Radical involvement in cobalt- and nickel-mediated dehalogenation reactions

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The first time I met Kris McNeill, he gave my friend and me half a sandwich. At that time, I was grateful and I thought he was a very nice person. Now I struggle to find a proper way to articulate how deeply grateful I am to have had the chance to know and work with Kris. He is not only a brilliant scientist and teacher, but he is an incredibly kind and thoughtful advisor. Most importantly, he is a friend, and someone who demonstrates with his actions what it means to be a good person. It is trite, but true that Kris’ patience, contagious enthusiasm, and optimism continue to nurture my development as a scientist.

Kris is fond of saying, “the molecules are the same everywhere, it’s the people that are different, you have to go somewhere where the people make you happy.” Whether or not the molecules are the same or different remains to be seen, but Kris, Doug, Laura, Ann, Joe, Kris W., Anne, Angela, Jeff W., Rose, Alicia, Betsy, Jeff B., Matt, Kristen, Britt, Elodie, Sarah P., Daniel, Paul, Rachel, Emily and many, many others at the University of Minnesota have challenged me, supported me, inspired me, and made me happy in ways I never anticipated.

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My papa, David Kliegman, has by example, shown me that there is always a way forward, but the best way generally includes a mission, goals, objectives, strategies, actions and measurable results.

My brother, Joe Kliegman, has given me an ideal of myself that I strive to live up to. A lot of people call him Lucky Joe Kliegman…but I am the lucky one, lucky to get to go through life with such a smart brother, a brother who gets really excited about things, and expects excellence in all aspects of life. Thank you for being a scientist. Thanks to all of you for believing in me.
“...protecting the environment is not about protecting the fishes and the birds for their own sake. It's about recognizing that nature is the infrastructure of our communities, and we must meet our obligation as a generation, as a civilization, as a nation, to create communities for our children that provide them with opportunities for dignity and enrichment and good health.”

Robert F. Kennedy Jr. (Sierra Summit, September 10, 2005)
Abstract

Halogenated chemicals represent a large and toxic class of environmental pollutants. Although regulation of certain halogenated organics resulted in decreasing production of these chemicals in the United States since the 1970s, others were yet unknown when the regulations were written and production is increasing. In many cases, halogenated organics are persistent in the environment, bioaccumulative, and bioactive, causing toxicological concerns. As such, environmental scientists have studied the processes by which these chemicals can be broken down, and the products that form in these breakdown reactions. In some cases, the toxic effects associated with halogenated organic pollutants can be ameliorated by complete dehalogenation, while incomplete dehalogenation or other transformations can result in the production of harmful compounds. The mechanisms of these transformations are in most cases not yet well understood, but a fundamental understanding of these reactions helps in the development of effective remediation strategies, and informs the fundamental chemistry inherent to these reactions.

Concern about halogenated environmental pollutants has led to investigations of a number of means of dehalogenation including biological attenuation. Microbially mediated dehalogenation represents a major transformation pathway for halogenated pollutants in the environment. Metal-containing cofactors have been implicated in these processes including cobalamin (vitamin B_{12}), factor F430, and hemitin. These cofactors are responsible for the reductive dehalogenation of environmental pollutants. These reactions can proceed by a various intermediates, but one of particular interest is the formation of radicals. Radicals have at least one unpaired electron, and as such are highly reactive and transient intermediates. These features can make them difficult to study but their powerful reactivity underscores their importance in environmental transformations.

Radical intermediates are often proposed but rarely fully understood in a range of environmental systems. In this thesis, the role of radicals in dehalogenation reactions is explored with particular attention to cobalamin-mediated and nickel-mediated reactions. The mechanism of cobalamin-mediated dechlorination has been studied
extensively and evidence for both outer-sphere (radical based) and inner sphere (nonradical based) mechanisms has been presented. In this thesis the literature concerning cobalamin-mediated dehalogenation is reviewed in detail (Chapter 1) and a mechanistic study on the role of radicals in cobalamin-mediated dechlorination of chloroethylenes reconciles previously seemingly contradictory data (Chapter 2).

Similarly, both radical and nonradical pathways have been invoked in nickel-mediated dehalogenation of a variety of substrates. Nickel-mediated dehalogenation has not been studied as extensively as cobalt-mediated reactions and the understanding is complicated by the fundamental chemistry of nickel complexes. In order to better understand the chemistry of reduced nickel complexes, particularly their reaction with halogenated organics, a series of nickel complexes was synthesized and characterized (Chapter 3). The relationship between reduced transition metal complexes and their ligands is inextricably linked to whether and how radical intermediates are formed in these systems. The reactivity of two reduced nickel complexes precursors show that these complexes are highly sensitive to slight changes in ligand structure (Chapter 4).
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Chapter I. Dechlorination of chloroethylenes by cob(I)alamin and cobalamin model complexes

Cobalt-mediated dehalogenation reactions, specifically those that employ cobalamin, have attracted particular attention because these complexes rapidly degrade tetrachloroethylene (PCE) and trichloroethylene (TCE), which are common groundwater contaminants. Although questions remain about the relative importance of several pathways, both radicals and organometallic intermediates, specifically chlorovinyl complexes, play an important role in these processes. This chapter highlights recent studies focused on elucidating the mechanism of chloroethylene degradation, including experimental studies on PCE and TCE dechlorination, computational studies, preparation of model complexes, and the study of model catalytic systems.
1.1 Introduction

Chlorocarbon-polluted groundwater is one of the legacies of our society’s love affair with chlorinated organics in the period between World War II and the 1970s. The acute toxicity, carcinogenicity, and other negative properties of these compounds are generally conferred through the chlorine atoms, whereas the corresponding parent hydrocarbons are normally benign. This phenomenon is exemplified by acutely carcinogenic vinyl chloride and nontoxic ethylene.\(^1\) Thus, removal of the chlorine substituents by reductive dechlorination reactions is a clear remediation approach.\(^2\) To this end, a number of dechlorination remediation strategies have been advanced and studied. These include bioremediation,\(^3\) permeable reactive barriers,\(^4^\text{-}^8\) and noble metal catalytic systems.\(^9^\text{-}^12\) Cobalamin (Figure 1.1) promoted dechlorination reactions have garnered special attention because reductive dehalogenases, the enzymes responsible for natural attenuation by microbes, almost always contain this cofactor.\(^13^,\!^14\) In addition, abiotic remediation strategies featuring cobalamin have been demonstrated at field sites,\(^15\) with packed bed reactors,\(^16\) and on modified electrodes,\(^17\) generating further interest in the mechanism of this dechlorination process.

Cob(II)alamin, a strong reductant\(^18\) and powerful nucleophile,\(^19^,\!^20\) can reduce chlorinated methanes,\(^21^\text{-}^26\) ethanes,\(^27\) higher alkanes,\(^28\) ethylenes,\(^15,\!^22,\!^29^\text{-}^36\) arenes,\(^37^\text{-}^39\) and other substrates.\(^40^\text{-}^44\) Among these, chloroethylenes (Figure 1.1) have a particularly diverse set of reaction modes, making their study appealing from a mechanistic standpoint. Furthermore, they have attracted a considerable amount of attention due to the widespread use of TCE and PCE.

While cobalt-mediated chloroethylene dehalogenation is a promising strategy, challenges remain. In fact, toxic and persistent intermediates, such as cis-dichloroethylene (cis-DCE) are produced. These problematic intermediates have motivated a number of recent studies focused on the mechanism of dechlorination reactions. This chapter highlights some of these studies on cobalamin and its functional models, including cobaloxime and tetraarylporphyrin cobalt, with an emphasis on (1) experimental and computational investigations of the dehalogenation mechanism with PCE and TCE, (2) studies of reaction intermediates and product forming steps, and (3) investigations of other dechlorination catalysts.
1.2 Initial Studies

Evidence for biologically mediated reductive dehalogenation of chloroethylenes in anaerobic systems was obtained as early as 1981.\textsuperscript{45} Attenuation of halogenated chemicals using biological organisms is an appealing method of detoxification, and as such, has been studied and reviewed extensively.\textsuperscript{3,14,46} Dehalogenases, the enzymes implicated in this process, are responsible for the transformation from higher to lower chlorinated congeners or to hydrocarbons.\textsuperscript{47} Many classes of halogenated substrates are reduced and the mechanisms are not well understood. Early support for the involvement of metallocofactors came from experiments with boiled bacterial extracts that retained dehalogenation activity.\textsuperscript{48} Krone and Thauer showed that reduced corrinoids, in the absence of the enzyme, dechlorinated chloromethanes, suggesting that the biologically derived reductive dehalogenation reactions were catalyzed by corrinoids in the organism.\textsuperscript{26} Since that time, all known reductive dehalogenases except for one have been found to utilize cobalamin or a cobalamin-like cofactor. The exception is \textit{D. tiedjei}, which is thought to contain a heme cofactor.\textsuperscript{13,14}
Figure 1.1: Structures and reduction potentials (vs SHE) of cobalamin and selected chloroethylenes. Potentiometry was used to determine the potential for cobalamin, whereas the values for the chloroethylenes are calculated at pH 7. The Co\textsuperscript{II}/Co\textsuperscript{I} reduction potential for cobalamin is pH independent above pH 4.7.

In 1991, Gantzer and Wackett tested a range of reduced transition metal complexes commonly associated with enzyme active sites, and found that cobalamin, F430, and hematin each catalyzed dehalogenation reactions in a sequential stepwise process. These results were significant because they supported the hypothesis that the natural attenuation of halogenated pollutants depended largely on the metal-containing
cofactor. This study set the stage for a series of investigations of the kinetics and mechanisms of chlorocarbon degradation reactions catalyzed by cobalamin.

Rate constants for cobalamin-mediated reductive dehalogenation of chloroethylenes have been determined under a range of experimental conditions (see Chapter I Supplement, page 24 for compilation).\textsuperscript{22,29,30,32,33,36} Unfortunately, since the temperature, pH, bulk reducing agent concentration, and cobalamin concentration varied among these studies, with each of these factors affecting the reaction rate, comparisons are difficult. Fortunately, the overall trends remain the same. In all cases, transformation from PCE to TCE is the fastest, transformations from TCE to various dichlorinated hydrocarbons are slower, and transformation from \textit{cis}-DCE to vinyl chloride is slowest (Figure 1.2). Although subsequent conversions from vinyl chloride to ethylene are relatively fast, the slow rate of conversion from \textit{cis}-DCE to vinyl chloride results in a build-up of \textit{cis}-DCE. The trends observed with the isolated cofactor have also been observed in pure cultures and field experiments, which show that \textit{cis}-DCE accumulates.\textsuperscript{50-52} Recent studies by Kittelmann and Friedrich suggest that in marine systems, microbial populations are responsible for the transformation of PCE to primarily \textit{trans}-DCE (85\% \textit{trans}-DCE, 15\% \textit{cis}-DCE) in marked contrast to the previous work.\textsuperscript{53,54} It is not clear, however, whether these organisms contain cobalamin or catalyze the dehalogenation reaction by some other means. A notable exception to either \textit{cis}- or \textit{trans}-DCE accumulation is observed with \textit{D. ethenogenes}, an organism that can completely dechlorinate PCE to ethane.\textsuperscript{55,56} This activity leads to an intriguing question about how \textit{cis}-DCE is processed or bypassed by this organism. It also bolsters the idea that a fundamental mechanistic understanding will uncover critical points in the pathway that can be exploited for more effective chloroethylene remediation. An example of this type of mechanistic critical point was found in abiotic experiments that showed the formation of acetylene products in addition to lower chlorinated ethylenes.\textsuperscript{29,32}
The product distributions for cobalamin-mediated reductive dechlorination of chloroethylene substrates have been determined in several studies (Table 1.1).\textsuperscript{22,29-33,36} Burris, et al. first reported a cobalamin-mediated dechlorination pathway for TCE that yields chloroacetylene in addition to cis-DCE (as well as trace amounts of trans-DCE and 1,1-DCE).\textsuperscript{30} While both chloroacetylene and cis-DCE are toxic, chloroacetylene is rapidly converted to acetylene under the reaction conditions.\textsuperscript{30,36} The conversion of TCE to acetylene was confirmed in a subsequent study.\textsuperscript{29,32} The observation of chloroacetylene suggested a vicinal dichlorine elimination (\textit{vic-Cl}_2-elimination) mechanism, (previously referred to as \textit{β}-elimination)\textsuperscript{30} similar to that observed with iron-mediated dechlorination.\textsuperscript{57}
Table 1.1: Product distributions from a series of chlorinated substrates. Abbreviations: tetrachloroethylene (PCE), trichloroethylene (TCE), cis-dichloroethylene (cDCE), trans-dichloroethylene (tDCE), 1,1-dichloroethylene (1,1-DCE), vinyl chloride (C₂H₃Cl), dichloroacetylene (C₂Cl₂), chloroacetylene (C₂HCl), acetylene (C₂H₂), ethylene (C₂H₄), ethane (C₂H₆)

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| * These products were not included in the model. It is not clear whether or not they were observed.

A relatively consistent mechanistic picture emerges from the product distribution and rate data. Two main pathways are operative in the cobalamin-mediated dechlorination of chloroethylenes. One involves sequential dechlorination giving lower chloroethylene products. The other gives acetylene products arising from formal vic-Cl-elimination. Subsequent in-depth mechanistic studies have provided rationalizations for this network of pathways.
1.3 Mechanistic Studies

1.3.1 Cobalt-Mediated Reductive Dehalogenation of PCE. Several mechanisms have been proposed for the reductive dehalogenation of PCE using cobalamin and cobalt-centered model complexes. Most broadly, the initial step can either be classified as an outer-sphere or an inner-sphere process. These can be further categorized as nucleophilic addition (inner-sphere), nucleophilic substitution (inner-sphere), or electron transfer (outer-sphere) (Figure 1.3).\(^{58}\)

In an inner-sphere process, the cob(I)alamin nucleophile can attack PCE and form either a 1,1,2,2-tetrachloroethyl complex (Path A) or eliminate chloride to form a trichlorovinyl complex (Path B) (Figure 1.3). These products correspond to nucleophilic addition and nucleophilic substitution, respectively. In an outer-sphere process, cob(I)alamin transfers an electron to PCE forming a trichlorovinyl radical and a cobalt(II) radical. The trichlorovinyl radical has several possible fates. It can be reduced to form a trichlorovinyl anion (Path C), quenched by a hydrogen atom donor to form TCE (Path D), or trapped by cob(II)alamin to form a trichlorovinyl complex, the same product as in Path B (Figure 1.3).

![Possible pathways for reductive dehalogenation of PCE.](image)

In an ongoing effort to understand the relative importance of each of the possible pathways involved in this process, a number of observations have been made. Addition of
PCE results in conversion of diamagnetic cobalt(I) to paramagnetic cobalt(II), as shown by EPR spectroscopy.\textsuperscript{32} Additionally, optical absorbance changes at 390 and 470 nm, associated with cob(I)alamin and cob(II)alamin, respectively, are consistent with this process.\textsuperscript{32} Although these results are consistent with an outer-sphere process, production of cob(II)alamin is expected in inner-sphere pathways as well. Therefore these results do not provide conclusive evidence for either mechanism.

Labeling studies conducted using trichloroalkene probes with pendant radical traps implicate organic radical intermediates.\textsuperscript{59} When subjected to dechlorination conditions, probes A and B underwent characteristic cyclization reactions resulting from formation of vinyl radicals.\textsuperscript{59} Again, although these results are consistent with an outer-sphere process, an inner-sphere mechanism cannot be ruled out as radical reaction pathways such as recombination to form an organocobalamin may have been prevented by both the fast intramolecular quenching process and by steric protection.

![Probe A and Probe B](image)

Dechlorination of PCE by cob(I)alamin conducted in the presence of increasing amounts of \(d_7\)-isopropanol, a D• donor, resulted in increased production of deuterated TCE, consistent with a trichlorovinyl radical intermediate.\textsuperscript{32} The level of deuterium incorporation was as high as 10\%,\textsuperscript{32} suggesting that Path D accounts for at least (because of a potential kinetic isotope effect) one-tenth of the total products. Reduction in \(D_2O\) gave ~90\% deuterated TCE,\textsuperscript{32} consistent with Path A, Path B, Path C or any combination.

There has been a significant effort to independently prepare a trichlorovinyl complex in the cobaloxime, tetraphenylporphyrincobalt, and cobalamin systems. Such a species, which has not been observed, is the hypothetical intermediate along Path B. The fact that this complex has not been observed is somewhat surprising given that trichlorovinyl metal complexes have been synthesized using nickel,\textsuperscript{60-63} palladium,\textsuperscript{63,64} and platinum.\textsuperscript{63,65} Although steric factors may play a role in the apparent instability of the trichlorovinylcobalt complex, successful synthesis of \textit{cis}-monochlorovinylcobalt
complexes in the cobalamin$^{66,67}$ and cobaloxime systems,$^{68}$ and trans-1,2-dichlorovinyl(tetraphenylporphyrin)cobalt,$^{69}$ suggests that steric factors alone are not preventing the synthesis of a trichlorovinylcobalt complex. The preparation of such a complex would clarify some of the questions that remain regarding the PCE degradation mechanism.

Computational studies have provided two possible explanations for the failure to synthesize a trichlorovinyl cobalt complex. First, a trichlorovinyl radical, if formed, would be rapidly reduced to the corresponding anion (Path C), preventing recombination with a cobalt(II) radical. In aqueous systems, the diffusion-controlled rate of protonation would control the fate of the trichlorovinyl anion resulting predominantly in TCE.$^{66}$ A second hypothesis supported by computational studies is that a trichlorovinylcobalt complex may have a reduction potential that is less negative than the Co$^{II}$/Co$^{I}$ couple (-0.59 V vs SHE)$^{20}$, causing it to be reduced in situ.$^{70}$ Pratt and van der Donk calculated that the base-off form is easily reduced under dechlorination conditions.$^{70}$

The viability of a tetrachloroethyl complex arising from Path A has been examined theoretically.$^{71,72}$ Such a complex is predicted to have a weak (8.8 kcal/mol) Co-C bond, and would be more easily reduced to TCE than the analogous trichlorovinyl complex.$^{71}$

### 1.3.2 Cobalt-Mediated Reductive Dehalogenation of TCE.

The mechanism of TCE dehalogenation is better understood than that of PCE. Studies focused on TCE have shed light on the participation of both outer-sphere and inner-sphere processes, the involvement of organometallic intermediates, and the origin of observed products.

Essentially the same mechanisms can be proposed for the transformation of TCE as those postulated for PCE (Figure 1.4). The cob(I)alamin nucleophile can attack TCE and form either a 1,2,2-trichloroethyl complex (Path A) or eliminate chloride to form a dichlorovinyl complex (Path B). In an outer-sphere process, cob(I)alamin can transfer an electron to TCE forming a dichlorovinyl radical and a cobalt(II) radical. The dichlorovinyl radical has several possible fates. It can undergo cis/trans isomerization, it can be reduced to form a dichlorovinyl anion (Path C), quenched by a hydrogen atom donor to form DCE (Path D or E), or trapped by cob(II)alamin to form a dichlorovinyl complex, the same product as in Path B (Figure 1.4). It should be noted that the
isomerization, reduction, quenching, and trapping pathways outlined in Figure 1.4 for the cis-DCE radical can also be proposed for the trans-DCE radical. However, based on the relative amounts of the products observed in previous studies, these are minor pathways at best.

With cobalamin-mediated dechlorination of TCE, 1,2-dichlorovinyl radical intermediates account for as much as 30% of the products based on deuterium incorporation from $d_7$-isopropanol, consistent with Paths D and E. Further support for vinyl radicals comes from Shey and van der Donk’s trichlorovinyl mechanistic probes, which can be viewed as models for both PCE and TCE. However, radical processes cannot account for all of the mechanistic observations. Indeed, there is considerable evidence for parallel inner-sphere pathways.

Strong evidence against outer-sphere processes comes from the distribution of cis- and trans-dichlorovinyl products. Outer-sphere electron transfer from cobalt(I) to TCE is expected to give a mixture of dichlorovinyl radicals. These species have several possible fates including trapping by a cobalt(II) radical, reduction to dichlorovinyl anion (Path C), quenching by a hydrogen atom donor (Path D), or facile isomerization to the other dichlorovinyl stereoisomer. Perhaps contrary to expectation based on steric effects, the cis geometry is favored thermodynamically for both the 1,2-dichlorovinyl radical (4:6:1) and 1,2-dichloroethylene (3:1) due to electronic factors and solvation energies. The final cis:trans ratio of the DCE products depends on the equilibration time before quenching and will not necessarily reflect the initial distribution of dichlorovinyl radicals, due to isomer interconversion. The product distribution was determined experimentally using a series of well-defined, outer-sphere electron transfer reagents of varying redox strengths. Ratios of cis-DCE to trans-DCE varied from 1:1 (strong reducing agents, short equilibration times) to 5:1 (weak reducing agents, long equilibration times). With cobalamin, much higher cis-DCE:trans-DCE ratios (>15:1) have been observed, suggesting that non-outer-sphere pathways are operative.

Further support for an inner-sphere mechanism can be derived from kinetic data. Rate constants, $k$ (M$^{-1}$s$^{-1}$) for the reaction between chloroethylene substrates and cobalamin, or anion radical mediators, were determined using changes in the cathodic peak potential upon addition of the substrate. Correlations between these experimentally
determined rate constants (log $k$) for the reduction of TCE (and PCE) and reduction potential for the reducing agent, showed that cob(I)alamin behaves differently than anion radicals.\textsuperscript{74} These results were consistent with the conclusion that neither a concerted nor stepwise electron transfer mechanism was viable in this system.\textsuperscript{74} Costentin \textit{et al.} proposed a mechanism whereby the reduced cobalt center and the chlorinated ethylene combine to form an organometallic cobalt complex.\textsuperscript{74} Theoretical calculations support the intermediacy of organometallic complexes, either in the form of a dichlorovinyl cobalt complex\textsuperscript{70} (Path B), or a trichloroethyl cobalt complex\textsuperscript{71,72} (Path A).

![Possible pathways in the cobalt-mediated dechlorination of TCE.](image)

An inner-sphere process, specifically the formation of chlorovinyl intermediates (Path B) has been hypothesized based on kinetic models,\textsuperscript{29} and mass balance considerations.\textsuperscript{36} The first direct evidence for chlorovinyl intermediates came from a report by Lesage \textit{et al}, in which TCE dechlorination reaction mixtures were analyzed by mass spectrometry and masses consistent with dichlorovinylcobalamin were observed.\textsuperscript{35} Computational studies suggest that a dichlorovinyl complex will be more stable to the reaction conditions than a trichlorovinyl complex explaining the lack of observation of
This expectation is borne out by successful independent synthesis of model complexes. Treatment of cob(I)aloxime with TCE yields cis-1,2-dichlorovinylcobaloxime.\textsuperscript{68,75,76} Interestingly, when TCE was reacted with tetraphenylporphyrincobalt(I), the trans-1,2-dichlorovinyl complex was isolated.\textsuperscript{77} These results support the viability of an inner-sphere pathway.

Chlorovinylcobaloxime complexes are remarkably stable, not reacting with dihydrogen or acid,\textsuperscript{76} calling into question the role of dichlorovinyl complexes in cobalt-mediated reductive dechlorination of TCE. However, they are unstable to reduction, yielding either cis-DCE (in protic solvent) or chloroacetylene (in aprotic solvents).\textsuperscript{78} These are the same products observed in the cobalamin-mediated dechlorination of TCE. The reduction of cis-dichlorovinylcobaloxime has been examined experimentally and theoretically, and the initial product is cis-1,2-dichlorovinyl anion.\textsuperscript{78,79} This intermediate is thought to be common to both the cis-DCE and chloroacetylene production pathways, and explains the solvent dependence on the product distribution (Figure 1.5).\textsuperscript{78} Protonation leads to cis-DCE, whereas elimination is favored in aprotic media.\textsuperscript{78}

![Reduction of cis-1,2-dichlorovinylcobaloxime](image)

Figure 1.5: Reduction of cis-1,2-dichlorovinylcobaloxime results in the formation of cis-1,2-dichlorovinyl anion. This anion can be protonated in protic media to form cis-DCE, or eliminate in aprotic media to form chloroacetylene.\textsuperscript{78}

An alternative mode of reduction where the chloroethylene is dechlorinated while bound to the cobalt center has been suggested based on mass spectrometry studies of reaction mixtures.\textsuperscript{35} Dechlorination while the chlorovinyl ligand is still attached was thought to explain the appearance of highly dechlorinated products at short reaction
times. McCauley et al., using cobaloxime model complexes, tested this proposed mechanism. They showed that although cis-1,2-dichlorovinylcobaloxime was transformed into the cis- and gem-chlorovinylcobaloximes in the presence of in situ generated cob(I)aloxime, this transformation did not result from dechlorination of an attached chlorovinyl ligand (Figure 1.6). Rather, their results were consistent with Co-C bond cleavage, formation of chloroacetylene, and reaction of chloroacetylene with cob(I)aloxime to form monochlorinated vinylcobaloximes. It is notable that monochlorovinylcobaloximes were not observed when cis-DCE was reacted with cob(I)aloxime.

\[
\begin{align*}
\text{Cl} & \quad \text{Cl} \\
\text{H} & \quad [\text{Co}] \\
\end{align*}
\]

\[
\begin{align*}
\text{H} & \quad \equiv \quad \text{Cl} \\
\text{Cl} & \quad \text{Cl} \\
\end{align*}
\]

\[
\begin{align*}
\text{H} & \quad \text{H} \\
\text{Cl} & \quad [\text{Co}] \\
\end{align*}
\]

\[
\begin{align*}
\text{H} & \quad \text{H} \\
\text{Cl} & \quad [\text{Co}] \\
\end{align*}
\]

Figure 1.6: Dechlorination of cis-1,2-dichlorovinylcobaloxime results in the formation of monochlorinated vinylcobaloximes, through the intermediacy of chloroacetylene. This transformation does not proceed while the chlorovinyl ligand attached to the metal center or via cis-DCE.

1.3.3 Computational Studies. A series of computational studies have provided significant insight into the viability of various intermediates and pathways. They have helped to rationalize experimental results and predicted the role of heretofore-unobserved intermediates.

Nonnenberg et al. as well as Pratt and van der Donk have examined the behavior and fate of simple organic fragments, such as chlorovinyl radicals and anions. These studies suggest that chlorovinyl radicals are expected to be stereochemically non-rigid (i.e. cis- and trans-dichlorovinyl radicals can interconvert) and are reducible to chlorovinyl anions under the dechlorination conditions. The chlorovinyl anions, by contrast, are calculated to have high barriers to inversion. They are also subject to
protonation by solvent and elimination to give acetylenes.\textsuperscript{70} The favorability of these processes for the various chlorovinyl anions determines the products observed.\textsuperscript{70} Elimination is calculated to be energetically unfavorable for trichlorovinyl anion, favoring protonation rather than dichloroacetylene formation.\textsuperscript{70} In contrast, \textit{cis}-1,2-dichlorovinyl anion is calculated to have competitive protonation and elimination rates.\textsuperscript{73} These results rationalize the experimental observation of chloroacetylene and not dichloroacetylene under aqueous conditions.

Reduction of chlorovinylcobalt complexes has been examined theoretically both in terms of thermodynamics and the pathways leading from the reduced complexes.\textsuperscript{70,79,80} The theoretical studies agree that reduction of these complexes is thermodynamically favorable under the redox conditions normally employed.\textsuperscript{70,79,80} The Co-C bond cleaves upon reduction and this process has been studied computationally by Follett \textit{et al.}\textsuperscript{79} At issue was whether Co-R cleavage leads to cobalt(I) and a carbon-based radical or to cobalt(II) and a carbanion (Figure 1.7).\textsuperscript{79}

![Figure 1.7: Possible cleavage pathways of the Co-C bond in alkyl- or vinylcobaloximes.](image)

The results indicate that the latter path leading directly to \textit{cis}-1,2-dichlorovinyl anion is favored (reaction energy of 20 kcal/mol) over the former radical-forming pathway (reaction energy 56 kcal/mol).\textsuperscript{79}

Computational studies have implicated chloroethyl complexes in the mechanism of reductive dechlorination reactions.\textsuperscript{71} Buhl \textit{et al.} suggest that cob(I)aloxime reacts with PCE to form (tetrachloroethylene)cobaloxime \pi-complex, which is subsequently protonated to form a tetrachloroethyl complex.\textsuperscript{72} The driving force for protonation of a tetrachloroethyl species was estimated to be -10 kcal/mol in aqueous solution.\textsuperscript{72}
Using a cobalamin-derived ligand set, Pratt and van der Donk argue that base-on tetrachloroethyl complexes formed by addition of cobalamin to PCE would be much more rapidly reduced to products than the analogous trichlorovinyl complexes formed by substitution of cobalamin for chloride in PCE.⁷¹

Similar analyses can be applied to TCE dechlorination, supporting trichloroethyl complexes from cobalamin and TCE.⁷¹ Furthermore, the formation of cis-DCE from trichloroethylcobalamin can be rationalized stereochemically. A simple Newman projection analysis (Figure 1.8) suggests that its most stable conformation would lead to trans-DCE via anti elimination. The calculations, however, indicate that the favored conformation does not have idealized 120° angles and would lead to cis-DCE, the observed product.⁷¹

Figure 1.8: Rationalization for observed products from trichloroethylcobalt complexes. Adapted from Pratt and van der Donk.⁷¹
1.3.4 Synthesis and characterization of chlorovinyl complexes. In order to study the role of organometallic intermediates in cobalamin-promoted dechlorination reactions, the van der Donk and McNeill research groups synthesized and characterized a range of cobalt chlorovinyl complexes using cobaloxime, tetraphenylporphyrin cobalt ((TPP)Co), and cobalamin. Cobaloxime complexes have long been used as functional mimics for cobalamin, and (TPP)Co has a similar coordination environment and reactivity to cobalamin. Several chemical approaches have been used in the syntheses of chlorovinylcobalt complexes (Tables 1.2 and 1.3). These methods have employed the cobalt center as both a nucleophile in the +1 oxidation state and an electrophile in the +3 oxidation state. Cobalt(I) was reacted with chlorinated ethylenes (Method I) and haloacetylenes in protic media (Method II), while cobalt(III) was reacted with chlorovinyl anions (Method III) and acetylene (Method IV).

Table 1.2: Chemical approaches used to synthesize chlorovinyl cobalt complexes

<table>
<thead>
<tr>
<th>Method</th>
<th>Reaction</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>$\text{Co}^I + \text{Cl} \xrightarrow{\text{X}} X$</td>
<td>69,75,76,84</td>
</tr>
<tr>
<td>II</td>
<td>$\text{Co}^I + \text{H} \xrightarrow{\text{X}} X + \text{H}^+$</td>
<td>66-68</td>
</tr>
<tr>
<td>III</td>
<td>$\text{Co}^\text{III} + \text{X} \xrightarrow{\text{H}}$</td>
<td>69</td>
</tr>
<tr>
<td>IV</td>
<td>$\text{Co}^\text{III} + \text{H} \xrightarrow{\text{H}} \text{H} + \text{Cl}^-$</td>
<td>77</td>
</tr>
</tbody>
</table>
Table 1.3: Chlorovinyl cobalt complexes shown have been synthesized using a range of synthetic methodologies with cobaloxime (designated by a), tetraphenylporphyrincobalt ((TPP)Co) (designated by b), and cobalamin (designated by c). Abbreviations: trichloroethylene (TCE), trans-dichloroethylene anion (tDCE$^-$), chloroacetylene (C$_2$HCl), trans-dichloroethylene (tDCE), acetylene (C$_2$H$_2$), chloride (Cl$^-$), 1,1-dichloroethylene (1,1-DCE), vinyl bromide (C$_2$H$_3$Br).

<table>
<thead>
<tr>
<th>Complex</th>
<th>System</th>
<th>#</th>
<th>Synthetic Method and Alkylating Agent</th>
<th>% Yield and Ref.</th>
</tr>
</thead>
<tbody>
<tr>
<td>![Cl-CCl]</td>
<td>Cobaloxime</td>
<td>--</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td>(TPP)Co</td>
<td>--</td>
<td>--</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td>Cobalamin</td>
<td>--</td>
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<td>--</td>
<td>--</td>
</tr>
<tr>
<td>![Cl-CCl]</td>
<td>Cobaloxime</td>
<td>2a</td>
<td>TCE</td>
<td>--</td>
</tr>
<tr>
<td>(TPP)Co</td>
<td>--</td>
<td>--</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td>Cobalamin</td>
<td>--</td>
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<td>--</td>
</tr>
<tr>
<td>![Cl-CCl]</td>
<td>Cobaloxime</td>
<td>--</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td>(TPP)Co</td>
<td>3b</td>
<td>TCE</td>
<td>--</td>
<td>tDCE$^-$</td>
</tr>
<tr>
<td>Cobalamin</td>
<td>--</td>
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<tr>
<td>![Cl-CCl]</td>
<td>Cobaloxime</td>
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<tr>
<td>(TPP)Co</td>
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<tr>
<td>Cobalamin</td>
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<tr>
<td>![Cl-CCl]</td>
<td>Cobaloxime</td>
<td>5a</td>
<td>C$_2$HCl</td>
<td>--</td>
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<tr>
<td>(TPP)Co</td>
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<tr>
<td>Cobalamin</td>
<td>5c</td>
<td>C$_2$HCl</td>
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</tr>
<tr>
<td>![Cl-CCl]</td>
<td>Cobaloxime</td>
<td>6a</td>
<td>tDCE</td>
<td>--</td>
</tr>
<tr>
<td>(TPP)Co</td>
<td>6b</td>
<td>--</td>
<td>--</td>
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</tr>
<tr>
<td>Cobalamin</td>
<td>--</td>
<td>--</td>
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<td>--</td>
</tr>
<tr>
<td>![Cl-CCl]</td>
<td>Cobaloxime</td>
<td>7a</td>
<td>1,1-DCE</td>
<td>--</td>
</tr>
<tr>
<td>(TPP)Co</td>
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<tr>
<td>Cobalamin</td>
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<td>--</td>
</tr>
<tr>
<td>![CCl]</td>
<td>Cobaloxime</td>
<td>8a</td>
<td>C$_2$H$_3$Br</td>
<td>--</td>
</tr>
<tr>
<td>(TPP)Co</td>
<td>--</td>
<td>--</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td>Cobalamin</td>
<td>8c</td>
<td>C$_2$H$_2$</td>
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</table>
The reaction of a cobalt(I) source with chlorinated ethylenes (Method I) was used to prepare 2a, 6a, 7a, and 8a in the cobaloxime system. Two different synthetic approaches were used. The van der Donk group generated reduced cobaloxime in situ via NaBH₄ reduction, and reacted it with halogenated ethylenes under a hydrogen atmosphere. They were able to synthesize and characterize 2a from the reaction with TCE (18% yield), 6a from reaction with trans-DCE, (1% yield), 7a from reaction with 1,1-DCE (23% yield), and 8a from the reaction with vinyl bromide (51% yield). In the McNeill lab, the synthesis of chlorovinylcobaloximes was adapted from the work of Pickin and Welker, where cob(I)aloxime was generated in situ from Co(OAc)₂, dimethylglyoxime, pyridine and zinc dust. Addition of chlorinated ethylenes produced the chlorovinyl complexes 2a (45% yield), 6a (21% yield) and 7a (48% yield). Notably both synthetic approaches yielded only 2a from the reaction with either PCE or TCE, and neither 1 nor 4 have been observed in any system. Furthermore, cis-DCE appears to be unreactive under both sets of conditions.

The mechanism of vinylcobaloxime formation has been the subject of several studies. Using vinyl chloride as a source of the vinyl group, Dodd et al. provided support for simultaneous attack of the cobalt nucleophile and displacement of the chloride ion with retention of configuration. In contrast, Stang and Datta, employing used alkylvinyl triflates, suggested that the reaction occurs by a stepwise addition-elimination mechanism, involving an anionic intermediate. McCauley et al. observed the transformation of monochlorovinylcobaloxime into vinyl cobaloxime. They found that 5a and 7a were slowly and incompletely converted to 8a under reducing conditions. They suggest the intermediacy of either vinyl chloride or acetylene intermediates, which could react with cobalt(I) via Method I or Method II respectively. The incomplete conversion is thought to result from volatilization of the organic intermediates.

Interestingly, in crystal structures of the chlorovinylcobaloxime complexes, the chlorovinyl ligands were observed to be coplanar with the axial pyridine ligands. Furthermore the chlorovinyl complexes are thought to be much more stable toward homolysis than chloroalkyl analogs, having bond dissociation energies 10 kcal/mol higher according to calculations. These observations suggested that π-bonding between the chlorovinyl ligand and the cobalt center may be important, and prompted a study of
Co-C bonding to evaluate the importance of this interaction. A series of cis-1,2-dichlorovinylcobaloxime complexes with different axial pyridine ligands were synthesized using Method I and characterized crystallographically. The bond lengths observed were not consistent with π-bonding, and neither were electronic structure calculations. The calculations did, however, support increased s-character in the interaction between the chlorovinyl ligand and the cobalt center.

Cob(I)alamin reacts with acetylenes to form chlorovinylcobalt complexes (Method II). This method was employed in the synthesis of the cis-chlorovinylcobalamin 5c from chloroacetylene (89% yield) and vinylcobalamin 8c from acetylene (50% yield). Interestingly, cis-dichlorovinyl cobaloxime 2a, was not formed during the reaction of cob(I)aloxime and dichloroacetylene. Reactivity studies employing 5c showed that this complex decomposed to 8c under dehalogenation conditions. Deuterium incorporation studies indicated that this transformation proceeded through an acetylene intermediate.

The trans-dichlorovinylcobalt complex, 3b, was generated in the tetraphenylporphyrin cobalt ((TPP)Co) system using Method I (23 % yield) and Method III (85 % yield). The trans-dichlorovinyl anions used in Method III were generated following Koebrich et al. via deprotonation of trans-DCE with butyl lithium. This type of chlorovinyl complex has not been synthesized using either cobaloxime or cobalamin.

The trans-chlorovinyl complex 6 is accessible in both the cobaloxime and (TPP)Co systems. In the former case, Method I is used to synthesize 6a. In the latter case, acetylene insertion into a Co-Cl bond results in chlorovinylcobalt complexes (Method IV). Reaction of acetylene with (TPP)CoCl resulted in the formation of 6b, the trans-monochlorovinyl, in 84% yield. Analogous trans-monobromovinyl and trans-monoiodovinylcobalt complexes were also synthesized. Interestingly the bromine and iodine atoms could be replaced by chloride under mild conditions, but only when the
halogen was trans to the cobalt. This study supports the intermediacy of an acetylene complex in these transformations, as proposed by Setsune et al.\textsuperscript{89}

\[
\begin{align*}
\text{LCo} & \rightleftharpoons X \text{H} & +X^- & \text{H} \text{H} & \text{LCo} \quad \oplus \\
\end{align*}
\]

1.3.5 Cobalt-carbon bond cleavage. The synthesis and characterization of chlorovinylcobalt complexes have facilitated studies of the Co-C bond cleavage component of the overall dehalogenation mechanism. As discussed above, reduction of the model complexes results in the same organic products as those observed under catalytic conditions with cobalamin. The Co-C bonds in the chlorovinyl complexes are expected to be stronger than their methyl analogues.\textsuperscript{66} This is exemplified by the rate of photochemical cleavage reactions for chlorovinyl and vinylcobalamin that were approximately 20 times slower than the methyl analogues.\textsuperscript{66} An alternative explanation for this result may be a large cage recombination effect, namely the vinyl and cobalt fragments may recombine much more rapidly than their methyl counterparts.\textsuperscript{66}

McCauley et al. examined the electrochemical properties of chlorovinylcobaloximes to probe the mode of reductive cleavage using cob(I)aloxime. Although neither cob(I)alamin nor cob(I)aloxime is generally reducing enough to transfer an electron to the chlorovinyl complexes, there is evidence that these species are involved in the decomposition of chlorovinyl complexes. Addition of cob(I)aloxime results in the conversion of dichlorovinylcobaloximes into the lower chlorinated vinylcobaloximes, a process known to involve Co-C bond cleavage.\textsuperscript{68} Electrochemical evidence also supports cob(I)aloxime’s involvement in the Co-C bond breaking step.\textsuperscript{68} This result is consistent with the autocatalytic evolution of methane from methylcobaloxime with dimeric cobaloxime described by Schrauzer.\textsuperscript{81,82}

Reduction of chlorovinyl complexes is the established decomposition pathway for these complexes.\textsuperscript{67,68,75,78} The Co-C bond can either cleave heterolytically forming a vinyl anion and a cobalt(II) complex, or homolytically forming a vinyl radical, which can then be reduced to the anion under dehalogenation conditions, and an anionic cobalt(I) complex. Recent calculations have clarified this dichotomy, providing support for the
heterolytic pathway.\textsuperscript{79} Solvation effects favor a small anionic organic fragment rather than the much larger cobalt anion because the free energy of solvation varies with effective radius.\textsuperscript{79} Furthermore, development of spin density, characteristic of radical fragments, was not observed for the dichlorovinyl fragment supporting the heterolytic pathway.\textsuperscript{79} These results contrast with those observed for an analogous methyl complex, where the data support homolytic dissociation followed by electron transfer.\textsuperscript{79}

1.4 Catalytic Model Systems

Concurrent with mechanistic studies of cobalt-mediated dehalogenation using cobalamin and its model systems, new cobalt-based catalysts have been developed. Early studies by Lewis and Morra showed that porphyrin complexes are effective catalysts for dechlorination of chloromethanes.\textsuperscript{23} Subsequent studies by Dror and Schlautmann demonstrated that water-soluble cobalt, iron and nickel porphyrins are catalysts for the reductive dechlorination of chlorinated ethylenes.\textsuperscript{90} Further, they showed that water-solubility is a key factor in the catalytic activity of these molecules.\textsuperscript{91} The functional and structural similarities of these complexes to cobalamin made them an interesting target for further studies of the dehalogenation mechanism.

Fritsch and McNeill studied the kinetics and mechanism of the reaction of \textit{tetrakis-(carboxyphenyl)porphyrincobalt}, (TCPP)Co, with chlorinated ethylenes.\textsuperscript{77} The results of this study, notably that PCE and TCE were degraded via a sequential stepwise process, with higher rate constants for the more chlorinated congeners, led to the conclusion that this system likely followed the same mechanism as cobalamin.\textsuperscript{77} Furthermore, both cobalt complexes had the same empirical rate laws and both required the cobalt(I) oxidation state for dechlorination activity.\textsuperscript{77}

1.5 Conclusions.

Fundamental inorganic and organometallic studies of the dechlorination of chloroethylenes using cobalt-centered complexes have provided insight into the operative mechanisms of these environmentally important reactions. It is hoped that the improved mechanistic understanding of these dechlorination mechanisms will lead to more effective remediation strategies. This is especially important in these systems since many
of the potential products are themselves toxic and recalcitrant. While the studies highlighted in this chapter have improved our understanding of the factors controlling the production of benign and toxic products, further studies are needed to address remaining questions.

PCE dechlorination appears to be relatively straightforward, leading to TCE with good mass balance. There is evidence for the participation of radicals and scant evidence for the intermediacy of Co-C bonded intermediates. Nevertheless, recent computational studies indicate that trichlorovinyl or tetrachloroethyl intermediates may be formed during this rapid transformation. The question remains whether these organometallic intermediates are formed and how these inner-sphere pathways compete with an outer-sphere electron transfer-based mechanism.

Examinations of TCE dechlorination have led to a number of conclusions. First, organometallic intermediates, specifically dichlorovinyl complexes, are believed to play an important role. Second, reduction of these dichlorovinyl complexes is thought to lead to dichlorovinyl anion that reacts to give cis-DCE and chloroacetylene. However, similar to PCE, the origin and significance of vinyl radical intermediates in cobalamin-catalyzed TCE dechlorination remains incompletely understood.

Acknowledgments. This work was supported the National Science Foundation under Grant No. CHE-0239461. We also thank Prof. Wilfred van der Donk for helpful comments.
### Chapter I Supplement: Compilation of rate constants and conditions for degradation of selected C₂ substrates by cobalamin.

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Chapter II. Reconciling disparate models of the involvement of vinyl radicals in cobalamin-mediated dechlorination reactions

Inner-sphere (nonradical) and outer-sphere (radical-based) mechanisms have been suggested for cobalamin-mediated dechlorination of tetrachloroethylene (PCE) and trichloroethylene (TCE). In this study, the role of free vinyl radicals was investigated using deuterated radical traps: $d_8$-isopropanol and $d_8$-tetrahydrofuran. For both substrates, addition of trap resulted in production of deuterated dechlorination products, and higher concentrations of trap resulted in increased amounts of deuterated products. However, only a finite proportion of the products were trappable – 8% of the PCE-derived products and 86% of the TCE-derived products result from free radicals. The data show that the reaction does not proceed solely by either an inner-sphere or an outer-sphere mechanism and led to the hypothesis that caged radical intermediates were involved in the mechanism. The untrappable fraction of products are hypothesized to result from in-cage reactions. This hypothesis was investigated using $d_5$-glycerol as a radical trap and viscogen. Although increased viscosity resulted in decreased formation of free radical-derived products, consistent with the cage hypothesis, these data were inconclusive. The role of $d_8$-isopropanol in enhancing the production of radicals in this system via an acetone ketyl radical chain mechanism was also investigated, and no evidence for such an effect was found.
2.1 Introduction

Cobalamin is the dominant catalyst responsible for microbially based reductive dechlorination reactions. The mechanism of cobalamin-mediated dechlorination of tetrachloroethylene (PCE) and trichloroethylene (TCE), has been studied extensively using cobalamin and various model systems, but a mechanism has yet to be proposed that reconciles all of the experimental observations. A key point of contention is the relative importance of carbon-centered radicals in the system, since there is contrasting data that supports inner-sphere (nonradical) and outer-sphere (radical-based) mechanisms.

Cob(I)alamin is responsible for the sequential, stepwise dehydrohalogenation of chlorinated ethylenes, PCE, TCE, cis- and trans-1,2-dichloroethylene (cis-DCE and trans-DCE), and vinyl chloride, resulting in the production of non-toxic ethylene. One of the most striking features of the dechlorination of TCE is that significantly more cis-DCE is produced than trans-DCE in a range of studies (greater than 15:1). This stereochemical product preference contrasts that observed with a series of known outer-sphere electron transfer agents, where low cis:trans ratios are observed (less than 5:1).

Furthermore, masses consistent with dichlorovinylcobalamin have been observed in mass spectra of dechlorination reactions, consistent with an inner-sphere process. Chlorovinyl cobalt complexes have been independently synthesized in several systems, and reactivity studies show that reduction of cis-1,2-dichlorovinylcobaloxime results in the same products observed with cobalamin-mediated dechlorination. The cleavage of the cobalt-carbon bond in these complexes proceeds heterolytically, leading to a chlorovinyl anion, and not a chlorovinyl radical, at this stage of the reaction.

In contrast, isotope labeling and trapping studies suggest that radicals play an important part in cobalamin-mediated dechlorination of PCE and TCE. Deuterated products were observed in dechlorination studies conducted in the presence of deuterated isopropanol and protiated water, and proportional protiated products were observed in analogous studies conducted with protiated isopropanol and deuterated water. Deuterium incorporation was as high as 10% of the PCE-derived products and 30% of the TCE-derived products. Products consistent with radical intermediates were also observed in cobalamin-mediated dechlorination of (1S,2R)-2-(1,2,2-
trichlorovinyl)cyclopropyl)benzene, which readily cyclizes if a radical is formed.\textsuperscript{59} Using this intramolecular radical trap, cyclized products accounted for 68\% of the total.\textsuperscript{59}

There has been some concern that the use of deuterated isopropanol as a radical trap may lead to enhancement of the amount of radical-derived products by a radical chain mechanism under basic conditions (Figure 2.1).\textsuperscript{59} This concern derives from the possibility that following deuterium abstraction, the isopropanol radical can be deprotonated, leading to the formation of the acetone ketyl radical. This strongly reducing species can be photochemically generated under basic conditions and has been shown to dehalogenate bromo- and iodobenzene but not chlorobenzene.\textsuperscript{93} It has been hypothesized that acetone ketyl radical may be responsible for reduction of chloroethylenes, leading to the enhancement in the population of chlorovinyl radicals.\textsuperscript{59} This study evaluates whether deuterated isopropanol is an “innocent” trap or if acetone ketyl radicals enhance the apparent radical-derived product yield.

\[ \text{Cl}_2\text{C}=\text{Cl} + \text{D}_2\text{C}_3\text{H}_6 \xrightarrow{\text{H}_2\text{O}} \text{Cl}_2\text{C}=\text{D} \]

Figure 2.1: Radical propagation cycle initiated by trichlorovinyl radical and isopropanol. Reduction potentials and pKa value from ref. 94.

Variation in the amounts of radical-derived products observed for the various substrates, combined with the strong evidence for non-outer sphere processes, inspired the current reinvestigation of the role of radicals in cobalamin-mediated dechlorination reactions. The purpose of this study was to reexamine the trapping of vinyl radicals by formal D-atom donors to understand the mechanism of this reaction.
2.2 Experimental Procedures.

2.2.1 Chemicals. Cobalamin (Acros), trichloroethylene (Aldrich), tetrachloroethylene (Aldrich), \(d_8\)-isopropanol (Aldrich), \(d_8\)-tetrahydrofuran (Cambridge Isotope Laboratories), \(d_5\)-glycerol (Cambridge Isotope Laboratories), and glycine (Aldrich) were used as received. Titanium citrate solution was prepared by adding TiCl\(_3\) (25 mL, 10% in 20-30% HCl, Aldrich) to a degassed solution of sodium citrate (16 g, Mallinckrodt) and tris(hydroxymethyl)aminomethane (8 g, Aldrich) in 25 mL DI-H\(_2\)O.

2.2.2 General. All studies were conducted in 20 mL crimp cap vials sealed with 20 mm, butyl/PTFE caps (Chromtech) containing 4 mL total reaction volume. The reactions were set up in a glove box (Coy Laboratory Products Incorporated) under nitrogen atmosphere containing ~1.5% hydrogen. Reactions contained glycine buffer, cobalamin, titanium citrate, deuterated trap, and chlorinated substrate; they were stirred for at least 30 minutes after substrate addition before analysis. Headspace samples (200 µL) were analyzed by GC-MS using an Agilent GC 6890 with Restek Rtx-1 Crossbond 100% dimethylpolysiloxane: 30 m x 0.32 mm x 5 µm film thickness column coupled to an Agilent MS 5973 mass selective detector operated in scan mode. Products were identified using extracted ion chromatograms.

2.2.3 GC/MS Method and Analysis. The oven program was 40 °C (7 min), ramp at 40 °C/min to 140 °C (9.5 min) for a total of 19 minutes. The products were identified by their retention times compared to standards: TCE, 15.5 min; cis-DCE, 13.3 min; trans-DCE 11.8 min. Protiated products were identified and quantified using extracted ion chromatograms (EIC) using the peak at 130 m/z for C\(_2\)HCl\(_3\) (\(h\)-TCE) and 96 m/z for protiated DCEs (C\(_2\)H\(_2\)Cl\(_2\), \(h\)-DCE). Deuterated products were identified using EIC peaks at 131 m/z for C\(_2\)DCl\(_3\) (\(d\)-TCE) and 97 m/z for the deuterated DCEs (C\(_2\)HDCl\(_2\), \(d_1\)-DCE). A correction factor was included for the 2.2% natural abundance of 131 m/z in the \(h\)-TCE mass spectrum. The \(d\)-TCE/\(h\)-TCE and \(d_1\)-DCE/\(h\)-DCE ratios reported in this study are the ratio of the corrected \(d\)-TCE and \(d_1\)-DCE values to the raw \(h\)-TCE and \(h\)-DCE values, respectively.

2.2.4 Trapping Studies. The concentration of deuterated trap was varied: \(d_8\)-THF, 0-310 mM; \(d_8\)-isopropanol, 0-650 mM; or \(d_5\)-glycerol, 0-4110 mM. All other reaction components were kept constant. The concentration of cobalamin was 2.5 µM in the PCE.
experiments and 25 μM in the TCE experiments. The titanium citrate solution (300 mM stock) was adjusted to pH 9 immediately prior to each study, and the final titanium citrate concentration was 8 mM. The reactions were buffered at pH 9 with glycine (90 mM). PCE (25 μM) or TCE (250 μM) were added to initiate reactions. Reactions were conducted at room temperature (24 °C) unless otherwise specified. Control studies to evaluate the effect of each of the reaction components were conducted. Titanium citrate concentration was varied (0-75 mM), glycine concentration was varied (0-750 mM), sodium citrate concentration was varied (90-410 mM), and cobalamin concentration was varied (0-40 μM).

2.2.5 Temperature variation. Trapping studies were conducted at 0 °C, 24 °C, 45 °C, and 60 °C. In these cases the reaction vials were equilibrated at the desired temperature for 15 minutes. The substrate was then added with a syringe through the septum. The tubes were then reacted with stirring for at least 30 minutes prior to analysis. All tubes were cooled to 0 °C for at least 5 minutes prior to analysis. These studies employed a saturating concentration of trap (d8-isopropanol, 163 mM).

2.2.6 Viscosity data fitting. In order to test the radical-cage hypothesis, d5-glycerol was added to reactions as a radical trap and viscogen. The viscosity of the solutions was calculated using the parameters described by Cheng. The diffusivity of the radicals from the cage is inversely related to the solution viscosity raised to the 1.14 power. As such, the ratio of the rate constant for cage escape in glycerol solution (viscous conditions, \( k_{esc,v} \)) to the rate constant for cage escape in water (\( k_{esc} \)) is related to the ratio of the viscosity of water (\( \mu \)) to the viscosity at some concentration of glycerol (\( \mu_v \)) raised to the 1.14 power given by:

\[
\frac{k_{esc,v}}{k_{esc}} = \left( \frac{\mu}{\mu_v} \right)^{1.14}.
\]

When this relationship is plotted versus glycerol concentration a function equal to the ratio of the viscosities raised to the 1.14 power can be obtained (eq 2.1):

\[
\frac{k_{esc,v}}{k_{esc}} = \left( \frac{\mu}{\mu_v} \right)^{1.14} = 1.66 \times 10^{-8} [\text{glycerol}]^2 - 2.39 \times 10^{-4} [\text{glycerol}] + 1
\]

when included in the function for \( d/h \) calculation (eq 2.4 for PCE and eq 2.7 for TCE dechlorination), accounts for the change in the diffusivity of the radicals due to increasing viscosity.
2.3 Results and Discussion

2.3.1 Trap identity. The cobalamin-mediated reductive dechlorination of PCE and TCE was investigated using titanium(III)citrate as a bulk reductant in the presence of deuterated radical traps: $d_8$-isopropanol and $d_8$-tetrahydrofuran (Figure 2.2).

![Figure 2.2: Reaction of chloroethylenes with cobalamin.](image)

The relative amount of deuterated dechlorination products increases with increasing concentrations of deuterated isopropanol. This observation supports the assertion that radicals are involved in the reaction since organic radicals are known to abstract deuterium from the tertiary C-D bond of deuterated isopropanol. One explanation for this result is that acetone ketyl radical, formed via deuterium atom abstraction from deuterated isopropanol and subsequent deprotonation, reacts with chloroethylenes and generates chlorovinyl radicals (Figure 2.1). Radical chain reactions involving acetone ketyl radical have been implicated in dehalogenation of some halobenzenes under basic conditions. If this process were operative, an enhancement in deuterated products would be observed with $d_8$-isopropanol but not with $d_8$-tetrahydrofuran, since the latter does not form a strongly reducing byproduct. In this study, the relative amounts of deuterated products were compared for $d_8$-isopropanol and $d_8$-tetrahydrofuran.

Consistent with previous work, the results of this study showed increasing concentrations of deuterated product with increasing deuterated trap concentrations. In order to determine whether there is an enhancement in radical-derived products due to the formation of acetone ketyl radical from $d_8$-isopropanol, trapping studies were performed with $d_8$-tetrahydrofuran as well (Table 2.1). The relative amount of deuterated product was not significantly different for the traps tested, suggesting that the ketyl radical effect does not play a significant role in the generation of radical-derived products.
Table 2.1: Product $d/h$ ratios and corresponding $\% d$ incorporation.

<table>
<thead>
<tr>
<th>Substrate</th>
<th>Trap</th>
<th>$d/h$ ratio$^a$</th>
<th>$% d$ incorporation$^b$</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 PCE</td>
<td>$d_8$-isopropanol</td>
<td>$8.1 \times 10^{-2} \pm 1.0 \times 10^{-2}$</td>
<td>$8.0 \pm 1.0 %$</td>
</tr>
<tr>
<td>2 PCE</td>
<td>$d_8$-tetrahydrofuran</td>
<td>$7.0 \times 10^{-2} \pm 1.1 \times 10^{-2}$</td>
<td>$7.0 \pm 1.1 %$</td>
</tr>
<tr>
<td>3 TCE</td>
<td>$d_8$-isopropanol</td>
<td>$6.0 \times 10^{-1} \pm 3.0 \times 10^{-1}$</td>
<td>$85 \pm 7 %$</td>
</tr>
<tr>
<td>3 TCE</td>
<td>$d_8$-tetrahydrofuran</td>
<td>$4.9 \times 10^{-1} \pm 5.2 \times 10^{-1}$</td>
<td>$83 \pm 11 %$</td>
</tr>
</tbody>
</table>

$^a$ The $d/h$ ratio is the ratio of the deuterated products to protiated products corrected for deuterium natural abundance. These values are extracted from fits of the trapping data to eq 3 and eq 6. $^b$ The $\% d$ incorporation ($d/(d+h) \times 100\%$) is the percentage of deuterated products corrected for deuterium natural abundance. These values are based on extrapolation to infinite trap concentration.

2.3.2 Trapping Studies. Perhaps surprisingly, the relationship between deuterium incorporation and deuterated trap was non-linear (Figure 2.3). Furthermore, the amount of deuterated products relative to the total amount of products was found to saturate at different levels for the two substrates. With TCE, 86$\%$ of the products were trappable with the deuterated trap, whereas with PCE only 8$\%$ were trappable when extrapolating to infinite trap concentration. Possible reasons for differences between substrates are discussed below.

Figure 2.3: Product ratio from cobalamin-mediated dechlorination of A) PCE and B) TCE with various concentrations of deuterated radical trap $d_8$-isopropanol (circles) or $d_8$-tetrahydrofuran (triangles).
2.3.3 Mechanistic hypotheses. The nonlinear relationship between trap concentration and deuterium incorporation and the fact that only a finite amount of the products are deuterated, even extrapolating to infinite D-atom donor concentration, led to the development of mechanistic hypotheses and prompted the studies described below.

One possible explanation for the data is that cob(I)alamin simultaneously reacts by two modes, an inner-sphere mode that does not involve radical intermediates and an outer-sphere electron transfer mode that involves “free” radicals (Figure 2.4, hypothesis A). In this model, PCE ($E^0 = -598$ mV vs SHE)$^{49}$ is expected to form radicals more readily via electron transfer than TCE ($E^0 = -674$ mV vs SHE).$^{49}$ In fact, the opposite is true, as significantly more deuterated dichlorovinyl than trichlorovinyl products are observed, suggesting that with TCE, the majority of the products are derived from free radicals making this pathway untenable.

An alternative explanation is that cob(I)alamin always reacts by outer-sphere electron transfer but involves the concept of a solvent cage (Figure 2.4, hypothesis B), wherein the solvent encapsulates the radical pair, which may react with each other prior to diffusing apart to become free radicals.$^{98-106}$ In this case, transfer of an electron to the substrate results in a caged radical pair—a substrate-derived vinyl radical and a cob(II)alamin metal-based radical. Deuterated products arise from the vinyl radicals that have escaped the cage while protiated products arise from several pathways including an in-cage reaction. The involvement of caged intermediates in this reaction system may explain why Shey, et al. observed relatively high levels of radical-derived products (68%) using intramolecular radical traps while Glod, et al. observed lower amounts of radical-derived products using intermolecular traps (30% for TCE and 10% for PCE).$^{32,59}$
In the cage, recombination of cobalamin radical and chlorovinyl radical may lead to a chlorovinyl cobalamin intermediate. Such a dichlorovinyl intermediate has been observed with TCE, but the analogous trichlorovinyl species has not been observed with PCE. The possible fates of the caged trichlorovinyl radical are discussed below. Although homolytic cleavage of the Co-C bond (if formed) would seem to be an important source of radicals, as is the case with alkyl-cobalt species, calculations, and trapping studies clearly show that reductive cleavage of Co-C bonds in chlorovinyl complexes leads to anionic and not radical intermediates. Consistent with this explanation, a study of the mechanism of living radical polymerization of methyl acrylate and vinyl acrylate by cobalt porphyrins shows that the vinyl case is much less active since the cobalt vinyl bond does not cleave homolytically.

Hypothesis B, as presented in Figure 2.4 is highly simplified. A more complete mechanistic hypothesis was developed on the basis of some general observations of cobalamin-mediated dechlorination of PCE.

2.3.4 General observations with PCE. Deuterated TCE (d-TCE) forms from cob(I)alamin-mediated dechlorination of PCE in the presence of deuterated trap and is believed to arise from abstraction of a deuterium atom from d₈-isopropanol by free trichlorovinyl radical. Since formation of d-TCE is indicative of radical involvement in the mechanism of reaction, the ratio of d-TCE/h-TCE can be used to determine the extent to which radical intermediates are involved. With PCE as a substrate, h-TCE was the major product, d-TCE was the minor product, and the ratio of d-TCE to h-TCE saturates
at a maximum of 8% (Figure 2.3A). Glod, et al. previously showed that the relative amount of $d$-TCE produced increased with increasing concentrations of deuterated isopropanol, but the greater number of trap concentrations employed in this study uncovered the saturation behavior.

In order to determine if the reaction components suppressed the deuterated product yield, a series of control experiments were conducted. In addition to the substrate (PCE), the catalyst (cob(I)alamin), and radical trap (usually $d_8$-isopropanol), the reaction solutions contained glycine (pH 9 buffer) and titanium(III)citrate (reductant). In these experiments, glycine, sodium citrate, titanium(III)citrate, and cobalamin were varied to determine their effects on the $d$-TCE/h-TCE ratio at different concentrations (Figure 2.5). Glycine was found to be a competitive radical scavenger at high concentrations, but the effect was minor under standard conditions (90 mM glycine). Neither sodium citrate nor cobalamin had an effect on the product ratio. When the concentration of titanium(III)citrate was increased, the amount of deuterated products decreased, consistent with reduction of trichlorovinyl radicals to trichlorovinyl anions and subsequent protonation by the solvent.
2.3.5 Proposed Mechanism with PCE. Based on the general observations noted above and previous results, the mechanism in Figure 2.6 is proposed. Single electron transfer from cob(I)alamin to PCE results in the formation of caged trichlorovinyl radical and cationic cob(II)alamin radical. Direct evidence for the formation of cob(II)alamin comes from UV-visible and EPR studies of similar reaction mixtures. The chlorovinyl
radical fragment can then either diffuse from the cage ($k_{esc}$) or undergo a reaction in the cage ($k_{cage}$). The in-cage reaction is hypothesized to yield a trichlorovinyl anion, which is protonated by the solvent to give $h$-TCE. The nature of the in-cage process is unknown; various possibilities are discussed below. Radicals that escape the cage have several possible fates. They may be reduced in a second-order process by the bulk reductant ($k_{Ti}$) to give the trichlorovinyl anion and subsequently $h$-TCE, or they can abstract a hydrogen atom from glycine ($k_{gly}$) to form $h$-TCE. Lastly, the chlorovinyl radicals can abstract a deuterium atom from deuterated trap molecules ($k_{trap}$) to form $d$-TCE.

![Figure 2.6: Proposed mechanism for cobalamin-mediated dechlorination of PCE.](image)

2.3.6 In-cage processes. With PCE reduction, the results of the current study indicate that a majority (as much as 92%) of the products are not derived from free radicals, suggesting an important role for in-cage processes. Although the fate of the caged trichlorovinyl radical is not known, there are at least three scenarios that lead to trichlorovinyl anion (Figure 2.7). Specifically, trichlorovinyl radical may be reduced in the solvent cage to form trichlorovinyl anion and cationic cob(III)alamin (pathway A), these ions could couple to form a transient trichlorovinyl complex (pathway B), or this intermediate could be formed via radical coupling (pathway C).\(^{109,110}\) A trichlorovinyl intermediate has never been observed and is hypothesized to be readily reduced to form trichlorovinyl anion under reducing conditions.\(^{70,73}\) Following either pathway B or pathway C, trichlorovinyl anion is formed and leads to the formation of protiated products in aqueous solution. Further investigation is necessary to determine the precise fate of the caged trichlorovinyl radical. Several species including cob(I)alamin ($E^0 = -0.59$ V vs NHE)$^{20}$, cob(II)alamin ($E^0 = 0.13$ V vs NHE at pH 9)$^{111}$, or Ti(III)citrate ($E^0 =$
-0.63 V vs NHE, would be capable of reducing trichlorovinyl radical (calculated $E^0 = 0.49-0.48$ V vs NHE), or dichlorovinyl radical (calculated $E^0 = 0.27-0.35$ V vs NHE).

Figure 2.7: Fate of caged intermediates.

2.3.7 Kinetic Model. Rate laws for the formation of the deuterated and protiated products are derived from the proposed mechanism (Figure 2.6) and given in eqs 2.2 and 2.3. The two rate expressions can be combined to describe the $d$-TCE/$h$-TCE ratio (eq 2.4). A generalized form of this expression was used to fit the data from the trapping studies (Figure 2.3A). At low trap concentrations, this model predicts a linear relationship between product ratio and trap concentration (eq 2.5). Under these conditions, the $d$-TCE/$h$-TCE ratio is a function of the fraction of radicals that escape the cage, $f_{esc}$, and the ratio of the relative rates of trapping ($k_{trap}$) to the rates of reduction ($k_{Ti}$) and hydrogen atom abstraction ($k_{gly}$). At high trap concentrations, the product ratio is entirely governed by the ratio of the rate constant for cage escape ($k_{esc}$) to the rate constant for the in-cage reaction ($k_{cage}$) (eq 2.6).
\[
\frac{d[d - TCE]}{dt} = \frac{k_{esc}k_{trap}[C_2Cl_3_{cage}]}{k_{trap}[\text{trap}]+k_{gly}[\text{gly}]+k_{T}[\text{Ti}]} \quad \text{eq 2.2}
\]

\[
\frac{d[h - TCE]}{dt} = \frac{k_{esc}[C_2Cl_3_{cage}]}{k_{trap}[\text{trap}]+k_{gly}[\text{gly}]+k_{T}[\text{Ti}]} + k_{cage}[C_2Cl_3_{cage}] \quad \text{eq 2.3}
\]

\[
\frac{d[d - TCE]}{d[h - TCE]} = \frac{\frac{k_{esc}}{k_{cage}}[\text{trap}]}{\left(\frac{k_{esc}}{k_{cage}} + 1\right)\left(\frac{k_{T}[\text{Ti}]+k_{gly}[\text{gly}]}{k_{trap}}\right) + [\text{trap}]} \quad \text{eq 2.4}
\]

at low [trap]; \[
\frac{d[d - TCE]}{d[h - TCE]} = f_{esc}\left(\frac{k_{trap}[\text{trap}]}{k_{T}[\text{Ti}]+k_{gly}[\text{gly}] \right) \quad ; \quad f_{esc} = \frac{k_{esc}}{k_{esc} + k_{cage}} \quad \text{eq 2.5}
\]

at high [trap]; \[
\frac{d[d - TCE]}{d[h - TCE]} = \frac{\frac{k_{esc}}{k_{cage}}}{[\text{trap}]} \quad \text{eq 2.6}
\]

The best-fit lines in Figure 2.3A correspond to non-linear fits of the data to eq 2.4. These fits give values for \( k_{esc}/k_{cage} \) of 0.08 ± 0.01 for \( d_8 \)-isopropanol and 0.07 ± 0.01 for \( d_8 \)-tetrahydrofuran. The values for \( (k_{T}[\text{Ti}]+k_{gly}[\text{gly}]/k_{trap} \) were 101 ± 28 and 96 ± 39 for \( d_8 \)-isopropanol and \( d_8 \)-tetrahydrofuran, respectively.

2.3.8 TCE Studies. As discussed above, there is evidence for and against the involvement of free radicals in TCE dechlorination. As such, TCE was evaluated to determine the relative importance of radicals in cobalamin-mediated dechlorination. The same general mechanistic hypotheses for PCE were adopted and expanded in evaluating the data from the TCE studies (Figure 2.8). The main difference in the schemes is that the intermediate cis- and trans-dichlorovinyl radicals can interconvert.\(^{73}\) In this mechanistic scheme, the in-cage process is shown explicitly proceeding via a cis-dichlorovinyl intermediate based on prior work that supports such a species.\(^{68,76,78}\)
2.3.9 General observations with TCE. TCE was dechlorinated in the presence of Ti(III)citrate by cob(I)alamin, producing a mixture cis- and trans-DCE. The reactions were buffered with glycine (pH 9), and a deuterated radical trap, usually $d_8$-isopropanol (0-650 mM), was added to determine the effect of increasing trap concentration on product deuterium incorporation. Control experiments, were used to evaluate the effect of the reagents on the product ratio and the same trends were observed with TCE as with PCE. Glycine (0-750 mM) and titanium(III)citrate (0-38 mM) were found to be a competitive radical scavengers, while sodium citrate (90-410 mM) and cobalamin (0-40 µM) had no effect on the product ratio (Figure 2.9).
Figure 2.9: Protiated to deuterated product ratio from cobalamin-mediated dechlorination of PCE using titanium(III)citrate as a bulk reductant in the presence of various concentrations of (A) glycine buffer, (B) titanium(III)citrate, (C) sodium citrate, and (D) cobalamin. Error bars are the standard deviation of duplicate samples.

The extent to which free radicals are involved in the mechanism of the reaction was deduced from the ratio of the sum of deuterated cis- and trans-DCE to the sum of protiated cis-DCE and trans-DCE observed.

\[
\frac{d_i - DCE}{h - DCE} = \frac{d_i - cDCE + d_i - tDCE}{h - cDCE + h - tDCE}
\]
At low trap concentration, the protiated product dominated and deuterated product was the minor product, at high trap concentration, the deuterated product was dominant. Rate laws for the production of each product were derived, and an expression for the \( d_1 / h \)-DCE ratio was obtained (eq 2.7) (see supplement, page 49, for derivation).

\[
\frac{d[d_1-DCE]}{d[h-DCE]} = \frac{k_{esc}}{k_{cage}} \frac{k_{\text{[trap]}}}{[\text{trap}]} \left( \frac{k_{\text{trans}}(k'_{\text{gly}}[\text{gly}]+k'[\text{Ti}]) + f_{\text{cis}}(k_{\text{gly}}[\text{gly}]+k[\text{Ti}])}{(f_{\text{trans}}k_{\text{trap}} + f_{\text{cis}}k_{\text{trap}})} + [\text{trap}] \right)
\]

The best-fit lines in Figure 2.3B correspond to non-linear fits of data to eq 2.7. These fits give values for \( k_{\text{esc}}/k_{\text{cage}} \) of 6.0 ± 0.4 for \( d_8 \)-isopropanol and 4.9 ± 0.5 for \( d_8 \)-tetrahydrofuran. The values for the ratio of the non-trap rate constants to the trapping rate constant were 215 ± 6 and 169 ± 10 for \( d_8 \)-isopropanol and \( d_8 \)-tetrahydrofuran, respectively. The ratio of the non-trap rate constants to the trapping rate constant is given by

\[
\frac{f_{\text{trans}}(k'_{\text{gly}}[\text{gly}]+k'[\text{Ti}]) + f_{\text{cis}}(k_{\text{gly}}[\text{gly}]+k[\text{Ti}])}{(f_{\text{trans}}k_{\text{trap}} + f_{\text{cis}}k_{\text{trap}})}
\]

The plot of \( d_1\)-DCE/\( h \)-DCE ratio versus \( d_8 \)-isopropanol is notably much less curved than the analogous plot in the PCE case, and a clear saturation point was not observed. When fit to eq 2.7, the extrapolated saturation point correlates to 86% deuterium incorporation. This striking result suggests that nearly all of the products of TCE dechlorination proceed through a free radical intermediate. The remainder of the products are hypothesized to derive from an in-cage reaction where caged dichlorovinyl radical and cob(II)alamin radical combine to form dichlorovinylcobalamin in the solvent cage. This idea is consistent with previous studies that strongly support the involvement of organometallic intermediates with TCE and lower chlorinated congeners in cobalamin-mediated reductive dechlorination reactions.\(^{31,35,66-68,74,76,78}\) Under the reaction conditions, this intermediate is expected to be reduced, yielding a dichlorovinyl anion,\(^{78}\) which, in protic solvent, is protonated at diffusion-controlled rates.

2.3.10 Stereochemical product preference. In previous work, the cis-DCE:trans-DCE ratio is used as a diagnostic of reaction mechanism, with cob(I)alamin-mediated dechlorination giving much higher cis-DCE:trans-DCE ratios than known outer-sphere electron transfer agents.\(^{31}\) This discrepancy is consistent with a non-outter-sphere process
for cobalamin. Furthermore the involvement of chlorovinylcobalt complexes is supported by mass spectrometry of reaction mixtures and independent synthesis and reactivity of chlorovinylcobalt complexes in several different systems. In this study, the cis-DCE:trans-DCE ratios were determined for the protiated and deuterated products. Consistent with previous results, a cis-DCE:trans-DCE ratio of 10:1 was observed for the protiated products. However among the deuterated products, a cis-DCE:trans-DCE ratio of 6:1 was observed. The marked preference for the cis isomer among the protiated products is consistent with a pathway where those products are derived from an organometallic intermediate. The cis-DCE:trans-DCE ratio for the deuterated products, which is at the high end of the calculated ratio of cis-DCE:trans-DCE isomers (3:1 for dichloroethylene and 4-6:1 for dichlorovinyl radicals), suggests that the deuterated products are derived from radicals that can freely isomerize. It is not clear whether the chlorovinyl radicals isomerize in the cage or upon diffusion out of the cage. However product distributions for meso and non-meso products from the decomposition of SS-azobis-a-phenylethane are consistent with radical isomerization in the cage prior to recombination.

2.3.11 Origin of the sterochemical preference. Two factors may contribute to the sterochemical preference for forming cis-1,2-dichlorovinylcobalt complexes. They are a preferred reactivity between cob(II)alamin and the cis-dichlorovinyl radical and preferential diffusion of trans-dichlorovinyl radical from the solvent cage. Coupling with cob(II)alamin is likely to be more facile for the cis-dichlorovinyl radical due to a less hindered transition state structure (Figure 2.10A). This route, which may lead to the formation of cis-dichlorovinylcobalamin, would generate cis-DCE under reducing conditions. The involvement of this pathway is likely to increase the cis-DCE:trans-DCE ratio since reduction of cis-dichlorovinylcobalamin results in the formation of the stereochemically rigid cis-dichlorovinyl anion.

It is known that molecular shape and stereochemistry contribute to diffusivity. Assuming both cis- and trans-dichlorovinyl radicals are initially formed in the cage, it is reasonable to expect that trans-dichlorovinyl radicals could escape faster given their more linear shape (Figure 2.10B)
Figure 2.10: A) Steric rationalization for preferential formation of cis-1,2-dichlorovinyl cobalt complexes. B) Molecular shape rationalization for preferential diffusion of trans-dichlorovinyl radical from the solvent cage.

2.3.12 Cage escape efficiency differences between trichlorovinyl and dichlorovinyl radicals. The results of the trapping studies indicate that the \( k_{\text{esc}}/k_{\text{cage}} \) ratio is 0.08 for trichlorovinyl radicals compared to 6.0 for dichlorovinyl radicals. Escape rates for dichlorovinyl radicals are expected to be 1.13 times faster than trichlorovinyl radical based on their molecular size.\(^{96}\) Clearly, escape rate alone cannot explain the difference observed, suggesting instead that the in-cage reaction is 65 times faster for trichlorovinyl radical than dichlorovinyl radical. We ascribe the superior in-cage reactivity of trichlorovinyl radical to its relative ease of reduction\(^{70,73}\) and favor the intermediacy of trichlorovinyl anion (Figure 2.7, pathways A and B).
2.3.13 Temperature dependence. In order to probe the involvement of a solvent cage in this reaction, trapping studies were conducted at 0 °C and 24 °C. Increased deuterium incorporation was observed at higher temperature (Figure 2.11); however due to the complexity of the various mass transfer and reaction rate processes involved in this system, it is not possible to attribute this result to a change in the rate of any one process.

Figure 2.11: Protiated to deuterated product ratio from cobalamin-mediated dechlorination using titanium(III)citrate as a bulk reductant at 24°C (filled circles) and 0 °C (open circles) for TCE (A) and PCE (B). Error bars are the standard deviation of duplicate samples.

Trapping studies were also conducted over a range of temperatures (0 °C to 60 °C). The relative amount of deuterium incorporation was found to increase linearly with inverse temperature over the temperature range studied and the response in the product ratio for PCE- and TCE-derived products had the same temperature dependence (Figure 2.12).
2.3.14 Viscosity Effects. In order to further examine the hypothesis that caged radical intermediates are involved, trapping studies were conducted using $d_5$-glycerol as both radical trap and viscogen. While glycerol is a well-known viscogen,\textsuperscript{95} it is also noteworthy that glycerol and isopropanol are close structural analogs. The proposed mechanism predicts increased deuterium incorporation with increasing $d_5$-glycerol concentration, similar to other traps. However, unlike other traps, at extreme glycerol concentrations the effect of viscosity on $k_{esc}$ is predicted to result in decreased $d/h$ ratios since increasing viscosity should limit cage escape. Although not conclusive, the observed trends are consistent with the proposed mechanism, addition of $d_5$-glycerol resulted in the formation of deuterated products; and at high viscosity (~3 cP), the $d/h$ ratio decreased (Figure 2.13).

Figure 2.12: Relationship between $d/h$ product ratio and inverse temperature for cobalamin-mediated dechlorination using titanium(III)citrate as a bulk reductant for TCE (A) and PCE (B).
The observed effect of increasing viscosity (Fig. 2.13, diamonds) on the \( d/h \) ratio deviates from the best-fit to the data (Fig. 2.13, dashed lines) at high \( d_5 \)-glycerol concentrations. This may be due to incorporation of trap molecules in the solvent cage.\(^{100,101}\) If this were the case, caged radicals may have access to the deuterated trap molecules before they diffuse from the cage, leading to the higher than expected \( d/h \) ratios at high trap concentrations.

### 2.4 Conclusions.

The results of this study suggest that cobalamin-mediated dechlorination of PCE and TCE proceeds via caged radical intermediates. With PCE, a maximum of 8% of the observed products are derived from free radicals (those that have escaped the cage and been trapped by a deuterated trap molecule). With TCE, 86% of the observed products are derived from free radicals. These results support the involvement of a caged radical intermediate because even at high trap concentrations, where reaction with the radical trap should overwhelm competing processes such as reduction by titanium(III)citrate or H-atom abstraction, only a finite number of free-radical derived products were observed.
Although not conclusive, under increased viscosity conditions the amount of free radicals that can be trapped decreases significantly with both substrates, and at $d_3$-glycerol concentrations of greater than 1 M, the trend of increasing product deuteration with increased trap is no longer observed. The involvement of caged intermediates in this system reconciles previous results, explaining the evidence for both apparent inner-sphere (nonradical) and outer-sphere (radical based) mechanisms.
Chapter II Supplement: Rate law derivations

The rate expressions for the formation of TCE-derived products were expressed using Figure 2.8. The product distribution is influenced in part by the equilibrium between the cis- and trans-dichlorovinyl radicals, $K_{iso}$.

$$K_{iso} = \frac{[cis - C_2HCl_2\cdot]}{[trans - C_2HCl_2\cdot]}$$

The total amount of free dichlorovinyl radicals in the reaction pool is given by:

$$[C_2HCl_{2,free\cdot}]_{ss} = [cis - C_2HCl_2\cdot] + [trans - C_2HCl_2\cdot]$$

where:

$$[trans - C_2HCl_2\cdot]_{ss} = \frac{[C_2HCl_{2,free\cdot}]_{ss}}{1 + K_{iso}} = f_{trans}[C_2HCl_{2,free\cdot}]_{ss} f_{trans} = \frac{1}{1 + K_{iso}}$$

$$[cis - C_2HCl_2\cdot]_{ss} = \frac{[C_2HCl_{2,free\cdot}]_{ss} K_{iso}}{1 + K_{iso}} = f_{cis}[C_2HCl_{2,free\cdot}]_{ss} f_{cis} = \frac{K_{iso}}{1 + K_{iso}}$$

The steady state concentration of dichlorovinyl radicals is given by:

$$[C_2HCl_{2,free\cdot}]_{ss} = \frac{k_{esc}[C_2HCl_{2,caged\cdot}]_{ss}}{f_{trans}(k'_{trap}[trap] + k'_{gly}[gly] + k'_{Tl}[Tl]) + f_{cis}(k_{trap}[trap] + k_{gly}[gly] + k_{Tl}[Tl])}$$

$$\frac{d[d_1 - tDCE]}{dt} = k'_{trap}[trap][trans - C_2HCl_2\cdot]$$

$$\frac{d[d_1 - tDCE]}{dt} = f_{trans} k'_{trap}[trap][C_2HCl_{2,free\cdot}]_{ss}$$

$$\frac{d[d_1 - tDCE]}{dt} = \frac{f_{trans} k'_{esc} k'_{trap}[trap][C_2HCl_{2,free\cdot}]_{ss}}{f_{trans}(k'_{trap}[trap] + k'_{gly}[gly] + k'_{Tl}[Tl]) + f_{cis}(k_{trap}[trap] + k_{gly}[gly] + k_{Tl}[Tl])}$$

$$\frac{d[d_1 - cDCE]}{dt} = k'_{trap}[trap][cis - C_2HCl_2\cdot]$$

$$\frac{d[d_1 - cDCE]}{dt} = f_{cis} k_{trap}[trap][C_2HCl_{2,free\cdot}]_{ss}$$

$$\frac{d[d_1 - cDCE]}{dt} = \frac{f_{cis} k_{esc} k_{trap}[trap][C_2HCl_{2,free\cdot}]_{ss}}{f_{trans}(k'_{trap}[trap] + k'_{gly}[gly] + k'_{Tl}[Tl]) + f_{cis}(k_{trap}[trap] + k_{gly}[gly] + k_{Tl}[Tl])}$$

The sum of the deuterated cis- and trans-dichlorovinyl products is given by:

$$[d_1 - DCE] = [d_1 - cDCE] + [d_1 - tDCE]$$
\[
\frac{d[d_1 - \text{DCE}]}{dt} = \frac{(f_{\text{trans}k_\text{trap}} + f_{\text{cis}k_\text{trap}})k_{\text{esc}}[\text{trap}]C_{\text{HC12-2,trap}^*}]_{\text{ss}}}{f_{\text{trans}}(k'_{\text{trap}}[\text{trap}] + k'_{\text{gly}}[\text{gly}] + k'r[Ti]) + f_{\text{cis}}(k_{\text{trap}}[\text{trap}] + k_{\text{gly}}[\text{gly}] + k-r[Ti])}
\]

\[
\frac{d[h - t\text{DCE}]}{dt} = \frac{(k'_{\text{gly}}[\text{gly}] + k'r[Ti])[\text{trans} - C_{\text{HC12}^*}]}{f_{\text{trans}}(k'_{\text{gly}}[\text{gly}] + k'r[Ti])}[C_{\text{HC12}_p^*}]_{\text{ss}}
\]

\[
\frac{d[h - t\text{DCE}]}{dt} = \frac{f_{\text{trans}}k_{\text{esc}}(k'_{\text{gly}}[\text{gly}] + k'r[Ti])[C_{\text{HC12}_p^*}]_{\text{ss}}}{f_{\text{trans}}(k'_{\text{trap}}[\text{trap}] + k'_{\text{gly}}[\text{gly}] + k'r[Ti]) + f_{\text{cis}}(k_{\text{trap}}[\text{trap}] + k_{\text{gly}}[\text{gly}] + k-r[Ti])}
\]

\[
\frac{d[h - c\text{DCE}]}{dt} = \frac{(k_{\text{gly}}[\text{gly}] + k_r[Ti])[\text{cis} - C_{\text{HC12}^*}]}{f_{\text{cis}}(k_{\text{gly}}[\text{gly}] + k_r[Ti])}[C_{\text{HC12}_p^*}]_{\text{ss}} + k_{\text{cage}}[C_{\text{HC12}_cage^*}]_{\text{ss}}
\]

\[
\frac{d[h - c\text{DCE}]}{dt} = \frac{f_{\text{cis}}k_{\text{esc}}(k_{\text{gly}}[\text{gly}] + k_r[Ti])[C_{\text{HC12}_cage^*}]_{\text{ss}}}{f_{\text{tran}}(k'_{\text{trap}}[\text{trap}] + k'_{\text{gly}}[\text{gly}] + k'r[Ti]) + f_{\text{cis}}(k_{\text{trap}}[\text{trap}] + k_{\text{gly}}[\text{gly}] + k-r[Ti])}
\]

The sum of the protiated \textit{cis}- and \textit{trans}-dichlorovinyl products is given by:

\[
[h - \text{DCE}] = [h - c\text{DCE}] + [h - t\text{DCE}]
\]

\[
\frac{d[h - \text{DCE}]}{dt} = \left[\frac{k_{\text{esc}}[f_{\text{trans}}(k'_{\text{gly}}[\text{gly}] + k'r[Ti]) + f_{\text{cis}}(k_{\text{gly}}[\text{gly}] + k_r[Ti])]}{f_{\text{trans}}(k'_{\text{gly}}[\text{gly}] + k'r[Ti]) + f_{\text{cis}}(k_{\text{gly}}[\text{gly}] + k_r[Ti])}\right]C_{\text{HC12}_p^*}]_{\text{ss}} + \left[\frac{k_{\text{cage}}[f_{\text{trans}}(k'_{\text{gly}}[\text{gly}] + k'r[Ti]) + f_{\text{cis}}(k_{\text{gly}}[\text{gly}] + k_r[Ti])]}{f_{\text{trans}}(k'_{\text{gly}}[\text{gly}] + k'r[Ti]) + f_{\text{cis}}(k_{\text{gly}}[\text{gly}] + k_r[Ti])}\right]C_{\text{HC12}_cage^*}]_{\text{ss}}
\]

\[
\frac{d[d_1 - \text{DCE}]}{dt} = \frac{(f_{\text{trans}k'_{\text{trap}} + f_{\text{cis}k_{\text{trap}}})k_{\text{esc}}[\text{trap}]C_{\text{HC12}_2,\text{trap}^*}]_{\text{ss}}}{[k_{\text{esc}}f_{\text{trans}}(k'_{\text{gly}}[\text{gly}] + k'r[Ti]) + f_{\text{cis}}(k_{\text{gly}}[\text{gly}] + k_r[Ti])][C_{\text{HC12}_2,\text{cage}^*}]_{\text{ss}} + [k_{\text{cage}}f_{\text{trans}}(k'_{\text{gly}}[\text{gly}] + k'r[Ti]) + f_{\text{cis}}(k_{\text{gly}}[\text{gly}] + k_r[Ti])][C_{\text{HC12}_2,\text{cage}^*}]_{\text{ss}}}
\]

\[
\frac{d[d_1 - \text{DCE}]}{dt} = \frac{(f_{\text{trans}k'_{\text{trap}} + f_{\text{cis}k_{\text{trap}}})k_{\text{esc}}[\text{trap}]C_{\text{HC12}_2,\text{cage}^*}]_{\text{ss}}}{k_{\text{esc}}[f_{\text{trans}}(k'_{\text{gly}}[\text{gly}] + k'r[Ti]) + f_{\text{cis}}(k_{\text{gly}}[\text{gly}] + k_r[Ti])] + [\text{trap}] + [\text{trap}]}
\]

\[\text{eq. 2.7}\]

50

A series of nickel complexes was synthesized using 6-[(2,6-dialkylphenylamino)-1-dimethyl]-2-[(2,6-dialkylphenylimino)methyl]pyridine ligands (alkyl = methyl, AIP\textsuperscript{Me}NiCl\textsubscript{2}; ethyl, AIP\textsuperscript{Et}NiCl\textsubscript{2}; and isopropyl, AIP\textsuperscript{iPr}NiCl\textsubscript{2}). The structures of these complexes were compared to 2,6-bis-[1-(2,6-diisopropylphenylimino)ethyl]pyridine nickel dichloride (BIP\textsuperscript{iPr}NiCl\textsubscript{2}). Solution state structures of each of these complexes were determined using paramagnetic \textsuperscript{1}H NMR spectroscopy, and solid-state structures were solved with X-ray crystallography. Cyclic voltammetry was used to assess the capacity of these complexes to undergo reduction. Evidence for chemical transformation following reduction was observed and this was further investigated using independently prepared cationic variants of the complexes.
3.1 Introduction.

Microbes dehalogenate environmental pollutants, and cofactors such as cobalamin (cobalt-containing macrocycle) and F430 (nickel-containing macrocycle) are essential to these processes.\textsuperscript{22,26,48} Although cobalamin-mediated dehalogenation is well studied,\textsuperscript{92,114} there is a relative lack of studies of nickel-mediated dehalogenation.

Nickel-mediated dehalogenation has primarily been studied with nickel(I)octaethylisobacteriochlorin anion (Ni(I)OEiBC\textsuperscript{−}), which catalytically degrades various halogenated substrates.\textsuperscript{115-118} In this mechanism, involvement of nickel(III)-alkyl intermediates has been proposed, but the product forming steps are not well-understood. Questions remain regarding the implications associated with the formation of coupling products, and whether or not they are derived from free organic radicals.\textsuperscript{115-118}

Well-defined nickel complexes can help to further elucidate the chemical basis for nickel-mediated dehalogenation. To this end, we synthesized and characterized a series of nickel complexes with varying ligand structure, since ligand structure can be integrally related to the reactivity of the complex.

Aminoiminopyridyl (AIP) ligands (Figure 3.1) have been employed in a variety of systems including aluminum,\textsuperscript{119-121} iron,\textsuperscript{122,123} lutetium,\textsuperscript{124,125} lanthanum,\textsuperscript{126} neodymium,\textsuperscript{126} yttrium,\textsuperscript{125,126} and scandium.\textsuperscript{125} These complexes have been studied primarily as polymerization catalysts and are also of fundamental interest. They are generated from bis(imino)pyridyl (BIP) ligands (Figure 3.1) via methylation with trimethylaluminum.\textsuperscript{120,122} The bis(imino)pyridyl ligand can also be alkylated at the imine when bound to a metal center, as was the case for the reaction of bis(imino)pyridyl iron dichloride with LiCH\textsubscript{2}Si(CH\textsubscript{3})\textsubscript{3}, although these reactions were quite complex and resulted in a mixture of alkylated products.\textsuperscript{123}
Zimmerman et al. note that significant internal charge-transfer processes are available with complexes of AIP ligands, giving rise to unique reaction pathways, coordination modes and complex stabilization. These features may enable nickel complexes of this ligand to be stabilized in a variety of oxidation states, and lead to interesting reaction pathways. The aminoiminopyridyl nickel complexes have, to the best of our knowledge, not yet been synthesized and characterized.

In this study, a series of nickel complexes with varying substituents on the aryl rings (R = methyl, ethyl, and isopropyl) were synthesized and characterized. For comparison, an analogous isopropyl substituted bis(imino)pyridyl nickel complex was also prepared in this study and further characterized. Solution and solid-state structures were obtained using NMR and X-Ray crystallography, and the reduction potential of each of the complexes was assessed.

3.2 Experimental Procedures.

3.2.1 General methods. The 2,6-bis-[1-(2,6-dialkylphenylimino)ethyl]pyridine (alkyl = methyl, BIPMe; alkyl = ethyl, BIPEt; and alkyl = isopropyl, BIPiPr) ligands were prepared as described. The ligands were methylated using trimethyl aluminum to prepare 6-[(2,6-dialkylphenylamino)-1-dimethyl]-2-[(2,6-dialkylphenylimino)methyl]pyridine (alkyl = methyl, AIPMe; alkyl = ethyl, AIPEt, and alkyl = isopropyl, AIPiPr) variants. All air- and moisture-sensitive manipulations were conducted in an MBraun Unilab glovebox under an atmosphere of purified nitrogen. Ferrocene (Aldrich) was used as received and tetrabutylammonium hexafluorophosphate (TBAPF$_6$) (Fluka) was used as received. $^1$H NMR spectra were recorded on Varian Inova
VI-300 or VXR-300 spectrometers. Paramagnetic NMR parameters $d_1 = 0.030$ s, $at = 0.063$ s, $sw = 70000$ Hz, $lb = 10$ Hz, were used for analysis of metal complexes. High-resolution electro-spray ionization mass spectrometry (ESI-MS) measurements were made on a Bruker BioTOF II instrument under positive ionization mode. UV-visible absorbance spectra were obtained on a Cary 14 Spectrophotometer (Olis Conversion) from 400 to 1200 nm.

3.2.2 Preparation of nickel(II) complexes. $\text{AIP}^{\text{Me}}\text{NiCl}_2$ was prepared using a method modified from Britovsek et al for the preparation of iron complexes$^{122}$ from NiCl$_2$$\cdot$$6$H$_2$O (0.070 g, 0.28 mmol) and AIP$^{\text{Me}}$ ligand (0.11 g, 0.28 mmol) in hot 1-butanol. The resulting reddish brown solution was heated to reflux for 10 minutes and then allowed to cool. The product crystallized from the reaction solution as an orange crystalline solid. These crystals were isolated by vacuum filtration. Further product was isolated by precipitation with Et$_2$O resulting in isolation of material in 68% yield (0.10 g, 0.19 mmol). X-ray quality crystals were grown from 1-butanol and the structure of this complex was confirmed with X-ray crystallography. $\mu_{\text{eff}}$ (Evans NMR method$^{130} \mu_B$): calcd 2.83; found 2.82. Paramagnetic $^1$H NMR (300 MHz, CD$_2$Cl$_2$, -20°C, $\delta$): 92.55 (s, 1H, meta pyridyl), 83.33 (s, 1H, meta pyridyl), 25.48 (s, 3H, imine CH$_3$), 24.59 (s, 1H, aryl), 19.18 (s, 1H, aryl), 18.61 (s, 9H, aryl CH$_3$), 14.63 (s, 1H, aryl), 13.38 (s, 1H, para pyridyl), 7.73 (s, 6H, gem dimethyl), 6.83 (s, 1H, aryl), 5.13 (s, 3H, CH$_3$), -6.87 (s, 1H, aryl), -6.97 (s, 1H, aryl). ESI-MS (m/z): [M$^+$ -Cl] calcd for C$_{26}$H$_{31}$ClN$_3$Ni 478.1554; found 478.1561.

$\text{AIP}^{\text{Et}}\text{NiCl}_2$ was prepared in a similar manner as $\text{AIP}^{\text{Me}}\text{NiCl}_2$ from NiCl$_2$$\cdot$$6$H$_2$O (0.19 g, 0.81 mmol) and AIP$^{\text{Et}}$ ligand (0.36 g, 0.81 mmol). The orange crystalline solid was isolated by vacuum filtration in 71% yield. (0.33 g, 0.58 mmol). X-ray quality crystals were grown from deuterated dichloromethane and the structure of this complex was confirmed with X-ray crystallography. $\mu_{\text{eff}}$ (Evans NMR method$^{130} \mu_B$): calcd 2.83; found 2.79. Paramagnetic $^1$H NMR (300 MHz, CD$_2$Cl$_2$, -20°C, $\delta$): 91.92 (s, 1H, meta pyridyl), 83.02 (s, 1H, meta pyridyl), 24.05 (s, 1H, aryl), 20.50 (s, 1H), 18.22 (s, 1H, aryl), 17.49 (s, 2H, ethyl), 17.09 (s, 3H, imine CH$_3$), 14.89 (s, 1H), 14.28 (s, 1H, aryl), 14.01 (s, 1H, para pyridyl), 13.68 (s, 2H, ethyl), 8.79 (s, 3H, ethyl), 8.10 (s, 3H, ethyl), 7.14 (s, 2H, ethyl), 5.77 (s, 1H, aryl), 1.63 (s, 6H, gem dimethyl), 1.23 (s, 2H, ethyl), -
2.05 (s, 3H, ethyl), -5.24 (s, 1H, aryl), -6.88 (s, 1H, aryl). ESI-MS (m/z): [M⁺ -Cl] calcd for C_{30}H_{39}ClN_{3}Ni 534.2181; found 534.2191.

**AIP^{iPr}NiCl_{2}** was prepared in a similar manner as **AIP^{Me}NiCl_{2}** from NiCl_{2}•6H_{2}O (0.24 g, 1.00 mmol) and AIP^{iPr} ligand (0.50 g, 1.00 mmol) in hot 1-butanol. The resulting reddish brown solution was heated to reflux for 10 minutes and then allowed to cool. The product crystallized from the reaction solution as an orange crystalline solid. These crystals were isolated by vacuum filtration. Further product was isolated by precipitation with ether resulting in isolation of material in 66% yield (0.42 g, 0.67 mmol). X-ray quality crystals were grown from 1-butanol and the structure of this complex was confirmed with X-ray crystallography. \( \mu_{\text{eff}} \) (Evans NMR method): calcd 2.8; found 2.7. Paramagnetic \( ^{1}H \) NMR (300 MHz, CD_{2}Cl_{2}, -20°C, \( \delta \)): 88.55 (s, 1H, meta pyridyl), 70.27 (s, 1H, meta pyridyl), 24.74 (s, 1H, aryl), 24.30 (s, 3H, iPr CH\(_{3}\)), 17.89 (s, 1H, aryl), 15.82 (s, 3H, imine CH\(_{3}\)), 14.13 (s, 1H, aryl), 13.77 (s, 1H, para pyridyl), 12.27 (s, 1H, iPr CH\(_{3}\)), 8.53 (s, 3H, iPr CH\(_{3}\)), 8.23 (s, 3H, iPr CH\(_{3}\)), 7.64 (s, 1H, aryl), 6.29 (s, 3H, iPr CH\(_{3}\)), 3.74 (s, 3H, iPr CH\(_{3}\)), 3.16 (s, 3H, iPr CH\(_{3}\)), 1.41 (s, 1H, iPr CH), 1.06 (s, 3H, iPr CH\(_{3}\)), -0.43 (s, 3H, gem CH\(_{3}\)), -1.26 (s, 3H, gem CH\(_{3}\)), -5.65 (s, 1H, aryl), -5.91 (s, 1H, aryl), -11.08 (s, 3H, iPr CH). ESI-MS (m/z): [M⁺ -Cl] calcd for C\(_{34}\)H\(_{47}\)ClN\(_{3}\)Ni 590.2807; found 590.2832.

**BIP^{iPr}NiCl_{2}** was prepared in a similar manner as **AIP^{Me}NiCl_{2}** from NiCl\(_{2}\)•6H\(_{2}O\) (0.0056 g, 0.024 mmol) and BIP\(^{iPr}\) ligand (0.011 g, 0.023 mmol). The orange crystalline solid was isolated by vacuum filtration (0.0070 g, 0.011 mmol, 52% yield). X-ray quality crystals were grown from 1-butanol and the structure of this complex was confirmed with X-ray crystallography. \( \mu_{\text{eff}} \) (Evans NMR method): calcd 2.8; found 2.5. \( ^{1}H \) NMR (300 MHz, CDCl\(_{3}\), 20°C, \( \delta \)): 77.86 (s, 2H, meta pyridyl), 13.73 (s, 4H, iPr CH), 12.30 (s, 4H, meta aryl), 4.35 (br s, 1H, para pyridyl), 2.01 (s, 12H, iPr CH\(_{3}\)), 1.50 (s, 12H, iPr CH\(_{3}\)), 0.53 (s, 6H, imine CH\(_{3}\)), -4.73 (s, 2H, para aryl). ESI-MS (m/z): [M⁺ -Cl] calcd for C\(_{33}\)H\(_{47}\)ClN\(_{3}\)Ni 574.2499; found 574.2469.

**[AIP^{iPr}NiCl]BPh\(_{4}\)** was prepared from **AIP^{iPr}NiCl\(_{2}\)**. Sodium tetraphenyl borate (0.027 g, 0.080 mmol) and **AIP^{iPr}NiCl\(_{2}\**) (0.051 g, 0.080 mmol) were dissolved in acetonitrile and stirred at room temperature for two hours. The mixture was then filtered.
and the filtrate was pumped down to solid resulting in isolation of material in a 96% yield (0.071 g, 0.078 mmol).

\[ \text{[BIP}^{\text{Pr}}\text{NiCl}]\text{BPh}_4 \] was prepared from \text{BIP}^{\text{Pr}}\text{NiCl}_2. Sodium tetraphenyl borate (0.019 g, 0.055 mmol) and \text{BIP}^{\text{Pr}}\text{NiCl}_2 (0.034 g, 0.055 mmol) were dissolved in acetonitrile and stirred at room temperature for two hours. The mixture was then filtered and the filtrate was pumped down to solid resulting in isolation of material in a 91% yield (0.045 g, 0.050 mmol).

3.2.3 X-Ray Crystallography. In all cases the crystal was placed onto the tip of a glass capillary and mounted on a either Siemens or a Bruker SMART Platform CCD diffractometer for a data collection. The structure was solved using SHELXS-97 and refined using SHELXL-97. The space group was determined based on systematic absences and intensity statistics. A direct-methods solution was calculated which provided most non-hydrogen atoms from the E-map. Full-matrix least squares/difference Fourier cycles were performed which located the remaining non-hydrogen atoms. All non-hydrogen atoms were refined with anisotropic displacement parameters. All hydrogen atoms except the amine hydrogens were placed in ideal positions and refined as riding atoms with relative isotropic displacement parameters. Crystallographic data for all structures are summarized in Table 3.1. \text{AlP}^{\text{Et}}\text{NiCl}_2 cocrystallized with CH\text{Cl}_2, which appears to interact with the chloride atoms in the complex. There is also a close contact (2.36 Å) between H17A, a methylene proton on one of the aryl ring ethyl groups, and the nickel center. \text{BIP}^{\text{Pr}}\text{NiCl}_2 cocrystallized with 1-butanol, and the solvent is hydrogen bonded to Cl2 (d(O1-H1A…Cl2 = 2.36 Å).
Table 3.1: Crystallographic data.

<table>
<thead>
<tr>
<th>Compound</th>
<th>AIP(^{\text{et}})NiCl₂</th>
<th>AIP(^{\text{t}})NiCl₂</th>
<th>AIP(^{\text{et}})NiCl₂(^*)</th>
<th>BIP(^{\text{et}})NiCl₂(^a)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Formula</td>
<td>C(<em>{26})H(</em>{31})Cl(_2)Ni</td>
<td>C(<em>{30})H(</em>{36})Cl(_2)Ni(_3)Ni, CH(_2)Cl(_2)</td>
<td>C(<em>{34})H(</em>{47})Cl(_2)Ni</td>
<td>C(<em>{37})H(</em>{43})Cl(<em>2)Ni(<em>3)Ni\cdot C(</em>{4})H(</em>{10})O</td>
</tr>
<tr>
<td>Color, shape</td>
<td>orange, needle</td>
<td>orange, plate</td>
<td>orange, needle</td>
<td>orange, prism</td>
</tr>
<tr>
<td>lattice type</td>
<td>monoclinic</td>
<td>tetragonal</td>
<td>monoclinic</td>
<td>monoclinic</td>
</tr>
<tr>
<td>space group</td>
<td>C(_2/c)</td>
<td>I-4</td>
<td>P(_2_1/c)</td>
<td>P(_2_1/c)</td>
</tr>
<tr>
<td>a, Å</td>
<td>37.881(4)</td>
<td>19.3040(19)</td>
<td>10.5365(12)</td>
<td>13.4331(11)</td>
</tr>
<tr>
<td>b, Å</td>
<td>7.9500(8)</td>
<td>19.3040(19)</td>
<td>15.0503(17)</td>
<td>15.1640(12)</td>
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<tr>
<td>c, Å</td>
<td>17.8591(18)</td>
<td>17.635(4)</td>
<td>21.001(2)</td>
<td>18.5296(15)</td>
</tr>
<tr>
<td>α, deg</td>
<td>90</td>
<td>90</td>
<td>90</td>
<td>90</td>
</tr>
<tr>
<td>β, deg</td>
<td>112.352(2)</td>
<td>90</td>
<td>98.124(2)</td>
<td>104.3410(10)</td>
</tr>
<tr>
<td>γ, deg</td>
<td>90</td>
<td>90</td>
<td>90</td>
<td>90</td>
</tr>
<tr>
<td>V, Å(^3)</td>
<td>4974.2(9)</td>
<td>6571.4(16)</td>
<td>3296.9(6)</td>
<td>3656.9</td>
</tr>
<tr>
<td>formula wt, g mol(^{-1})</td>
<td>515.15</td>
<td>571.25, solvent</td>
<td>627.36</td>
<td>685.43</td>
</tr>
<tr>
<td>D(_c), g cm(^{-3})</td>
<td>1.376</td>
<td>1.326</td>
<td>1.264</td>
<td>1.245</td>
</tr>
<tr>
<td>µ, mm(^{-1})</td>
<td>1.014</td>
<td>0.940</td>
<td>0.777</td>
<td>0.708</td>
</tr>
<tr>
<td>F(000)</td>
<td>2160</td>
<td>2752</td>
<td>1336</td>
<td>1464</td>
</tr>
<tr>
<td>θ range, deg</td>
<td>2.29 to 25.08</td>
<td>1.56 to 25.04</td>
<td>1.67 to 25.08</td>
<td>1.56 to 25.06</td>
</tr>
<tr>
<td>reflns collected</td>
<td>20499</td>
<td>31769</td>
<td>31627</td>
<td>32487</td>
</tr>
<tr>
<td>independent reflns</td>
<td>4422 [R(int) = 0.0599]</td>
<td>5810 [R(int) = 0.0666]</td>
<td>5840 [R(int) = 0.0672]</td>
<td>6468 [R(int) = 0.0609]</td>
</tr>
<tr>
<td>max, min transmission</td>
<td>0.819 and 0.1918 and 0.9118 and 0.925 and 0.986 and 0.986</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>data/restraint/parameters</td>
<td>4422 / 0 / 300</td>
<td>5810 / 0 / 363</td>
<td>5840 / 0 / 372</td>
<td>6468 / 0 / 409</td>
</tr>
<tr>
<td>R(_I), wR(_2) (I &gt; 2σ(I))</td>
<td>0.0511, 0.0863</td>
<td>0.0650, 0.1729</td>
<td>0.0424, 0.815</td>
<td>0.0389, 0.8033</td>
</tr>
<tr>
<td>R(_I), wR(_2) (all data)</td>
<td>0.0758, 0.0926</td>
<td>0.0749, 0.1815</td>
<td>0.0764, 0.0906</td>
<td>0.0688, 0.0986</td>
</tr>
<tr>
<td>GOF</td>
<td>1.107</td>
<td>1.122</td>
<td>1.028</td>
<td>1.056</td>
</tr>
<tr>
<td>largest diff peak, hole, e Å(^3)</td>
<td>0.519 and - 1.220 and - 0.238 and - 0.849 and -</td>
<td>0.384 and 0.822 and 0.256 and 0.821</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

\(^{a}\)This crystallographic data is also reported in Chapter 4.\(^{114}\)

3.2.4 Electrochemistry. Cyclic voltammetry experiments were conducted using a BAS 100B electrochemical analyzer with a Pt auxiliary electrode, a highly polished glassy carbon working electrode (A = 0.07 cm\(^2\)) and a Ag\(^+\)/AgCl reference electrode containing 1.0 M KCl. A modified Luggin capillary separated the working compartment from the reference compartment. The reference, auxiliary, and working compartments of the cell were filled with a solution of dry tetrahydrofuran containing 0.1 M tetrabutylammonium hexafluorophosphate (TBAPF\(_6\)) as the supporting electrolyte. In all of the experiments, the working compartment of the cell was bubbled with argon to deoxygenate the solution. Background cyclic voltammograms of the electrolyte solution were collected prior to addition of each solid sample, ferrocenium was added at the end of each set of experiments to provide an internal reference. The potentials are reported...
verses Ag+/AgCl and are not corrected for the junction potential. The cyclic voltammograms were recorded at similar concentrations (0.7 mM) and scan rates (250 mV/s).

3.3 Results and Discussion.

A series of arylaminoiminopyridyl (AIP) nickel complexes were synthesized and characterized in the solid state and in solution. Electrochemical characterization was used to determine whether these complexes were competent to reduction. These data were compared data from the analogous isopropyl substituted bisaryliminopyridyl nickel complex, which was previously crystallized. All of the complexes were synthesized using variations of previously published syntheses for other metal complexes, and isolated as orange crystalline solids in good yields.

3.3.1 Solid state structures. X-ray quality crystals for AIPMeNiCl₂, AIPiPrNiCl₂, and BIPiPrNiCl₂ were obtained by recrystallization from 1-butanol, and crystals of AIPEtNiCl₂ were grown by slow evaporation from deuterated dichloromethane. High quality structures were obtained for all four complexes (Figure 3.2). Each of the AIP complexes is neutral and five-coordinate, with three sites occupied by the neutral nitrogen donor ligands – the imine, the amine, and the pyridine – and two sites occupied by the two chloride ions. These complexes have distorted square pyramidal geometries around the metal center. Selected bond angles and τ values are reported in Table 3.2.
Figure 3.2. ORTEP diagrams of complexes. The ellipsoids are shown at the 50% probability level.
position of the aryl ring, not surprisingly increases with increasing steric bulk of the aryl
AIP
axial chloride, and increasing steric bulk of the aryl substituents results in decreasing
amine side aryl group with
methylene proton on one of the aryl ring ethyl groups, and the nickel center.
ring is situated in the open coordination site of the five
NH group retains its proton in

Table 3.2. Selected bond lengths (Å) angles (˚) for AIpMeNiCl2, AIpEtNiCl2,
AIPiPrNiCl2, and BIPiPrNiCl2. Esds are shown in parentheses.

<table>
<thead>
<tr>
<th></th>
<th>AIPMeNiCl2</th>
<th>AIPEtNiCl2</th>
<th>AIPiPrNiCl2</th>
<th>BIPiPrNiCl2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ni-Nimin1 (Ni-N1)</td>
<td>2.114(3)</td>
<td>2.127(5)</td>
<td>2.128(2)</td>
<td>2.135(2)</td>
</tr>
<tr>
<td>Ni-Nimin2 (Ni-N3)</td>
<td>--</td>
<td>--</td>
<td>--</td>
<td>2.124(2)</td>
</tr>
<tr>
<td>Ni-Npyridyl (Ni-N2)</td>
<td>1.988(3)</td>
<td>1.988(4)</td>
<td>1.996(2)</td>
<td>1.992(2)</td>
</tr>
<tr>
<td>Ni-Namine (Ni-N3)</td>
<td>2.176(3)</td>
<td>2.167(4)</td>
<td>2.246(2)</td>
<td>--</td>
</tr>
<tr>
<td>Ni-Clax (Ni-C11)</td>
<td>2.2504(9)</td>
<td>2.2546(16)</td>
<td>2.2426(8)</td>
<td>2.2381(8)</td>
</tr>
<tr>
<td>Camine-Namine (C1-N1)</td>
<td>1.291(4)</td>
<td>1.289(8)</td>
<td>1.285(3)</td>
<td>1.279(4)</td>
</tr>
<tr>
<td>Camine-Nimin1 (C7-N3)</td>
<td>--</td>
<td>--</td>
<td>--</td>
<td>1.285(4)</td>
</tr>
<tr>
<td>Camine-Nimin2 (C6-C7)</td>
<td>1.479(5)</td>
<td>1.483(9)</td>
<td>1.488(4)</td>
<td>1.486(4)</td>
</tr>
<tr>
<td>Camine-Namine (C7-N3)</td>
<td>--</td>
<td>--</td>
<td>--</td>
<td>1.494(4)</td>
</tr>
<tr>
<td>Camine-Namine (C6-C7)</td>
<td>1.532(5)</td>
<td>1.552(8)</td>
<td>1.530(4)</td>
<td>--</td>
</tr>
<tr>
<td>Camine-Namine (C7-N3)</td>
<td>1.527(4)</td>
<td>1.526(7)</td>
<td>1.529(3)</td>
<td>--</td>
</tr>
<tr>
<td>Camine-Namine (C7-N3)</td>
<td>1.348(4)</td>
<td>1.326(7)</td>
<td>1.349(3)</td>
<td>1.340(4)</td>
</tr>
<tr>
<td>Camine-Namine (C6-N2)</td>
<td>1.330(4)</td>
<td>1.324(8)</td>
<td>1.333(3)</td>
<td>1.335(4)</td>
</tr>
</tbody>
</table>

Npyridyl-Ni-Namine (N2-Ni-N1) | 78.47(11) | 78.22(18) | 78.54(9)    | 76.84(9)    |
Npyridyl-Ni-Nimin2 (N2-Ni-N3) | --         | --         | --          | 76.85(9)    |
Npyridyl-Ni-Namine (N2-Ni-N3) | 78.94(11)  | 79.22(19)  | 77.62(8)    | --          |
Namine-Namine (N3-Ni-N1) | 154.67(11) | 155.62(2)  | 154.36(8)   | --          |
Namine-Namine (N3-Ni-N1) | --         | --         | --          | 150.23(9)   |
Namine-Ni-Clax (N2-Ni-C12) | 96.18(8)   | 101.17(14) | 94.77(6)    | 93.34(7)    |
Namine-Ni-Clax (N2-Ni-C11) | 157.39(8)  | 152.77(14) | 160.96(6)   | 153.77(7)   |
Namine-Ni-Clax (N1-Ni-C12) | 100.55(8)  | 102.91(14) | 101.21(6)   | 97.44(7)    |
Namine-Ni-Clax (N1-Ni-C11) | 99.12(8)   | 98.04(14)  | 101.15(6)   | 98.42(7)    |
Namine-Ni-Clax (N3-Ni-C12) | --         | --         | --          | 97.78(7)    |
Namine-Ni-Clax (N3-Ni-C11) | --         | --         | --          | 98.99(7)    |
Namine-Ni-Clax (N3-Ni-C12) | 93.12(9)   | 90.58(15)  | 90.08(6)    | --          |
Namine-Ni-Clax (N3-Ni-C11) | 97.32(8)   | 97.69(13)  | 98.30(6)    | --          |
Clax-Ni-Clax (C12-Ni-C11) | 106.32(4)  | 105.93(6)  | 105.88(3)   | 112.89(3)   |

τ values132 | 0.05 | 0.05 | 0.10 | 0.06 |

Like the analogous AIP iron complexes characterized by Britovsek et al.,122 the
NH group retains its proton in the metal-bound form, resulting in distorted tetrahedral
geometry around the amine nitrogen. A consequence of this orientation is that the aryl
ring is situated in the open coordination site of the five-coordinate square-base pyramidal
structure. In fact, with AIPEtNiCl2, a close contact (2.36 Å) is observed between H17A, a
methylene proton on one of the aryl ring ethyl groups, and the nickel center.

A second consequence of the protonated amine nitrogen is the orientation of the
amine side aryl group with respect to the chloride ligands. The aryl group is anti to the
axial chloride, and increasing steric bulk of the aryl substituents results in decreasing
absolute torsion angles for Clax-Ni-Namine-Caryl of 141.3(2), 133.8(5), and 132.8(2) for
AIPMeNiCl2, AIPEtNiCl2, and AIPiPrNiCl2. The Ni-Namin-Caryl angle, which dictates the
position of the aryl ring, not surprisingly increases with increasing steric bulk of the aryl
substituent and is 118.2(2), 120.5(3), and 123.6(2) for \( \text{AIP}^{\text{Me}}\text{NiCl}_2 \), \( \text{AIP}^{\text{Et}}\text{NiCl}_2 \), \( \text{AIP}^{\text{iPr}}\text{NiCl}_2 \), respectively.

The bond lengths around the nickel center are fairly similar for the three AIP complexes (Table 3.2). Notably, the Ni-N_amine bonds average 0.073(7) Å longer than the Ni-N_imine bonds suggestive of weaker Ni-N bonding. Interestingly, the Ni-N_amine bond in the isopropyl substituted complex was 2.246(2) Å, whereas the corresponding bonds in the methyl and ethyl substituted complexes are nearly identical at 2.176(3) and 2.167(4) Å, respectively. This bond length is suggestive of a particularly weak bond Ni-N_amine bond in \( \text{AIP}^{\text{iPr}}\text{NiCl}_2 \).

3.3.2 Magnetic properties. The \( ^1\text{H} \) NMR spectra of these complexes had broad resonances spread over a wide frequency range, and lack of coupling, characteristic of paramagnetic complexes. Results gathered using the Evans Method\textsuperscript{130} of determining the number of unpaired electrons support the presence of two unpaired electrons for each of the complexes when compared to the calculated value of 2.83 (Table 3.3).

Table 3.3: Effective magnetic moments of nickel complexes determined by the Evans NMR Method.\textsuperscript{130}

<table>
<thead>
<tr>
<th>Complex</th>
<th>( \mu_{\text{eff}} ) (( \mu_\text{B} ))</th>
</tr>
</thead>
<tbody>
<tr>
<td>( \text{AIP}^{\text{Me}}\text{NiCl}_2 )</td>
<td>2.82</td>
</tr>
<tr>
<td>( \text{AIP}^{\text{Et}}\text{NiCl}_2 )</td>
<td>2.79</td>
</tr>
<tr>
<td>( \text{AIP}^{\text{iPr}}\text{NiCl}_2 )</td>
<td>2.50</td>
</tr>
<tr>
<td>( \text{BIP}^{\text{iPr}}\text{NiCl}_2 )</td>
<td>2.51</td>
</tr>
</tbody>
</table>
3.3.3 Solution state structure. Although broad, uncoupled, and spread over a large frequency range, the numbers of resonances observed in the paramagnetic $^1$H NMR spectra for AIP$^{Me}$NiCl$_2$, AIP$^{Et}$NiCl$_2$, and BIP$^{iPr}$NiCl$_2$ corresponded to the expected number of peaks based on the number of distinct proton environments. The peaks were assigned using integrations, COSY and EXSY correlations, and the knowledge that the meta pyridyl protons in these types of complexes are shifted far downfield.$^{133}$ However with AIP$^{iPr}$NiCl$_2$, at room temperature (24 °C), only a fraction of the predicted resonances were observed, indicating that the molecule is fluxional. At low temperature (-20 °C) 21 of 25 potential resonances were observed, consistent with all of the proton groups being distinct (Figure 3.3). This spectrum was integrated, and the integrations, and correlations observed in COSY (Figure 3.4) and EXSY (Figure 3.5) spectra were used to assign the protons in the spectrum to their atom group (Table 3.4).

![Figure 3.3: Paramagnetic $^1$H NMR spectrum of AIP$^{iPr}$NiCl$_2$ recorded at -20 °C. CH protons are represented in bold, and CH$_3$ protons are numbered in italics.](image)

The correlations in the COSY (Figure 3.4) were used to identify the pyridyl and aryl groups, as well as one of the isopropyl groups. The correlations in the EXSY (Figure 3.5) were used to identify the relationships between the isopropyl methyl groups and the meta aryl protons on a particular group.
Figure 3.4: COSY of AIP\textsuperscript{IPr}NiCl\textsubscript{2} recorded at -20 °C. CH protons are represented in bold, and CH\textsubscript{3} protons are numbered in italics.

Figure 3.5: EXSY of AIP\textsuperscript{IPr}NiCl\textsubscript{2} recorded at -10 °C. CH protons are represented in bold, and CH\textsubscript{3} protons are numbered in italics.
Table 3.4: Correlations and integrations used to assign the NMR of $\text{AIP}^{\text{iPrNiCl}_2}$.

<table>
<thead>
<tr>
<th>Peak</th>
<th>COSY</th>
<th>EXSY</th>
<th>Integration</th>
<th>Assignment</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>8</td>
<td>--</td>
<td>1</td>
<td>$meta$ pyridyl</td>
</tr>
<tr>
<td>2</td>
<td>8</td>
<td>--</td>
<td>1</td>
<td>$meta$ pyridyl</td>
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<td>3</td>
<td>19</td>
<td>12</td>
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<tr>
<td>4</td>
<td>--</td>
<td>13</td>
<td>3</td>
<td>iPr CH$_3$</td>
</tr>
<tr>
<td>5</td>
<td>7, 20</td>
<td>7</td>
<td>1</td>
<td>$meta$ aryl</td>
</tr>
<tr>
<td>6</td>
<td>--</td>
<td>--</td>
<td>3</td>
<td>imine CH$_3$</td>
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<tr>
<td>7</td>
<td>5, 20</td>
<td>5</td>
<td>1</td>
<td>$meta$ aryl</td>
</tr>
<tr>
<td>8</td>
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<td>3</td>
<td>iPr CH$_3$</td>
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<td>1</td>
<td>$meta$ aryl</td>
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<td>--</td>
<td>4</td>
<td>3</td>
<td>iPr CH</td>
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<td>9</td>
<td>11</td>
<td>3</td>
<td>iPr CH$_3$</td>
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<td>--</td>
<td>15</td>
<td>3</td>
<td>iPr CH$_3$</td>
</tr>
<tr>
<td>17</td>
<td>--</td>
<td>--</td>
<td>3</td>
<td>gem CH$_3$</td>
</tr>
<tr>
<td>18</td>
<td>--</td>
<td>--</td>
<td>3</td>
<td>gem CH$_3$</td>
</tr>
<tr>
<td>19</td>
<td>3,12</td>
<td>--</td>
<td>1</td>
<td>$para$ aryl</td>
</tr>
<tr>
<td>20</td>
<td>5,7</td>
<td>--</td>
<td>1</td>
<td>$para$ aryl</td>
</tr>
<tr>
<td>21</td>
<td>10</td>
<td>3</td>
<td>3</td>
<td>iPr CH$_3$</td>
</tr>
</tbody>
</table>

The nature of the fluxional process with $\text{AIP}^{\text{iPrNiCl}_2}$ is unknown, but there are a couple of observations that improve our understanding. First, fluxional processes are frozen at -20 °C. At this temperature, two resonances are observed for the gem dimethyl protons, four for the meta aryl protons, and eight for the isopropyl methyl groups. The observation of distinct resonances for the gem dimethyl protons indicates that the ‘top’ and ‘bottom’ of the molecule are distinct environments, which would require the amine arm to be bound to the metal, as it is in the solid state (Figure 3.6)
Figure 3.6: Proposed fluxional process for AIPiPrNiCl₂.

The observation of four meta aryl protons and eight isopropyl methyl groups suggests that at cold temperatures, Caryl-N and Caryl-Cisopropyl bonds no longer freely rotate or that rotation is slow relative to the NMR timescale. In fact, evidence for the latter explanation is inherent to the EXSY data. The rotation process on the EXSY timescale transfers magnetization between distinct methyl groups on the same isopropyl group and meta aryl sites on the same ring that are related by rotation.

The room temperature spectrum (24 °C) appears to be an intermediate state between the totally asymmetric spectrum observed at low temperature, and the symmetrized spectrum observed at high temperature (50 °C). At 50 °C, only two meta aryl resonances and two isopropyl methyl resonances are observed indicating that the Caryl-N and Caryl-Cisopropyl bonds freely rotate. The peaks corresponding the gem dimethyl protons coalesce into a single peak, suggesting that the ‘top’ and the ‘bottom’ of the molecule become identical at higher temperatures. Structurally, this suggests that the amine arm of the ligand dissociates, allowing the Cpyridyl-Camine bond to rotate, making the gem dimethyl protons equivalent.

The rate constants for exchange between the free-amine and bound-amine forms of the molecule can be calculated using line shape analysis and used to calculate the free energy barrier for the process (ΔG‡). In this system, ΔG‡ was calculated to be 12 kcal/mol, indicating that it is a facile process at room temperature. This is not surprising considering the relatively long Ni-Namine bond (2.246(2) Å), observed with AIPiPrNiCl₂ in the solid state.
3.3.4 Visible spectroscopy. Absorbance spectra of the orange nickel(II) complexes were recorded in methylene chloride, and there were not significant differences between them in the visible range. The absorbance data is summarized in Table 3.5.

Table 3.5: Molar absorbtivities for each of the nickel(II) complexes.

<table>
<thead>
<tr>
<th></th>
<th>AIP\textsuperscript{ipr}NiCl\textsubscript{2} $\lambda_{\text{max}}$ (\textepsilon\textsuperscript{M\textsuperscript{-1} cm\textsuperscript{-1}})</th>
<th>BIP\textsuperscript{ipr}NiCl\textsubscript{2} $\lambda_{\text{max}}$ (\textepsilon\textsuperscript{M\textsuperscript{-1} cm\textsuperscript{-1}})</th>
</tr>
</thead>
<tbody>
<tr>
<td>458 (150)</td>
<td>456 (150)</td>
<td>544 (50)</td>
</tr>
<tr>
<td>544 (50)</td>
<td>568 (40)</td>
<td>811 (30)</td>
</tr>
<tr>
<td>811 (30)</td>
<td>778 (10)</td>
<td>1092 (40)</td>
</tr>
<tr>
<td>1092 (40)</td>
<td>1018 (20)</td>
<td></td>
</tr>
</tbody>
</table>

3.3.5 Electrochemistry. Cyclic voltammetry of this series of complexes was used to evaluate whether the nickel(I) form was electrochemically accessible. In particular, since related complexes that employ the BIP\textsuperscript{ipr}, and $\alpha$-iminopyridine ligands preferentially undergo ligand-centered reductions, the aminoiminopyridyl nickel complexes are of interest. AIP\textsuperscript{Me}NiCl\textsubscript{2}, AIP\textsuperscript{Et}NiCl\textsubscript{2}, AIP\textsuperscript{ipr}NiCl\textsubscript{2}, and BIP\textsuperscript{ipr}NiCl\textsubscript{2} were analyzed at concentrations of $\sim$ 0.7 mM in dry tetrahydrofuran with 0.1 M tetrabutyl ammonium hexafluorophosphate as the supporting electrolyte (Figure 3.7). The steric bulk of the aryl substituents and the level of ligand saturation effect the redox properties of the complexes. Among the aminoiminopyridyl complexes, the reduction peaks become progressively more negative and the oxidation peaks become progressively more positive along the series from methyl to ethyl to isopropyl substituents (Table 3.6). When comparing AIP\textsuperscript{ipr}NiCl\textsubscript{2}, and BIP\textsuperscript{ipr}NiCl\textsubscript{2}, not surprisingly, BIP\textsuperscript{ipr}NiCl\textsubscript{2} has a less negative reduction potential than AIP\textsuperscript{ipr}NiCl\textsubscript{2}. 
Figure 3.7: Cyclic voltammograms for AIP$^{*}$NiCl$_2$, AIP$^{*}$NiCl$_2$, AIP$^{*}$NiCl$_2$, and BIP$^{*}$NiCl$_2$ in tetrahydrofuran with 0.1 M tetrabutyl ammonium hexafluorophosphate. Reference: Ag$^{+}$/AgCl, scan rate 250 mV/s.

Table 3.6: Redox potentials for complexes recorded in tetrahydrofuran with 0.1 M tetrabutyl ammonium hexafluorophosphate as supporting electrolyte. Reference: Ag$^{+}$/AgCl, scan rate 250 mV/s.

| Complex               | $E_{Ni^{II} \rightarrow Ni^{I}}$ (V) | $E_{Ni^{I} \rightarrow Ni^{II}}$ (V) | $|E_{Ni^{II} \rightarrow Ni^{I}} - E_{Ni^{I} \rightarrow Ni^{II}}|$ (V) |
|-----------------------|--------------------------------------|--------------------------------------|--------------------------------------------------|
| AIP$^{*}$MeNiCl$_2$   | -0.922                               | -0.582                               | 0.340                                            |
| AIP$^{*}$EtNiCl$_2$   | -0.966                               | -0.530                               | 0.436                                            |
| AIP$^{*}$PrNiCl$_2$   | -0.992                               | -0.484                               | 0.508                                            |
| BIP$^{*}$PrNiCl$_2$   | -0.840                               | -0.348                               | 0.492                                            |
| [AIP$^{*}$PrNiCl]BPh$_4$ | -0.526                               | -0.384                               | 0.142                                            |
| [BIP$^{*}$PrNiCl]BPh$_4$ | -0.376                               | -0.246                               | 0.130                                            |

Interestingly, for all of the complexes, the reduction and oxidation waves were significantly separated. The difference between the peaks ranged from 0.34 V (AIP$^{*}$MeNiCl$_2$) to 0.51 V (AIP$^{*}$PrNiCl$_2$). Similar behavior was previously observed with bis(pyridine-2,6-diiminemanganese.$^{135}$ In that case, the reduction and oxidation waves were separated by 0.59 V, and was hypothesized to arise from the chemical tranformation of the complex after reduction.$^{135}$
In the complexes under study in this investigation, there is a facile route to chemical transformation after reduction (Figure 3.8). We hypothesized that LNiCl$_2$ was reduced, forming LNiCl$^-$, which subsequently loses chloride, generating neutral LNiCl. Oxidation of LNiCl results in the formation of LNiCl$^+$, a species that is chemically distinct from LNiCl$_2$. In order to test this hypothesis, LNiCl$^+$ was independently prepared from LNiCl$_2$ for L = AIP$_{iPr}$ and BIP$_{iPr}$, and sodium tetraphenyl borate. Voltammograms of [AIP$_{iPr}$NiCl$^+$]BPh$_4$ and [BIP$_{iPr}$NiCl$^+$]BPh$_4$ were reversible, and the difference between the reduction and oxidation waves was 0.14 and 0.13 V, respectively. Furthermore, the redox potentials of the cations were largely coincident with the oxidation wave observed with AIP$_{iPr}$NiCl$_2$ and BIP$_{iPr}$NiCl$_2$. The cyclic voltammograms of the cationic complexes are compared to the neutral complexes in Figure 3.9.

![Figure 3.8: Mechanistic hypothesis for reduction and subsequent chemical transformation of nickel complexes.](image-url)
Figure 3.9: Cyclic voltammograms for $\text{AIP}^{\text{iPr}}\text{NiCl}_2$, $[\text{AIP}^{\text{iPr}}\text{NiCl}]\text{BPh}_4$, $\text{BIP}^{\text{iPr}}\text{NiCl}_2$, and $[\text{BIP}^{\text{iPr}}\text{NiCl}]\text{BPh}_4$ in tetrahydrofuran with 0.1 M tetrabutyl ammonium hexafluorophosphate. Reference: $\text{Ag}^+$/AgCl, scan rate 250 mV/s.

3.4 Conclusions.

A series of $\text{AIPNiCl}_2$ complexes and $\text{BIP}^{\text{iPr}}\text{NiCl}_2$ were prepared and characterized, and they have several important similarities. These orange complexes have relatively similar spectroscopic characteristics. All of the $\text{d}^8$ complexes have paramagnetic NMR spectra, and room temperature magnetic susceptibility values consistent with two unpaired electrons. Electrochemically, all four complexes have related reduction and oxidation processes that are significantly separated (by at least 0.34 V); this is thought to be related to a chemical transformation that occurs after reduction. Each of the $\text{AIPNiCl}_2$ complexes and $\text{BIP}^{\text{iPr}}\text{NiCl}_2$ contain a neutral tridentate nitrogen donor ligand and two inner-sphere chloride ligands.

Among the AIP complexes, and between the AIP complexes and $\text{BIP}^{\text{iPr}}\text{NiCl}_2$, there are some notable differences. $\text{AIP}^{\text{iPr}}\text{NiCl}_2$ distinguishes itself with a fluxional NMR spectrum at room temperature, a feature hypothesized to be imparted by the dissociation of the of the amine ligand from the metal. In support of this hypothesis, the bonds from the amine ligands to the metal center are significantly longer than the bonds from the imine ligands, and $\text{BIP}^{\text{iPr}}\text{NiCl}_2$ did not exhibit a fluxional spectrum. However, as the
methyl- and ethyl-substituted complexes did not exhibit fluxional NMR spectra either, the steric bulk of the isopropyl substituents on the aryl rings is thought to play a synergistic role with the flexibility imparted by the amine ligand. Lastly, in solution, cyclic voltammetry shows that BIP^{iPr}NiCl₂ is more readily reduced than AIP^{iPr}NiCl₂.

Acknowledgments. The authors thank Dr. Victor G. Young, Jr. of the University of Minnesota X-ray Crystallographic Facility for assistance with crystallography, Dr. Letitia Yao for help with NMR experiments and for the NMR figures, Dr. Jason England for advice about paramagnetic NMR, and Dr. Kent Mann for use of the cyclic voltammetry set-up. The National Science Foundation (CHE-0239461, CHE-0809575) supported this work.
Chapter IV. Evaluation of structurally similar nickel complexes: evidence for metal-based and ligand-based radicals

Reduced nickel complexes were synthesized using 6-[(2,6-dialkylphenylamino)-1-dimethyl]-2-[(2,6-dialkylphenylimino)methyl]pyridine (AIP\textsuperscript{ipr}) and 2,6-bis-[1-(2,6-dialkylphenylimino)ethyl]pyridine (BIP\textsuperscript{ipr}) ligands. These complexes were crystallographically characterized, and the difference in the pattern of the bond lengths in the reduced complexes compared to the nickel(II) precursors are consistent with the formation of a nickel(I) complex with AIP\textsuperscript{ipr}NiCl and a nickel(II) complex with a ligand radical with BIP\textsuperscript{ipr}NiCl.
4.1 Introduction.

Reduced nickel centers are important in a number of interesting and useful transformations including catalytic cross coupling of alkyl electrophiles,\textsuperscript{136,137} evolution of dihydrogen by protonation of nickel hydrides,\textsuperscript{138} dioxygen activation,\textsuperscript{139} as well as imparting catalytic activity to several metalloenzymes.\textsuperscript{140} Our interest in nickel(I) centers derives from our longstanding interest in reductive dehalogenation reactions using transition metal complexes.\textsuperscript{31,69,76-79,92,141-143}

Nickel-mediated dehalogenation has been observed with factor F430 (Figure 4.1), the nickel-containing prosthetic group associated with methyl-coenzyme M reductase in methanogenic organisms.\textsuperscript{22,48,144} This cofactor has been shown to dehalogenate a range of substrates in its reduced form and its dehalogenation activity has been modeled experimentally using reduced nickel octaethylisobacteriochlorin anion,\textsuperscript{115-118,145} variously saturated nickel porphyrins,\textsuperscript{145,146} and tetraazamacrocyclic nickel complexes.\textsuperscript{147,148}

![Figure 4.1: Structure of F430](image)

One challenge in understanding the reactivity of F430 and other nickel-containing complexes is the interactions between the nickel atom and the surrounding ligands in the reduced form, specifically, whether the unpaired electron resides on the metal or is delocalized onto the ligand. Reduction of nickel(II) complexes can result in the formation of nickel(I) complexes, nickel(II) complexes with a ligand radical, or a mixed species with both nickel(I) character and ligand radical character (Figure 4.2). The degree to which the metal and/or ligand is reduced can significantly affect the structure of the reduced complex, its spectroscopic features, and its reactivity.
Theoretical studies confirm experimental demonstration that F430, unlike other macrocyclic nickel centers, is able to attain a true nickel(I) oxidation state. However with nickel-containing model complexes the picture is more complicated.

Among the macrocyclic nickel complexes, there is a link between cavity size, ligand flexibility, saturation, and the oxidation state of the metal and the ligand under reducing conditions. For example, flexible and saturated tetraaza macrocyclic ligands were found to readily reorganize to stabilize the nickel(I) oxidation state, while analogous complexes with imine functionality underwent ligand reduction. Similar trends were observed with various nickel porphyrins, chlorin, porphycene, and isobacteriochlorin. Axial ligation, solvent, and ligand substituents also play a role in the oxidation state of the metal and the ligand.

Non-macrocyclic reduced nickel complexes have been stabilized by phosphine or sulfur ligand spheres and aromatic amines or imine functionality. With the aromatic amine and imine donor ligands, the complexes are thought to be stabilized by the π-accepting capability of the ligands. The low-lying π* orbitals on these ligands have led to the formation of ligand-based radicals in a number nickel complexes including bis(pyridine-2,6-diimine)nickel, α-iminopyridine, α-iminoketone, and α-diimine nickel. Structural, spectroscopic, and electronic features indicated the formation of ligand-based radicals. Crystal structure data shows that the imine bond lengths in reduced and oxidized complexes are indicative of the oxidation state of the ligand.

In order to further understand the fundamental chemistry of reduced nickel complexes, we prepared two new reduced nickel complexes employing the bis(imino)pyridine and aminooiminopyridine ligands. We hypothesized that the bis(imino)pyridine ligand with its tendency to accept an electron would form a nickel(II) species with a ligand radical under reducing conditions. Indeed, after we initiated this
work, Manuel and Rhode prepared the same complex and came to the same conclusion.\textsuperscript{169}

Nickel(II) precursor complexes: arylaminoiminopyridinenickel (AIP\textsuperscript{iPr}NiCl\textsubscript{2}) and bis-(arylmino)pyridinenickel (BIP\textsuperscript{iPr}NiCl\textsubscript{2})\textsuperscript{127,128} were synthesized and characterized.\textsuperscript{114} These were subsequently reduced using zinc amalgam, characterized, and reacted with benzyl bromide. The differences in the reactivity of the two reduced complexes, AIP\textsuperscript{iPr}NiCl and BIP\textsuperscript{iPr}NiCl, (Figure 4.3) illustrate the surprisingly large impact of a single unit of ligand unsaturation on the reactivity of the complex. These systems not only provide simple models with which to illustrate the fundamental chemistry of reduced nickel complexes, but they enhance understanding of reductive dehalogenation in the biological context that may lead to development of inexpensive and effective catalysts for pollution remediation.

Figure 4.3: Structures of A) AIP\textsuperscript{iPr}NiCl and B) BIP\textsuperscript{iPr}NiCl, the reduced nickel complexes used in this study.

4.2 Experimental Procedures.

4.2.1 General methods. All air- and moisture-sensitive manipulations were conducted in an MBraun Unilab glovebox under an atmosphere of purified nitrogen. Acetonitrile was dried with calcium hydride, hexanes were dried with sodium, and tetrahydrofuran was dried with sodium with benzophenone as an indicator. All solvents were deoxygenated prior to use. Zinc amalgam was prepared as previously described.\textsuperscript{78} Ferrocene (Aldrich) was used as received. \textsuperscript{1}H NMR spectra were recorded on Varian Inova VI-500. High-resolution mass spectrometry (HRMS) measurements were made on a Bruker BioTOF II instrument under positive ionization mode. UV-visible absorbance spectra were obtained on a Cary 14 Spectrophotometer (Olis Conversion) from 400 to 1200 nm. Electron Paramagnetic Resonance (EPR) spectra were recorded on a Bruker
ELEXSYS E-500 with an OXFORD ESR910 cryostat attached in frozen tetrahydrofuran (10 K). Frequency: 9.64 GHz, attenuation 40 dB, power 200 mW.

4.2.2 Preparation of complexes. The 2,6-bis-[1-(2,6-diisopropylphenylimino)ethyl]pyridine ligand (BIP\textsuperscript{ipr}) was prepared as previously described,\textsuperscript{129} and methylated to prepare 6-[(2,6-diisopropylphenylamino)-1-dimethyl]-2-[(2,6-diisopropylphenylimino)methyl]pyridine (AIP\textsuperscript{ipr}).\textsuperscript{119,120,122} Nickel(II) complexes were prepared with AIP\textsuperscript{ipr}, and BIP\textsuperscript{ipr}. For full characterization of AIP\textsuperscript{ipr}NiCl\textsubscript{2} and BIP\textsuperscript{ipr}NiCl\textsubscript{2} see Chapter 3.\textsuperscript{114}

AIP\textsuperscript{ipr}NiCl was prepared from AIP\textsuperscript{ipr}NiCl\textsubscript{2} that was dissolved in acetonitrile (0.093 g, 0.15 mmol). Zinc amalgam (0.3 g) was added and the mixture stirred at ambient temperature in the nitrogen filled glove box for 20 minutes. The zinc amalgam was filtered off, and the solvent was removed under reduced pressure. The purple solids were washed with hexanes. The resulting solids were extracted into THF, filtered, and the solvent was removed under reduced pressure (0.036 g, 0.060 mmol, 40\% yield). Crystals were grown by slow evaporation from acetonitrile and the structure of this complex was confirmed with X-ray crystallography. UV-visible (tetrahydrofuran) $\lambda_{\text{max}}$, nm ($\varepsilon$): 222 (16,000), 279 (7,200), 345 (sh, 2,300), 488 (1,400), 668 (500), 889 (1,500). $\mu_{\text{eff}}$ (Evans NMR method,\textsuperscript{130} $\mu_B$): calcd 1.7; found 1.8.

BIP\textsuperscript{ipr}NiCl was prepared in the same way as AIP\textsuperscript{ipr}NiCl from BIP\textsuperscript{ipr}NiCl\textsubscript{2} (0.053 g, 0.087 mmol) and zinc amalgam (0.3 g). The purple product was isolated by filtration (0.039 g, 0.068 mmol, 78\% yield). Crystals were grown from tetrahydrofuran layered with hexanes and the structure of this complex was confirmed with X-ray crystallography. UV-visible (tetrahydrofuran) $\lambda_{\text{max}}$, nm ($\varepsilon$): 239 (18,000), 325 (7,100), 436 (1,700), 475 (sh, 1,500), 510 (sh, 1,200), 670 (600), 952 (800). $\mu_{\text{eff}}$ (Evans NMR method,\textsuperscript{130} $\mu_B$): calcd 1.7; found 1.3.

4.2.3 Reactivity. Both reduced nickel complexes were reacted with benzyl bromide in $d_3$-acetonitrile. Stock solutions of benzyl bromide (8.413 mM) and ferrocene (44 mM) were prepared in $d_3$-acetonitrile. In sealable NMR tubes, the benzyl bromide stock (700 $\mu$L) and the ferrocene stock (24 $\mu$L) were combined and mixed by inversion. Initial quantitative NMR spectra were collected, ($d_1 = 20$, $at = 5$) and the benzyl peak was integrated with respect to the ferrocene peak (4.17 ppm). To these solutions were
added solutions of $\text{AIP}^{\text{iPr}}\text{NiCl}$ (8.3 mg, 0.014 mmol) and $\text{BIP}^{\text{iPr}}\text{NiCl}$ (7.0 mg, 0.012 mmol) in $d_3$-acetonitrile. The solutions were mixed by inversion, and quantitative NMR spectra were collected. The percent conversion to bibenzyl was quantified using eq. 4.1.

$$\% \text{conversion} = \frac{\text{bibenzyl}}{\text{BnBr}_i - \text{BnBr}_f} \quad \text{eq (4.1)}$$

$[\text{BnBIP}^{\text{iPr}}\text{NiCl}]_2$ was prepared via reaction of $\text{BIP}^{\text{iPr}}\text{NiCl}$ (0.039 g, 67 µmol) with benzyl bromide (1.7 g, 10 µmol) in $d_3$-acetonitrile. The orange product crystallized from the reaction solution and was isolated by filtration (6.5 mg, 4.9 µmol, 97 % yield). The structure of this complex was confirmed with X-ray crystallography. $^1$H NMR (300 MHz, CD$_2$Cl$_2$, 20°C, δ): 7.48 (m, 8H, ortho- and meta-benzyl), 7.35 (m, 2H, para-benzyl), 7.17 (t, $J = 7.2$ Hz, 4H, para-aryl), 7.02 (d, $J = 7.5$ Hz, 8H, meta-aryl), 3.81 (m, 8H, iPr CH$_2$), 2.67 (d, $J = 11.7$ Hz 4H, benzyl CH$_2$), 2.36 (m, 2H, para-pyridyl), 2.15 (s, 4H, meta-pyridyl), 1.56 (s, 12 H, imine CH$_3$), 1.59 (d, $J = 6.9$ Hz 12H, iPr CH$_3$), 1.49 (d, $J = 6.9$ Hz 12H, iPr CH$_3$), 1.28 (d, $J = 6.9$ Hz 12H, iPr CH$_3$), 1.21 (d, $J = 6.9$ Hz 12H, iPr CH$_3$). ESI-MS (m/z): [M – 2Cl + 2(CH$_3$CN)]$^{2+}$ calcd for C$_{84}$H$_{106}$N$_8$Ni$_2$ 671.3624; found 671.3618.

4.2.4 X-Ray Crystallography. In all cases the crystal was placed onto the tip of a glass capillary and mounted on either a Siemens or a Bruker SMART Platform CCD diffractometer for a data collection. The structures were solved using SHELXS-97$^{131}$ ($\text{AIP}^{\text{iPr}}\text{NiCl}_2$, $\text{BIP}^{\text{iPr}}\text{NiCl}_2$, and $\text{AIP}^{\text{iPr}}\text{NiCl}$) or SIR-97$^{170}$ ($\text{BIP}^{\text{iPr}}\text{NiCl}$) and refined using SHELXL-97.$^{131}$ The space group was determined based on systematic absences and intensity statistics. A direct-methods solution was calculated which provided most non-hydrogen atoms from the E-map. Full-matrix least squares/difference Fourier cycles were performed which located the remaining non-hydrogen atoms. All non-hydrogen atoms were refined with anisotropic displacement parameters in the $\text{AIP}^{\text{iPr}}\text{NiCl}_2$, $\text{BIP}^{\text{iPr}}\text{NiCl}_2$, and $\text{BIP}^{\text{iPr}}\text{NiCl}$ structure, and most were anisotropic in the $\text{AIP}^{\text{iPr}}\text{NiCl}$ structure. All hydrogen atoms except the amine hydrogen were placed in ideal positions and refined as riding atoms with relative isotropic displacement parameters. $\text{BIP}^{\text{iPr}}\text{NiCl}_2$ cocrystallized with 1-butanol, and the solvent is hydrogen bonded to Cl$_2$ (d(O1-H1A…Cl2 = 2.36 Å). Crystallographic data for all structures are summarized in Table 4.1.
Table 4.1: Crystallographic data.

<table>
<thead>
<tr>
<th>Compound</th>
<th>AIP^{iPr}NiCl₂</th>
<th>AIP^{iPr}NiCl</th>
<th>BIP^{iPr}NiCl₂</th>
<th>BIP^{iPr}NiCl</th>
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*This crystallographic data is also reported in Chapter 3.*

4.3 Results.

Two reduced nickel complexes, AIP^{iPr}NiCl and BIP^{iPr}NiCl, were chemically prepared by reduction of AIP^{iPr}NiCl₂ and BIP^{iPr}NiCl₂ with zinc amalgam in acetonitrile. AIP^{iPr}NiCl is new; BIP^{iPr}NiCl was recently reported. Upon reduction, the solutions changed from orange to dark purple. The reduced complexes AIP^{iPr}NiCl and BIP^{iPr}NiCl, were isolated in 40% and 78% yield, respectively. Both were stable to reduced pressure, soluble in acetonitrile, tetrahydrofuran, and dimethylformamide, and slightly soluble in toluene. They are both paramagnetic as determined by their EPR and NMR spectra, and their magnetic susceptibility was found to be 1.8 μB and 1.3 μB for AIP^{iPr}NiCl and BIP^{iPr}NiCl, respectively. These magnetic susceptibility values, determined using the
Evans NMR method, are consistent with the calculated value of 1.7 for one unpaired electron. Although these data may support the formation of a d⁹ nickel(I) center, they are also consistent with a d⁸ nickel(II) center complexed to a ligand radical. In fact, there is a significant evidence that supports ligand non-innocence with bis(imino)pyridine¹³⁵,¹⁷¹ and related ligands.⁷²,¹⁶⁴,¹⁶⁶,¹⁶⁷ A recent crystal structure of BIP⁻PrNiCl showed bond lengths consistent with ligand reduction.¹⁶⁹ As such, a more detailed study of the nature of the reduced nickel complexes was undertaken.

4.3.1 Crystallography of reduced complexes. Crystals of AIP⁻PrNiCl were obtained by slow evaporation from acetonitrile, and crystals of BIP⁻PrNiCl were grown from a solution of tetrahydrofuran layered with hexanes. Molecular structures were determined at −100 °C and −150 °C for AIP⁻PrNiCl and BIP⁻PrNiCl, respectively. Crystallographic details are shown in Table 4.1. Both complexes (Figure 4.4) were four-coordinate, square planar, and overall neutral, with three sites occupied by the neutral tridentate nitrogen donor ligand and one site occupied by a single chloride ligand.

Both the BIP⁻PrNiCl structure reported here and the structure reported by Manuel and Rhode¹⁶⁹ were monoclinic, although they were P2₁/n and P2₁/c, respectively. The ligand bond lengths in the coordination spheres for the two structures are very similar, although C₈pyridine–N₈pyridine bonds in this work were 0.012(7) Å longer than Manuel and Rhode’s. Overall the conclusions that can be drawn from both structures are the same.

Figure 4.4. ORTEP diagrams of reduced nickel complexes. The ellipsoids are shown at the 50% probability level.
Ligand radicals have been observed and characterized in a variety of complexes with imine donor ligands; changes in the imine bond lengths is indicative of ligand reduction.\textsuperscript{135,164-167,169,171} Other bonds in the coordination sphere are also affected. Specifically, in the ligand radical complexes, the imine bond lengthens, the C$_{\text{imine}}$-C$_{\text{pyridine}}$ shortens, and C$_{\text{pyridine}}$-N$_{\text{pyridine}}$ lengthens. In this study, bond lengths from the reduced complexes were compared to the bond lengths of the precursor nickel(II) complexes to determine whether the complexes were truly nickel(I) complexes, or nickel(II) complexes with a ligand radical. The bond lengths for the nickel(II) complexes, their reduced counterparts, and the difference between them are shown in Table 4.2.

Table 4.2: Selected bond lengths for BIP$_{\text{ipPr}}$NiCl$_2$, BIP$_{\text{ipPr}}$NiCl, AIP$_{\text{ipPr}}$NiCl$_2$, AIP$_{\text{ipPr}}$NiCl, and the differences between the bond lengths for the reduced and neutral complexes.

<table>
<thead>
<tr>
<th>Bond</th>
<th>BIP$_{\text{ipPr}}$NiCl$_2$</th>
<th>BIP$_{\text{ipPr}}$NiCl</th>
<th>BIP$_{\text{ipPr}}$NiCl$<em>2$ - BIP$</em>{\text{ipPr}}$NiCl$_2$</th>
<th>AIP$_{\text{ipPr}}$NiCl$_2$</th>
<th>AIP$_{\text{ipPr}}$NiCl</th>
<th>AIP$_{\text{ipPr}}$NiCl$<em>2$ - AIP$</em>{\text{ipPr}}$NiCl$_2$</th>
</tr>
</thead>
<tbody>
<tr>
<td>C$<em>{\text{imine}}$-N$</em>{\text{imine}}$ (C1-N1)</td>
<td>1.279(4)</td>
<td>1.321(3)</td>
<td>0.042(5)</td>
<td>1.287(3)</td>
<td>1.262(10)</td>
<td>-0.015(10)</td>
</tr>
<tr>
<td>C$<em>{\text{imine}}$-N$</em>{\text{imine}}$ (C7-N3)</td>
<td>1.285(4)</td>
<td>1.321(3)</td>
<td>0.036(5)</td>
<td>--</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td>C$<em>{\text{imine}}$-C$</em>{\text{pyridine}}$ (C1-C2)</td>
<td>1.486(4)</td>
<td>1.442(3)</td>
<td>-0.044(5)</td>
<td>1.487(4)</td>
<td>1.482(13)</td>
<td>-0.005(13)</td>
</tr>
<tr>
<td>C$<em>{\text{imine}}$-C$</em>{\text{pyridine}}$ (C6-C7)</td>
<td>1.494(4)</td>
<td>1.443(3)</td>
<td>-0.051(5)</td>
<td>--</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td>C$<em>{\text{pyridine}}$-N$</em>{\text{pyridine}}$ (C2-N2)</td>
<td>1.340(4)</td>
<td>1.362(3)</td>
<td>0.022(5)</td>
<td>1.350(3)</td>
<td>1.415(11)</td>
<td>0.065(11)</td>
</tr>
<tr>
<td>C$<em>{\text{pyridine}}$-N$</em>{\text{pyridine}}$ (C6-N2)</td>
<td>1.335(4)</td>
<td>1.367(3)</td>
<td>0.032(5)</td>
<td>1.332(3)</td>
<td>1.352(11)</td>
<td>0.002(11)</td>
</tr>
</tbody>
</table>

The bond lengths in BIP$_{\text{ipPr}}$NiCl are consistent with the involvement of a ligand based radical, as the imine bonds lengthened, the bonds connecting the imine carbons to the pyridyl ring carbons shortened, and the pyridyl C-N bonds lengthened. The changes in all three types of bonds is strong evidence for ligand reduction with this complex, consistent with previous results with bis(imino)pyridine iron,\textsuperscript{171} and bis(pyridine-2,6-dimine) manganese,\textsuperscript{135} Manuel and Rhode arrived at the same conclusion.\textsuperscript{169}

With AIP$_{\text{ipPr}}$NiCl the bond lengths did not follow the expected pattern for ligand reduction. The imine bond, which is expected to lengthen if the ligand is reduced, in fact, shortened by 0.015 Å. The change in the C$_{\text{imine}}$-C$_{\text{pyridine}}$ bond length was insignificant. One of the C$_{\text{pyridine}}$-N$_{\text{pyridine}}$ lengthened significantly, whereas the other did not change within error. If ligand reduction were to occur, this bond would be expected to lengthen.
(although not by as much as was observed with C2-N2). It should be noted that the AIP$^{\text{Pr}}$NiCl structure is not of particularly high quality (completeness to $2\theta = 89.1\%$), as a result there was insufficient data to model C16 anisotropically. However, the pattern in the bond lengths is clear and is not consistent with ligand reduction.

4.3.2 EPR spectroscopy. AIP$^{\text{Pr}}$NiCl and BIP$^{\text{Pr}}$NiCl were EPR active. However, the EPR spectra were not readily interpretable for the two reduced complexes, as both AIP$^{\text{Pr}}$NiCl and BIP$^{\text{Pr}}$NiCl spectra appeared to contain more than one paramagnetic component (Figure 4.5). AIP$^{\text{Pr}}$NiCl had an anisotropic signal with $g = 2.1335$ while BIP$^{\text{Pr}}$NiCl had a relatively sharp anisotropic signal with $g = 2.0049$, perhaps consistent with ligand radical character.

Figure 4.5: EPR spectra of AIP$^{\text{Pr}}$NiCl and BIP$^{\text{Pr}}$NiCl in frozen tetrahydrofuran (10 K). Frequency: 9.64 GHz, attenuation 40 dB, power 200 mW.

4.3.3 UV-visible spectroscopy. The absorbance spectrum of AIP$^{\text{Pr}}$NiCl was recorded in tetrahydrofuran at room temperature in sealed cuvettes. The spectrum consists of strong absorbances in the UV, and relatively weak bands in the visible and near infrared region (Figure 4.6A). The UV bands are likely due to the absorbance of the ligand, which absorbs in a similar region, and are assigned as the $\pi$ to $\pi^*$ transitions of the ligand. Some of the visible bands are proposed to be assigned as metal to ligand charge transfer (MLCT), d–$\pi^*$ bands based on their relative intensity, while others appear to be
d–d transitions (Figure 4.6B). The spectrum of **BIP\textsuperscript{iPr}NiCl** was recently reported in toluene with $\lambda_{\text{max}}$ at 465, 505, 730, and 820 nm.\textsuperscript{169}

![Graph of absorption spectra](image)

Figure 4.56: A) Absorption spectra of **AIP\textsuperscript{iPr}NiCl** in tetrahydrofuran (solid line) and **AIP\textsuperscript{iPr}NiCl\textsubscript{2}** (dotted line) in dichloromethane. B) Assignments of observed transitions for **AIP\textsuperscript{iPr}NiCl**. Absorbances (nm) are shown in italics with corresponding energies (cm\textsuperscript{-1}) in parentheses, the molar absorptivities (M\textsuperscript{-1}cm\textsuperscript{-1}) are shown in bold. Assignments are color coded: $\pi – \pi^*$ in blue, $d – \pi^*$ in green, and $d – d$ in red.

### 4.3.4 Reactivity

Given the structural differences between **AIP\textsuperscript{iPr}NiCl** and **BIP\textsuperscript{iPr}NiCl**, it is not surprising that they react differently. When the purple **AIP\textsuperscript{iPr}NiCl** was added to benzyl bromide the solution immediately turned orange, while reaction with **BIP\textsuperscript{iPr}NiCl** gave a green solution. The products of these reactions were analyzed with $^1$H NMR, GC/MS, and X-ray crystallography. With **AIP\textsuperscript{iPr}NiCl**, the main product is bibenzyl (68 % conversion), whereas with **BIP\textsuperscript{iPr}NiCl**, the product is a benzylated dimer ([BnBIP\textsuperscript{iPr}NiCl\textsubscript{2}]) (97 % isolated yield) (Figure 4.7). The relative amount of bibenzyl was quantified using quantitative $^1$H NMR with ferrocene ($\delta = 4.17$ ppm, singlet) as an internal standard. Ferrocene does not influence the outcome of the reaction, as the same product suite was observed with and without addition of ferrocene.
Figure 4.7: Reaction of $\text{AIP}^{\text{Pr}}\text{NiCl}$ and $\text{BIP}^{\text{Pr}}\text{NiCl}$ with benzyl bromide.

The formation of a tricyclic complex analogous to $[\text{BnBIP}^{\text{Pr}}\text{NiCl}]_2$ (Figure 4.8) has precedent, as analogous structures have been reported with aluminum\textsuperscript{121} and chromium.\textsuperscript{172} In both previous cases, dimer formation was thought to be preceded by alkylation at the para-position on the pyridine ring. The alkylated complex apparently dimerizes via an asynchronous biradical mechanism wherein the one carbon-carbon bond between the monomers is formed, followed by a spatial rearrangement and a second carbon-carbon bond forming event.\textsuperscript{121} Calculations of the energies associated with dimer formation showed that a synchronous [3+3] dimer formation reaction is symmetry forbidden.\textsuperscript{121}

In the dimer, the pyridine ring is dearomatized and the bond lengths in the coordination sphere are consistent with ligand conjugation (Table 4.3). The resulting ligand is a dianion, which, together with the two chloride ions in the coordination sphere, stabilize two nickel(II) centers.

Figure 4.8: ORTEP diagram of $[\text{BnBIP}^{\text{Pr}}\text{NiCl}]_2$. The ellipsoids are shown at the 50% probability level.
Table 4.3: Selected bond lengths for BIP<sup>iiiPr</sup>NiCl<sub>2</sub>, BIP<sup>iiiPr</sup>NiCl, [BnBIP<sup>iiiPr</sup>NiCl]<sub>2</sub>.

<table>
<thead>
<tr>
<th>Bond</th>
<th>BIP&lt;sup&gt;iiiPr&lt;/sup&gt;NiCl&lt;sub&gt;2&lt;/sub&gt;</th>
<th>BIP&lt;sup&gt;iiiPr&lt;/sup&gt;NiCl</th>
<th>[BnBIP&lt;sup&gt;iiiPr&lt;/sup&gt;NiCl]&lt;sub&gt;2&lt;/sub&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>C&lt;sub&gt;imine&lt;/sub&gt;-N&lt;sub&gt;imine&lt;/sub&gt;</td>
<td>1.279(4)</td>
<td>1.321(3)</td>
<td>1.319(3)</td>
</tr>
<tr>
<td>(C1-N1)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>C&lt;sub&gt;imine&lt;/sub&gt;-N&lt;sub&gt;imine&lt;/sub&gt;</td>
<td>1.285(4)</td>
<td>1.321(3)</td>
<td>1.316(3)</td>
</tr>
<tr>
<td>(C7-N3)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>C&lt;sub&gt;imine&lt;/sub&gt;-C&lt;sub&gt;pyridine&lt;/sub&gt;</td>
<td>1.486(4)</td>
<td>1.442(3)</td>
<td>1.423(4)</td>
</tr>
<tr>
<td>(C1-C2)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>C&lt;sub&gt;imine&lt;/sub&gt;-C&lt;sub&gt;pyridine&lt;/sub&gt;</td>
<td>1.494(4)</td>
<td>1.443(3)</td>
<td>1.426(4)</td>
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<tr>
<td>(C6-C7)</td>
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<td></td>
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</tr>
<tr>
<td>C&lt;sub&gt;pyridine&lt;/sub&gt;-N&lt;sub&gt;pyridine&lt;/sub&gt;</td>
<td>1.340(4)</td>
<td>1.362(3)</td>
<td>1.338(3)</td>
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<tr>
<td>(C2-N2)</td>
<td></td>
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</tr>
<tr>
<td>C&lt;sub&gt;pyridine&lt;/sub&gt;-N&lt;sub&gt;pyridine&lt;/sub&gt;</td>
<td>1.335(4)</td>
<td>1.367(3)</td>
<td>1.342(4)</td>
</tr>
<tr>
<td>(C6-N2)</td>
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</table>

The formation of bibenzyl in the reaction with AIP<sup>iiiPr</sup>NiCl and benzyl bromide is consistent with previous observations of coupling products in the reaction between nickel(I) centers and alkyl halides.<sup>116,117</sup>

4.4 Discussion.

The data support ligand-centered reduction with BIP<sup>iiiPr</sup>NiCl and metal centered reduction with AIP<sup>iiiPr</sup>NiCl. In general, this is consistent with a model where complexes with more saturated, flexible ligands are reduced at the metal, while complexes with less saturated, inflexible ligands are reduced at the ligand. These results highlight a subtle dividing line between nickel complexes that when reduced can attain a true nickel(I) oxidation state, and those that form nickel(II) complexes with ligand based radicals. Although nickel(I) complexes have been characterized (F430 is a notable example), they are still relatively rare, particularly those with nitrogen coordination spheres.

Crystallographic data in this study show that the reduced complexes AIP<sup>iiiPr</sup>NiCl and BIP<sup>iiiPr</sup>NiCl, have significantly different C<sub>imine</sub>-N<sub>imine</sub>, C<sub>imine</sub>-C<sub>pyridine</sub>, C<sub>pyridine</sub>-N<sub>pyridine</sub> bond lengths. Historically, nickel macrocycles including porphyrins, porphycenes, chlorins, and other tetraazamacrocycles have been used to investigate the nickel(I) oxidation state.<sup>145,147,148,152</sup> EPR and the Ni-N bond lengths were the indicators of metal or ligand-centered reduction.<sup>173</sup> More recently crystallographic data and accompanying density functional theory (DFT) calculations have provided quantitative methods for
characterizing the ways that electrons are distributed in complexes containing imine functionality. A number of bis(ligand)nickel complexes and mono(ligand)nickel complexes with ligand radical functionality have been prepared from Ni(COD)$_2$ (COD = cyclooctadiene) and neutral ligand. In this method, $\alpha$-iminopyridine, and $\alpha$-diimine complexes were prepared that had nickel(II) centers coupled to ligand radicals. Elongated imine and shortened carbon-carbon bond lengths characterize these complexes. In a recent contribution, Manuel and Rhode report a reductive pathway to BIP$_{\text{Pr}}$NiCl, using sodium amalgam as the reducing agent, structural characterization of that complex had bond lengths consistent with ligand reduction. Like Manuel and Rhode, our BIP$_{\text{Pr}}$NiCl structure had a pattern of ligand bond lengths that is consistent with the involvement of a ligand based radical. However, the AIP$_{\text{Pr}}$NiCl structure did not follow the expected trend for ligand reduction.

It is clear that the structural and electronic differences between the AIP$_{\text{Pr}}$ and BIP$_{\text{Pr}}$ ligands lead to significantly different imine bond lengths in the two reduced complexes. There is precedent for formation of nickel(I) species with imine functionality. It is noteworthy that, unlike other first row transition metal complexes, oxidation of of $\alpha$-iminopyridine, and $\alpha$-diimine ligand radical nickel(II) complexes afforded cationic nickel(I) species where one of the ligands has been oxidized to the neutral ligand, and the other has transferred its electron to the metal center. This process has been described as an oxidatively induced reduction of the central nickel atom. In our study, a reductive, rather than an oxidative, pathway to nickel(I) species was identified with AIP$_{\text{Pr}}$NiCl.

Accurate knowledge of the location of the electron in transition metal complexes can help to rationalize reactivity differences. The two reduced complexes in this study have vastly different reactivity, with AIP$_{\text{Pr}}$NiCl reacting with benzyl bromide to form bibenzyl while BIP$_{\text{Pr}}$NiCl reacts with benzyl bromide to form a benzylationated dimer (Figure 4.7). The observed products from the reaction with benzyl bromide are indicative of the differences in electronic structure. The bis(imino)pyridine ligand system has long been known to be redox non-innocent, and has been shown to accommodate up to three electrons in the conjugated imine and pyridine moieties. Manuel and Rhode also observed ligand-based reactivity with BIP$_{\text{Pr}}$NiCl in the reaction with dioxygen.
As both the metal and ligand can play an active role in reactions, including catalysis, it is particularly important to understand the role of ligand reduction. In the nickel-mediated cross coupling reaction, the distinction between metal-based and ligand-based radicals with a variety of nickel complexes highlights the fact that the electronic structure of transition metal complexes will directly influence the yield of the reaction. The electronic properties of the ligand also govern the available oxidation states of the metal. Both nickel(I) and nickel(III) oxidation states have been hypothesized to be involved in nickel-mediated dehalogenation reactions. The involvement of ligand-based radicals or metal-based radicals may be crucial to understanding the mechanisms of these reactions.

Finally, the results of this study suggest that the ability of a complex to attain a true metal-based nickel(I) oxidation state is contingent on very slight tuning of the ancillary ligands. There is a body of evidence that suggests that F430, with its relatively saturated ligand sphere, is reduced to nickel(I) in its active form. There are various reasons that have been proposed for this, including the saturation, flexibility, and exocyclic ketone functionality of the ligand. The results of the current study support the proposal that these features may indeed be necessary for a complex to attain nickel(I). Specifically, we show that less saturation, and more flexibility lead to nickel(I), whereas extended conjugation and rigidity lead to a ligand-based radical.
V. References.


