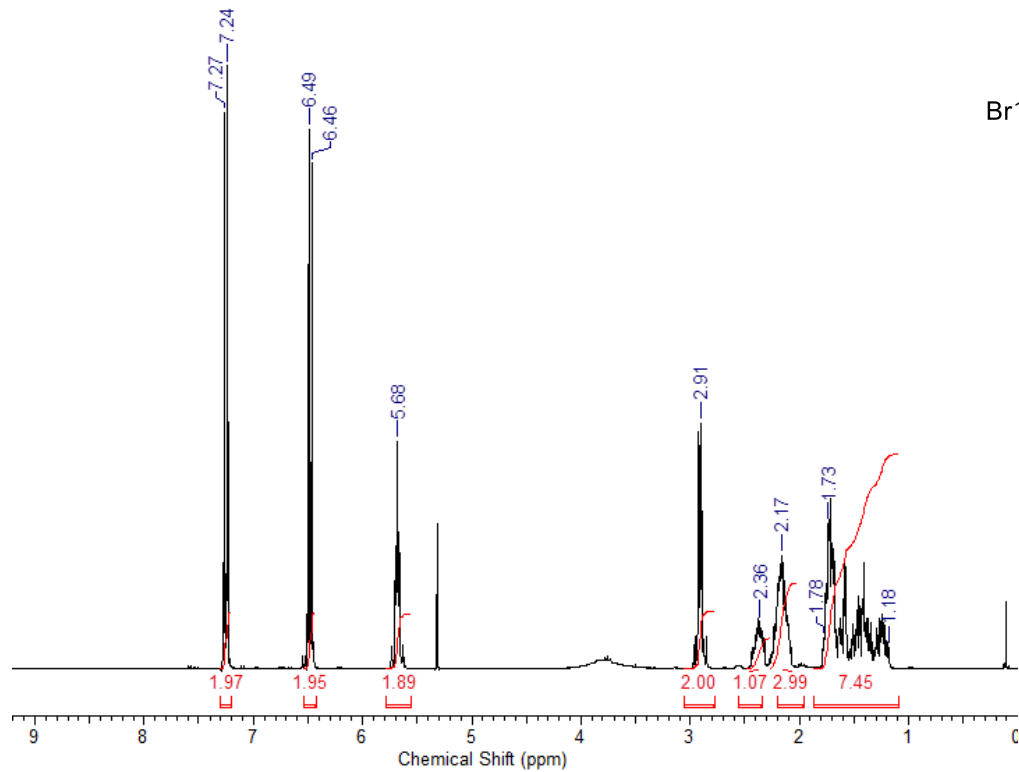
$^{13}\text{C}\{^1\text{H}\}$ NMR spectrum (75 MHz, CDCl_3):



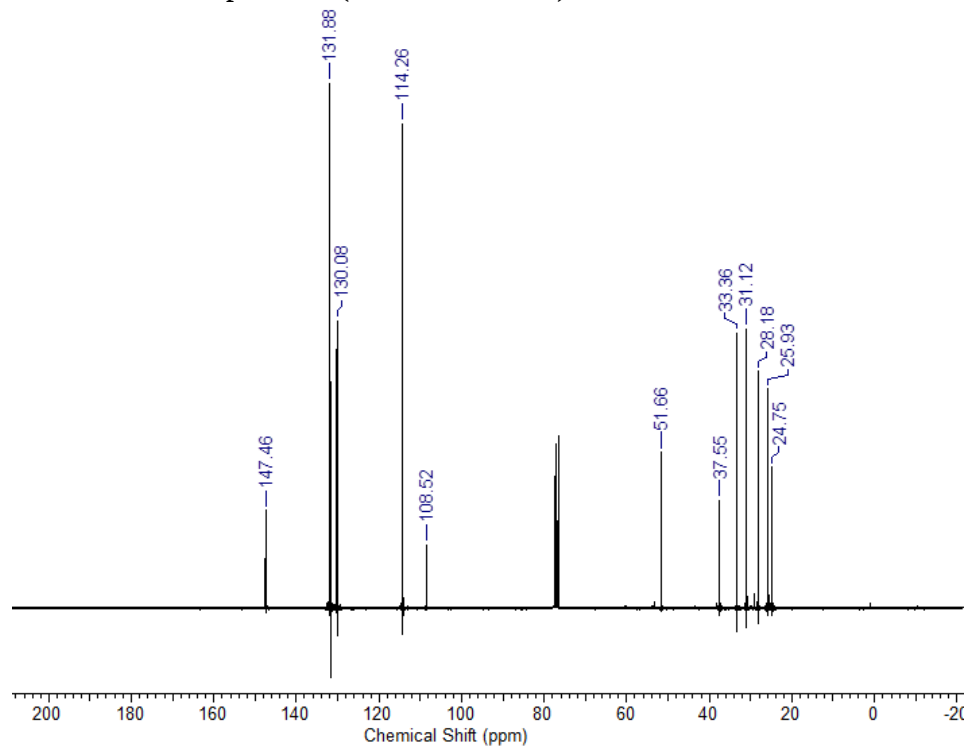
$^{19}\text{F}\{^1\text{H}\}$ NMR spectrum (282 MHz, CDCl_3):



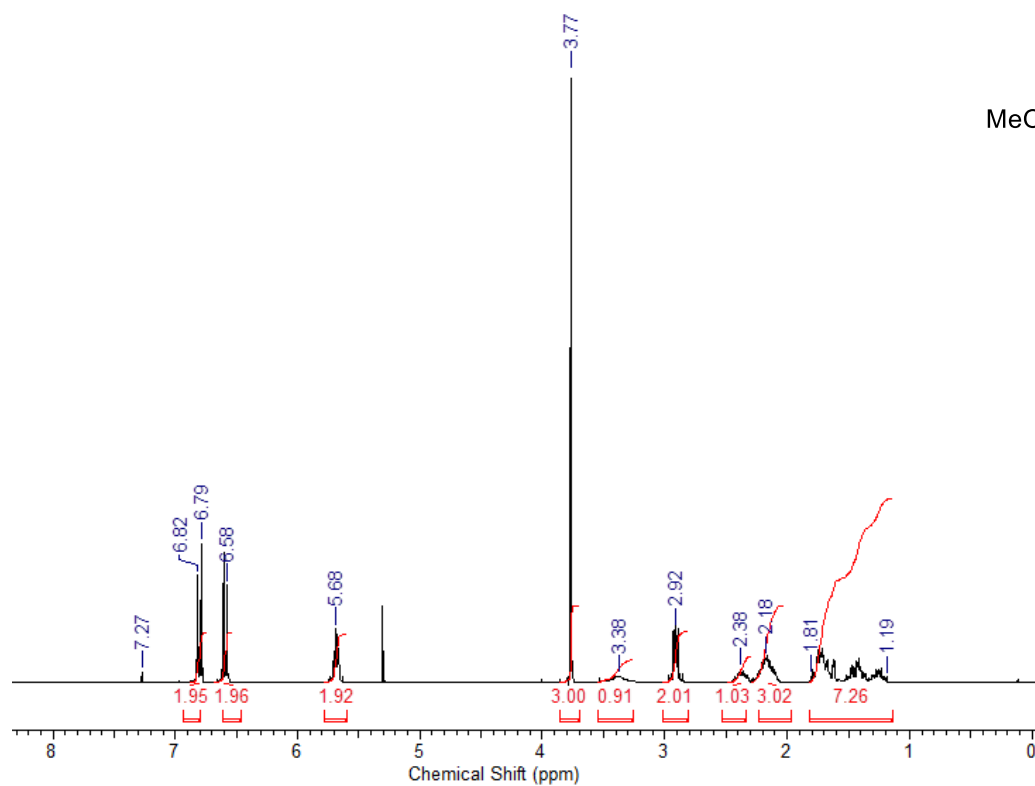
ACC-3 ^1H NMR spectrum (300 MHz, CDCl_3):



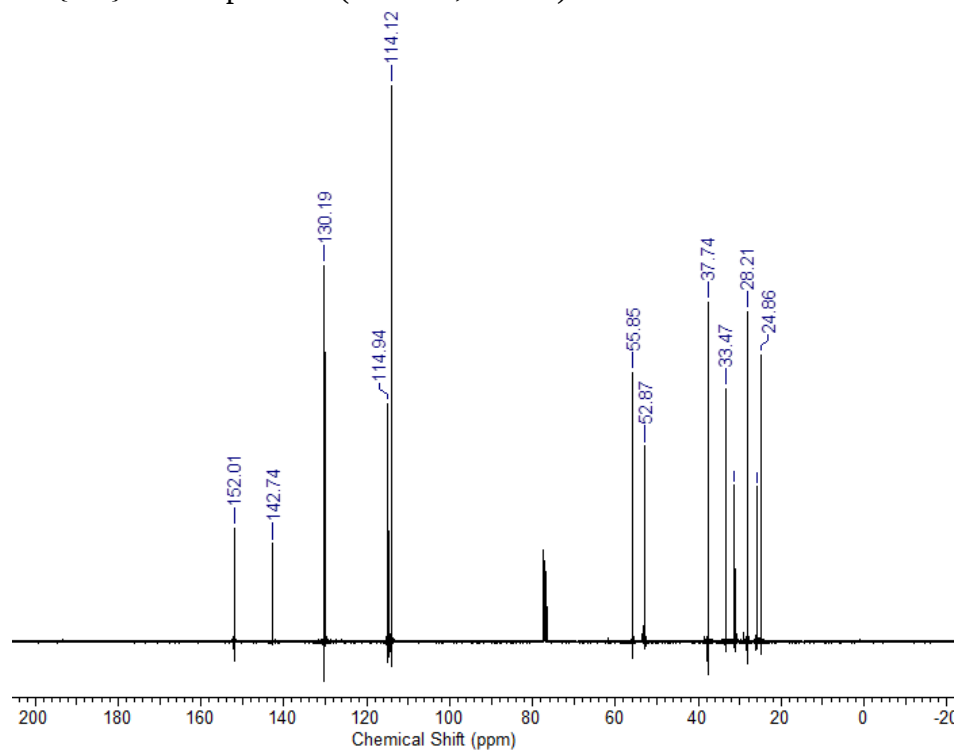
$^{13}\text{C}\{^1\text{H}\}$ NMR spectrum (75 MHz, CDCl_3):



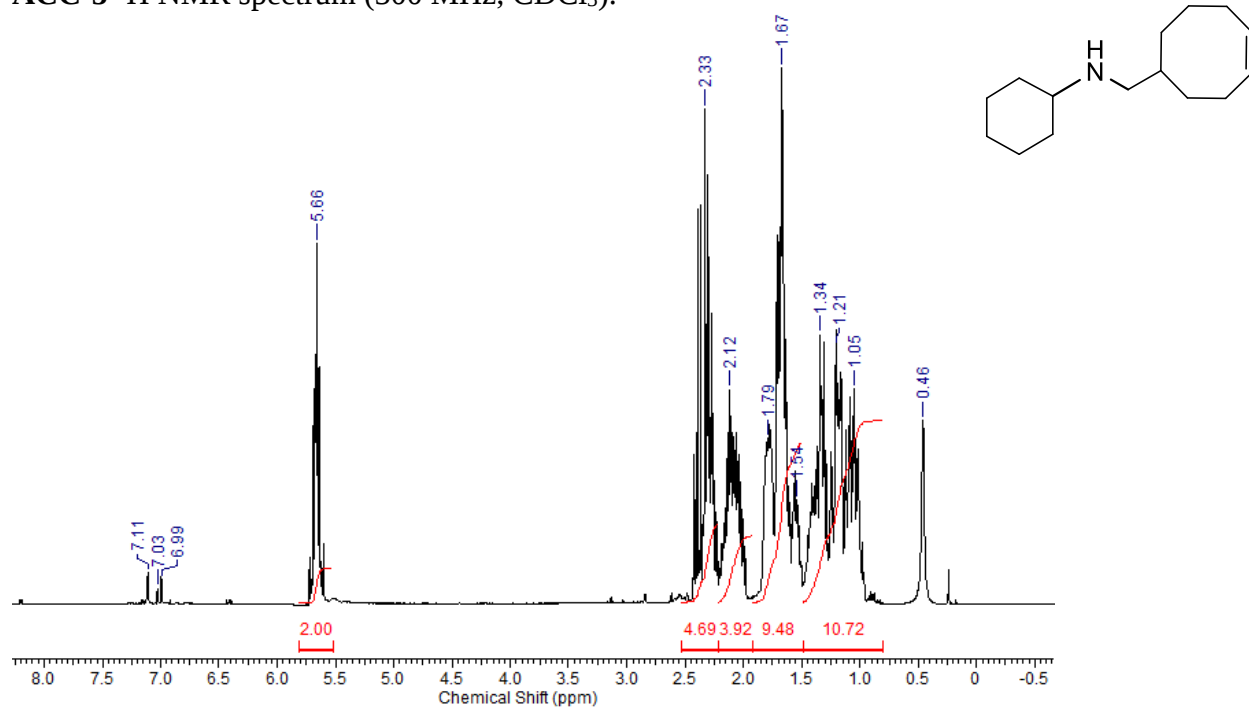
ACC-4 ^1H NMR spectrum (300 MHz, CDCl_3):



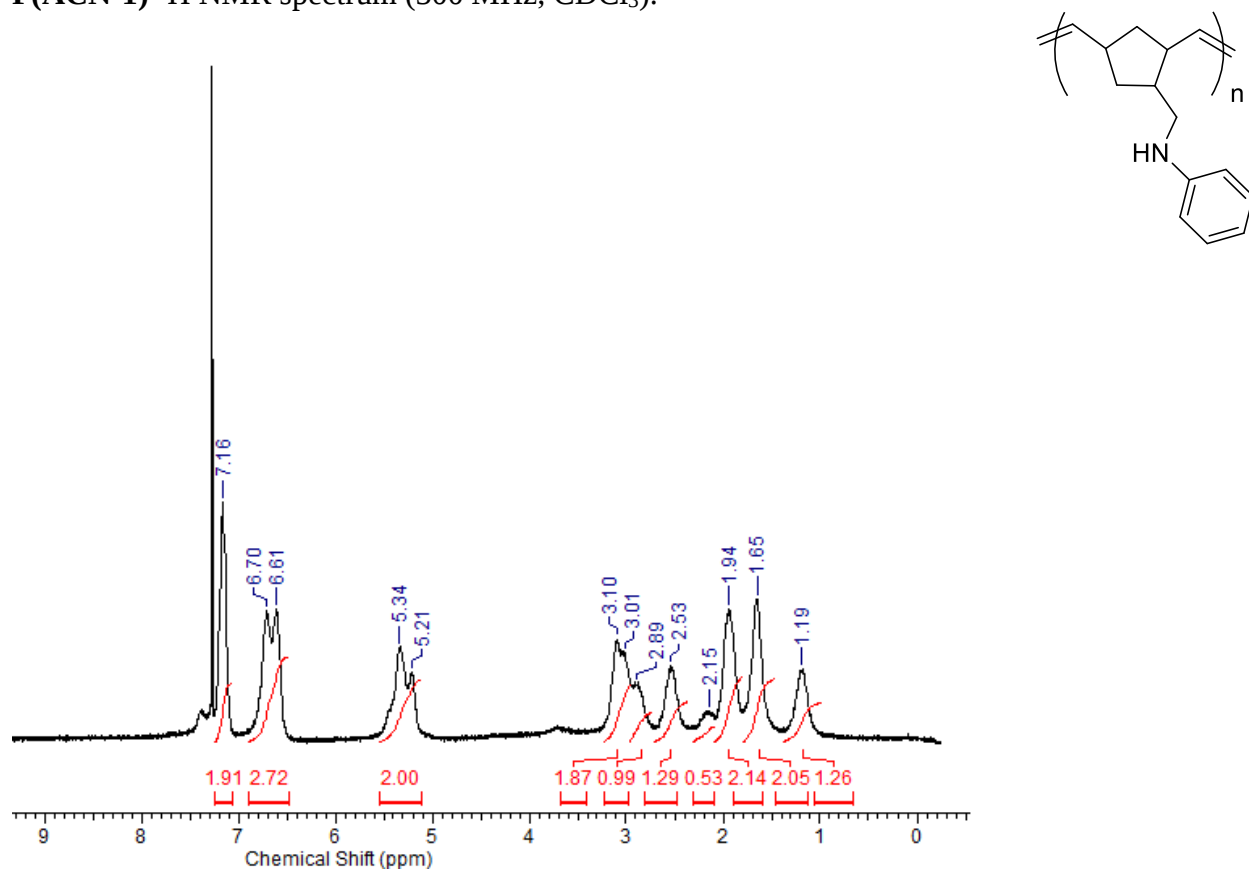
$^{13}\text{C}\{^1\text{H}\}$ NMR spectrum (75 MHz, CDCl_3):



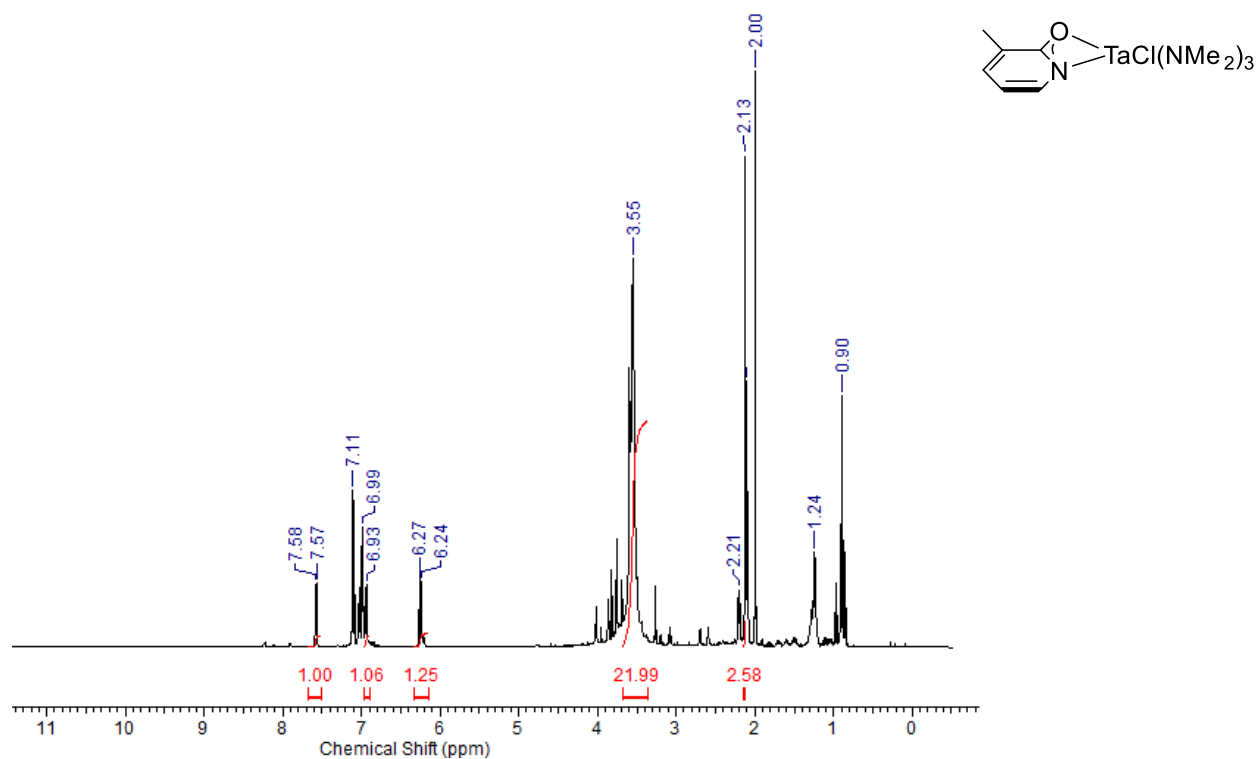
ACC-5 ^1H NMR spectrum (300 MHz, CDCl_3):



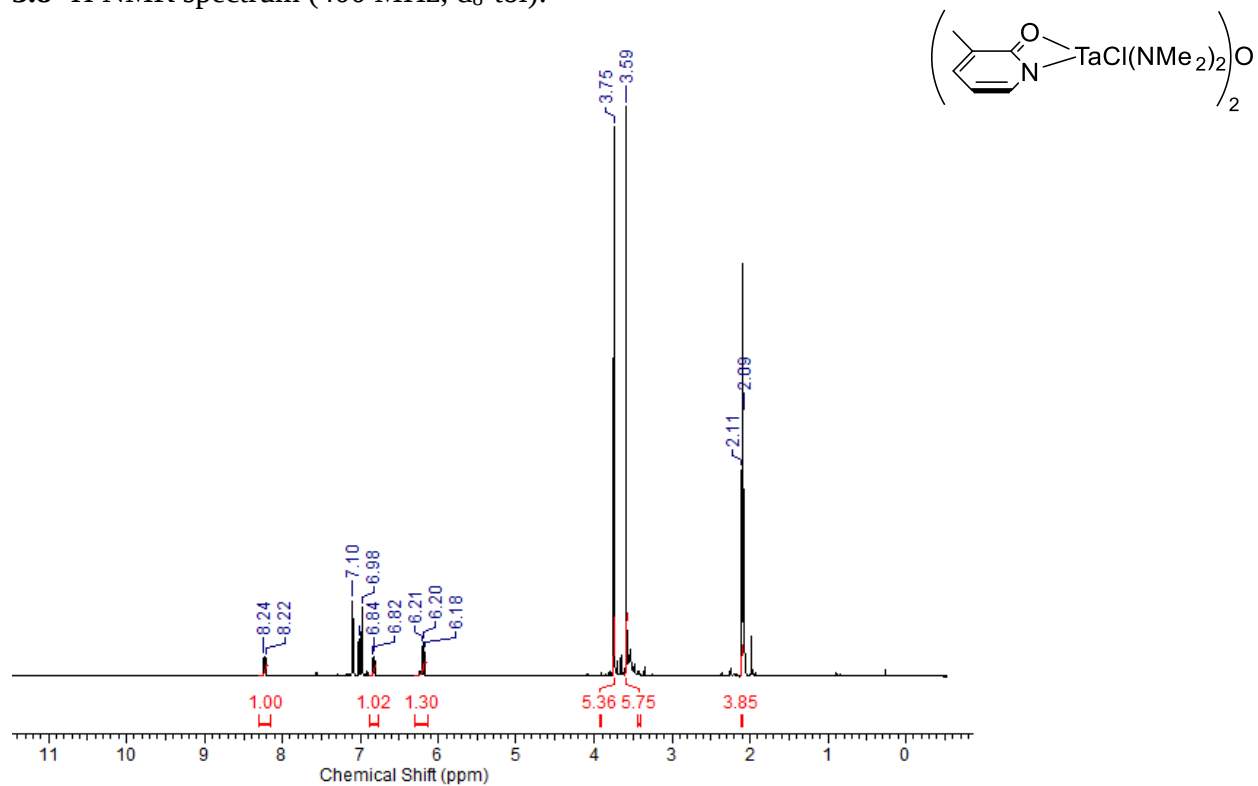
P(ACN-1) ^1H NMR spectrum (300 MHz, CDCl_3):



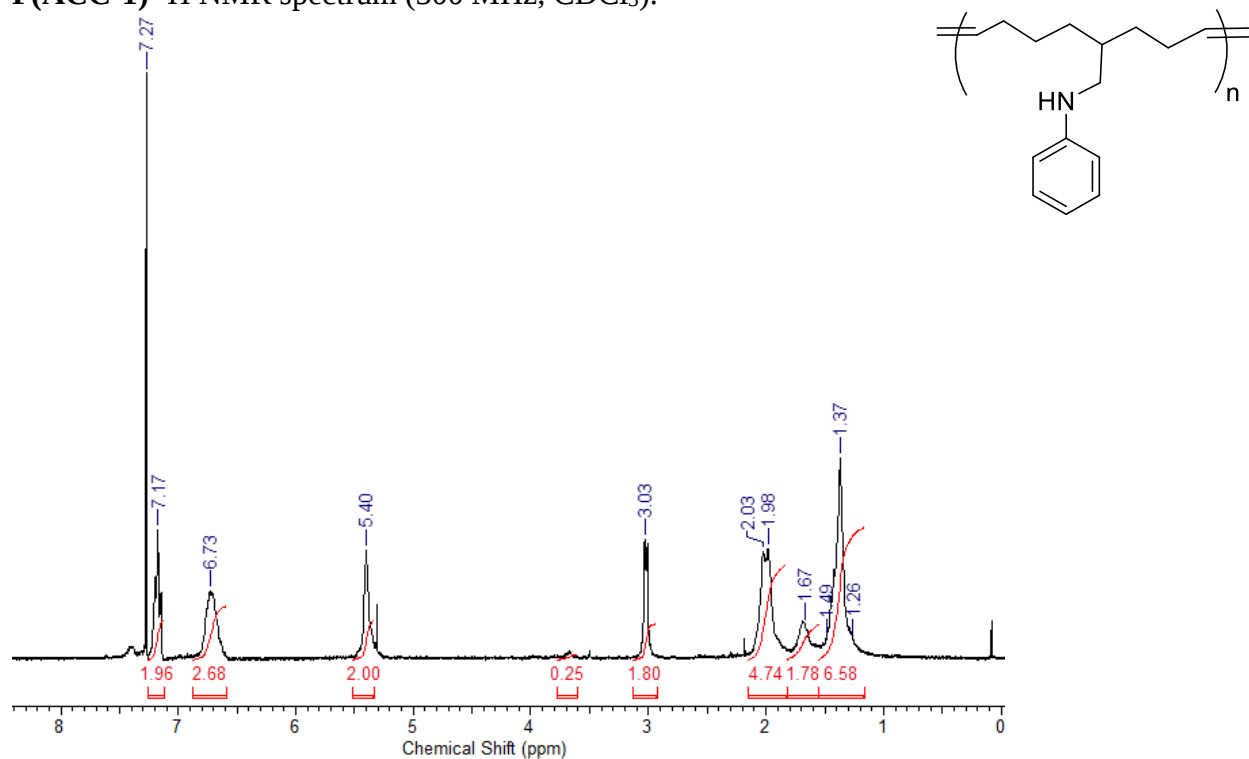
1.9 (Crude Mixture) ^1H NMR spectrum (400 MHz, $\text{d}_8\text{-tol}$):



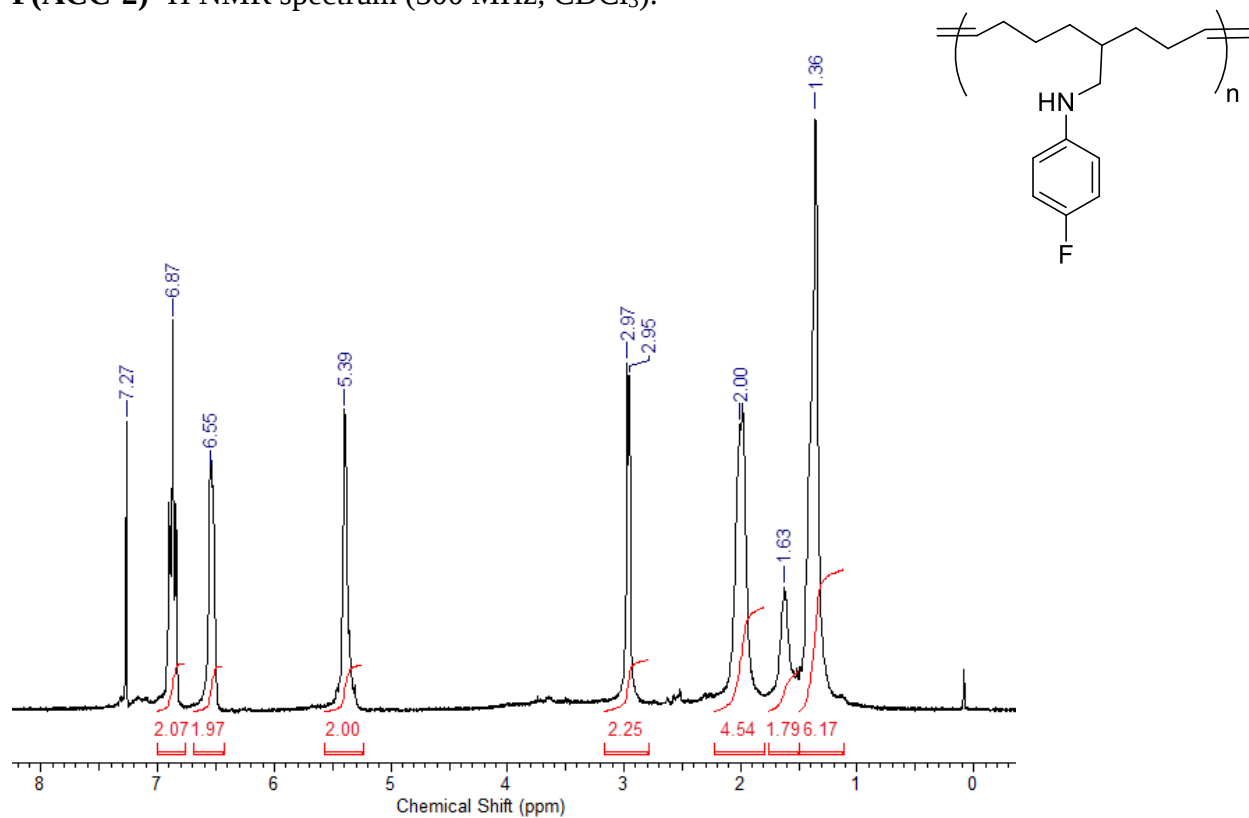
3.8 ^1H NMR spectrum (400 MHz, $\text{d}_8\text{-tol}$):



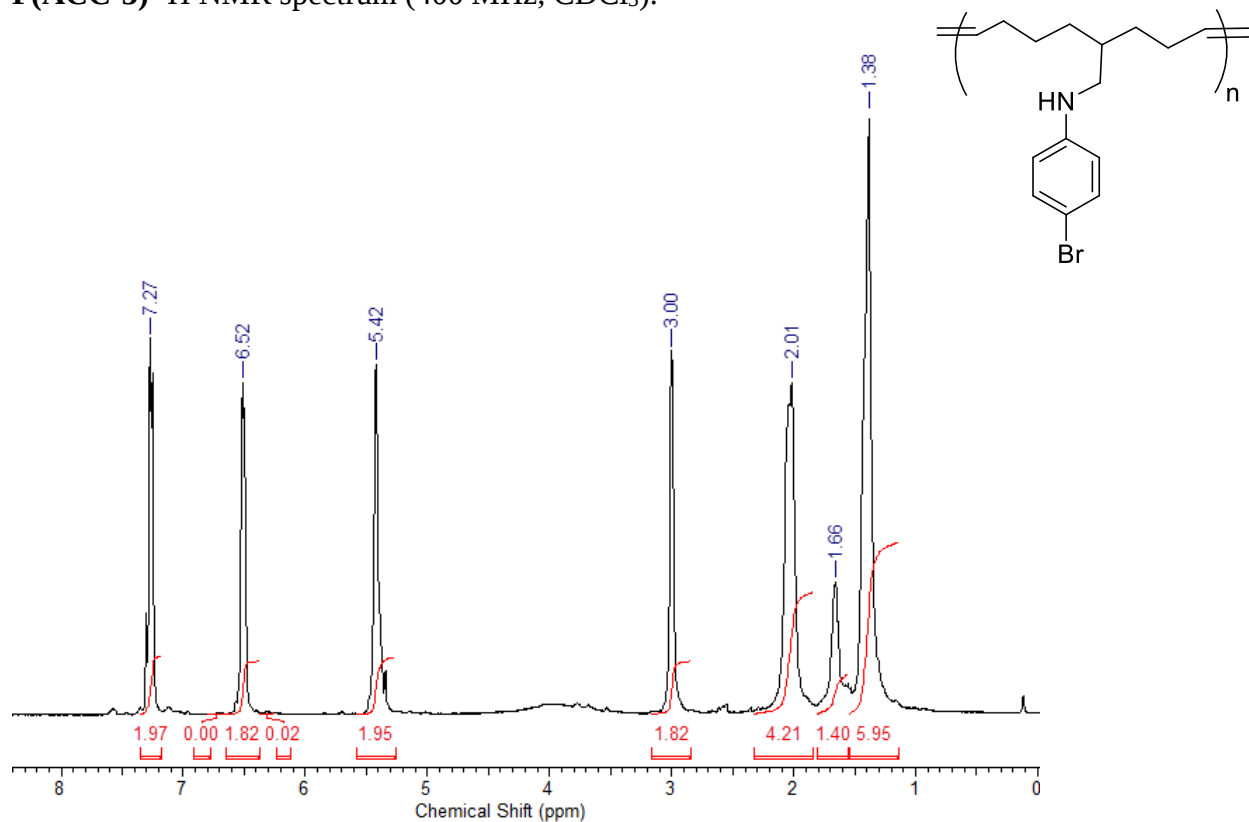
P(ACC-1) ^1H NMR spectrum (300 MHz, CDCl_3):



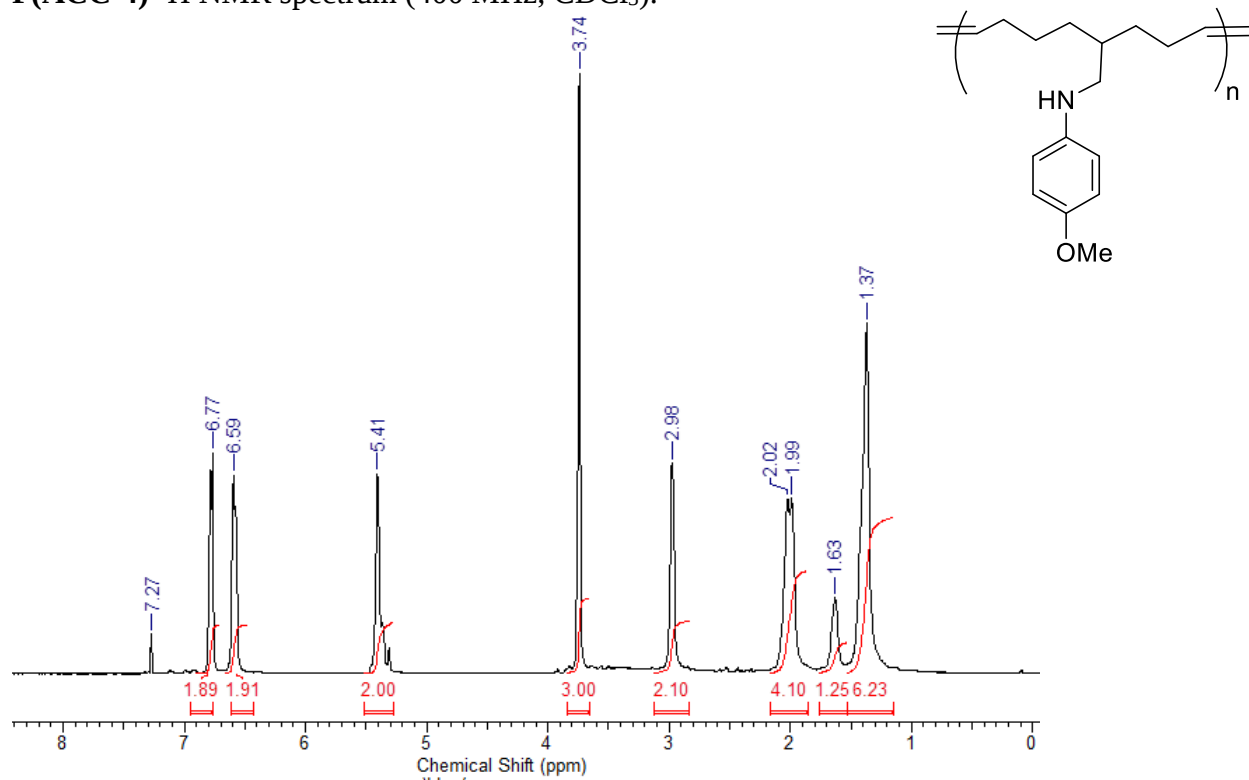
P(ACC-2) ^1H NMR spectrum (300 MHz, CDCl_3):



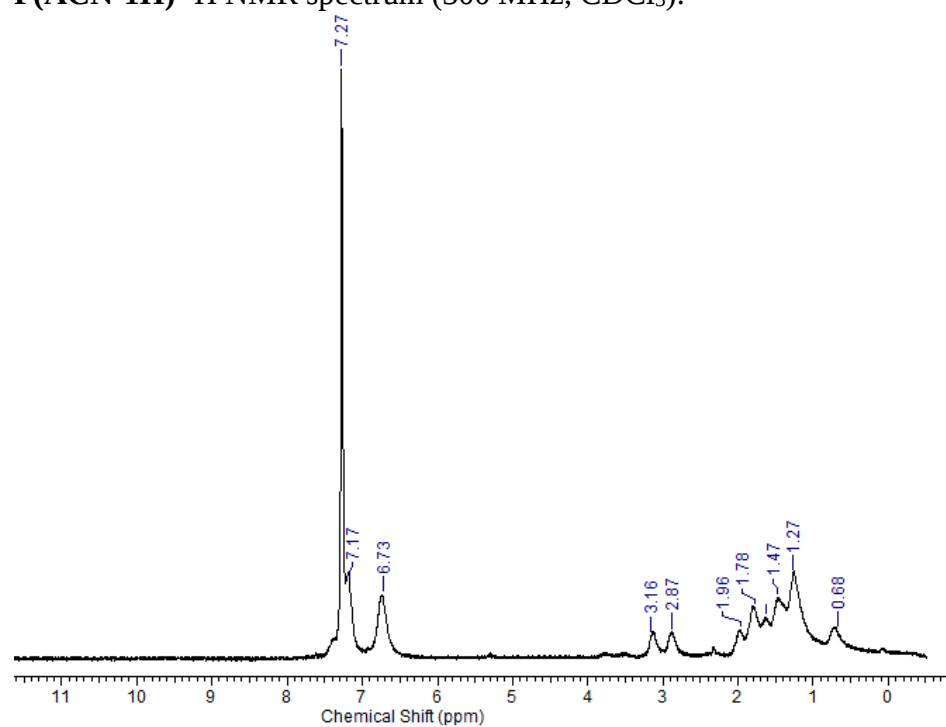
P(ACC-3) ^1H NMR spectrum (400 MHz, CDCl_3):



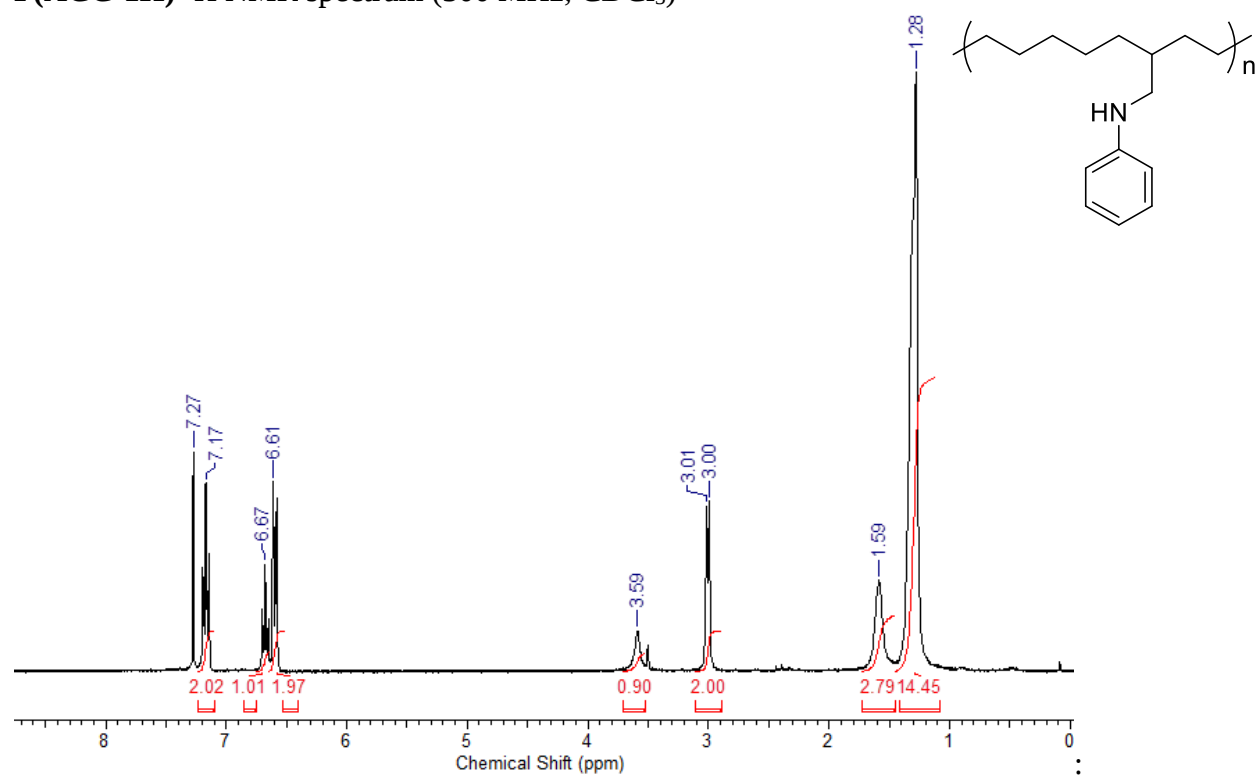
P(ACC-4) ^1H NMR spectrum (400 MHz, CDCl_3):



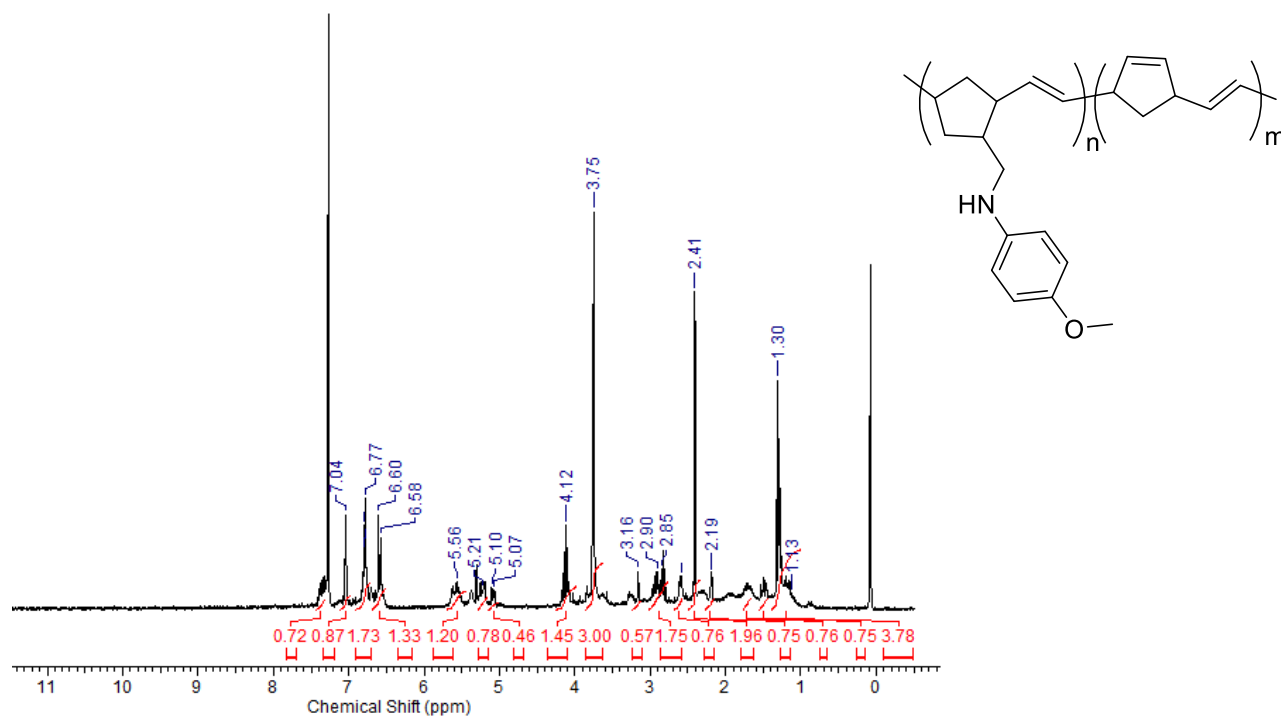
P(ACN-1H) ^1H NMR spectrum (300 MHz, CDCl_3):



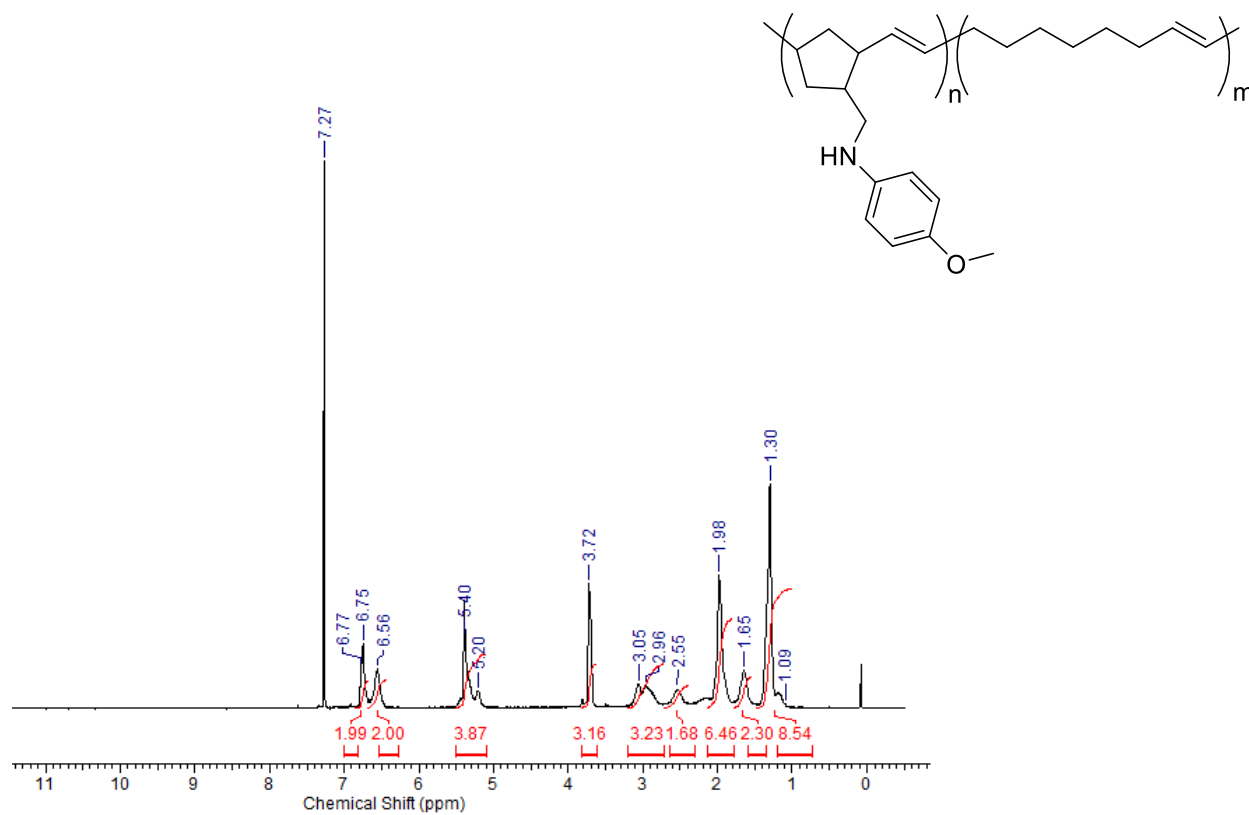
P(ACC-1H) ^1H NMR spectrum (300 MHz, CDCl_3)



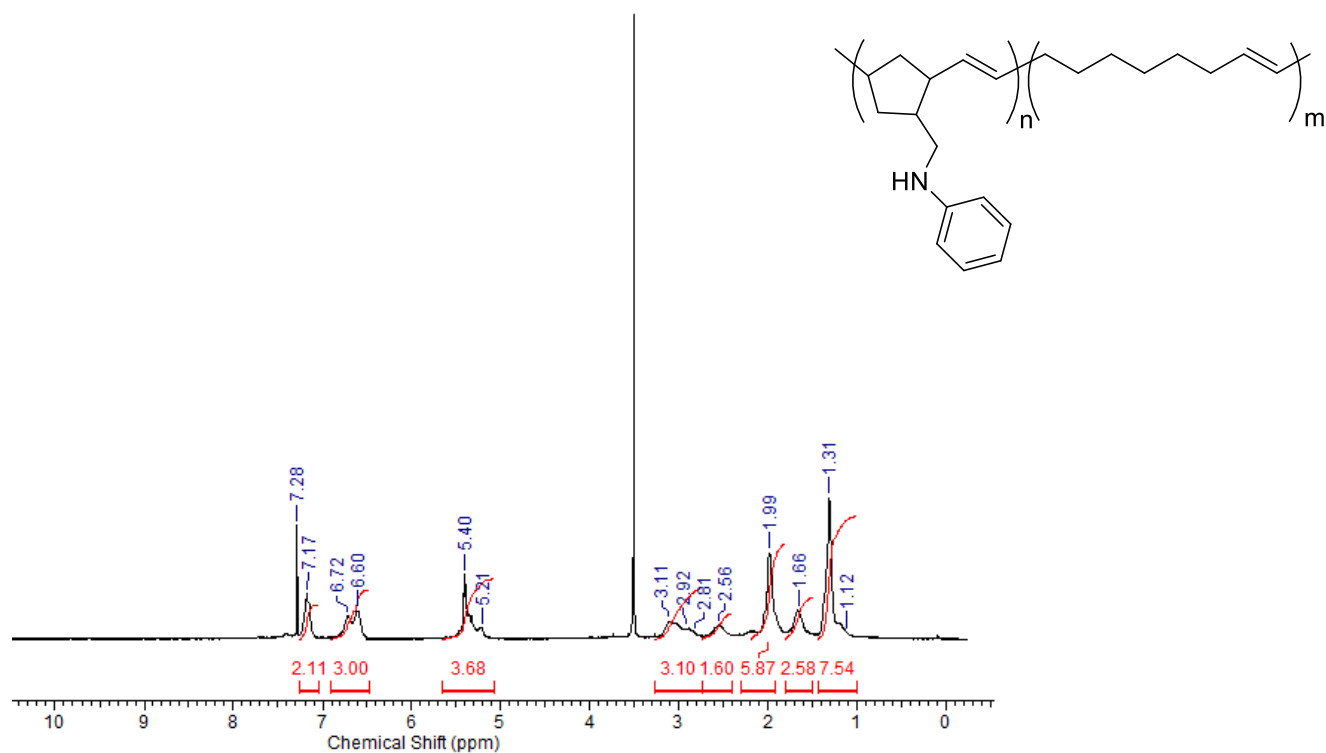
P(ACN-4-*co*-norbornadiene) ^1H NMR spectrum (300 MHz, CDCl_3):



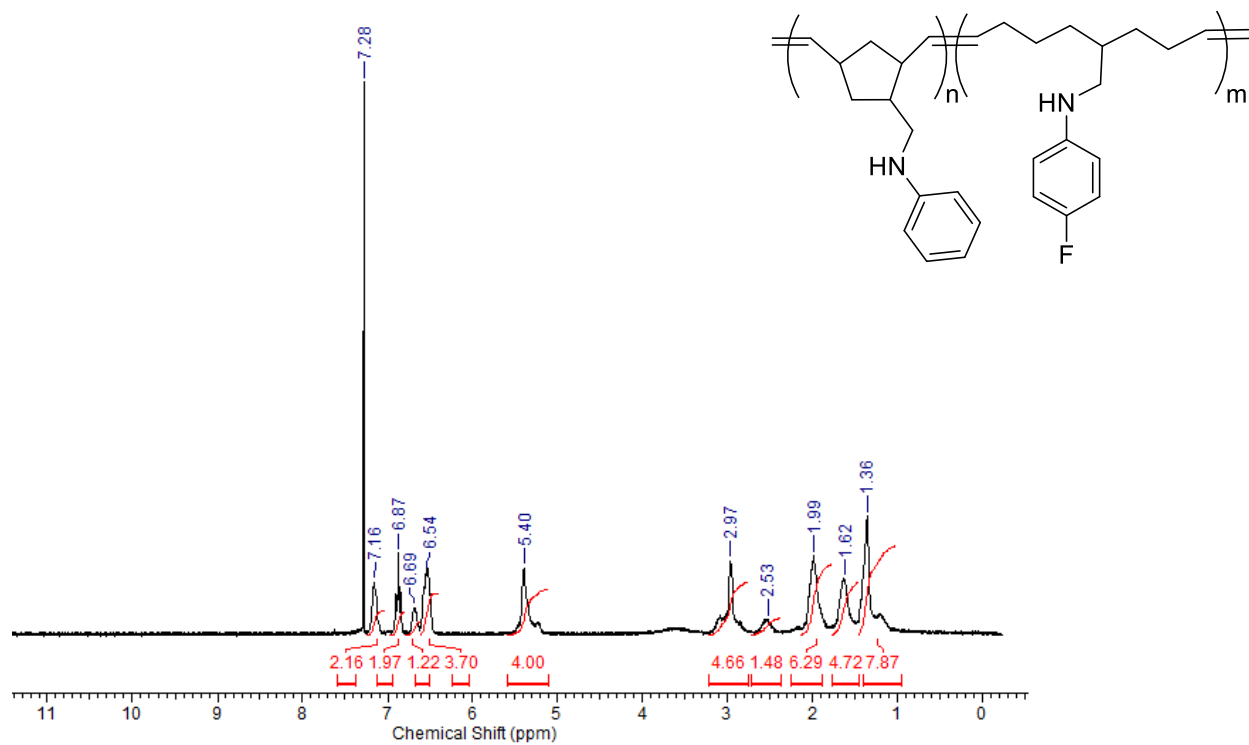
P(ACN-4-*co*-cyclooctene) ^1H NMR spectrum (300 MHz, CDCl_3):



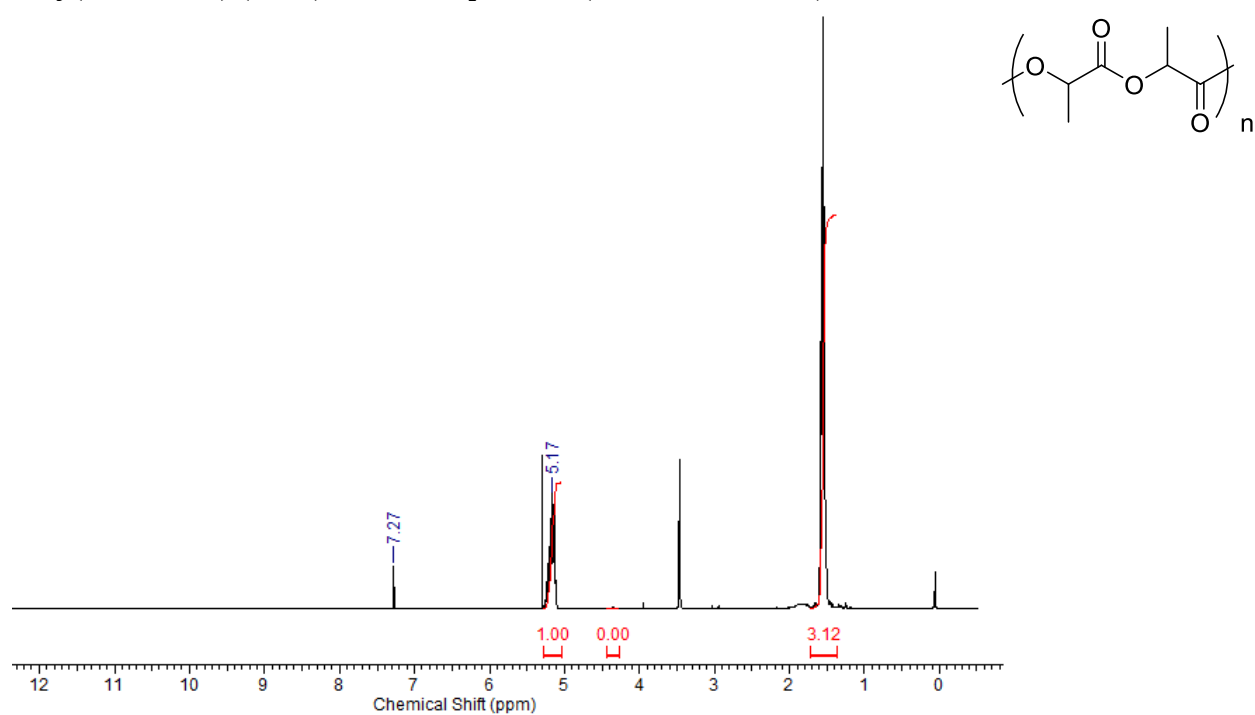
P(ACN-1-co-cyclooctene) (Alternating addition) ^1H NMR spectrum (300 MHz, CDCl_3):



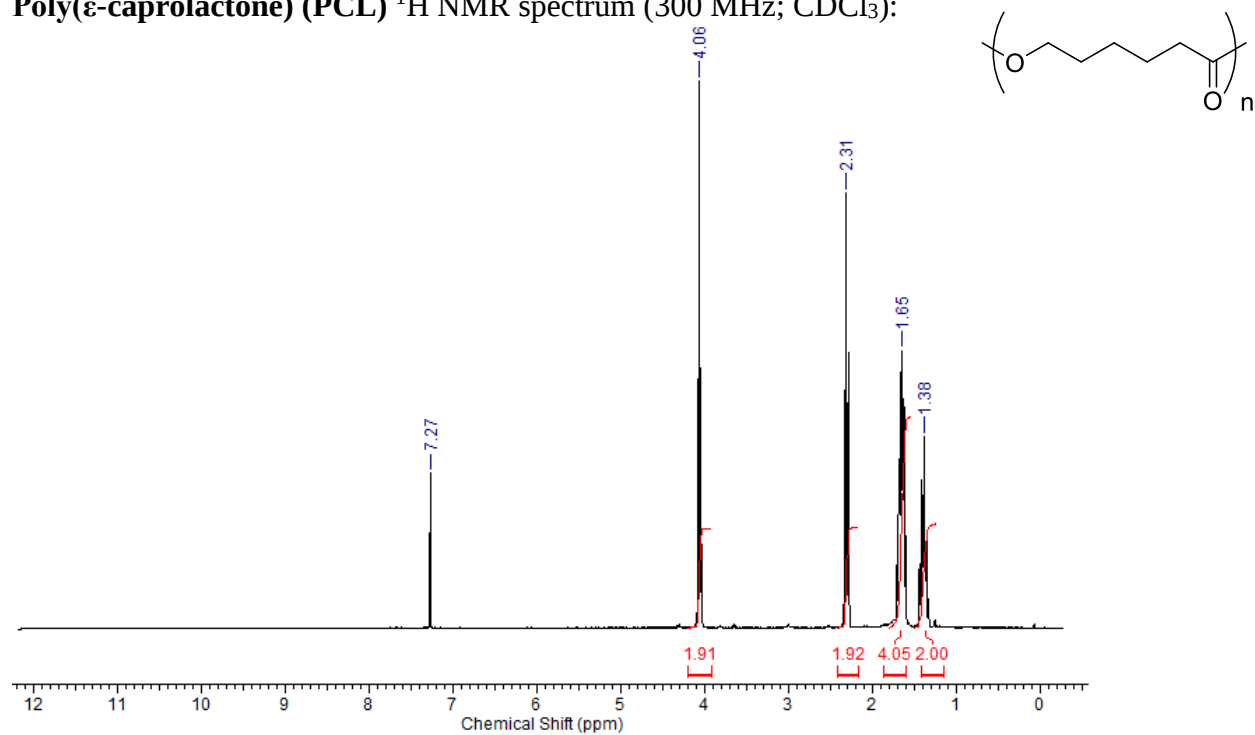
P(ACN-1-co-ACC-2) ^1H NMR spectrum (300 MHz, CDCl_3):



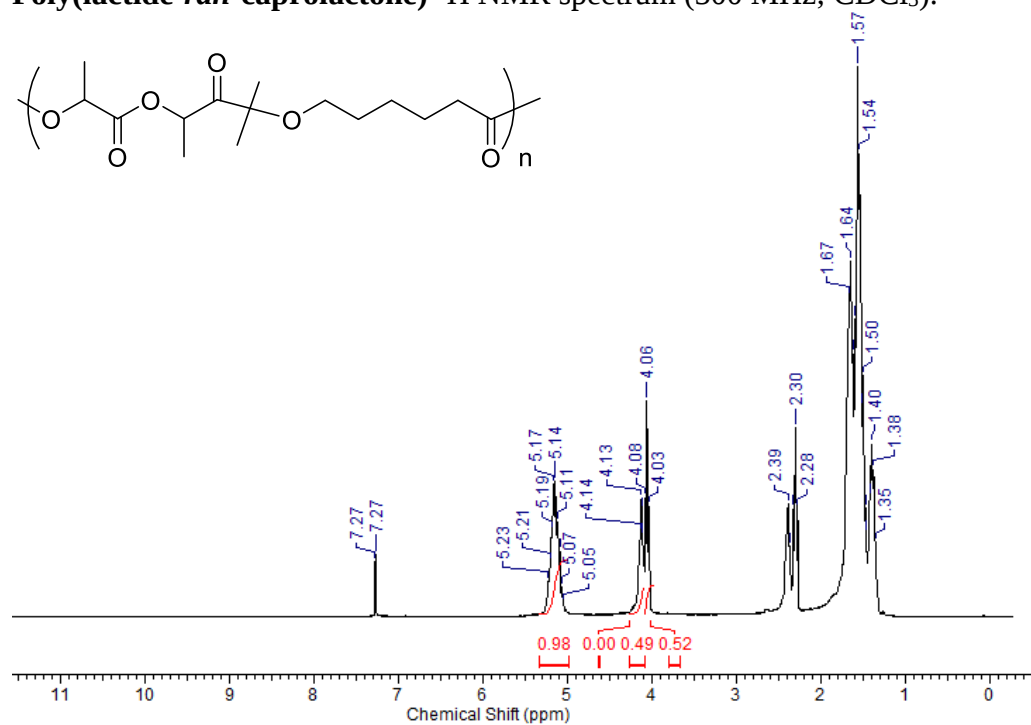
Poly(lactic acid) (PLA) ^1H NMR spectrum (300 MHz; CDCl_3):



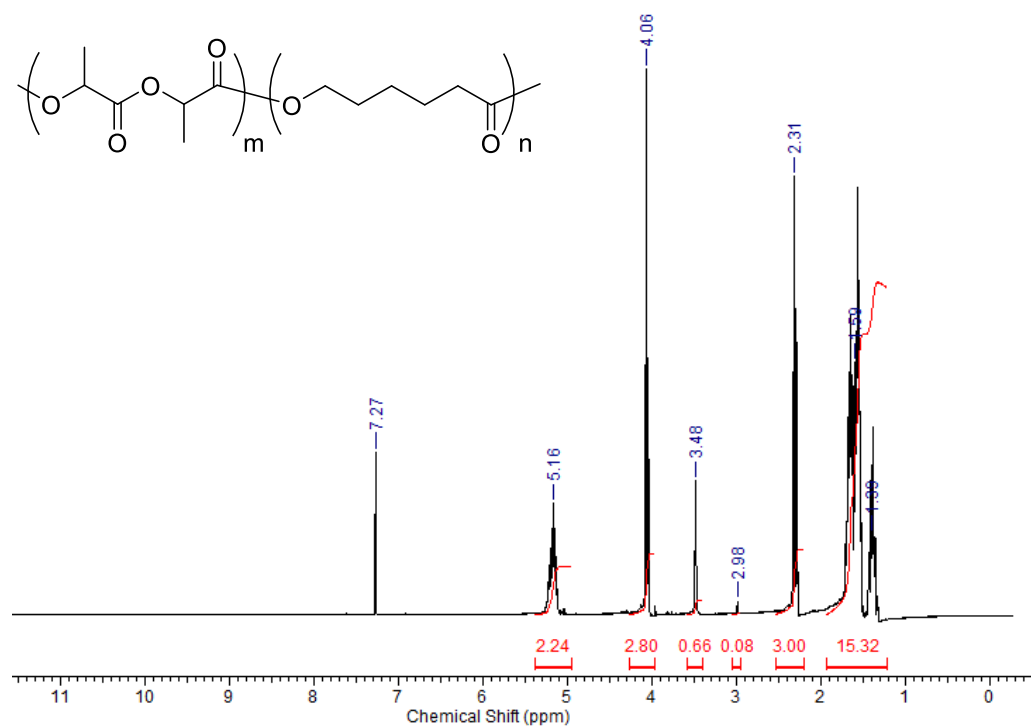
Poly(ϵ -caprolactone) (PCL) ^1H NMR spectrum (300 MHz; CDCl_3):



Poly(lactide-*ran*-caprolactone) ^1H NMR spectrum (300 MHz; CDCl_3):

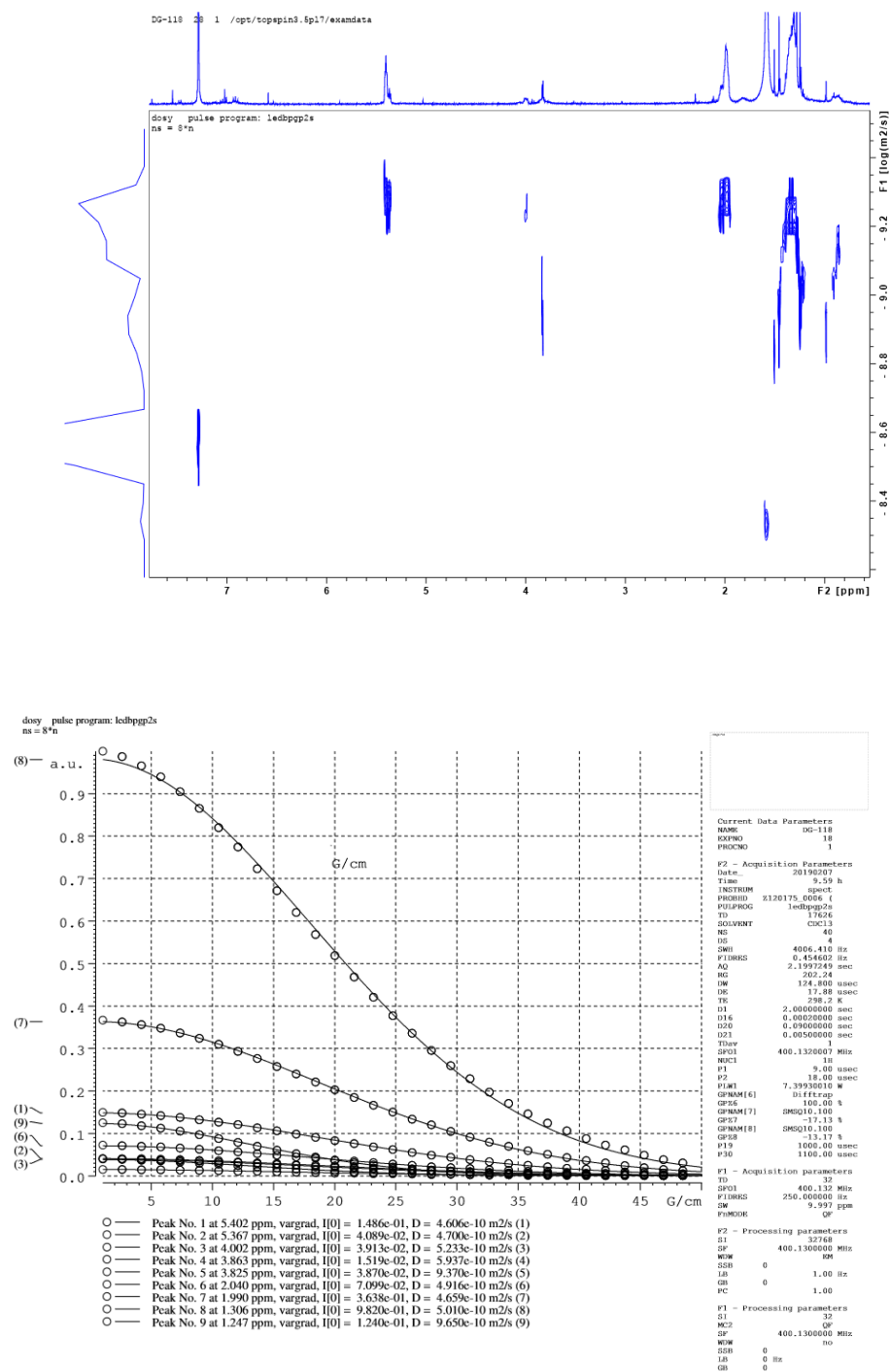


Poly(lactide-*b*-caprolactone) ^1H NMR spectrum (300 MHz; CDCl_3):



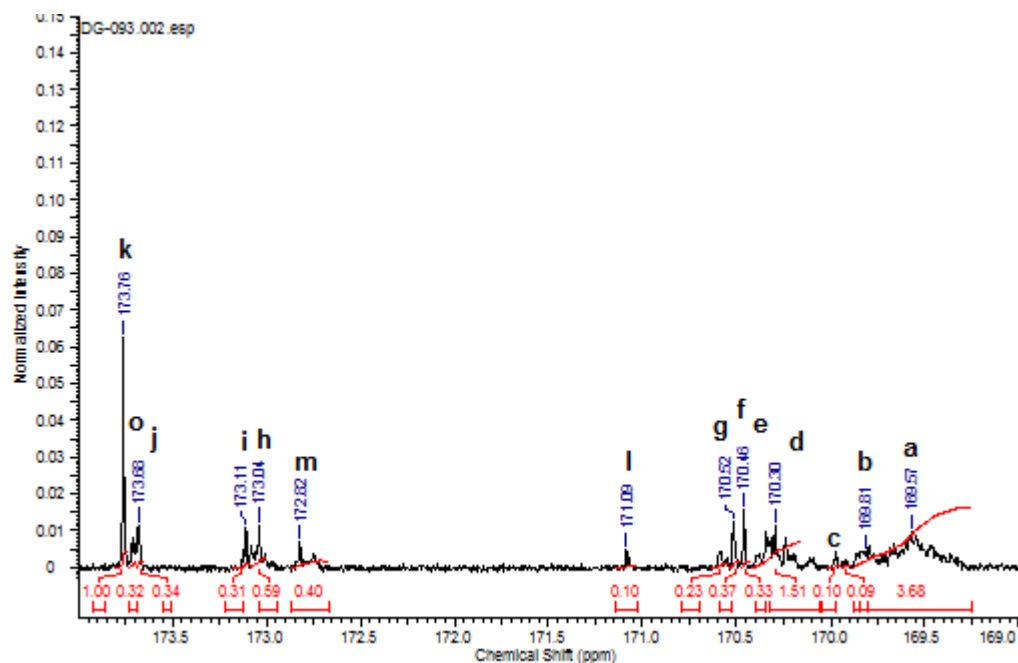
Appendix E NMR spectra calculations

E.1 DOSY NMR spectrum of attempted block copolymer with cyclooctene and an amine-containing norbornene derivative (Chapter 3)



E.2 Average sequence lengths in random copolymers (Chapter 4)

^{13}C NMR Spectrum (600 MHz, CDCl_3) of **Table 4.3, Entry 2** (zoom-in to region between 169 and 174 ppm)



Calculation of $L_{\text{CL}}/L_{\text{LA}}$ sequence lengths determined using method described by Kasperczyk and Bero:

$$L_{\text{LL}} = (1/2) \cdot (LLL + LLC + CLL + CLC) \cdot ((CLC + (1/2) \cdot (LLC + CLL))^{-1}$$

$$L_{\text{CL}} = (LCL + CCL + LCC + CCC) \cdot ((LCL + (1/2) \cdot (CCL + LCC))^{-1}$$

Where:

$$LLL = (1/2)(c + g) + (1/2)(d) + (1/3)(b + e) + a$$

$$LLC = (1/2)(d) + (1/2)(f) + (1/3)(b + e)$$

$$CLL = (1/2)(c + g) + (1/2)(f) + (1/3)(b + e)$$

$$CLC = l$$

$$LCL = h + m$$

$$CCL = i + o$$

$$LCC = j + o$$

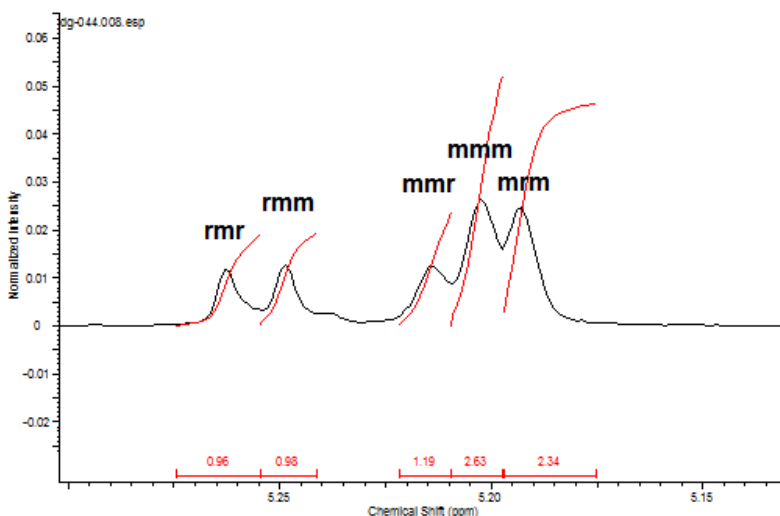
$$CCC = k$$

Values of a through o calculated based on the integrations of the assigned sequences shown above

E.3 Calculation of P_m in the ROP of *rac*-lactide (Chapter 4)

^1H $\{^1\text{H}\}$ NMR Spectrum (400 MHz, CDCl_3) of **Table 4.4, Entry 5** (zoom in to δ 5.30-5.10)

-Irradiated at δ 1.57 to minimize coupling to methine protons



PLA tacticity P_m , calculated using Bernoullian statistics based on the assignments made by Coates²⁵⁷

$$P_m + P_r = 1$$

$$\text{rmr} \quad P_r = (2\text{rmr})^{1/2}$$

$$\text{rmm} \quad P_r^2 - P_r + 2\text{mmr} = 0$$

$$P_r^2 - P_r + x = 0 \quad x = 2\text{rmm}$$

$$P_r = (1 \pm (1-4x)^{1/2}) / 2$$

$$\text{mmr} \quad P_r^2 - P_r + 2\text{mmr} = 0$$

$$P_r^2 - P_r + x = 0 \quad x = 2\text{mmr}$$

$$P_r = (1 \pm (1-4x)^{1/2}) / 2$$

$$\text{mmm} \quad P_r^2 - 3P_r + 2 - 2\text{mmm} = 0$$

$$P_r^2 - 3P_r + 2 - x = 0 \quad x = 2\text{mmm}$$

$$P_r^2 - 3P_r + y = 0 \quad y = 2-2x$$

$$P_r = (3 \pm (9-4y)^{1/2}) / 2$$

$$\text{mrm} \quad P_r = 2\text{mrm}$$

Values of rmr, rmm, mmr, mmm, and mrm were determined using the integrals of the assigned peak over the total integration. Resulting P_r values from above equations were then averaged.

E.4 Evans Method analysis on complex 5.2

^1H NMR (300 MHz; CDCl_3) of complex 5.2 (zoom-in to δ 1.65 to 1.35)

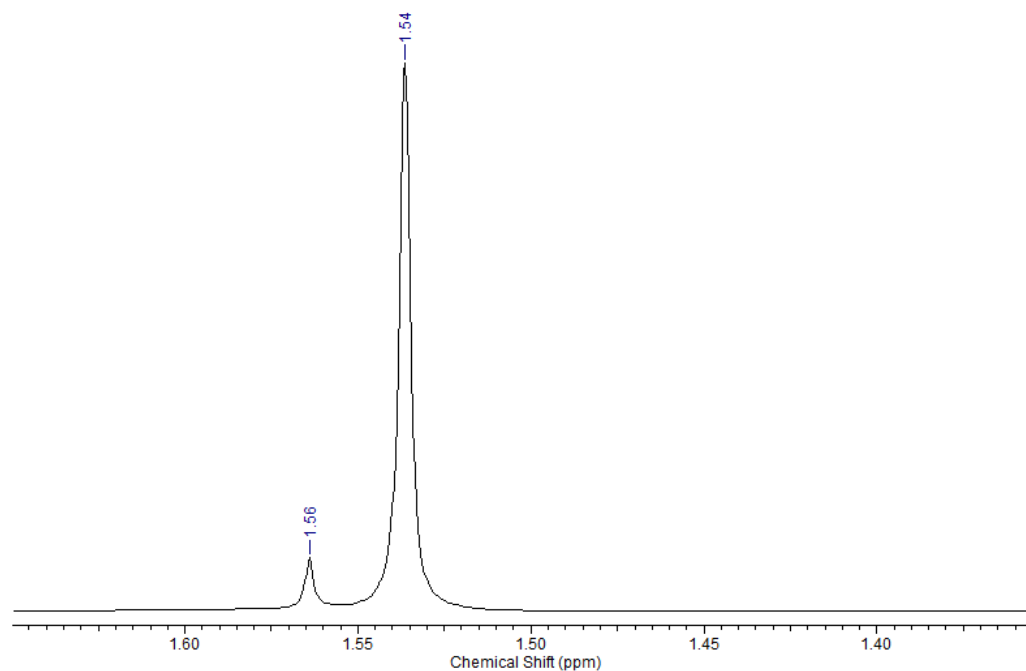


Table E.1 Tabulated values to determine μ_{exp}

M.W.	1101
Δf (Hz)	11.1
f (Hz)	400000000
m (g) per 1mL	0.00455
χ (mL/g) solvent	-7.40E-07
d (g/mL) solvent	1.48
d (g/mL) solution	1.48455
T	293
χ (mL/g) sample	1.46E-06
χ (mL/mol)	1.60E-03
μ_{exp}	1.95E+00

****Sample****
**** Difference between COA peaks in Chloroform ****
**** Instrument field Strength ****
****Sample****
 CDCl_3
 CDCl_3