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DEPARTMENT OF CHEMISTRY

SYNTHESIS AND CHARACTERIZATION OF POLYMERIZATION-POWERED MOTOR SYSTEMS

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A thesis submitted in partial fulfillment of the requirements for a baccalaureate degree in Chemistry with honors in Chemistry

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ABSTRACT

1 micron gold/silica particles have been modified by covalently binding Grubbs 1st and 2nd generation catalyst to the silica surface. The particles are capable of performing ring-opening metathesis polymerization of norbornene monomer to give polynorbornene. More interestingly though, the particles bearing these catalysts display enhanced diffusion when placed in a monomer solution. At 1 M norbornene, the Grubbs 2nd generation motor showed its highest increase in diffusion, a 70 % increase over the 0 M solution. GC analysis was conducted to determine the turnover frequency of the motor as a function of time and ¹H NMR was used to determine the that the product of polymerization was polynorbornene. The synthesis of a dye-tagged Grubbs catalyst was also attempted to determine the diffusion coefficient for a single molecule during polymerization. The first step of the synthetic route was completed to give 1-(2,4,6-Trimethylphenyl)-1H-imidazole with a yield of 52 %. The products' identity was confirmed with ¹H NMR.

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Chapter 1

Introduction: Diffusion, Nanomotors, and Grubbs Catalyst

1.1 Diffusion

In 1812, Robert Brown, a Scottish botanist, made a significant discovery while observing pollen grains with his microscope – the grains displayed a constant, random motion. It was nearly 100 years later when Einstein described this "Brownian motion" as being a function of the random spread of a particle's displacement over time, or diffusion (1). In a solution, a particle is constantly colliding with solvent molecules with a kinetic energy of kT/2 in each direction (2). Asymmetry in these collisions will result in a net gain of momentum for the particle; however, this momentum is short-lived (on the order of 10^{-13} s) as the particle will quickly collide with another solvent molecule to dissipate this energy (2). The random aspect of this motion comes from the fact that there is an equal likelihood for this asymmetry in collisions to happen in any direction. Quantitatively, diffusion can be represented by the diffusion coefficient (D), a function of the thermodynamic temperature (T), the Boltzmann constant (k) and the frictional drag from the medium (f) (Equation 1-1) (3).

$$D = \frac{kT}{f}$$
(1-1)

The frictional drag can be defined as a function of the viscosity of the medium (η) and the hydrodynamic radius of the particle (a) and if we are assuming the particle is spherical, then geometric terms can be added to modify equation 1-1 to give the Stokes-Einstein equation (Equation 1-2) (3).

$$D = \frac{kT}{6\pi\eta a}$$
(1-2)

The diffusion of a particle can also be thought of as a relationship between its inertial forces and the drag forces acting on it in solution. For a particle with length L, in a solution with velocity v, density ρ , and viscosity η , this relationship can be defined by its dimensionless Reynolds number, Re (Equation 1-3) (2). Thus, very small particles (with a small L term) are described by an Re << 1; meaning the viscous forces of the medium dominate the particles' motion.

$$\operatorname{Re} = \frac{\nu L \rho}{n} \tag{1-3}$$

1.2 Nanomotors

A rapidly growing avenue of research is centered around understanding motion at the micro and nanoscales (4). Ultimately, one of the primary goals of this research is to develop an autonomously powered nanomotor. Such a system could be applied to selfassembly and drug-delivery applications. One of the primary obstacles for a nanomotor is overcoming Brownian motion. Collisions between the motor and solvent molecules are capable of rotating the motor and giving randomized motion (3). An effective motor must be able to generate enough inertial force to overcome the drag forces from the medium as well as the Brownian motion from the solvent. Some of the most complex motors are found in biological systems. One well-known example is the polymerization of actin in eukaryotes (5). Actin polymerization occurs via an insertion polymerization mechanism that results in a "site-directed tread-milling" of actin filaments (5).

One method of generating autonomous motion is by applying a force or gradient to the medium, either electrical or chemical, to give a so-called phoretic transport (6). An example of the former could be demonstrated by applying an electric field across an ionic solution (6). The electric field would cause a charged particles' counter ion cloud to diffuse in a direction opposite to the particle; this induces a velocity difference between the particles relative to the bulk solution (6). The latter is achieved by creating an electrolytic gradient across a colloidal suspension. Such a gradient drives the particles toward the region of higher concentration with a diffusion rate nearly fifty times larger than by Brownian diffusion alone (7).

If a particle could generate its own local field or concentration gradient, then its motion would be truly autonomous (6). The Whitesides group at Harvard synthesized one of the first autonomous motors when they placed a platinum strip onto a polydimethylsiloxane boat that was capable of propelling itself through a hydrogen peroxide solution by creating bubbles on the platinum strip (8). Platinum is able to catalytically decompose hydrogen peroxide into oxygen and water, which allows the particle to create a constant concentration gradient (6). Gold/platinum nanorods capable of self-electrophoresis through a similar mechanism were reported by Paxton *et al.* (9).

1.3 Grubbs Catalyst

Grubbs catalyst, a ruthenium carbene-complex, has been shown to be capable of performing an array of olefin methathesis reactions (Figure 1-1) (10). Olefin methathesis refers to a class of reactions that result in a rearrangement of carbon-carbon double bonds (11). The mechanism of olefin metathesis proceeds through the formation of a metallocyclobutane intermediate from the coordination of an olefin to a metal alkylidene before a cycloreversion occurs to give the product (Figure 1-2) (12).



Figure 1-1. Grubbs 1st and 2nd generation catalysts.



Figure 1-2. Scheme for Chauvin mechanism of olefin metathesis.

Ring-opening methathesis polymerization (ROMP) is one such form of olefin methathesis that is performed by Grubbs catalyst (10). In this reaction, the catalyst rapidly polymerizes the monomer subunits to give a polymer chain (13). Often, the driving force for these reactions is the alleviation of ring strain on the monomer subunits (13). This function of Grubbs catalyst would make them appealing reaction sources for an asymmetric nanomotor since it occurs continuously to give a useful product (10).

N-heterocyclic carbenes (NHC) are a class of stable carbenes commonly used as organometallic ligands (10). These ligands are desirable because they are excellent σ -donors, easily modified, and often afford metal-carbon bonds that are less labile than the analogous metal-phosphine bond (13). NHCs can be produced through the treatment of an imidazolium or imidazolinium salt with a strong base, typically potassium *tert*-butoxide or sodium hydride; once produced, the NHC can readily displace a phosphine group on the catalyst (10).

Chapter 2

Polymerization-Powered Nanomotors

2.1 Introduction

Another widely studied class of motors are those mounted onto Janus particles. Earlier work has resulted in Janus particle motor systems capable of self-phoresis. Howse *et al.* synthesized platinum/polystyrene Janus particles that were capable of decomposing aqueous hydrogen peroxide to give the particles enhanced diffusion (6). The asymmetric Janus particles followed much longer trajectories, thus had larger diffusion coefficients, than the pure polystyrene controls (6).

More generically, the term Janus particle can be used to describe any particle with two different faces. For the following investigation, gold/silica Janus particles were mounted with different versions of Grubbs catalyst to enhance the diffusion of the particles in solution. Grubbs catalysts are powerful polymerization catalysts that are ideal for such a study due to their stability at room temperature, their tolerance toward air, water, and many functional groups (10). Varying concentrations of "fuel" in the form of the strained monomer, norbornene, were used to determine a relationship between the rate of the diffusion and the rate of catalysis as a function of monomer concentration.

2.2 Fabrication of Au/PS Janus particles

The Janus particles are prepared by half-coating silica particles with gold (Figure 2-1). A glass slide was placed in a petri dish containing water. Hexane was added to form a thin film above the water layer. A concentrated suspension of silica microspheres in ethanol was added to the bilayer. The glass slide was slowly lifted to get a monolayer

of polystyrene particles. The glass slide was dried and thin layers of chromium (7 nm) followed by gold (56 nm) were deposited on the exposed silica surface by chemical vapor deposition (CVD). Finally, gold/silica Janus particles were collected by sonication. The FESEM images of the particles are shown in (Figure 2-2).



Figure 2-1. Fabrication of gold/silica Janus particles.



Figure 2-2. FESEM images of 1.5 µm polystyrene/gold Janus particles.

2.3 Reaction Scheme

2.3.1 Grubbs 2nd Generation Motor

The catalyst was tethered to the gold/silica Janus particle surface via a linker molecule capable of associating with the silica surface at one end and the catalyst at the other (Figure 2-3). The linker was attached to the silica surface through silane chemistry, while it was modified at the other end with an imidazole group, that was capable of being deprotonated to form an NHC. The NHC was used to displace a tricyclohexylphosphine group on the catalyst to give the Grubbs 2nd generation motor.



Figure 2-3. Synthetic scheme for the Grubbs 2nd generation motor.

2.3.2 Grubbs 1st Generation Motor

The catalyst was tethered to the gold/silica Janus particle surface via a linker molecule that was capable of associating with the silica surface at one end and the catalyst at the other (Figure 2-4). The linker was attached to the silica surface through silane chemistry, while a diphenylphosphine group at the other end that was capable of displacing a tricyclohexylphoshphine group to give the Grubbs 1st generation motor.



Figure 2-4. Synthetic scheme for the Grubbs 1st generation motor.

2.4 Experimental

2.4.1 General Methods

All solvents and reagents were used as obtained from Alfa Aeser (Ward Hill, MA) without further purification unless otherwise noted. ¹H NMR spectra were recorded on a Bruker DPX-300 MHz spectrometer and XPS spectra were obtained on a Kratos Ultra XPS. The particles were tracked using a Zeiss Axiovert-200 MAT microscope and PhysVis software and the data analysis was conducted with MatLab software.

2.4.2 Grubbs 2nd Generation Motor

Gold/silica Janus particles (1 µm, 1 equivalent) and 3-

imidazoliumpropyltrimethoxysilane (excess) were stirred in dichloromethane overnight at room temperature. The particles were washed several times with dichloromethane and then potassium tert-butoxide in THF (1 equiv.) was added and stirred for 1 hour at 25 °C. Grubbs 2nd generation catalyst (1.5 equiv.) was added and stirred overnight at 25 °C before being washed several times with dichloromethane.

2.4.3 Grubbs 1st Generation Motor

Gold/silica Janus particles (0.96 μ m, 1 equiv.) and 3-(diphenylphosphino) propyltriethoxysilane (excess) were heated in toluene at 100 °C overnight. The particles were washed several times with toluene and suspended in a solution of excess Grubbs 1st generation catalyst (1.5 equiv.). The solution was stirred overnight and the particles were washed with dichloromethane under nitrogen.

2.5 Results and Discussion

2.5.1 Grubbs 2nd Generation Motor

Grubbs 2nd generation catalyst was mounted to 1 μ m gold/silica Janus particles via a silane linker molecule. Following the synthesis, the particles were suspended in a norbornene solution to monitor the catalytic activity. Characterization of the product was achieved through XPS and catalytic activity was characterized by analyzing the resulting polymer with ¹H NMR.

The turnover frequency (TOF) for the catalyst was determined. A solution of particles in 0.15 M norbornene in dichloromethane with a 0.5 mM chlorobenzene internal standard was stirred for 50 h. GC analysis was used to determine the ratio of norbornene to standard, which was then compared to a calibration curve to give the number of moles of monomer in the solution. Initially, the monomer concentration depleted linearly with time and after ten hours the frequency began to decrease (Figure 2-5). One possible

explanation is that the catalyst on the surface is deactivating over time due to backbiting and crosslinking; two effects commonly observed in other Grubbs supported systems (10). Alternatively, the growth of the polymer on the surface could be impeding monomers from reaching the catalytic site, which would lead to a decrease in TOF.



Figure 2-5. Plot of the amount of monomer consumed versus time.

The surface coverage of the particles was determined to be 10⁻⁶ mol cm⁻² through back calculations using the moles of norbornene consumed and the molecular weight of the polymer (Table 2-1). This calculated value is much higher than expected, suggesting that there is either free catalyst contamination or errors in the assumptions used in the calculation.

	Unit	Theoretical	Experimental	Theoretical /
				Experimental
Flux	$mol / cm^2 s$	3.09e-5	1.19e-8	2605
Accumulation	mol / s	4.57e-13	1.75e-16	2605
TOF	mol norb. /	3.09e5	119	2605
	mor cut . s			
TOF per gram	mol norb. / g s	1.59e-2	6.11e-6	2605

Table 2-1. Theoretical values versus experimental data from GC analysis.

XPS was employed because it offers high selectivity for characterizing the elements on a surface. The XPS spectra confirmed that Grubbs catalyst was mounted to the surface of the Janus particles (Appendix). The spectra showed signals corresponding to ruthenium, carbon, nitrogen, oxygen, silicon and gold; however, a peak for phosphorus was missing. One explanation is that free linker molecules are replacing both of the tricyclohexylphosphine groups on the catalyst, thus removing phosphorous altogether. Another possibility is that the tricyclohexylphosphine groups had not recoordinated with the catalyst. This is plausible because the samples were run immediately after the particles were used to perform a polymerization. The XPS showed a nitrogen to ruthenium to chlorine ratio of 4:1:2, which suggests that the former explanation is most likely occurring. Sodium and potassium were also detected as impurities. The potassium most likely came from the potassium *tert*-butoxide and the sodium could have come from any number of sources.

¹H NMR was used to characterize the resultant polymer. The spectra showed all of the key peaks for polynorbornene (Appendix); however, water was also present in the spectra as an impurity. These results suggest that Grubbs catalyst was bound to the surface of the silica particles and was carrying out the predicted catalytic cycle.

The particles were studied in several different concentrations of norbornene in 1,1,1-trichloroethane to monitor their diffusion. The relatively low vapor pressure of 1,1,1-trichloroethane allowed for a non-evaporating environment for the experiments. The particles were suspended in the solvent and then added to norbornene solutions in a spacer on a glass slide. Particle diffusion was monitored under a microscope and 10 s videos were taken. The videos were analyzed using PhysVis software and their movement was tracked as a function of time. The spatial coordinates of each particle were recorded at each frame for a total of 80 particles per each sample concentration of norbornene analyzed – 0.01, 0.1, 0.5 and 1 M. Several controls were also run, including 0 M, 0.1 M with inhibitor, 0.5 M with inhibitor, as well as 0, 0.01, 0.1, 0.5 and 1 M using silica particles uniformly coated with Grubbs catalyst. MatLab was employed to evaluate the data to give a diffusion coefficient for each particle for different time steps before averaging them together. The values were then adjusted to account for changes in viscosity of different monomer solutions to show a positive, linear relationship between norbornene concentration and the observed diffusion coefficient (Figure 2-6). At 1 M norbornene, the diffusion increased by over 70 % compared the 0 M sample (Figure 2-7).



Diffusion Coefficient of Gold/Silica-Grubbs Particles in Norbornene

Figure 2-6. Calculated diffusion coefficient at varying monomer concentrations.



Figure 2-7. The percentage increase in the calculated diffusion coefficient at each concentration.

2.5.2 Grubbs 1st Generation Motor

A Grubbs 1st generation motor was synthesized by mounting the 1st generation catalyst onto 0.96 µm gold/silica particles via a linker molecule, 3-(diphenylphosphino) propyltriethoxysilane. Tracking and analysis was carried out in the same manner as for the Grubbs 2nd generation motor. The tracking data (Table 2-2) was inconclusive for these particles due to the fact that the particles became stuck to the slides at 0, 0.5 and 1 M; at 0.5 and 1 M, also the polymerization increased the viscosity of the solution, which caused them to adhere to the slides. The 0.1 M with inhibitor sample exhibited faster diffusion than the 0.1 M. It is likely that the particles in the 0.1 M solution began to slow down as the viscosity caused by polymerization increased and the 0.1 M with inhibitor sample resembled a system without monomer. It is possible that free catalyst is present as a contaminant that is causing the solution to polymerize too rapidly, which will in turn increase the viscosity of the solution and decrease diffusion.

Concentration (M)	Diffusion Coefficient (µm s ⁻¹)	Standard Deviation
0	-	-
0.1	0.26	0.02
0.5	-	-
1	-	-
0.1 with inhibitor	0.30	0.03

 Table 2-2.
 Diffusion data for the Grubbs 1st generation motor.

2.6 Conclusions and Future Work

The data for the Grubbs 2nd generation motor presents a well-defined motor system. Spectral analysis indicates that the catalyst is bound to the surface of the Janus particles and the motors are polymerizing norbornene. GC analysis was performed to calculate the TOF as a function of time. The results showed that the amount of monomer consumed increased linearly for the first six hours before the rate of consumption decreased sharply at the ten hour mark. This is likely due to deactivation of the catalyst or crowding around the catalytic site from the newly formed polymer.

The results for the Grubbs 1st generation motor are inconclusive. The synthesis yields active particles, capable of rapid polymerization. One explanation for these results is that free catalyst contamination is causing the solution to polymerize too quickly, which is leading to a sudden increase in viscosity that is slowing the particles.

This working system should be explored in more detail. Work should be done to elucidate the mechanism of motility and applications for the system should be determined. For the former, two possible models are described in the literature, but neither fully describe this system. Figueroa *et al.* suggest that a catalytic, asymmetric motor consumes fuel on one side of the particle and releases either a low concentration of products and/or a slower diffusing product creates an osmotic force across the particle (14). This model qualitatively fits our system, as our motor consumes high amounts of monomer but only releases small amounts of polymer; however, it does not quantitatively fit our system. The authors define TOF in units of meters per second, which is not applicable to the context of a chemical reaction. This model needs to be altered to determine if osmotic force is causing the enhanced motion from the motor system. A

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diffusiopheretic mechanism can also potentially explain our motor; however, this model is typically applied to a catalytic site making more products than reactants consumed (15, 16). Our motor works oppositely but this can just be interpreted as a difference in the direction of the motor.

One of the most promising applications of the motors is as an autonomous repair device. Directed transport of the particle can be achieved utilizing salt gradients or a magnetic field, if the particle is magnetically susceptible (17, 18). Salt gradient transport is described equation 2-1, where U is velocity, Z is the charge number, e is the charge of an electron, κ is the Debye length, η is viscosity, D₊ is the diffusivity of the positive electrolyte, D. is the diffusivity of the negative electrolyte, k is the Boltzmann constant, T is temperature, n_o is the bulk concentration, and ζ is the zeta potential (17). While transport by a magnetic field on a magnetically susceptible particle is described by equation 2-2, where U is velocity, χ_p is the magnetic susceptibility of the particle, χ_m is the magnetic susceptibility of the medium, μ_o is the vacuum magnetic permeability, and B is the magnetic flux density (18).

$$U = \frac{2Ze}{\kappa^2 \eta} \left[\left(\frac{D_+ - D_-}{D_+ + D_-} \right) \zeta - \frac{2kT}{Ze} \ln(1 - \gamma^2) \right] V n_{o}, \qquad \gamma = \tanh(\frac{Ze\zeta}{4kT})$$
(2-1)

$$U = -\frac{(x_p - x_m)}{2\mu_o} V B^2$$
 (2-2)

Chapter 3

SYNTHESIS OF DYE-TAGGED GRUBBS CATALYST

3.1 Introduction

A logical extension of our prior work is the investigation of the diffusion of a single molecule during polymerization. Since Grubbs catalyst is employed to drive our motor systems, it was determined to be the most appropriate substrate for the study. Unlike a silica particle, a single molecule cannot be tracked by optical microscopy. Fluorescent correlation spectroscopy (FCS) can be employed to monitor the diffusion of the catalyst; however this would first require a fluorescent dye molecule to be covalently linked to the catalyst (19). Previously, it had been shown that FCS is capable of accurately determining the diffusion coefficient of the enzyme urease while performing a catalytic reaction (19).

3.2 Retrosynthetic Analysis

Retrosynthetic analysis was conducted to determine an appropriate synthetic scheme for the target molecule (Figure 3-1). Due to the large variety of functional groups on a fluorescent dye molecule, it was deemed appropriate to attach it last to decrease the likelihood of an unwanted side reaction. Fluorescent dyes are commonly mounted to substrates via an amide bond; thus, the dye should either have an amine or carboxylic acid functionality and it should be tethered to the catalyst via a linker molecule with a complementary functional group. First generation Grubbs-Hoveyda catalysts are modified to the more stable second generation versions by displacing a tricyclohexylphosphine group with an NHC. In contrast to a tricyclohexylphosphine group, an NHC is a more mutable ligand capable of being modified by the addition of the desired linker molecule. Such a transformation could be achieved through the S_N^2 displacement of the leaving group on an alkyl halide by the nucleophilic amine at the 3-position of the imidazole.



Figure 3-1. Retrosynthetic analysis of the target, a dye-tagged Grubbs catalyst.

3.3 Reaction Scheme

With the retrosynthetic analysis in mind, the proper scheme for the synthetic route was developed (Figure 3-2). Mesityl was chosen as the substituent on the imidazole as is provides greater stability for the NHC that will be formed in a later step (10). Occhipinti *et al.* reported a means of synthesizing the desired mesityl-substituted imidazole, imidazole **1**, from 2,4,6-trimethylaniline, glyoxal, formaldehyde and ammonium acetate (20). The acid-catalyzed reaction of glyoxal with ammonium acetate and 2,4,6trimethylaniline results in the formation of a diimine intermediate. Cyclization is completed with the acid-catalyzed, nucleophilic attack of the diimine on formaldehyde to give imidazole **1** (Figure 3-3). The amine functionality on the linker molecule, 3bromopropylamine, should be protected using fluorenylmethyloxycarbonyl (FMoc) chloride to reduce its reactivity. The protected linker can be attached to imidazole **1** via an S_N^2 displacement of the bromide group to give imidazolinium salt 2. The formation of the NHC can be achieved through the deprotonation of the 2-position of the imidazolinium salt 2. The NHC is then capable of displacing one of the tricyclohexylphosphine ligands on a first generation Grubbs-Hoveyda catalyst to give Grubbs catalyst 3. Deprotection, by removal of the FMoc group, is achieved by reacting Grubbs catalyst 3 with 20 % piperidine in DMF to give Grubbs catalyst 4. The final product is achieved through the coupling of the amine group on Grubbs catalyst 4 with a carboxylic acid functionality on the desired dye molecule.



Figure 3-2. Scheme for the synthesis of the target, a dye-tagged Grubbs catalyst.



Figure 3-3. Mechanism for the formation of imidazole 1.

3.4 Experimental

3.4.1 General Methods

2,4,6-trimethylaniline was obtained from Tokyo Chemical Industry (Boston, MA), while all other chemicals and reagents were obtained from Alfa Aeser (Ward Hill, MA). All solvents and reagents were used without further purification unless otherwise noted. ¹H NMR spectra were recorded on a Bruker DPX-300 MHz spectrometer.

3.4.2 1-(2,4,6-Trimethylphenyl)-1H-imidazole

Aqueous formaldehyde (37 % w/w H₂O, 0.55 mL, 20 mmol) and aqueous glyoxal (40 % w/w H₂O, 2.28 mL, 50 mmol) were added to acetic acid (10 mL), stirred and heated to 70 °C. A solution of ammonium acetate (1.17 g, 20 mmol) in water (2 mL), 2,4,6-trimethylaniline (2.81 mL, 20 mmol) and acetic acid (10 mL) was added dropwise to the stirring reaction mixture over a period of 30 min. The resulting solution was heated at 70 °C for 18h. The reaction mixture was cooled to 25 °C, and then added dropwise to a stirring solution of NaHCO₃ (29.4 g) in water (300 mL) to give a precipitate. The solid was washed with water (3 x 20 mL) and air-dried to give a crude product (2.74 g). The precipitate was recrystallized using ethyl acetate to give **1** as a brown-red solid (1.98 g, 53.23 %), mp 109-112 °C. ¹H NMR (300 MHz, CDCl₃): δ 7.48 (s, 1H), 7.29 (s, 1H), 7.00 (s, 2H), 6.93 (s, 1H), 2.37 (s, 3H), 2.02 (s, 6H).

3.5 Results and Discussion

Only the first step of the synthetic route has been completed. 1-(2,4,6-Trimethylphenyl)-1H-imidazole was synthesized from 2,4,6-trimethylaniline, glyoxal, formaldehyde and ammonium acetate with a yield of 52 %. The product was characterized by ¹H NMR and melting point.

The ¹H NMR spectra contained all of the expected peaks for the product at chemical shifts similar to those reported in the literature (Appendix). The singlet at 2.02 ppm corresponds to the six equivalent methyl protons at the ortho positions on the mesityl group, while the methyl group at the para position of the mesityl group appears as a singlet integrating to three protons at 2.37 ppm. The singlet at 7.00 ppm corresponds to the two aromatic protons on the mesityl group. The singlets at 7.48, 6.93, and 7.29 ppm correspond to the aromatic protons on the imidazole at the 2, 4, and 5 positions, respectively. There were few impurities present in the ¹H NMR spectrum; however, the small peaks between 2.02 and 2.37 ppm caused the methyl singlets to artificially integrate to higher values than expected. The experimentally observed melting range (109 °C – 112 °C) was consistent with the literature value (110 °C – 112 °C). The minor discrepancy can be attributed to the aforementioned impurities observed in the ¹H NMR spectrum.

The highest yield of the purified product was 53.23 %, which is comparable to the literature yield (69.7 %). The primary loss of product can be attributed to the recrystallization of the crude product. Ethyl acetate was the only solvent that was able to dissolve the crude product; however it did so at room temperature. Recrystallization only occurred when the dissolved product was cooled in an ice bath; but, even under those conditions the process was slow. It is likely that a significant amount of the product never dropped out of solution. However, recrystallization was still used as the primary

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method of purification because an appropriate mobile phase for column chromatography was never determined.

3.6 Conclusions and Future Work

The synthesis of the first product in the reaction scheme, 1-(2,4,6trimethylphenyl)-1H-imidazole, was completed. It was isolated and purified to give a sufficient yield of 52 %. ¹H NMR and melting point were employed to confirm its purity. The purification process could be refined to increase the yield; however, it was not prohibitively low enough to necessitate such an investigation.

The successful synthesis of this product allows for the continuation of the synthetic route. Once the final product is obtained, fluorescence correlation spectroscopy can be employed to monitor the diffusion of the catalyst under an array of experimental conditions.

Works Cited

- 1. Mirkovic, T.; Zacharia, N.; Scholes, G.; Ozin, G. *Small*, **2010**, *6*, 159.
- 2. Van de Ven, T. Colloidal Hydrodynamics, New York: Academic Press, 1984.
- Houston, P. Chemical Kinetics and Reaction Dynamics. Dover Publications, 2006.
- 4. Wang, J.; Manesh, K. *Small*, **2010**, *6*, 338.
- 5. Pantaloni, D.; Le Clainche, C.; Carlier, M. Science, 2001, 292, 1502.
- 6. Ebbens, S.; Howse, J. Soft Matter, **2010**, *6*, 726.
- 7. Ebel, J.; Anderson, J. *Langmuir*, **1988**, *4*, 396.
- Ismagilov, F.; Schwartz, A.; Bowden, N.; Whitesides, G. Angew. Chem. Int. Ed.,
 2002, 41, 652.
- 9. Paxton, W.; Sen, A.; Mallouk, T. Chem. Eur. J. 2005, 11, 6462.
- 10. Vougioukalakis, G.; Grubbs, R. Chem. Rev. 2010, 110, 1746.
- 11. Trnka, T.; Grubbs, R. Acc. Chem. Res., 2001, 34, 18.
- 12. Katz, T.; McGinnis, J. J. Am. Chem. Soc. 1975, 97, 1592.
- 13. Cardin, D.; Cetinikaya, B.; Lappert, M. Chem. Rev. 1972, 72, 545.
- 14. Co'rdova-Figueroa, U.; Brady, J. Phys. Rev. Lett. 2008, 100, 158303.
- 15. Anderson, J.; Lowell, M.; Prieve, D. Fluid Mech. 1982, 117, 107.
- 16. Anderson, J. Ann. N. Y. Acad. Sci. 1986, 469, 166.
- 17. Prieve, D.; Anderson J.; Ebel, J.; Lowell, M. J. Fluid Mech. 1984, 148, 247.
- 18. Watari, H.; Suwa, M.; Iiguni, Y. Anal. Bioanal. Chem. 2004, 378, 1693.
- 19. Muddana, H.; Sengupta, S.; Mallouk, T.; Sen, A.; Butler, P. J. Am. Chem. Soc.
 2010, 132, 2110.

20. Occhipinti, G.; Jensen, V.; Törnroos, K.; Froystein, N.; Bjorsvik, H. *Tetrahedron*.
2009, 65, 7186.

Appendix



Chapter 2.5.1 NMR spectrum of polynorbornene produced by the polymerization nanomotors.



Chaper 2.5.1 XPS spectrum for Grubbs 2nd generation catalyst showing the presence of Ruthenium.



Chapter 2.5.1 XPS spectrum for Grubbs 2nd generation catalyst showing all the elements in the spectrum.



Chapter 3.5 NMR spectrum of 1-(2,4,6-trimethylphenyl)-1H-imidazole.

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EDUCATION

The Pennsylvania State University, University Park, PA

- Bachelor of Science in Chemistry, expected December 2010
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HONORS AND AWARDS

- Bruce and Elsa Ottinger Weldner Scholarship in Analytical Chemistry, 2010
- Fleming-Meyer Analytical Award, 2010
- Teas Science Scholarship, 2010
- Schreyer Honors Academic Excellence Scholarship, 2006-2010
- Huck Trustee Scholarship in Science, 2009
- University Trustee Scholarship, 2006
- ACS Project SEED Scholarship, 2006

RESEARCH EXPERIENCE

Research Assistant, Penn State University

- Research Advisor: Prof. Ayusman Sen
- Interdisciplinary research in nanochemistry, organic synthesis, organometallics, and polymer chemistry

RELATED EXPERIENCE

Undergratduate Assistant, Penn State University

Chemistry 431W (Organic and Inorganic Preparations)

- Supervise students performing inorganic and organic laboratory experiments
- Assist in the interpretation of spectra

Teaching Assistant, Penn State University

Undergraduate Instrument Room

- Supervise undergraduate students in organic chemistry laboratories running various spectroscopy techniques, including NMR, IR, UV-Vis, GC
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2006 - Present

August, 2010 - Present

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Chemistry Tutor, Penn State University

• Tutor both individuals and groups of students in general and organic chemistry lectures and labs

Teaching Assistant, Penn State University

Chemistry 202 (Organic Chemistry I)

- Graded homework assignments and exams
- Held office hours and review sessions
- Assisted in generating class materials

Teaching Assistant, Penn State University

Chemistry 203 (Organic Chemistry II)

- Supervised one section of undergraduates performing organic laboratory experiments
- Lectured on laboratory techniques and safety procedures
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