KINETIC STUDY AND MECHANOCHEMICAL SYNTHESES OF α- AND β- ISOMERS OF DITETRADECYL 2,2'-BIPYRIDINE-4,4'-DICARBOXYLATE COMPLEXES OF PALLADIUM AND 1,3-DIMETHYL BENZIMIDAZOLIUM IODIDE

Alexandra Nicole Underwood Ms
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KINETIC STUDY AND MECHANOCHEMICAL SYNTHESSES OF α- AND β-ISOMERS OF DITETRADECYL 2,2'-BIPYRIDINE-4,4'-DICARBOXYLATE COMPLEXES OF PALLADIUM AND 1,3-DIMETHYL BENZIMIDAZOLIUM IODIDE

A Thesis
Presented to
the Faculty of the Department of Chemistry
Jesse D. Jones Hall
Murray State University
Murray, Kentucky

In Partial Fulfillment
of the Requirements for the Degree
of Masters of Chemistry

By: Alexandra Underwood
December 2019
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Abstract

Mechanochemistry involves milling reagents to induce reactions and is considered a greener alternative to solution-based synthesis. This work will address the mechanochemical syntheses of the $\alpha$- and $\beta$-isomers of ditetradecyl 2,2'-bipyridine-4,4'-dicarboxylate complexes of palladium as well as the kinetics of these reactions. This work will also address the improved mechanochemical synthesis of 1,3-dimethyl benzimidazolium iodide as well as its kinetics.

The study of ditetradecyl 2,2'-bipyridine-4,4'-dicarboxylate complexes of palladium utilized $^1$H NMR spectroscopy for kinetic analysis. The total reaction completion time for $\text{PdL}_{\alpha14}^{}\text{I}_2$ was 55 minutes while the total reaction completion time for $\text{PdL}_{\beta14}^{}\text{I}_2$ was 600 minutes. Based on coefficients of determination, it was ascertained that only the Johnson-Mehl-Avarami-Yerofeev-Kolmogrov (JMAYK) model could be used to fit both reactions.

Values of the rate constant, $k$ obtained from the JMAYK model for $\text{PdL}_{\alpha14}^{}\text{I}_2$ were $0.05\pm0.01 \text{ min}^{-1}$ while values of $k$ from the JMAYK model for $\text{PdL}_{\beta14}^{}\text{I}_2$ were $0.011\pm0.008 \text{ min}^{-1}$ and $0.005\pm0.004 \text{ min}^{-1}$ for mixing and non-mixing, respectively. These decreased values for $\text{PdL}_{\beta14}^{}\text{I}_2$ were consistent with the rate differences observed during milling for both complexes. Average values of $n$ obtained for $\text{PdL}_{\alpha14}^{}\text{I}_2$ were $1.1\pm0.2$ and indicate pre-existing nucleation sites are present on the material before milling as well as two-dimensional growth. While average $n$ values obtained for $\text{PdL}_{\beta14}^{}\text{I}_2$ were $0.5\pm0.1$ and $0.30\pm0.06$ for mixing and non-mixing, respectively. These values also indicate pre-existing nucleation sites are present on the material prior to mixing, however, growth is one-
The differences in growth cause the differences in observed reaction rates between the two complexes.

Values of nucleation, $k_1$ and autocatalytic growth, $k'_2$ for PdL$_{a^{14}}$I$_2$ were $0.04 \pm 0.02$ min$^{-1}$ and $0.02 \pm 0.03$ min$^{-1}$. While values of $k_1$ for PdL$_{b^{14}}$I$_2$ were $0.01 \pm 0.01$ min$^{-1}$ and $0.004 \pm 0.002$ min$^{-1}$ for mixing and non-mixing, respectively. However, values of $k'_2$ were consistently negative, therefore; restricted modeling was utilized to only yield positive values. This gave values of zero for both mixing and non-mixing which would indicate autocatalytic growth does not occur during the synthesis of PdL$_{b^{14}}$I$_2$. Differences in the physical properties of the complexes were observed throughout milling as $\alpha$-substituted reactions yielded products that were soft while $\beta$-substituted reactions yielded products that were hard and sticky.

Finally, this work will address the improved mechanochemical synthesis of 1,3-dimethyl benzimidazolium iodide where both LAG (liquid assisted grinding) and neat methods were utilized. Kinetic analysis for this study also utilized $^1$H NMR spectroscopy. For neat methods, complete conversion occurred within 350 minutes, whereas complete conversion for LAG methods occurred at 600 minutes. Coefficients of determination were found to be between 0.9834-0.9951 and 0.9450-0.9912 for JMAYK and Finke-Watzky (FW) models, respectively. Values of $k$ from the JMAYK model for neat methods were $5.644 \times 10^{-3}$ min$^{-1}$ and $5.246 \times 10^{-3}$ min$^{-1}$ while the $k$ value obtained for the LAG methods were smaller. This was consistent with the differences in rates observed during the course of the reactions. Values of $n$ cannot be broken down to give information of
nucleation and growth as the values obtained were larger than four for the neat methods. This would indicate, however, that increasing nucleation is occurring.

Values of $k_1$ and $k'_2$ for neat methods were also similar to each other while the values of $k_1$ were in between those of neat methods. Values of $k'_2$ were smaller than that of the LAG methods which was consistent with the reaction rates observed. Due to the slow reaction times for LAG methods, it was determined that LAG methods actually hindered conversion to product.
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Chapter 1: Introduction

1.1 Mechanochemistry

Mechanochemical synthesis, a greener, alternative methodology to traditional synthesis, involves inducing reactions by the input of mechanical energy. The benefits of these methods have been well reviewed\textsuperscript{1} and include significant decreased or elimination of solvent use and decreased reaction times for many types of syntheses as well as being more cost effective than traditional synthesis. Historically, these types of preparations have been a “sideline” approach. However, the current dependence on solvents is becoming increasingly more unsustainable and mechanochemical based syntheses are increasing in popularity due to their benefits.\textsuperscript{1}

Despite the recent rise in popularity, mechanochemistry is not a new concept. According to Takacs,\textsuperscript{2} mechanochemistry was potentially utilized as early as 4\textsuperscript{th} century B.C. through the grinding of cinnabar alongside acetic acid in copper vessels to produce elemental mercury. A recent \textit{Faraday Discussion} presented a wide variety of modern processes and mechanochemical energy sources that are implied under the heading of mechanochemistry.\textsuperscript{3} Kinetic understanding of “molecular” mechanochemistry is in early development, as was first reviewed by Ma and coworkers in 2014.\textsuperscript{4} “Molecular” mechanochemistry refers to the mechanochemical preparation of discrete molecules and complexes, rather than extended network materials.\textsuperscript{1, 2, 5-14} Since then, work by our group\textsuperscript{15-17} and others\textsuperscript{18-21} has focused on determining whether or not the models\textsuperscript{22} originally
developed for the synthesis of inorganic network materials (e.g. metal oxides and nitrides) are applicable to molecular mechanochemistry.

This work will initially focus on the mechanochemical syntheses of the \( \alpha \)- and \( \beta \)-isomers of ditetradecyl 2,2'-bipyridine-4,4'-dicarboxylate complexes of palladium (1 and 2, Figure 1) and the kinetics of their preparation. A thorough study of kinetics of these reactions is necessary in order to reliably predict reaction times for mechanochemical synthesis to be utilized for routine small molecule and transition metal complex preparation.

![Figure 1. The structures of PdL\(^{\alpha 14}I_2\) (left) and PdL\(^{\beta 14}I_2\) (right).](image)

Secondly, this work will address the improved mechanochemical synthesis of 1, 3-dimethyl benzimidazolium iodide (HBZM-Me\(_2\)I, Figure 2); which is used as a reagent for the synthesis of a catalyst for coupling reactions.\(^\text{23}\) This molecule has demonstrated antimicrobial properties as it has been evaluated against \textit{Staphylococcus aureus, Escherichia coli, Pseudomonas aeruginosa, Bacillus subtilis, and Bacillus proteus.}\(^\text{24}\) Since this work is a culmination of two different
projects, the material will be treated individually, with the initial discussion of the palladium complex synthesis and kinetic analysis, on page 14, before addressing 1, 3-dimethyl benzimidazolium iodide, on page 34.

Figure 2. The structure of HBZM-Me2I.

Before addressing each of the syntheses mentioned above, some consideration will be given to kinetic modeling as it will be applied to both topics later in the discussion. All models considered for this work will be presented, but the main focus will be on the two most applicable. This will include a discussion of the models as well as their relevant derivations.

The mechanochemical methods from this study will be compared to the results of literature solution syntheses. Literature solution syntheses are illustrated in Scheme 1. Solvent heavy conditions are utilized for traditional methods in which the reacting species need to be dissolved before reaction (Scheme 1, blue arrows) and purification is required and carried out by column chromatography. Mechanochemical methods (Scheme 1, green arrows) give complete conversion and eliminates the need for heavy solvent use. Thus, providing a more sustainable method for syntheses.
Scheme 1. The traditional preparation of complexes (blue arrows) requires vast use of solvents due to incomplete conversion. Purification is necessary and carried out by column chromatography. Mechanochemical synthesis (green arrows) yields complete conversion in the absence of solvent.

1.2 Kinetic Modeling

One of the main focuses of this study was the kinetics of reactions. Specifically, consideration was given to the time to conversion from starting materials to product and the rate at which conversion occurred. This was done by preparing conversion fraction ($\alpha$) plots; where $\alpha$ is plotted versus time for the reaction of each complex. Conversion fraction is the mole abundance of products compared to the total, theoretical, moles of product of the reaction at a given point in time. This is defined in Equation 1 where $n(p)$ is moles of synthesized product and $n(ty)$ is theoretical yield in moles.

$$\alpha = \frac{n(p)}{n(ty)}$$ (1)
The study and understanding of reaction kinetics are necessary to maximizing the benefits of these more sustainable reaction methods. There are several mathematical models to consider presented by Khawam and Flanagan\textsuperscript{22} as well as two proposed by Finney and Finke\textsuperscript{25}. These models are shown in Table 1. These kinetic models have been applied to several different solid-state reactions and transitions such as nanocluster formation\textsuperscript{26}, solid-state crystallizations\textsuperscript{27}, and protein aggregation relevant to neurological diseases.\textsuperscript{28-30}
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<table>
<thead>
<tr>
<th>Model</th>
<th>Abbrev.</th>
<th>$f(\alpha) = \frac{1d\alpha}{kdt}$</th>
<th>$g(\alpha) = kt$</th>
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<tbody>
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<td>P2</td>
<td>$2\alpha^{1/2}$</td>
<td>$\alpha^{1/2}$</td>
</tr>
<tr>
<td></td>
<td>P3</td>
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<td>P4</td>
<td>$4\alpha^{3/4}$</td>
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<tr>
<td>Prout-Tompkins</td>
<td>B1</td>
<td>$\alpha(1 - \alpha)^{1/2}$</td>
<td>$\ln\left[\frac{\alpha}{(1 - \alpha)}\right] + c$</td>
</tr>
<tr>
<td>Contracting Area</td>
<td>R2</td>
<td>$2(1 - \alpha)^{1/2}$</td>
<td>$1 - (1 - \alpha)^{1/2}$</td>
</tr>
<tr>
<td>Contracting Volume</td>
<td>R3</td>
<td>$3(1 - \alpha)^{2/3}$</td>
<td>$1 - (1 - \alpha)^{1/3}$</td>
</tr>
<tr>
<td>1-D Diffusion</td>
<td>D1</td>
<td>$\frac{\alpha}{2}$</td>
<td>$\alpha^2$</td>
</tr>
<tr>
<td>2-D Diffusion</td>
<td>D2</td>
<td>$\frac{\ln (1 - \alpha)}{3(1 - \alpha)^{2/3}}$</td>
<td>$[1 - (1 - \alpha)^{1/3}]^2$</td>
</tr>
<tr>
<td>3-D Diffusion, Jander</td>
<td>D3</td>
<td>$\frac{3}{2[1 - (1 - \alpha)^{1/3}]}$</td>
<td>$1 - \frac{2}{3} \alpha - (1 - \alpha)^{2/3}$</td>
</tr>
<tr>
<td>Ginstling-Brounshtein</td>
<td>D4</td>
<td>$\frac{1}{2[1 - (1 - \alpha)^{1/3}]}$</td>
<td>$1 - \frac{2}{3} \alpha - (1 - \alpha)^{2/3}$</td>
</tr>
<tr>
<td>Zero-Order</td>
<td>F0</td>
<td>$1$</td>
<td>$\alpha$</td>
</tr>
<tr>
<td>First-Order</td>
<td>F1</td>
<td>$(1 - \alpha)$</td>
<td>$-\ln (1 - \alpha)$</td>
</tr>
<tr>
<td>Second-Order</td>
<td>F2</td>
<td>$(1 - \alpha)^2$</td>
<td>$\frac{1}{(1 - \alpha)^2} - 1$</td>
</tr>
<tr>
<td>Third-Order</td>
<td>F3</td>
<td>$(1 - \alpha)^3$</td>
<td>$\frac{1}{2}[(1 - \alpha)^{-2} - 1]$</td>
</tr>
<tr>
<td>Johnson-Mehl-Avrami-Yerofeev-Kolmogrov</td>
<td>JMAYK</td>
<td>$\alpha = 1 - e^{-(kt)^n}$</td>
<td>$\ln[-\ln(1 - \alpha)] = n\ln(k) + n\ln(t)$</td>
</tr>
<tr>
<td>Finke-Watzky</td>
<td>FW</td>
<td>$\alpha = \frac{k_1 + k_1'}{k_1' + k_1 e^{(k_1 + k_1')t}}$</td>
<td></td>
</tr>
</tbody>
</table>

Traditionally, there are two methods by which kinetic data can be fitted to determine reaction models. The term $f(\alpha)$ corresponds to the differential form of the rate equation for the reaction model. Since these functions are non-linear for all reaction models with the exception of zero-order reaction kinetics, it is
common to utilize an integrated version of each model, termed here, \( g(\alpha) \) instead. For this method of fitting, values of \( g(\alpha) \) are calculated from \( \alpha \) and are plotted versus time (\( t \)) according to Equation 2.

\[
g(\alpha) = Ae^{-\frac{Ea}{RT}t} = kt
\]  

(2)

Khawam and Flanagan have outlined four different classes of mechanochemical reaction models in their review.\(^{22}\) The first class is nucleation which includes power laws (P2-4), Johnson-Mehl-Avrami-Yerofeev-Kolmogrov (JMAYK), and Prout Tompkins models (B1). The second class is geometrical contraction models including the contracting volume and contracting area models (R2 and R3). The third class is diffusion-based models, including one-, two-, and three-dimensional diffusion models (D1-4), where the three-dimensional diffusion models include both Jander and Ginsling-Brounshtein types. The fourth class is reaction order models (F0-3), which follow typical models observed for solution reactions.

While each of these kinetic models have been given consideration in this work, similar, past research\(^{15}\) has indicated that reaction kinetics for other 2,2'-bipyridine-4,4'-dicarboxylate complexes of palladium were sigmoidal. Additionally, the initial plotting of conversion fraction versus time curves for 1, 3-dimethyl benzimidazolium iodide were sigmoidal in nature. Therefore, only the nonlinear JMAYK and FW models were utilized to fit the data in this study.
1.2.1 JMAYK Model

The Johnson-Mehl-Avrami-Yerofeev-Kolmogrov (JMAYK) model has both linear and nonlinear versions and is an empirical model. The nonlinear version of the JMAYK model, (JMAYK, Table 1) was utilized for data fitting in the study as this model exhibits sigmoidal behavior. The Avrami exponent, \( n \), can be broken down according to the work of Cumbrera and coworkers as shown in Equation 3.\(^{31}\) This equation contains a nucleation rate term, \( a \), (\( a \) is zero for preexisting nucleation sites or one for instantaneous formation of nucleation sites) growth mechanism, \( p \), (\( p = 1 \) for interfacial growth or \( 1/2 \) for parabolic growth) and dimensionality of growth term, \( b \). The JMAYK equation is derived from the rate of nucleation equation presented by Avrami\(^{32}\) (Equation 4) where \( N \) is the number of nuclei that appear in a sample of volume \( V \), \( \dot{N} \) is the nucleation rate of new particles, and \( T \) is the time constant of phase growth.

\[
\begin{align*}
n &= a + bp \\
N &= V\dot{N}dT
\end{align*}
\]

Since growth is isotropic, each nucleus will grow into a sphere of radius \( \dot{G} (t - T) \) where \( \dot{G} \) is growth rate and \( t \) is the time interval where the growth occurs. The extended volume, \( dV_{\beta}^e \) where \( e \) is the initial volume and \( \beta \) is the maximum volume, is also growing due to nuclei appearing in the time interval is given in Equation 5. Integration of Equation 5 between \( T = 0 \) and \( T = t \) gives Equation 6.
\[ dV^e_\beta = \frac{4\pi}{3} \dot{G}(t - T)^3 V \dot{N}t \]  
\[ V^e_\beta = \frac{\pi}{3} V \dot{N} \dot{G}^3 t^4 \]  

Nucleation occurs randomly and the fraction of the extended volume that forms during each time increment will be proportional to the volume fraction of untransformed conversion fraction, which gives Equation 7. Rearranging Equation 7 gives us Equation 8, which provides the ability to integrate giving Equation 9 where \( Y \) is the volume fraction of \( \beta \) (\( V_\beta / V \)). This equation can be reduced to give the JMAYK equation, Equation 10 where \( k = \pi \dot{N} \dot{G}^3 / 3 \) and \( n \) is the Avrami exponent from Equation 3. Note that in this study, \( \alpha \) is utilized instead of \( Y \) because this study measures conversion fraction as opposed to volume fraction.

\[ dV_\beta = dV^e_\beta (1 - \frac{V_\beta}{V}) \]  
\[ \frac{1}{1 - V_\beta/V} dV_\beta = dV^e_\beta \]  
\[ \ln(1 - Y) = -V^e_\beta/V \]  
\[ Y = 1 - e^{-(kt)^n} \]

1.2.2 Finke-Watzky Models

The Finke-Watzky model was also examined for this study.\(^{25}\) The FW model is a two-step kinetic scheme consisting of nucleation followed by autocatalytic growth as seen in Equations 11 and 12. The FW model has historically fit the data for loss of concentration of nanocluster precursor, \( A \) in
Equations 11 and 12, as opposed to most solid state reactions that are typically given in terms of the amount of starting material transformed into product, $\alpha$, which increases with time.

$$A \rightarrow k_1 B$$  \hspace{1cm} (11)

$$A + B \rightarrow k_2 2B$$ \hspace{1cm} (12)

The integrated rate equation for the loss of $A$ over time is given in Equation 13. This is calculated by taking the applicable rate equation, Equation 14, for the kinetically important steps and starting the kinetic derivation with the rate-determining steps, $k_1$ and $k'_2$. Substituting the mass balance equation, $[B]=[A]_0-[A]$, yields Equation 15. Equation 15 can then be evaluated at limits of zero and $t$ through Equations 16, 17, and 18.

$$[A] = \frac{k_1/[A]_0}{1 + \frac{k_2}{[A]_0} e^{(k_1+k_2/[A]_0)t}}$$ \hspace{1cm} (13)

$$\frac{-d[A]}{dt} = \frac{d[B]}{dt} = k_1 [A] + k_2 [A][B]$$ \hspace{1cm} (14)

$$[A] = k_1 [A] + k_2 [A]([A]_0 - [A])$$ \hspace{1cm} (15)

$$[A] = k_1 [A] + k_2 [A]([A]_0 - [A]) \int_0^t \frac{-d[A]}{[A](k_1+k_2([A]_0-[A]))} dt$$ \hspace{1cm} (16)

$$[A] = dt \frac{1}{k_1+k_2[A]_0} \ln \left[ \frac{k_1+k_2([A]_0-[A])}{[A]} \right]_0^t$$ \hspace{1cm} (17)

$$[A] = t \ln \left[ \frac{(k_1+k_2([A]_0-[A]))[A]_0}{k_1[A]} \right] = (k_1 + k_2([A]_0)t$$ \hspace{1cm} (18)
Expressing Equation 18 in exponential form gives Equation 13. According to Finney and Finke,\textsuperscript{25} in order to compare model fits between the JMAYK and FW models, Equation 13 must be converted into a form that expresses $\alpha$ as a function of time. This is done by recognizing that in the FW model, $\alpha = (\{A\}_0 - \{A\}_0 t)/\{A\}_0$. In order to get Equation 19, $\{A\}_0 t = [A]_0 (1 - \alpha)$ is substituted in the left-hand side of Equation 13 and then the equation is solved for $\alpha$. It is important to note that in Equation 19, $k'_2 = k_2 [A]_0$ to remove the concentration dependences from the FW model because concentration is not a useful concept in the solid-state. The Finke-Watzky model gives separate rate constant values for nucleation ($k_1$) and autocatalytic growth ($k'_2$) as shown in Equation 19. This differs in that the JMAYK model combines nucleation and growth under a single rate related parameter, ($k$).

$$\alpha = \frac{k_1 + k'_2}{k_1 e^{(k_1 + k'_2)t}}$$  \hspace{0.5cm} (19)

These models were fit to the data in this study based on the coefficients of determination ($R^2$ values). This was done using Equation 20. The residual sum-of-squares, $SS$, is given by Equation 21 where $N$ is the number of data points, $y_i$ is the experimental value, and $f_i$ is the value predicted from the model. The total sum-of-squares, $S_{tot}$, is given by Equation 22 where $\bar{y}$ is the average of all the data values.

$$R^2 = 1 - \frac{SS}{S_{tot}}$$  \hspace{0.5cm} (20)

$$SS = \sum_{i=1}^{N} (y_i - f_i)^2$$  \hspace{0.5cm} (21)
\[ SS_{tot} = 1^N(y_i - \bar{y})^2 \]  

(22)

Akaike’s Information Criterion (\(AIC_{ci}\)) is another statistical method that can be applied to model fitting. This method calculates the probability that one model should be used over another for a given data set. Akaike’s second-order method,\(^{34}\) Equation 23, was utilized in this study. In Equation 23, \(SS\) is the residual sum of squares as defined above; \(N\) is the number of data points and \(K\) is the number of parameters in the model. PSI-Plot version 8.81 was utilized to carry out fitting to each model to determine \(SS\), \(N\), and \(K\). Since there are two parameters for each model, \(K\) is two for both JMAYK and FW models.

\[
AIC_{ci} = Nln \left( \frac{SS}{N} \right) + 2K + \frac{2K(K+1)}{N-K-1} 
\]

(23)

Because lower \(SS\) values correspond to better fits and because Equation 23 imposes a positive penalty for a model with more parameters, the model with the lowest value of \(AIC_{ci}\) will be statistically favored. In order to make this determination more quantitative, the differences in \(AIC_{ci}\) values can be converted to Akaike weights, \(w\), Equation 24, which represents the probability that a given model is favored. Akaike weights can vary from zero to one based on how strongly one model fits the data compared to others. In order to determine \(w\), the difference in \(AIC_{ci}\) values between each model and the lowest \(AIC_{ci}\), value for all models compared (\(\Delta AIC_{ci}\)) must also be determined.

\[
w = \frac{e^{-\frac{AIC_{ci}}{2}}}{\sum_{y=1}^{R} e^{-\frac{\Delta AIC_{ci}}{2}}} 
\]

(24)
To make a comparison of the utility of the two models to each other, evidence ratios ($ER$) were calculated using Equation 25 from Akaike weights for both the JMAYK and FW models were utilized.\textsuperscript{25} An $ER \geq 10^4$ would indicate that the JMAYK model was significantly better while and $ER \leq 10^{-4}$ would indicate that the FW model was a significantly better fit even if both models gave acceptable fits based on $R^2 \geq 0.95$. Now that relevant information that pertains to both topics of this work has been presented, the focus will shift to a discussion specifically of palladium complexes.

$$ER = \frac{w_{JMAYK}}{w_{FW}}$$

(25)
Chapter 2: Palladium Complexes

2.1 Introduction

The kinetics of the syntheses of α- and β-ditetradecyl 2,2’-bipyridine-4,4’-dicarboxylate complexes of palladium (Scheme 2) were considered in this study. This study was carried out as a continuation of previous research from the Allenbaugh group\(^{15}\) which established that other ditetradecyl 2,2’-bipyridine-4,4’-dicarboxylate complexes of palladium reaction kinetics were sigmoidal by fitting complexes to the linear and sigmoidal models listed in Table 1.

**Scheme 2.** The synthesis of PdL\(^{\alpha14}\)I\(_2\) (R\(^1\)=H, R\(^2\)=C\(_{13}\)H\(_{27}\)) and PdL\(^{\beta14}\)I\(_2\) (R\(^1\)=CH\(_3\), R\(^2\)=C\(_{12}\)H\(_{25}\)).

Based on poor \(R^2\) values obtained, it was determined that none of the data correlated well with linear models. However, the data did correlate well with the sigmoidal version of the JMAYK and the FW models. Therefore, two sigmoidal reaction models were considered (Table 1) for this study. This was done in order to see if one single kinetic model would fit both reactions as the α/β isomers have
the same mass, but very different physical properties that will be discussed later on.

2.2 Experimental

2.2.1 General Procedures

The \(^1\)H NMR spectra were recorded on a JEOL-ECS 400 MHz spectrometer at room temperature in CDCl\(_3 \) solution. The CDCl\(_3 \) was stored over activated alumina in order to remove any trace acid. Trace acids can potentially result in the protonation of the complexes below. Differential scanning calorimetry (DSC) measurements were obtained using a TA instruments DSC Q200 with a ramp rate 10° C min\(^{-1} \). Two heating/cooling cycles were performed for each sample. The data discussed in this work were obtained from the second heating/cooling cycle.

2.2.2 Synthetic Procedures

Both ligands, L\(^{a14} \) and L\(^{b14} \), were synthesized were prepared using solution methods by Hyatt et al.\(^{35} \) and Allenbaugh et al.\(^{15} \) Various alcohols as well as PdI\(_2 \) were obtained from Sigma Aldrich; 2,2’-bipyridine-4,4’- dicarboxylic acid was obtained from Ark Pharm. All reagents were utilized without further purification. The ligands were then purified by triple recrystallization from hot ethanol. Characterization information for all ligands have been reported previously.\(^{35-37} \)
2.2.3 Conditions for Kinetic Studies

Kinetic runs were carried out in either a SPEX 5100 mill (α-substituted reactions) or a SPEX 8000M mill (β-substituted reactions) in 2.5-mL stainless steel vials with one 6.35-mm steel ball. One single run was sampled multiple times for both complexes. A total of four runs were carried out for the α-substituted reactions, while a total of six runs were carried out for the β-substituted reactions. All kinetic studies were carried out in CDCl₃ and the mixtures were first filtered to remove unreacted PdI₂ prior to ¹H NMR spectroscopic analysis. For α-substituted reactions, PdI₂ (0.4377 mmol±0.0047 mmol) and ligand (0.3406 mmol±0.0028 mmol) were milled in a SPEX 5100 Mixer Mill. Samples were milled for a total of 65 minutes with kinetic sampling occurring at one, two, three, four, five, and ten-minute intervals and then sampling every five minutes thereafter.

It is important to note that for some trials the order of adding reagents to the vial was changed. In some cases, PdI₂ was added to vial first, whereas in some instances, ligand was added first. The reaction mixture was dissolved in 5-mL of chloroform and filtered to remove excess PdI₂. The solvent was then evaporated to yield dark red crystals. The material is hygroscopic and may be dried under vacuum.

For β-substituted reactions, PdI₂ (0.3673 mmol±0.0363 mmol) and ligand (0.4407 mmol±0.0041 mmol) were milled in a SPEX 8000M Mixer Mill. Samples were milled for a total of 600 minutes with kinetic sampling occurring at 10, 20, and 30-minute intervals and then sampling every 30 minutes thereafter. It is
important to note that at a certain point in the synthesis, the sample had to be hand mixed at 30-minute time intervals to achieve conversion. The reaction mixture was dissolved in 5-mL of chloroform and filtered to remove excess PdI₂. The solvent was then evaporated to yield dark crystals. All kinetic studies were carried out in CDCl₃ and the mixture was filtered to remove unreacted PdI₂ prior to ¹H NMR spectroscopic analysis.

2.3. Results and Discussion

The focus of this study was to determine if one single, kinetic model could fit both reactions. In order to do this, α- and β-substituted reactions were treated individually and then compared. The conversion fraction, α, was tracked by ¹H NMR spectroscopy as seen in Figure 3 where the relative amounts of ligand and complex are determined using the boxed resonances along with Equation 1 on page 4 to determine α. At 330 minutes, a conversion fraction of 86% was observed. Partial ¹H NMR spectra of PdLβ₁₄I₂ from 0-600 minutes are pictured in Figure 3. Only PdLβ₁₄I₂ shown below as PdLα₁₄I₂ has similar resonances to PdLβ₁₄I₂. A full ¹H NMR spectrum of PdLα₁₄I₂ can be found on page A1 of the Appendix.
2.3.1 The Study of α-Ditetradecyl 2,2'-Bipyridine-4,4'-dicarboxylate Complex of Palladium

During the synthesis of PdLα14I2 the order in which PdI2 and Lα14 were added to the vial prior to milling was changed to determine if this had any effect on the reaction or conversion to product. This was done by alternating between adding PdI2 to the bottom or the top of the vial. Initially, a decreased reaction rate for was observed for adding PdI2 to the top of the vial. This decreased rate was attributed to poor initial mixing. However, this did not affect the completion of the overall reaction as homogenization occurred during milling and complete conversion to product was attained. This is shown in Figures 4 and 5 below where kinetic plots were obtained by plotting conversion fractions taken from
sampling intervals and plotted versus time. From this, it is was possible to fit the JMAKY and FW models to the data and the resulting curves are pictured below in Figures 4 and 5, respectively. Results from these fittings will be discussed later.

**Figure 4.** Kinetic plots of the four trials for the synthesis of PdL^{α14}I\textsubscript{2} for the JMAKY model. Whether the L^{α14} (● and ▲) or PdI\textsubscript{2} (× and ○) is placed at the top of the vial affects initial reaction rate, because the reaction mixture is not well mixed initially.
Figure 5. Utilizing the same data for PdL$^{14}$ as in Figure 4, kinetic plots can also be made using the FW model (Table 1). The resulting curves are very similar to the JMAK results, regardless of whether L$^{14}$ (● and ▲) or PdI$_2$ (× and ○) is placed at the top of the vial initially.

2.3.2 The Study of β-Ditetradecyl 2,2′-Bipyridine-4,4′-dicarboxylate Complex of Palladium

Conversion fraction for β-substituted complex was also tracked by $^1$H NMR spectroscopy. While the spectrum for β-substituted complex was similar to the α-substituted complex (Figure 3), the $^1$H NMR spectrum for the β-substituted complex can be found on page A2 in the Appendix. These samples were initially powdery but proceeded to become smoother and more uniform as bulk mixing of the reagents occurred during milling. However, it was determined that at 60% conversion ($\alpha = 0.60$), the reaction mixture became hard and sticky. This inhibited bulk mixing and necessitated hand mixing at 30-minute sampling intervals. It was
determined that hand mixing samples resulted in complete conversion while samples that were not hand mixed never achieved complete conversion. This is shown in Figures 6 and 7. Conversion fraction from sampling intervals was plotted versus time in order to obtain kinetic plots of the data. From this, model fitting of the JMAYK and FW models was possible as pictured below in Figures 6 and 7, respectively.

![Figure 6. Kinetic plots for the six trials for the synthesis of PdL^{14}\text{I}_2 for the JMAYK model (Table 1). Samples mixed by hand (●, ▲, and ×) resulted in complete conversion. Unmixed samples (Ο, ■, and ♦) did not reach complete conversion.](image-url)
Once the models were fit to the data, it was apparent in Figure 7 that the FW model gave a poor fit to the data. Although the FW model fits the initial and final portions of the data well when the samples are mixed by hand at 30-minute intervals the overall fit is poor. The FW model does not fit the results for the unmixed samples well at any point in the reaction sequence. Results from these fittings will be discussed later on.

2.3.3 Thermal Studies

One of the considerations given to this study was the effect the physical properties of the ligands and the complexes had upon the reaction. Thermal properties of the ligands are shown below in Table 2 for Lα14 and Lβ14 and were determined from DSC traces (Figures 8 and 9). For comparative purposes, Lβ12 that had been previously studied16 is also included. While each ligand has
different transitions phases, both of the β-substituted ligands have a transition that was not observed for the α-substituted ligand. The glass transition observed in both of the β-substituted ligands would indicate that this is a characteristic of this type of substitution of ligands.

Table 2. Thermal properties of ligands.\textsuperscript{16, a}

<table>
<thead>
<tr>
<th>Species (decomp, °C)</th>
<th>Transition</th>
<th>Temp. (°C)</th>
<th>∆H (kJ/mol)</th>
</tr>
</thead>
<tbody>
<tr>
<td>( \text{L}^{\alpha14} ) (384.5)</td>
<td>Cr-I</td>
<td>70.4</td>
<td>93.6</td>
</tr>
<tr>
<td></td>
<td>I-Cr</td>
<td>61.5</td>
<td>93.3</td>
</tr>
<tr>
<td></td>
<td>G-Cr1</td>
<td>-45.0</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>Cr1-Cr2</td>
<td>-11.6</td>
<td>79.1</td>
</tr>
<tr>
<td></td>
<td>Cr2-I</td>
<td>75.4</td>
<td>150.0\textsuperscript{b}</td>
</tr>
<tr>
<td></td>
<td>I-G</td>
<td>-49.3</td>
<td>-</td>
</tr>
<tr>
<td>( \text{L}^{\beta14} ) (377.2)</td>
<td>G-Cr1</td>
<td>20.1</td>
<td>55.8</td>
</tr>
<tr>
<td>( \text{L}^{\beta12} ) (333.6)</td>
<td>Cr1-I</td>
<td>71.0</td>
<td>66.8\textsuperscript{b}</td>
</tr>
<tr>
<td></td>
<td>I-G</td>
<td>12.3</td>
<td>-</td>
</tr>
</tbody>
</table>

\textsuperscript{a} Transition temperatures for compounds from DSC maxima/minima during second heat/cool, decomposition temperatures from TGA first mass loss inflection points; glass (G), crystalline phase (Cr), liquid crystalline phase (LC), isotropic liquid (I).

\textsuperscript{b} A series of unresolved transitions, likely due to alkyl chain rearrangements, occur and a single ∆H is provided for all transitions along with the temperature of the main transition event.
Figure 8. A DSC trace for L$^{\alpha 14}$. Traces are for the second heat/cool cycle.

Figure 9. A DSC trace for L$^{\beta 14}$. Traces are for the second heat/cool cycle.

Some consideration was also given to the physical properties of the complexes and how they affected the overall reaction. Thermal data for PdL$^{\alpha 14}$I$_2$
and PdL^{14}I_2 are shown below in Table 3. For comparative purposes, previously studied^{15, 38} PdL^{a16}I_2 and PdL^{b16}I_2 complexes are also included. As shown in Table 3, PdL^{a14}I_2 demonstrates a lamellar liquid crystalline phase while PdL^{b14}I_2 is not liquid crystalline. For PdL^{a16}I_2, a lamellar liquid crystalline phase is also observed while PdL^{b16}I_2 is not liquid crystalline. These similarities would indicate that these properties are characteristic of these substitutions of complexes. Thermal properties of PdL^{a14}I_2 and PdL^{b14}I_2 were determined from DSC traces below in Figure 10.
Table 3. Thermal properties of PdL_{α14}I_{2}, PdL_{β14}I_{2} PdL_{α16}I_{2}, and PdL_{β16}I_{2}.\(^a\)

<table>
<thead>
<tr>
<th>Species (decomp, °C)</th>
<th>Transition</th>
<th>Temp. (°C)</th>
<th>ΔH (kJ/mol)</th>
<th>Ref.</th>
</tr>
</thead>
<tbody>
<tr>
<td>PdL_{α14}I_{2} (342.4)</td>
<td>Cr1-Cr2</td>
<td>68.2</td>
<td>65.8</td>
<td>(^b)</td>
</tr>
<tr>
<td></td>
<td>Cr2-LC*</td>
<td>116.0</td>
<td>0.6</td>
<td></td>
</tr>
<tr>
<td></td>
<td>LC+C-LC</td>
<td>122.8</td>
<td>3.3</td>
<td></td>
</tr>
<tr>
<td></td>
<td>LC-I</td>
<td>189.3</td>
<td>25.2</td>
<td></td>
</tr>
<tr>
<td></td>
<td>I-LC</td>
<td>186.2</td>
<td>25.3</td>
<td></td>
</tr>
<tr>
<td></td>
<td>LC-Cr2</td>
<td>111.7</td>
<td>4.0</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Cr2-Cr1</td>
<td>53.0</td>
<td>65.7</td>
<td></td>
</tr>
<tr>
<td>PdL_{β14}I_{2} c</td>
<td>Cr-I</td>
<td>164.2</td>
<td>18.4</td>
<td>(^b)</td>
</tr>
<tr>
<td></td>
<td>I-Cr</td>
<td>143.4</td>
<td>18.2</td>
<td></td>
</tr>
<tr>
<td>PdL_{α16}I_{2} (337.0)</td>
<td>LC-I</td>
<td>170.1</td>
<td>13.0</td>
<td>[38]</td>
</tr>
<tr>
<td></td>
<td>I-LC</td>
<td>172.0</td>
<td>12.9</td>
<td></td>
</tr>
<tr>
<td></td>
<td>LC-Cr2</td>
<td>59.4</td>
<td>5.3</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Cr2-Cr1</td>
<td>33.8</td>
<td>26.4</td>
<td></td>
</tr>
<tr>
<td>PdL_{β16}I_{2} (289.1)</td>
<td>Cr1-Cr2</td>
<td>24.7</td>
<td>29.7</td>
<td>[15]</td>
</tr>
<tr>
<td></td>
<td>Cr2-I</td>
<td>168.8</td>
<td>27.7</td>
<td></td>
</tr>
<tr>
<td></td>
<td>I-Cr2</td>
<td>150.7</td>
<td>26.4</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Cr2-Cr1</td>
<td>16.8</td>
<td>32.3</td>
<td></td>
</tr>
</tbody>
</table>

\(^a\) Transition temperatures for compounds from DSC maxima/minima during second heat/cool, decomposition temperatures from TGA first mass loss inflection points; glass (G), crystalline phase (Cr), liquid crystalline phase (LC), isotropic liquid (I).

\(^b\) This work.

\(^c\) Species decomposition temperature not reported.

\(^d\) Lack of reported heating transitions as data was taken from previous research that did not report heating transitions.

\(^*\) As POM gave no apparent difference from the main phase, and small alkyl chain rearrangements are the likely cause, these have been designated with an asterisk rather than as separate phases.
Changes in physical properties were observed throughout milling. The reaction of PdL$^{\alpha 14}$I$_2$ is initially a voluminous powder as the microcrystalline ligand is relatively fine and fluffy. The reaction mixture quickly mills to a soft, soap-like consistency. Due to the ease of mixing the reaction mixtures during milling, these reactions are considered to be “soft”, and easily mixed as the ball mill provided enough energy to induce the reactions. This can be explained by the lamellar liquid crystalline phase observed in Table 3. Lamellar liquid crystalline phases consist of neatly ordered sheets that allow the layers of the material to easily slip past each other; which leads to the formation of a softer product. These layers are expected to persist in the solid state, which leads to easier milling.

The physical properties of PdL$^{\beta 14}$I$_2$ were much different than that of PdL$^{\alpha 14}$I$_2$. For one, the $\beta$-substituted ligand is not as voluminous or fluffy as the $\alpha$-substituted ligand. While the reaction mixture becomes smoother, almost clay-like during milling, as the reaction proceeds, it becomes harder and stickier.
These reactions are considered to be “sticky” and as a result, bulk mixing is hindered, which affects the reaction mixtures ability to homogenize which significantly increases the time it takes to attain complete conversion. Thus hand-mixing the reaction mixture at sampling intervals was utilized and while hand-mixing the reaction sample does help drive the reaction to completeness, it still takes a significantly longer time to attain complete conversion when compared to PdL$^{\alpha14}$I$_2$.

The difference in physical properties of PdL$^{\alpha14}$I$_2$ and PdL$^{\beta14}$I$_2$ can be attributed to the substitution of the R$^1$ of the ligands. The methyl group on the PdL$^{\beta14}$I$_2$ is bulkier than that of the proton on PdL$^{\alpha14}$I$_2$. This leads to a poorer packing efficiency of PdL$^{\beta14}$I$_2$, leading to the hard and sticky reaction mixture observed during milling. This is consistent with the glass inflection point observed for the $\beta$-substituted complex as poor packing likely leads to disordered, interdigitated chains. This led to disordered (glass) solid state, which is likely what caused the mixture to be harder to mill.

2.3.4 Kinetic Studies

One other area of focus in this study was determining if one kinetic model could be applied to both isomers. This was done by utilizing coefficients of determination or $R^2$ values once the data was fit to the kinetic models. For this study successful kinetic modeling was defined as $R^2 \geq 0.95$. Values of $R^2$ for the JMAYK and FW models for each reaction for PdL$^{\alpha14}$I$_2$ using Equation 20 on page 11 were determined and tabulated below in Table 4. Of the four reactions in this study, only one gave an $R^2$ value less than 0.95; However, it was very close.
Based on these values, it was determined that both the JMAYK and FW models gave acceptable fits for the data as seven of the eight reactions conducted produced values of $R^2 \geq 0.95$.

**Table 4.** Results of model fitting for reactions of PdL$^{\alpha14}$I$_2$ where symbols are from Figures 4 and 5.

<table>
<thead>
<tr>
<th>Model</th>
<th>Run</th>
<th>Top?</th>
<th>Parameters</th>
<th>$R^2$</th>
</tr>
</thead>
<tbody>
<tr>
<td>JMAYK</td>
<td>L$^{\alpha14}$</td>
<td>•</td>
<td>$k = 0.06$ min$^{-1}$, $n = 0.8$</td>
<td>0.9604</td>
</tr>
<tr>
<td></td>
<td></td>
<td>▲</td>
<td>$k = 0.05$ min$^{-1}$, $n = 1.0$</td>
<td>0.9778</td>
</tr>
<tr>
<td></td>
<td></td>
<td>×</td>
<td>$k = 0.04$ min$^{-1}$, $n = 1.2$</td>
<td>0.9728</td>
</tr>
<tr>
<td></td>
<td></td>
<td>O</td>
<td>$k = 0.04$ min$^{-1}$, $n = 1.4$</td>
<td>0.9874</td>
</tr>
<tr>
<td>FW</td>
<td>L$^{\alpha14}$</td>
<td>•</td>
<td>$k_1 = 0.06$ min$^{-1}$, $k'_2 = 0.000$ min$^{-1}$</td>
<td>0.9498</td>
</tr>
<tr>
<td></td>
<td></td>
<td>▲</td>
<td>$k_1 = 0.04$ min$^{-1}$, $k'_2 = 0.005$ min$^{-1}$</td>
<td>0.9778</td>
</tr>
<tr>
<td></td>
<td></td>
<td>×</td>
<td>$k_1 = 0.02$ min$^{-1}$, $k'_2 = 0.04$ min$^{-1}$</td>
<td>0.9773</td>
</tr>
<tr>
<td></td>
<td></td>
<td>O</td>
<td>$k_1 = 0.02$ min$^{-1}$, $k'_2 = 0.05$ min$^{-1}$</td>
<td>0.9901</td>
</tr>
<tr>
<td>JMAYK</td>
<td>avg</td>
<td></td>
<td>$k_{avg} = 0.05 \pm 0.01$ min$^{-1}$, $n_{avg} = 1.1 \pm 0.2$</td>
<td></td>
</tr>
<tr>
<td>FW</td>
<td>avg</td>
<td></td>
<td>$k_{1\ avg} = 0.04 \pm 0.02$ min$^{-1}$, $k'_{2\ avg} = 0.02 \pm 0.03$ min$^{-1}$</td>
<td></td>
</tr>
</tbody>
</table>

The values of $R^2$ for six PdL$^{\beta14}$I$_2$ trials were also determined once the models were fitted. All but one of the $R^2$ values obtained for each reaction for the JMAYK model gave values greater than 0.95; However, it was very close. Based on this, it was determined that while the JMAYK model gave acceptable fits to the data as five of the six reactions carried out in this study gave values of $R^2 \geq 0.95$. However, none of the $R^2$ values obtained for the FW model were near 0.95. Therefore, the FW model was not an acceptable fit for the data for either mixing or non-mixing. These values are given below in Table 5. Based on this, it can be determined that only the JMAYK model can be successfully applied to both isomer syntheses.
Table 5. Results of model fitting for reactions of PdL$^{\beta14}$I$_2$ where symbols are from Figures 6 and 7.

<table>
<thead>
<tr>
<th>Model</th>
<th>Run</th>
<th>Mix?</th>
<th>Parameters</th>
<th>$R^2$</th>
</tr>
</thead>
<tbody>
<tr>
<td>JMAYK</td>
<td>●</td>
<td>yes</td>
<td>$k = 0.010 \text{ min}^{-1}, n = 0.5$</td>
<td>0.9678</td>
</tr>
<tr>
<td></td>
<td>▲</td>
<td></td>
<td>$k = 0.011 \text{ min}^{-1}, n = 0.6$</td>
<td>0.9740</td>
</tr>
<tr>
<td></td>
<td>×</td>
<td></td>
<td>$k = 0.012 \text{ min}^{-1}, n = 0.4$</td>
<td>0.9453</td>
</tr>
<tr>
<td></td>
<td>O</td>
<td>no</td>
<td>$k = 0.009 \text{ min}^{-1}, n = 0.3$</td>
<td>0.9842</td>
</tr>
<tr>
<td></td>
<td>■</td>
<td></td>
<td>$k = 0.003 \text{ min}^{-1}, n = 0.4$</td>
<td>0.9856</td>
</tr>
<tr>
<td></td>
<td>♦</td>
<td></td>
<td>$k = 0.001 \text{ min}^{-1}, n = 0.3$</td>
<td>0.9612</td>
</tr>
<tr>
<td>FW</td>
<td>●</td>
<td>yes</td>
<td>$k_1 = 0.008 \text{ min}^{-1}, k'_2 = 0 \text{ min}^{-1}$</td>
<td>0.8583</td>
</tr>
<tr>
<td></td>
<td>▲</td>
<td></td>
<td>$k_1 = 0.029 \text{ min}^{-1}, k'_2 = 0 \text{ min}^{-1}$</td>
<td>0.8202</td>
</tr>
<tr>
<td></td>
<td>×</td>
<td></td>
<td>$k_1 = 0.007 \text{ min}^{-1}, k'_2 = 0 \text{ min}^{-1}$</td>
<td>0.6458</td>
</tr>
<tr>
<td></td>
<td>O</td>
<td>no</td>
<td>$k_1 = 0.006 \text{ min}^{-1}, k'_2 = 0 \text{ min}^{-1}$</td>
<td>-0.1693</td>
</tr>
<tr>
<td></td>
<td>■</td>
<td></td>
<td>$k_1 = 0.003 \text{ min}^{-1}, k'_2 = 0 \text{ min}^{-1}$</td>
<td>0.3774</td>
</tr>
<tr>
<td></td>
<td>♦</td>
<td></td>
<td>$k_1 = 0.002 \text{ min}^{-1}, k'_2 = 0 \text{ min}^{-1}$</td>
<td>-0.2373</td>
</tr>
<tr>
<td>JMAYK</td>
<td>avg</td>
<td>yes</td>
<td>$k_{avg} = 0.0110 \pm 0.0008 \text{ min}^{-1}$, $n_{avg} = 0.5 \pm 0.1$</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>$k_{avg} = 0.005 \pm 0.004 \text{ min}^{-1}$, $n_{avg} = 0.30 \pm 0.06$</td>
<td></td>
</tr>
<tr>
<td>FW</td>
<td>avg</td>
<td>yes</td>
<td>$k_{1avg} = 0.01 \pm 0.01 \text{ min}^{-1}, k'_{2avg} = 0 \text{ min}^{-1}$</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>$k_{1avg} = 0.004 \pm 0.002 \text{ min}^{-1}, k'_{2avg} = 0 \text{ min}^{-1}$</td>
<td></td>
</tr>
</tbody>
</table>

Another parameter from kinetic modeling that can be evaluated from the JMAYK model is the rate parameter, $k$. The values given for $k$ for the synthesis of PdL$^{\alpha14}$I$_2$ are larger than that of PdL$^{\beta14}$I$_2$. This is expected based on the differences in rates of the reactions. Slower reactions, like that of PdL$^{\beta14}$I$_2$ will have smaller values of $k$, while faster reactions, like that of PdL$^{\alpha14}$I$_2$ will be larger. Additionally, from the FW model another kinetic parameter that can be evaluated is $k_1$. Values for $k_1$ of PdL$^{\beta14}$I$_2$ were also smaller than $k_1$ values for PdL$^{\alpha14}$I$_2$. This is also consistent with what was observed during the course of the reactions as smaller values of $k_1$ indicate that nucleation is occurring slowly.
Additionally, $k'_2$ values obtained for both isomers are consistently low for PdL$^{14}$I$_2$ and zero in the case of PdL$^{14}$I$_2$. This is due to the use of restricted modeling for fitting the FW model to PdL$^{14}$I$_2$. The initial attempts to fit the model gave back negative values for $k'_2$ which is not logical from a physical standpoint. Restricting the model to positive values resulted in returning values of zero. This would indicate a lack of autocatalytic growth for the synthesis of PdL$^{14}$I$_2$; however, $k'_2$ values were obtained for PdL$^{14}$I$_2$ indicating autocatalytic growth does occur in that synthesis.

Another parameter from both model fittings that can be evaluated is $n$, the Avrami exponent. The breakdown of $n$ from Equation 3 was previously discussed on page 8. Given that $n_{\text{avg}}$ is 1.1±0.2 for the synthesis of PdL$^{14}$I$_2$ and that $p$ is $\frac{1}{2}$, (as the reaction is carried out under a constant temperature) would indicate that $a$ is zero and $b$ is two. This would indicate that pre-existing nucleation sites must be present before milling and that the dimensionality of the growth of product is two-dimensional. However, given that $n_{\text{avg}}$ is 0.5±0.1 and 0.30±0.06 for mixing and non-mixing, respectively for the synthesis of PdL$^{14}$I$_2$ and that $p$ is also $\frac{1}{2}$, would indicate that $a$ is also zero and that $b$ is one. This is also indicative of pre-existing nucleation sites that are present before milling. However, it would indicate that the dimensionality of the growth of product is one-dimensional. This is consistent with what was observed during the course of the reactions as the slow synthesis of PdL$^{14}$I$_2$ would be a result of one-dimensional growth.

Further support for these pre-existing sites on the surface of PdI$_2$ is provided by previous research in the Allenbaugh group through pre-milling
experiments where PdI$_2$ was milled in the absence of ligand then used for synthesis of a similar palladium complex. Results from that study saw a decrease in percent conversion from 90-100% down to 13.4%. This would indicate that pre-milling PdI$_2$ appears to destroy these pre-existing sites and that additional sites do not appear to be generated throughout the course of the synthesis. These pre-existing sites are located in defects on the lattice of PdI$_2$. These defects are high energy sites where nucleation can occur.

Additional support that these pre-existing sites exist on the surface of PdI$_2$ were observed in the synthesis of PdL$^{\beta 14}$I$_2$. In the synthesis of PdL$^{\beta 14}$I$_2$, at 60% conversion, bulk milling becomes more difficult. This is due to the fact that there is more product in the reaction mixture than starting material and the product is hard and sticky. The product is actually covering up those nucleation sites and thus, conversion cannot occur. Hand-mixing actually alleviates this problem in that when the reaction mixture is scraped with a spatula, the product is being removed from covering up these nucleation sites and conversion can continue.

2.4 Conclusion

These syntheses furthered the previous research of the Allenbaugh group of 2,2'-bipyridine-4,4'-dicarboxylate complexes of palladium. It was determined that the physical properties of the ligands and complexes did have an effect on completion time of the reactions as PdL$^{\alpha 14}$I$_2$ had a lamellar liquid crystalline phase observed while PdL$^{\beta 14}$I$_2$ did not. This difference in the texture of the reaction mixture lead to a difference in the ease of homogenization between the two. While both the JMayK and the FW models were applied to both complexes
studied, it was determined that only the JMayK model could be used to fit the data of both complexes as the FW model was only effective for PdL\(^{a14}\)I\(_2\).

Values of \(k_{avg}\) for PdL\(^{a14}\)I\(_2\) were 0.05±0.01 min\(^{-1}\) and were 0.0110±0.0008 min\(^{-1}\) and 0.005±0.004 min\(^{-1}\) for PdL\(^{b14}\)I\(_2\), mixing and non-mixing, respectively. Smaller values of \(k\) observed in PdL\(^{b14}\)I\(_2\) are consistent with the slower rate of the reaction. Average values of \(n\) obtained led to the determination of two-dimensional growth for PdL\(^{a14}\)I\(_2\) and one-dimensional growth for PdL\(^{b14}\)I\(_2\) which is consistent with the rates in synthesis observed. Additionally, \(n\) values indicated that the nucleation sites must be pre-existing in the system before milling. The \(k_1\) values obtained for PdL\(^{b14}\)I\(_2\) were smaller than that of PdL\(^{a14}\)I\(_2\), also consistent with the difference in rates observed for both reactions. While \(k_2'\) values were obtained for PdL\(^{a14}\)I\(_2\), negative values were generated for PdL\(^{b14}\)I\(_2\) leading to the utilization of restricted modeling. This indicated that autocatalytic growth did not occur in PdL\(^{b14}\)I\(_2\).
Chapter 3: 1, 3-Dimethyl Benzimidazolium Iodide

3.1 Introduction

Some consideration was given to another area where mechanochemistry could be applied was improving upon previous research from the Allenbaugh group of the synthesis of 1, 3-dimethyl benzimidazolium iodide (HBZM-Me$_2$I). This synthesis was part of a larger work, shown in Scheme 3, that focused on the first mechanochemical synthesis of a palladium benzimidazole-2-ylidene complex using solvent free preparation and a kinetic study of the complex.$^{17}$

Scheme 3. Mechanochemical synthesis of HBZM-Me$_2$I proceeds through intermediate HBZM-Me.

This was done in order to further research as preparations of ligands as a part of a total mechanosynthesis of organometallic complexes is limited$^9,40$ Of the existing types of organometallic mechanosynthesis including (1) ligand exchange/functionality and/or co-crystallization or organometallic species prepared by non-mechanochemical methods,$^{41-46}$ (2) preparation of carbonyl complexes,$^{46,47}$ and (3) formation of new metal-organic ligand bonds$^5,7-9,48-56$ less than half involve mechanochemical C-H bond activation.$^5,7-9,52-56$ This lack of total synthesis is a problem for widespread adoption of mechanochemistry, as maintaining both solution and mechanochemical systems can be impractical.
Initially, it was theorized that HBZM-Me$_2$I could be synthesized mechanochemically, as attempts to synthesize similar molecules by Beillard et al.$^5$ proved successful. This similar synthesis is shown below in Scheme 4. Successful mechanosynthesis of HBZM-Me$_2$I would be considered a superior method than that of the traditional, solution-based synthesis. Traditional synthesis of HBZM-Me$_2$I utilizes a pressure tube prepared with excess, toxic methyl iodide (MeI)$^{57}$ and can be seen below in Scheme 5.

**Scheme 4.** Similar mechanosynthesis of a benzimidazolium species.$^5$

**Scheme 5.** Literature synthesis of HBZM-Me$_2$I.$^{57}$

Initial research in the Allenbaugh group attempted to synthesize HBZM-Me$_2$I using mechanochemical methods to minimize environmental impact. One of the first considerations for improving upon traditional synthesis began with the utilization of new, Teflon$^\text{TM}$ vials for synthesis as the steel vials previously used by the group were not applicable to synthesis with liquid reagents. Initial studies
began with custom built 4-mL Teflon™ vials that were airtight and chemically inert. However, these vials were difficult to fabricate and clean. Later attempts at improving synthesis utilized the Dynalon 5-mL Teflon™ bottle. While these bottles were also chemically inert and airtight, they were more readily available online. The major difference between the two is that the inner volume of the bottle is not uniform in shape. This is shown below in Figure 11.

**Figure 11.** Teflon™ vial (left) and bottle (right) used for improved synthesis.

Early mechanochemical studies produced hydroiodic acid as a byproduct. Therefore, initial attempts to utilize mechanochemical synthesis determined that sodium carbonate (Na₂CO₃) could be used a base for synthesis. While this effectively neutralized the acid, full conversion to product was not attained. This initial attempt at improvement is shown below in Scheme 6.

**Scheme 6.** Initial attempts at improved mechanochemical synthesis of HBZM-Me₂I where excess MeI was also utilized.
However, it was also determined in initial studies that each time the reaction vial was opened for sampling, MeI was released due to its volatility. This gave poor yields as the loss of MeI caused the carbonate salts to cake around the milling balls, limiting conversion. This is shown in Figure 12. In an attempt to improve this previous research, liquid assisted grinding, or LAG methods utilizing CDCl₃ as well as modified sampling methods were considered in this study.

![Figure 12. Results from previous research of carrying out the mechanochemical reaction in the absence of LAG where HBZM (♦), HBZM-Me (▲), and HBZM-Me₂I (●).](image)

### 3.2 Experimental

#### 3.2.1 General Procedures

The $^1$H NMR spectra were recorded on a JEOL-ECS 400 MHz spectrometer at room temperature in CDCl₃ solution. The CDCl₃ was stored over activated alumina to remove any trace acid. Reagents were purchased from Aldrich or Fisher Scientific and used without further purification. Some
preliminary reactions for yield were carried out in a SPEX 5100 mill, while other bulk preparations and all kinetic studies were carried out in a SPEX 8000M mill.

3.2.2 Synthetic Procedures

1, 3-dimethyl benzimidazolium iodide. In a 5-mL Teflon™ vial, two 6.35-mm stainless steel balls, benzimidazole (208.8mg, 1.767 mmol), sodium carbonate (375.1mg, 3.539 mmol), and methyl iodide (221μL, 3.550 mmol) were premixed before milling for 350 minutes in a SPEX 8000M mill. The reaction mixture was placed in hot ethanol, and hot filtered to remove sodium carbonate and bicarbonate. The desired product was crystallized from the ethanol, collected by vacuum filtration, and dried in a desiccator. The ¹H NMR spectrum agreed with the literature and commercial reagent from Sigma Aldrich. Yield: 449.4 mg, 92.8%.

3.2.3 Conditions for Kinetic Studies

All kinetic runs were carried out in a SPEX 8000M mill in 5-mL Teflon™ screw-cap vials using two 6.35-mm stainless steel balls. In the case of the benzimidazolium salt preparations, separate trials had to be carried out for each time interval sampled because significant alkyl halide was lost during sampling. Three replicates were taken at each time interval. Liquid reagents were dispensed via micropipette. Reagent amounts are given in Table 6. Small samples were taken at a time interval of 50 minutes up to 350 minutes with each vial only being sampled once in order to prevent MeI loss. Solution reaction to produce alkyl-benzimidazole and benzimidazolium salts in CDCl₃ does occur;
however, these reactions are very slow. All NMR samples were filtered prior to analysis.

Table 6. Average reagent masses and volumes used for kinetic studies.

<table>
<thead>
<tr>
<th>Conditions</th>
<th>Reagent</th>
<th>Amount</th>
</tr>
</thead>
<tbody>
<tr>
<td>3 MeI, neat</td>
<td>HBZM</td>
<td>0.2090±0.005g</td>
</tr>
<tr>
<td></td>
<td>Na₂CO₃</td>
<td>0.377±0.003g</td>
</tr>
<tr>
<td></td>
<td>MeI</td>
<td>331μL</td>
</tr>
<tr>
<td></td>
<td>CDCl₃</td>
<td>0μL</td>
</tr>
<tr>
<td>3 MeI, LAG</td>
<td>HBZM</td>
<td>0.2091±0.0003g</td>
</tr>
<tr>
<td></td>
<td>Na₂CO₃</td>
<td>0.378±0.004g</td>
</tr>
<tr>
<td></td>
<td>MeI</td>
<td>331μL</td>
</tr>
<tr>
<td></td>
<td>CDCl₃</td>
<td>567μL</td>
</tr>
<tr>
<td>2 MeI, neat</td>
<td>HBZM</td>
<td>0.2093±0.0004g</td>
</tr>
<tr>
<td></td>
<td>Na₂CO₃</td>
<td>0.377±0.002g</td>
</tr>
<tr>
<td></td>
<td>MeI</td>
<td>221μL</td>
</tr>
<tr>
<td></td>
<td>CDCl₃</td>
<td>0μL</td>
</tr>
</tbody>
</table>

3.3 Results and Discussion

Using $^1$H NMR spectroscopy, the relative amounts of HBZM, or HBZM-Me, and HBZM-Me₂I were used to determine the conversion fraction. In the synthesis of HBZM-Me₂I the signal for the proton on the imidazolium moiety at 8.08 ppm was integrated relative to the signals for the methyl moieties of the intermediate HBZM-Me and the desired product at 3.85 and 4.15 ppm, respectively, to determine the relative amounts of each species. Figure 13 shows example NMR spectra for a preparation of HBZM-Me and HBZM-Me₂I under neat conditions.
Figure 13. Portions of the $^1$H NMR spectra for the neat synthesis of HBZM-Me and HBZM-Me$_2$I from 0-300 minutes using two equivalents of MeI. The signal for the proton on the imidazole moiety at 8.08 (red) was integrated to the signals for the methyl moieties of the intermediate (blue) and the desired product (green) at 3.85 and 4.15 ppm, respectively. Samples were taken every 50 minutes up to 300 minutes starting from the bottom spectrum.

Attempts at improving the synthesis of HBZM-Me$_2$I focused on the utilization of LAG methods. It is important to note that multiple replicate reactions were milled simultaneously over the course of several sampling intervals. Each vial was only opened one time for sampling in order to eliminate MeI loss during sampling and improve conversion. The results from this can be seen below in Figure 14. Because of the many replicates utilized in this study, average conversion fraction was plotted versus time for model fitting. It was determined from these initial attempts that LAG methods did give a complete conversion to product around 600 minutes.
Initial attempts at improved synthesis of HBZM-Me₂I utilizing LAG methods where HBZM (♦), HBZM-Me (△), and HBZM-Me₂I (○) and the FW (dashed lines) and JMAKY (solid lines) models were fit to data.

While successful, this was considered to be a long time for synthesis, so attempts to improve reaction times were considered. This utilized the original neat methods, paired with the modified sampling methods mentioned previously. These neat methods used different equivalents of MeI for each reaction as seen in Table 6. Average conversion fraction for the various preparations of HBZM-Me₂I was plotted versus time and the JMAKY and FW models were fit to the data as shown in Figure 15. This kinetic analysis is somewhat unique because the synthesis of a well-defined intermediate can be simultaneously tracked as shown in Figure 16. The relative amount of intermediate that builds up in the reaction mixture relates directly to the amount of liquid, MeI or CDCl₃, present in the reaction mixture.
Figure 15. Kinetic data for the synthesis of HBZM-MeI₂ using 2 equivalents of MeI under neat conditions (□), 3 equivalents of MeI under neat conditions (△), and 3 equivalents of MeI under LAG conditions (○). The results of JMAYK (solid lines) and FW modeling (dashed lines) are shown.

Figure 16. Kinetic data for the synthesis of intermediate HBZM-Me using 2 equivalents of MeI under neat conditions (□), 3 equivalents of MeI under neat conditions (△), and 3 equivalents of MeI under LAG conditions (○).
Results from neat methods using modified sampling methods indicated faster reaction times than that of LAG methods. It was observed that increasing the amount of MeI to three equivalents in the neat method study, did not affect the overall completion time of the reaction. The models were evaluated for their fit to the data based on coefficients of determination ($R^2$ values); however, to compare the utility of the two models to each other, evidence ratios ($ER$) were utilized and calculated using Equations 23-25. An $ER \geq 10^4$ would indicate that the JMayK model was significantly better while and $ER \leq 10^4$ would indicate that the FW model was a significantly better. The statistical parameters for each of the models evaluated are below in Table 7 and the results of kinetic modeling are below in Table 8.

### Table 7. Statistical parameters for the comparison of the JMayK and FW models.

<table>
<thead>
<tr>
<th>Cond.</th>
<th>N</th>
<th>$SS_{JMayK}$</th>
<th>$SS_{FW}$</th>
<th>$AIC_{C_i, JMayK}$</th>
<th>$AIC_{C_i, FW}$</th>
<th>$W_{JMayK}$</th>
<th>$ER$</th>
</tr>
</thead>
<tbody>
<tr>
<td>3 MeI</td>
<td>8</td>
<td>0.0074</td>
<td>0.0180</td>
<td>-49.4557</td>
<td>-42.3633</td>
<td>0.9720</td>
<td>34.6808</td>
</tr>
<tr>
<td>3 MeI</td>
<td>14</td>
<td>0.0309</td>
<td>0.0289</td>
<td>-80.5222</td>
<td>-81.4296</td>
<td>0.3885</td>
<td>0.6354</td>
</tr>
<tr>
<td>2 MeI</td>
<td>8</td>
<td>0.0089</td>
<td>0.0130</td>
<td>-47.9247</td>
<td>-44.9698</td>
<td>0.8142</td>
<td>4.3820</td>
</tr>
</tbody>
</table>

a Neat conditions.
b LAG conditions.
Table 8. Results of kinetic modeling, where parameters are defined as in Equations 10, 19, and 25. In cases where FW model fitting gave negative values of the rate related parameter $k'_2$, the data were modeled a second time with the restriction $k'_2\geq0$.

<table>
<thead>
<tr>
<th>Conditions</th>
<th>JMAYK</th>
<th>FW</th>
<th>ER</th>
</tr>
</thead>
<tbody>
<tr>
<td>3 Mel</td>
<td>$k = 5.644\times10^{-3}$ min$^{-1}$</td>
<td>$k_1 = 1.028\times10^{-4}$ min$^{-1}$</td>
<td>34.68</td>
</tr>
<tr>
<td>neat</td>
<td>$n = 5.904$</td>
<td>$k'_2 = 3.562\times10^{-2}$ min$^{-1}$</td>
<td></td>
</tr>
<tr>
<td></td>
<td>$R^2 = 0.9951$</td>
<td>$R^2 = 0.9882$</td>
<td></td>
</tr>
<tr>
<td>2 Mel</td>
<td>$k = 2.981\times10^{-3}$ min$^{-1}$</td>
<td>$k_1 = 5.225\times10^{-4}$ min$^{-1}$</td>
<td>0.6354</td>
</tr>
<tr>
<td>LAG</td>
<td>$n = 2.171$</td>
<td>$k'_2 = 1.020\times10^{-2}$ min$^{-1}$</td>
<td></td>
</tr>
<tr>
<td></td>
<td>$R^2 = 0.9834$</td>
<td>$R^2 = 0.9845$</td>
<td></td>
</tr>
<tr>
<td>2 Mel</td>
<td>$k = 5.246\times10^{-3}$ min$^{-1}$</td>
<td>$k_1 = 8.271\times10^{-5}$ min$^{-1}$</td>
<td>4.382</td>
</tr>
<tr>
<td>neat</td>
<td>$n = 5.366$</td>
<td>$k'_2 = 3.438\times10^{-2}$ min$^{-1}$</td>
<td></td>
</tr>
<tr>
<td></td>
<td>$R^2 = 0.9939$</td>
<td>$R^2 = 0.9912$</td>
<td></td>
</tr>
</tbody>
</table>

For this study, values of $k$ from the JMAYK model for the neat methods were similar while $k$ for the LAG method were smaller. This was consistent with the differences in rates that were observed. The values of $k_1$ from the FW model obtained for neat methods were similar to each other while the $k_1$ for LAG methods were in between these values. Values for $k'_2$ from the FW model for neat methods were similar while the $k'_2$ value for LAG methods were smaller. This would indicate that while both nucleation and autocatalytic growth are occurring, the autocatalytic growth has more of an influence over the reaction. It is important to note that $n$ cannot be broken down by Equation 3 like in that of the previous chapter. This is due to the fact that Equation 3 only holds true when the value of $n$ is one to four. A value of $n$ greater than four indicates increasing nucleation, and thus, the breakdown cannot be applied.

For this study, values of $R^2\geq0.95$ were considered to be good fits to the data. For the JMAYK model, $R^2$ values were between 0.9834-0.9951. While $R^2$
values for the FW model were between 0.9450-0.9912. This indicated that both
the JMAYK and FW models were applicable to this synthesis. When comparing
the utility of the two, neither model was preferable based on $ER$ values as
$10^{-4} < ER < 10^4$.

Because the FW model has separate parameters for nucleation and
autocatalytic growth, it was the simpler model to use in examining the effects of
reaction parameters. In the synthesis of HBZM-Me$_2$I, significant amounts of the
intermediates HBZM-Me build up in the reaction mixture and reaction does occur
in the absence of added Na$_2$CO$_3$, so the rate limiting step would seem to involve
the alkyl-benzimidazole species. That increasing the amount of MeI added does
not significantly alter the rate points to alkyl-benzimidazole based nucleation
sites.

The effect of using CDCl$_3$ as a LAG solvent is to increase nucleation, as
reflected in increased $k_1$, while autocatalytic growth remains constant or
decreases. This gives an initially faster rate compared to neat reactions, but a
slower time to complete conversion as seen in Figure 15. While initial research
determined that LAG methods did improve upon previous research in the group
and give complete conversion to product, further studies into neat methods
suggested that LAG conditions can actually hinder the production of 1, 3-dimethyl
benzimidazolium iodide. As reaction times using neat methods attained
conversion around 300 minutes, less than half of time completion time of LAG
methods, neat methods are considered to be a better method of synthesis when
compared to the LAG methods of this study.
3.4 Conclusion

This study improved upon the synthesis of 1, 3-dimethyl benzimidazolium iodide from previous research of the Allenbaugh group. This also furthered research of limited preparations of ligands as a part of a total mechanosynthesis of organometallic complexes. While initial studies utilizing LAG methods and modified sampling methods attained complete conversion, the reaction time was not favorable. Synthesis using neat methods while utilizing modified sampling methods yielded conversion in a significantly shorter period of time than that of the LAG methods and so it was concluded that LAG methods actually hinder the preparation of 1, 3-dimethyl benzimidazolium iodide. Sigmoidal behavior was observed while plotting conversion fraction versus time.

Upon fitting the data to the JMAYK and FW models, $R^2$ values were obtained and all but one met the criteria $R^2 \geq 0.95$ while the one that did not was extremely close, $R^2 = 0.945$. This indicated that both the JMAYK and FW models were applicable to data from the synthesis of 1, 3-dimethyl benzimidazolium iodide. For neat methods, similar values of $k$, $k_1$, and $k_2'$ values were obtained which was consistent with the observed reaction rates. Based on $ER$ values obtained neither model was preferable when comparing the utility of the two models.
Appendix
Figure A1. The full $^1$H-NMR spectrum of PdL$^{a14}$I$_2$. 
Figure A2. The full $^1$H-NMR spectrum of PdL$^{814}$I$_2$. 
Figure A3. The full $^1$H-NMR spectrum of HBZM-Me$_2$I.
References


19. Ahmadian Baghbaderani, H.; Rahimipour, M. R.; Delshad Chemahini, M., A combined experimental and modeling study of thermodynamics and kinetics of mechanochemical treatment for synthesis of Ni_{0.5}Co_{0.5}Fe_{2}O_{4}. Mater. Des. 2016, 95, 54-62.
23. Muskawar, P. N.; Karthikeyan, P.; Aswar, S. A.; Bhagat, P. R.; Senthil Kumar, S., NHC-metal complexes based on benzimidazolium moiety for chemical transformation. Arabian J. Chem. 2016, 9 (Suppl. 2), S1765-S1778.


