Silylene and Germylene Activation of Alkane, Ether and Amine C-H Bonds Mediated by an Aryl Halide. Observation of an Aryl Halide Kinetic Isotope Effect for the C-H Activation Reaction.

by

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A dissertation submitted in partial fulfillment
of the requirements for the degree of
Doctor of Philosophy
(Chemistry)
in The University of Michigan
2009

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Acknowledgments

There are numerous individuals who were of support during my time at the University of Michigan. Most importantly, I need to thank Professor Mark Banaszak Holl for the help, guidance encouragement and intellectual challenges he has provided as a mentor.

Some of the other individuals that I wish to highlight for their help and assistance with the experimental work that I have carried out are: Amy Gottfried, Zuzanna Cygan, Sara Scott, Jeff Bartolin, Jia Wang, Ajdin Kavara and Ahleah Rohr. Additional group members who made sure the days were enjoyable include: Bonnie Ludwig, Stacci DiMagio, Kevin Landmark, Kandarpa Cousineau, Doug Mullen, Dan McNerny, Pascale Leroueil, and numerous graduate students who had a rotation with the group.

I would also like to single out some individuals within the Chemistry Department who provided technical assistance. Chris Kojiro and Eugenio Alvarado for help with NMR. Roy Wentz for his expertise in manufacturing glassware. Al Wilson for advice and parts to maintain equipment. Jim Windak, Paul Lennon and Jeff Kampf for their time running mass spectra and X-ray structures.

I give special thanks to my family and parents for their encouragement and support. My family may have rarely seen me, but they have been an invaluable support system over the years.

Finally, I gratefully acknowledge the University of Michigan and the Department of Chemistry for the opportunity they provided me to pursue a Doctorate of Philosophy in Chemistry. I am indebted to the National Science Foundation for the grant Mark Banaszak Holl received to support a large portion of this work.

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1.1- What is Activation?

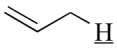
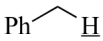
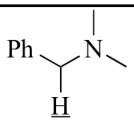
In sciences, the term activate describes a conversion from a lower energy and less reactive state to a higher energy and more reactive state. In the discipline of chemistry, activation has a similar meaning as in other science related fields. Two stereotypical reasons for activating a molecule are for spectroscopy or chemical reactivity. When performing spectroscopy, excitation is commonly used for achieving a difference in population of various energy states. Traditionally, more reactive forms of a compound are achieved through functional group and protecting group manipulations. The development of synthetic methods not requiring protecting group and functional group manipulations are of great interest in industrial and academic groups for increasing productivity, efficiency and providing different methods of carrying out desired chemical transformations.

1.2- Activation of C-H Bonds

The occurrence of C-H bonds is ubiquitous in organic molecules, biological compounds and pharmaceuticals. Though C-H bonds are ubiquitous, the C-H bond might not be the weakest or most reactive bond within a molecule. The strength of C-H bonds can be viewed through two different bond strength comparisons. The relative bond strength corresponding to heterolytic bond cleavage can be estimated with pKa tables. With a heterolytic bond cleavage, one atom will end up with all of the electrons from the

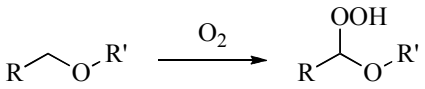
broken bond, while the other atom of the bond ends up with no electrons from the broken bond. A second way in which a chemical bond can be broken is through homolytic bond cleavage. A homolytic bond cleavage will result in the electrons of a bond being divided equally between the two atoms of the cleaved bond. In **Table 1.1** the homolytic bond strengths for select C-H bonds of hydrocarbons,[1] ethers[2, 3] and amines[4-6] are listed. Simplified logic leads to the presumption that weaker chemical bonds should be the easiest bonds to activate. Under the correct conditions, even molecules and bonds perceived as inert react. An example of a molecule typically viewed as inert, but that does react under the appropriate conditions is the noble gas xenon. Combining xenon gas and fluorine gas in a sealed nickel container and subsequently increasing temperature and pressure results in formation of xenon fluorides. Another example of a molecule typically thought of as inert, but the molecule does react, is nitrogen gas. Though nitrogen is thought of as an inert gas, storing or heating lithium metal under a nitrogen atmosphere is a potentially combustible combination and extremely dangerous. The reaction of lithium metal with nitrogen gas is why lithium metal should be stored in an argon environment. Finding reaction conditions capable of selectively reacting a relatively inert C-H bond presents a challenge that various groups are researching.

Table 1.1- Homolytic Bond Dissociation Energies

Bond	Bond Strength (kcal/mol)	Reference
CH_3—H	105.1	1
	98.2	1
	95.1	1
	93.2	1
Cyclohexane C-H Bond	95.5	1
Cyclopentane C-H Bond	94.5	1
	86.3	1
	88	1
Ph—H	110.9	1
Et_2O	88.8	2
1,4-dioxane	96.0	3
Me_2N^tBu	90.0	5
Et_3N	90.7	5
Pr_3N	90	4
$PhNMe_2$	91.7	5
	84.8	6

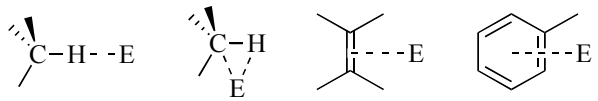
A reaction that breaks C-H bonds, the combustion of gasoline and other hydrocarbon fuel sources, occurs on a nonstop basis worldwide. The prolonged heating of hydrocarbons in the presence of oxygen, without combustion, will oxidize C-H bonds to C-O bonds. The diradical ground state of O_2 is a fairly reactive ground state configuration. Typically, the O_2 oxidation of C-H to C-O bonds favors the oxidation of the weakest C-H bond, **Figure 1.1**, but the oxidation can produce a variety of isomeric products. One of the first challenges of C-H activation in synthetic chemistry is finding reaction conditions capable of selectively reacting the relatively inert C-H bond. Next, the challenge becomes controlling the extent to which the C-H bonds react. As the combustion of hydrocarbons demonstrates, controlling the number of C-H bonds activated and the extent of activation presents a challenge.

Figure 1.1– Oxidation of Ethers by Molecular Oxygen



Chemists have gone about controlling the extent of C-H bond activation by using reagents capable of interacting with hydrocarbons in a way that weakens the C-H bonds present within the molecule, while avoiding the conversion of substrates into combustion products. Representative examples of some intramolecular interactions between hydrocarbons and a reagent, represented by E, are depicted in **Figure 1.2**. The chemical literature of the past decade contains various examples of C-H activation, along with numerous review articles on the topic of C-H activation.[7-24] **Figure 1.2.A** represents an end-on interaction of a reactive species with a C-H bond. The interaction depicted with **Figure 1.2.A** could be described as a bimolecular nucleophilic or electrophilic C-H

Figure 1.2- Representative Interactions Capable of Weakening C-H Bonds



1.2.A **1.2.B** **1.2.C** **1.2.D**

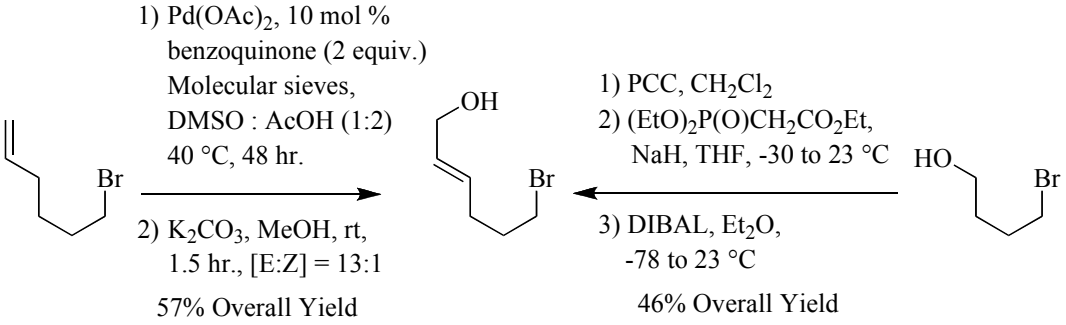
activation reaction. **Figure 1.2.B** would represent a σ-bond or a C-H insertion type activation of a C-H bond. The interaction depicted with **Figure 1.2.B** indicates a possible manner for how an active species might directly interact with a C-H σ-bond. **Figure 1.2.C** depicts an interaction between an alkene π bond and E. The π–E complex could be such that the allylic C-H bond is weakened and will react. A π–E interaction such as **Figure 1.2.C** could lead directly to formation of a π-allyl complex through loss of an allylic hydrogen atom. **Figure 1.2.D** depicts an interaction between an aryl group and E. Formation of the aryl-E complex could result in the formation of a formal carbon-E bond, and subsequently form products similar to electrophilic and nucleophilic aromatic substitution reactions. The C-H bond interactions depicted in **Figure 1.2** represent some of the methods that have been used for the activation of C-H bonds over the last decade.

1.3- Why the Interest in Activation of C-H Bonds?

Conversion of a readily available, and less expensive, starting material to a more valuable, complex and/or desired product can be viewed as the reason for all synthetic transformations. A quick glance of the literature demonstrates various uses for C-H bond activation and various reactions of C-H bonds in alkyl, alkenyl and aryl containing compounds. The possibility of eliminating functional group or protecting group manipulations, and finding more efficient synthetic schemes, are simplified explanations for the great interest in C-H activation methods by research groups in industry and

academia.[25] Minimizing the number of steps needed for obtaining a specific intermediate can improve yields, reduce the overall amount of waste generated and decrease the amount of time required to obtain desired intermediates and products.[26] Typically, multistep reactions encounter a concern regarding compatibility of a functional group(s) present in the starting material with a well established method that would achieve a desired transformation. Incompatibility of functional groups with proposed reaction conditions has brought about the use of protecting groups. Volumes of chemical literature are devoted to functional group compatibility and functional group conversions.[27-33] The use of protecting groups and functional group manipulations introduces additional steps to a synthetic scheme. For example, in **Scheme 1.1** of a classical functional group manipulation route is compared to a C-H activation route for

Scheme 1.1- Competitive Routes for Synthesis of the Same Intermediate

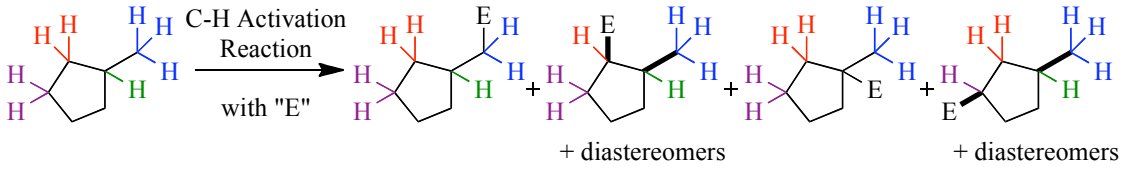


the construction of an intermediate used in the synthesis of (−)-Swainsonine.[34] The ability to avoid protecting groups and functional group manipulations should increase yields of desired intermediates and products, while increasing the efficiency of the synthetic chemist. New synthetic options afforded by development of new methodologies, including C-H activation methods, invariably leads to new approaches of synthesizing compounds and development of new problem methods for synthesizing

compounds. The development of synthetic methodologies that selectively activate a C-H bond provides more options to the synthetic chemist when considering a synthetic route.

One challenge with C-H activation has been the relative strength of C-H bonds when compared with other functional groups. When comparing heterolytic bond strengths, C-H bonds are typically among the strongest bonds present in functionalized molecules. A second challenge arises due to the ubiquitous nature of the C-H bond. With numerous methine, methylene and methyl C-H bonds present within a molecule, selectively activating one methylene over another methylene is a challenge. C-H activation of a substrate as simple as methylcyclopentane demonstrates the challenge of C-H bond selectivity, see **Figure 1.3**. Methylcyclopentane contains three different types of C-H bonds (1°, 2° and 3°) that could be activated to form six regioisomeric or steroisomeric products. A vast majority of the selectively C-H bond activation reactions

Figure 1.3- Isomeric Products from C-H Activation of Methylcyclopentane



utilize some type of directing group. Directing groups have varied from functional groups capable of directing reactivity to a proximal C-H bond, activation of the weakest C-H bond or reversible C-H activation that eventually forms the thermodynamically favored C-H activation product. The ability to directly activate C-H bonds has resulted in more rapid, higher yielding and less waste intensive methods of accessing desirable intermediates and products from cheap, readily available, chemical feedstocks. A long term goal of C-H activation would be the ability to selectively activate any compound

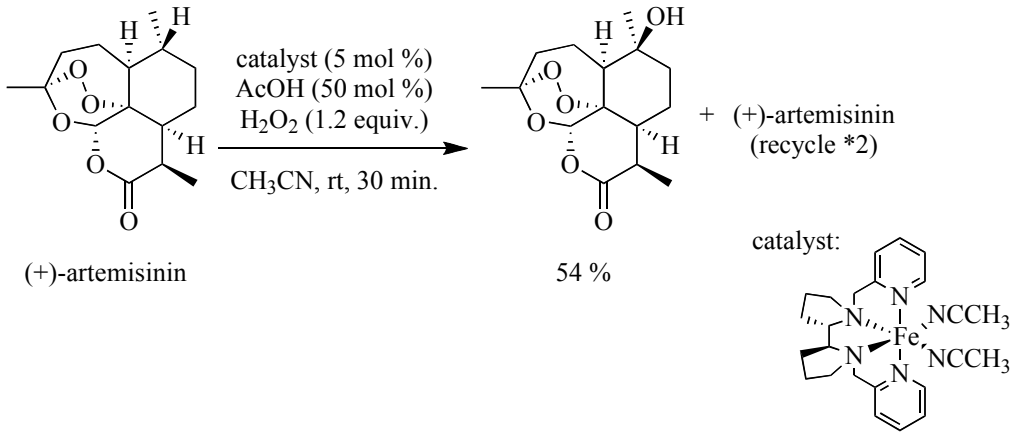
containing a C-H bond at a predetermined position; i.e. the C-H bond could be viewed as another easily manipulated functional group.

1.4- Types of C-H Activation Methods for Breaking C-H Bonds

Numerous methods can be found in the literature for the homolytic and heterolytic cleavage of C-H bonds. Within the last decade various reports and reviews on transition metal catalyzed methods for breaking C-H bonds have been published.[16, 35-50] Many transition metal catalyzed reactions that reversibly activate a C-H bond and formally form a carbon-transition metal bond eventually form the thermodynamically favored C-M product as the major product. A quick screening of the chemical literature also demonstrates intramolecular and intermolecular C-H activation reactions are possible with transition metal catalyzed reactions.

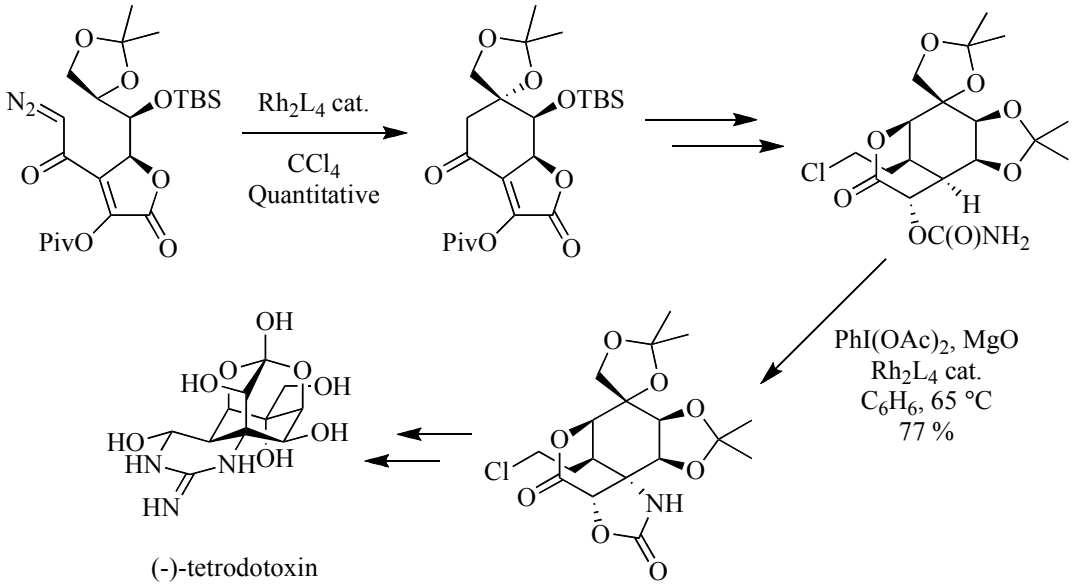
M. C. White et al. have developed intermolecular C-H activation methods that oxidize C-H bonds to the corresponding C-O and C-N bonds.[34, 50-52] One method developed by White et al. is a palladium catalyzed allylic oxidation. These palladium catalyzed allylic oxidations have resulted in shorter linear sequences and higher yields of intermediates used for the synthesis of various natural products. A second C-H activation method also developed by White et al. is a Fe(II) catalyzed oxidation of a C-H bond to a C-O bond using H_2O_2 as the terminal oxidant. The Fe(II)/H_2O_2 method is selective for weak C-H bonds, and converts the weak C-H bond to a C-O bond. White et al. have used the Fe(II)/H_2O_2 method for the one step conversion of (+)-artemisinin to (+)-10β-hydroxyartemisinin, **Scheme 1.2**.[50]

Scheme 1.2- Conversion of (+)-Artemisinin to (+)-10β-Hydroxyartemisinin



H. M. L. Davies et al. and J. Du Bois et al. have published extensively on intramolecular and intermolecular C-H activations mediated by rhodium-carbenes or rhodium-nitrenes inserting into C-H bonds. H. M. L. Davies et al. have used the rhodium catalyzed C-H activation method for synthesizing libraries of pharmaceutical derivatives.[53, 54] J. Du Bois et al. have used rhodium catalyzed C-H activation reactions in the synthesis of highly functionalized natural products. Examples of the natural products synthesized by J. Du Bois et al. are the neurotoxins (–)-tetrodotoxin and (+)-saxitoxin, **Scheme 1.3**.[55, 56]

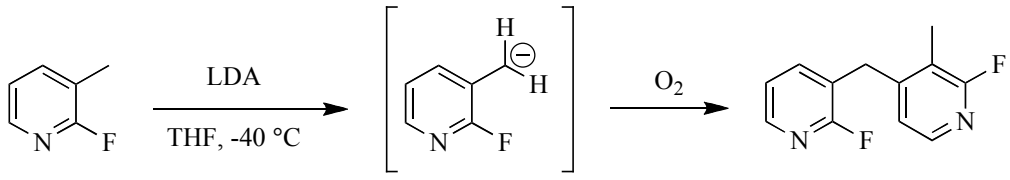
Scheme 1.3- Synthesis of (–)-Tetrodotoxin



1.4.1- Use of Strong Bases for Deprotonation Reactions

The presence of appropriate functional groups can make deprotonation a facile and high yielding reaction capable of rapidly forming complex compounds. Bases capable of deprotonating hydrocarbon C-H bonds are typically incompatible with numerous functional groups. Synthetic methods using deprotonation of alkyl chain C-H bonds are limited due to the functional group intolerance of the strong bases required to achieve the deprotonation. The use of strong bases for the formation of carbanions is not described as a C-H activation, rather the label of an acid-base reaction is the traditional way of describing this method of breaking a C-H bond. For an example of a deprotonation reaction that forms a reactive carbanion see **Scheme 1.4**.[57] For the purposes of consistency with established terminology, and traditions, the use of strong bases for breaking C-H bonds will be referred to as an acid-base reaction.

Scheme 1.4- Use of Acid-Base Reaction for Reacting a C-H Bond



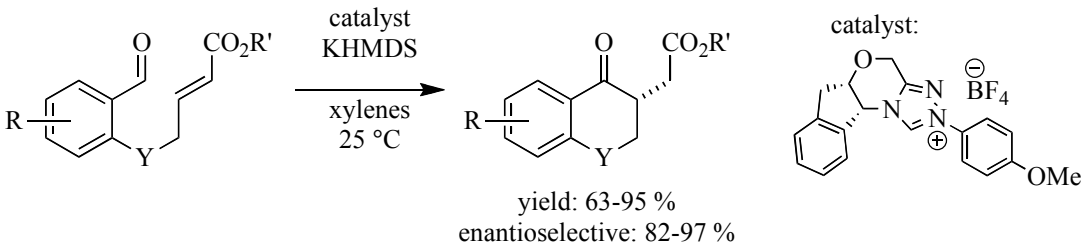
1.5- Carbenes, Silylenes, Germylenes and Stannylenes

The fourteenth column of the periodic table contains the elements carbon, silicon, germanium, tin and lead. One of the most typical bonding patterns for these atoms, when lacking a formal charge, involves four covalent bonds to the central atom. The four covalent bonds result in a filled valence shell configuration. A less common configuration with no formal charge, involves two covalent bonds and two electrons at the central atom. These divalent neutral forms of the fourteenth column elements are referred to as carbenes, silylenes, germylenes, stannylenes and plumbylenes. There are two possible electronic configurations for carbenes and the heavier atom analogs. One possible electronic configuration is the two electrons having opposite spins, known as the singlet state. A second possible electronic configuration is the two electrons having the same spins, know as a triplet state. The triplet ground state can be thought of as a diradical, just like the oxygen we breathe.

Within the last decade numerous uses of carbenes have been demonstrated in the literature, including the specialized publication *Advances in Carbene Chemistry*. Carbenes are most frequently used as ligands that replace the phosphine ligands on transition metal compounds and in transition metal catalyzed reactions.[58-60] A commonly cited example for demonstrating the usefulness of carbenes involves the replacement of tricyclohexylphosphine with a nitrogen heterocyclic carbene (NHC) for making Grubb's

second generation type olefin metathesis catalysts.[61-63] NHC's with varying amounts of steric bulk, slightly varying electronic properties and asymmetric variations of all types have been readily synthesized and are found throughout the literature. Beyond the use of carbenes as ligands in transition metal catalyzed reactions, carbenes can function as the actual catalysts that turnover in a catalytic cycle. The Stetter reaction is an example of a reaction in which a carbene functions as the actual catalyst, see **Scheme 1.5**.[64] The use of carbenes is well documented throughout the literature, yet the use of silylenes, germylenes and stannylenes as ligands with transition metals or as catalysts is not as common.

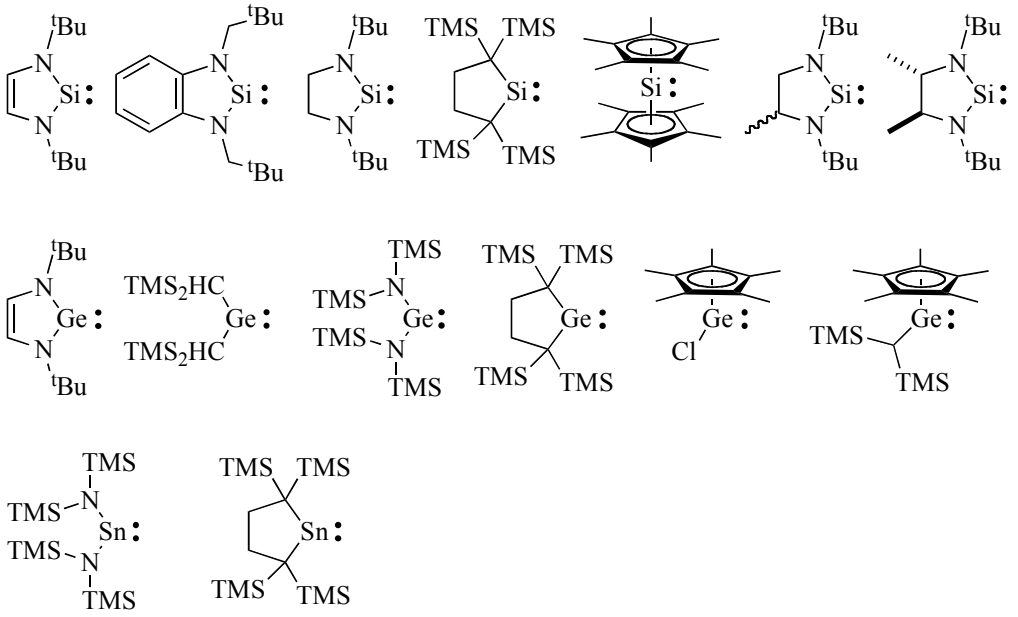
Scheme 1.5- Asymmetric Stetter Reaction



1.6- Why use Heavy Atom Analogues of Carbenes?

Carbene analogues can be synthesized using the fourteenth column heavier elements silicon, germanium, tin and lead. Due to differences in size and electronegativity, the reactivity and applications of silylenes, germylenes and stannylenes are expected to vary slightly from analogous carbenes. Numerous attempts at synthesizing heavier atom analogues of carbenes have demonstrated steric hindrance of the divalent silicon, germanium or tin atom is required to synthesize and isolate the heavier atom carbene analogs.[65-70] Some select examples of these heavier atom carbene analogs are shown below, **Figure 1.4**.[65, 68, 70-75] Differences in electronegativity and size

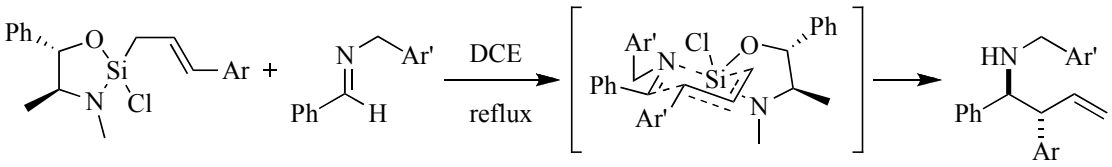
Figure 1.4- Various Silylenes, Germylenes and Stannylenes



of silicon, germanium and tin does not guarantee similar Lewis acidity and basicity between the compounds. As previously stated, one notable difference between carbenes and the heavier atom analogs are the increased steric demands about the divalent atom. Without the sterically bulky environment about the divalent atom, dimerization is very commonly observed.

Banaszak Holl et al. have demonstrated that germylenes and stannylenes are capable of directly forming C-Ge and C-Sn bonds from C-H bonds. Combining the new method of forming C-Ge or C-Sn bonds with the known methods of cleaving C-Ge, or C-Sn, and potentially C-Si bonds presents a new means of constructing synthetically useful compounds. Some of the methods for reacting C-Si bonds are Fleming-Tamoa Oxidation, Hiyama type cross-coupling and alkylation reactions like that of **Scheme 1.6**.[76] The number of examples demonstrating the reactivity of a C-Ge bond using cross-coupling and alkylation reactions are few, due to the rare use of germanium containing

Scheme 1.6- Allylation of an Imine via a Closed Transition State



54 - 68 % yield
94 - 99 % ee

compounds.[77, 78] Compounds containing C-Sn bonds are frequently used with Stille type cross-couplings and allylation reactions, but there is a major concern with using organotin containing compounds. Due to toxicity concerns with organotin compounds, the large-scale use of tin containing compounds is typically avoided in the synthesis of pharmaceuticals and biologically interesting compounds. The toxicity concerns over organotin containing compounds has provided a driving force for developing synthetic methodologies capable of reacting the C-Si and C-Ge bonds.

1.7- C-H Activation and Formation of Carbon-Main Group Element Bonds

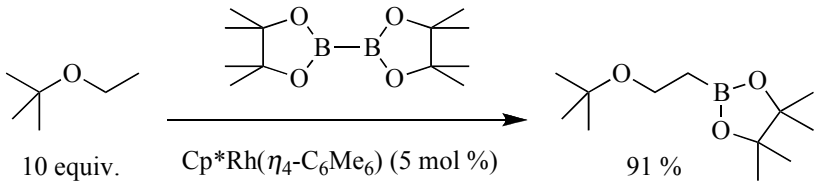
Academic and industrial groups are interested in developing new synthetic methods that directly convert C-H bonds to more reactive C-E bonds. The majority of research on methods for activating C-H bonds has focused on using transition metal catalyzed reactions. In comparison to the transition metal catalyzed methods, less research efforts have been published on the activation of C-H bonds using main group catalysts or main group containing compounds.

Examples of main group containing compounds, or main group catalysts, used for the activation of C-H bonds can be found in the literature. Crabtree et al. have used a mercury photosensitized method for the activation of C-H bonds and a subsequent C-C bond formation via radical coupling.[79] P. R. Schreiner et al. have developed a biphasic

method for converting C-H bonds to carbon-halogen bonds. The mechanism proposed for the reaction was that of a single electron transfer (SET) process. The halogenation reaction developed by P. R. Schreiner could be viewed as a controlled version of the $Br_2/h\nu$ radical halogenation of organic compounds.[80]

A more synthetically useful C-H activation reaction that forms a bond between carbon and a main group element is the transition metal catalyzed C-H activation and C-B bond forming reaction from Hartwig et al. and Smith et. al., see **Figure 1.5**.[15, 81, 82] The synthetic utility of C-B bond containing compounds in Suzuki type cross-coupling reactions is one reason why the C-H activation and C-B bond forming reactions are synthetically useful.[83]

Figure 1.5- C-H Activation Reaction forming a C-B Bond



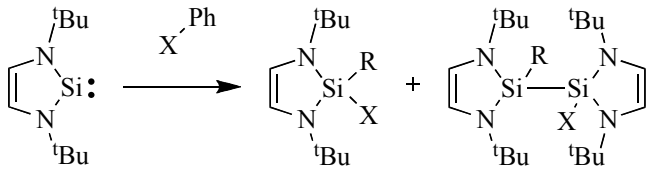
1.8- Silylene, Germylene, and Stannylene Reactivity with C-X Bonds

The reaction of silylenes, germylenes, and stannylenes with halogenated molecules has been documented through out the literature.[84-86] These carbene analogs will readily undergo an oxidative addition (OA) of carbon-halogen (C-X) bonds. Studies on the mechanism of C-X bond OA to Me_2Ge produced two different mechanisms that are dependent on the hybridization at the carbon of a C-X bond. A concerted insertion type mechanism has been proposed for the OA of C(sp)-X and C(sp^2)-X type bonds to

Me_2Ge.[87, 88] While the OA of $C(sp^3)$-X type bonds has been proposed to occur via a SET type mechanism.[89]

West et al. have also proposed a SET type mechanism for the OA of C-X bonds to silylenes. Careful analysis of all products from the OA reaction of $CHCl_3$ with a silylene demonstrated that Cl_2HC-$CHCl_2$, the coupled product of two Cl_2HC radicals, had been formed.[86] Observation of the C-C radical coupled products has been interpreted as evidence supporting a SET mechanism. West et al. have also observed that the OA of various other halocarbons, in hexanes, produced two distinct OA products, see **Figure 1.6**. Formation of the second OA product can be described as the OA of C-X across the Si-Si bond. Published work would indicate West et al. support a SET type pathway to form the OA products from reactions of silylenes with C-X.

Figure 1.6- OA of Halocarbons to a Silylene



X = Br	67 %	33 %
X = I	>98 %	-

Lappert et al. were one of the first groups to publish on the mechanism of OA of C-X's to a stannylene and germylene. Lappert et al. studied the mechanism of OA with kinetics and through the measurement of any electron paramagnetic resonances (EPR).[65, 66, 84, 90] Lappert et al. found the reaction demonstrated a first order dependence on the stannylene according to their interpretation of kinetic data. Additionally, the EPR data was consistent with a SET type mechanism as EPR active intermediates were observed. Another interesting result from Lappert et al. comes from reactions carried out with Ph-

Br in the presence of THF solvent. There are only two products mentioned for this reaction, one was the OA of Ph-Br to the stannylene and the second was formation of a R_2SnBr_2 type compound. The presence or absence of trace Br_2 in the Ph-Br was not noted in the published results. Commenting on the absence of trace Br_2 would aid in understanding if a SET type mechanism involved the formation of solvated or un-solvated radical intermediates.

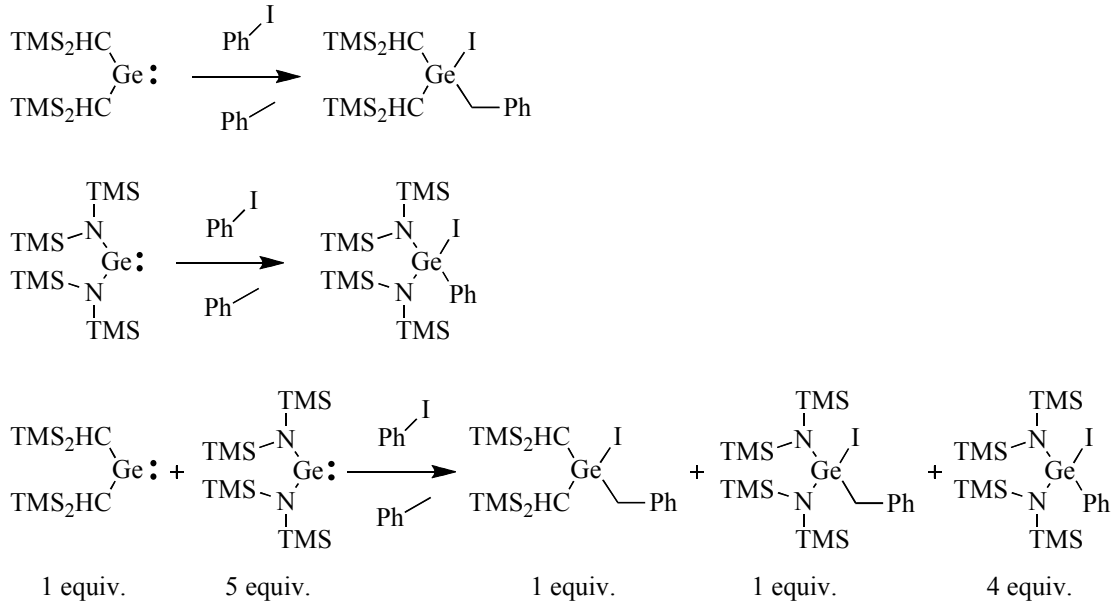
1.9- Germylenes and Stannylenes in the Activation of C-H Bonds

Banaszak Holl et al. have used germylenes and stannylenes, in combination with an aryl halide, for the activation of alkane and ether C-H bonds. The reaction reported by Banaszak Holl et al. tolerated temperatures below 0 °C, absence of light, various aryl halides, different alkane substrates, various ether substrates and the use of different germylenes and stannylenes. These C-H activations demonstrated a preference for activating the weakest C-H bond of the alkane or ether substrate. The alkane substrates demonstrated a selectivity consistent with a cationic or radical forming reaction, meaning the observed C-H bonds selectivity was 3° >2° >1° C-H. For ether substrates, the C-H bond α to the oxygen atom is selectively activated over all other C-H bonds.

Banaszak Holl et al. have used a stannylene that does not react directly with π-bonds to demonstrate that allylic, benzylic and propargylic C-H activations are also possible. Alkene substrates containing C=C bonds that are not sterically encumbered, like a terminal π bond, add a Ph and Sn-I fragment across the C=C bond with the fragments adding anti to each other. The anti addition across the C=C bond would be consistent with a SET type mechanism.

The aryl halide component of the C-H activation reaction reported by Banaszak Holl et al. demonstrated a general trend for reaction rates of Ph-I >Ph-Br >>Ph-Cl. The relatively slow reacting germylene/Ph-Br combination was used for collecting a series of kinetic traces; the kinetic data was consistent with a second order dependence on the germylene. For these C-H activations, insights on the mechanism were gained through the use of competition and labeling experiments. Labeling experiments with deuterated substrates had a primary kinetic isotope effect (KIE) similar to the hydrogen abstraction KIE of phenyl-diazo-triphenylmethane (PAT), an *in situ* source of a phenyl radical. The KIE for the hydrogen abstraction and competition experiments between germylenes and PAT were similar, but statistically different. Banaszak Holl et al. noted that although similar reactivity trends are observed, a difference in the reactivity of germylenes was observed. The most notable difference in the reactivity of germylenes was observed with the attempted benzylic C-H activation of toluene. The germylene $(TMS_2CH)_2Ge$ activates the benzylic C-H bond of toluene. Yet the germylene $(TMS_2N)_2Ge$ does not activate the benzylic bond of toluene and results exclusively in OA. Interestingly a mixture of $(TMS_2CH)_2Ge$ and $(TMS_2N)_2Ge$ was observed to form the benzylic C-H activation product derived from each germylene, see **Scheme 1.7**. These mixed reactivity results have been interpreted as further support of the second order dependence of the germylenes or stannylenes.[91]

Scheme 1.7- Empirical Evidence Supporting the Second Order in Germylene



The remaining chapters contain a report on efforts aimed at expanding germylene/Ar-X and stannylene/Ar-X type C-H activations to include the use of silylene/Ph-I for activating C-H bonds. Additionally, the use of deuterium labeled compounds is described along with the mechanistic insight gained from measured isotope effects.

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Chapter 2- C-H Activation of Alkanes and Ethers with Silylene/Ph-I

2.1- Background on Silylenes

2.1.1- Activation of Ethers and Alkanes using Germylenes/Ar-X as a Mixed Reagent

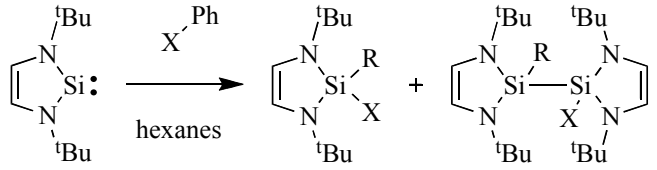
As mentioned in Chapter 1, Banaszak Holl et al. have used germylene/Ph-I for the activation of C-H bonds in small organic molecules. A quick glance over published results reveals ethers functioned as substrates that gave higher yields of C-H activation products when compared to hydrocarbons.[1] The work demonstrated that use of motor driven syringe techniques increased the ratio of C-H activation products to oxidative addition (OA). The original proposed purpose of this work was to synthesize a silylene, and then observe if the C-H activation reactions reported by Banaszak Holl et al. with germylenes/Ph-I could be repeated using silylene/Ph-I. Additionally, if the C-H activation reactions could be observed with silylene/Ph-I, will selectivity be similar to the germylene/Ph-I alkane and ether C-H activation reactions.

2.1.2- Reaction Chemistry of Silylenes

The reactive nature of silylenes has been demonstrated with various reactions throughout the chemical literature. The research groups of West and Denk et al. and Kira et al. have reported on the reactivity of silylenes with various small molecules. West and Denk et al. have looked at the reactivity of $[(CH)_2{}^tBu_2N_2]Si$ (**1**) with transition metals, azides, dioxygen, sulfur, selenium, alcohols and radicals.[2-4] Also, West and Denk et al. discovered the oxidative addition of halocarbons, $C(sp^2)$-X and $C(sp^3)$-X type bonds, to **1**

would form two different oxidative addition products, **Scheme 2.1**.[5] The oxidative addition of halocarbons to **1** has been examined with computational models in attempts to gain a better understanding of the mechanism of oxidative addition.[6, 7] The theoretical investigation by McKee et al. was consistent with a single electron transfer type mechanism for explaining how the oxidative addition reaction can occur.[7]

Scheme 2.1- OA of Halocarbons to Silylene **1**

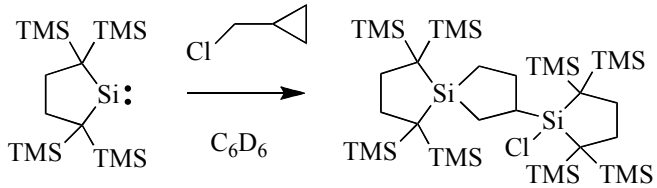


1

X = Br 67 % 33 %
X = I >98 % -

Kira et al. have also looked at the reactivity of an alkyl silylene (**32**) that exhibits greater steric hinderance around the silicon atom than **1**. Some of the observed reactivity of **32** that Kira et al. have reported includes reactions with transitions metals, alcohols, radicals, elemental sulfur, alkenes, isocyanides and halocarbons.[8, 9] Kira et al. have also noted the reactivity of **32** with halocarbons, which resembles the dimer like products observed from reactions of **1** with halocarbons, **see Scheme 2.2**. Su et al. have carried out a theoretical analysis on the OA of **32** to halocarbons. The theoretical analysis was

Scheme 2.2- OA of a Halocarbon to **32**



70 %

interpreted as showing that a single electron transfer process was a feasible mechanism for the OA of halocarbons to **32**.[6, 10]

The work of West and Denk et al. and Kira et al. contained promising results hinting that the desired C-H activation might occur with the proper conditions. As depicted in **Scheme 2.1** and **Scheme 2.2**, a second order dependence of the silylene for reactions with halocarbons is supported empirically. Additionally, theoretical studies supported the feasibility of a single electron transfer mechanism for the reaction of silylenes with halogen containing substrates.

After successfully synthesizing the desired silylene, numerous C-H activation reactions have been carried out using various substrates. The first substrates screened are the simple hydrocarbon and ether substrates previously reported by Banaszak Holl et al.[1] The remainder of the chapter is based on the recently published C-H activation of ethers and hydrocarbons using silylene/Ph-I.[11]

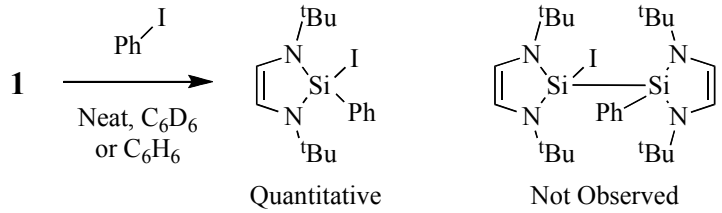
2.2- C-H Activation of Small Molecules

2.2.1- Silylene/Ph-I C-H Activation of Ethers

Silylene/Ph-I was used for the successful C-H activation of the C-H bond α to the oxygen atom of Et_2O. In addition to the desired C-H activation occurring, the formation of the oxidative addition (OA) adduct derived from addition of Ph-I to **1** was also observed. Upon combining **1**, Et_2O and then Ph-I in a reaction vessel, in the order listed, the instantaneous change from colorless to a golden-yellowish color was observed. After removal of volatiles, a ^1H NMR spectrum of the crude product mixture supported the formation of two products, the hoped for C-H activation of Et_2O and the OA product. The ratio of the C-H activation and OA products was ~1:1 when adding reagents in the

order listed above. Independently mixing together **1** with Ph-I, neat or in C_6D_6, provided reference ^1H and ^{13}C NMR spectra of the OA product. The ^1H NMR of the OA product revealed a shift of the silylene backbone vinyl hydrogen peak from 6.75 ppm for **1** to 5.91 ppm for the OA product, **2**, see **Figure 2.1**. Characterization of the OA product was consistent with the absence of any dimer like OA product formation. The ^1H NMR spectrum of **2** contains two unique features that have provided a method for quickly diagnosing for the presence of the OA product. The first feature is a broad peak at 8.05 ppm, the *ortho* aromatic protons of the OA product. The broad peak at 8.05 ppm was expected, as a similar peak has been reported for the oxidative addition of Ph-I to germylenes and stannylenes.[1, 12, 13] The second feature was the singlet at 5.91 ppm, corresponding to the silylene backbone alkenyl protons.

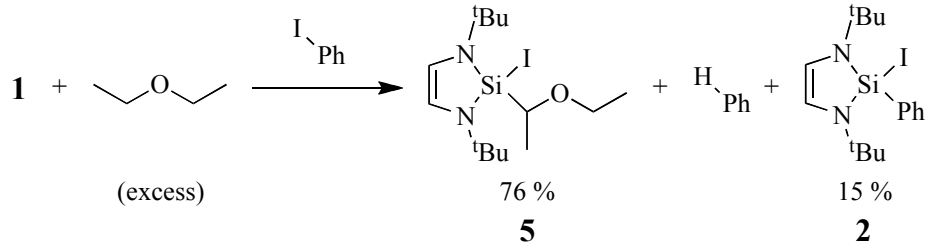
Figure 2.1- Oxidative Addition of Ph-I to **1**



2

The previous work of Banaszak Holl et al. indicates the sequential addition of **1**, excess Et_2O and finally Ph-I was not likely to be the ideal reaction conditions for maximizing the amount of C-H activation product. Typical reaction conditions of ~20 mg of silylene, ~10 g of Et_2O and then ~14 mg Ph-I consistently resulted in a ~1:1 formation of C-H activation product and OA product. When using a motor driven syringe with an addition rate of 3.17 mL/hr., the addition of a 0.0515 M silylene solution

Figure 2.2- C-H Activation of Et_2O with **1**/Ph-I

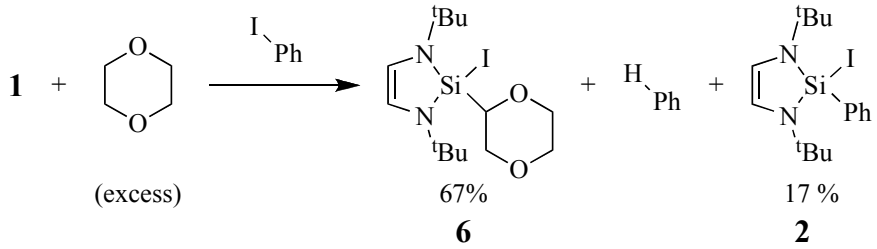


to a 0.0237 M solution of Ph-I resulted in 76 % C-H activation of Et_2O and 15 % OA of the silylene, **Figure 2.2**.

The use of deuterium labeled compounds provided a method for determining what became of the activated H atom. The published work on C-H activation of ethers and alkanes with $(TMS_2CH)_2Ge$ (**21**)/Ph-I demonstrated the activated H ended up attached to what was Ph-I, forming an equivalent of benzene. Gas chromatography–mass spectroscopy (GC-MS) analysis of volatiles from the reactions of **1**/Ph-I with Et_2O-d_{10} and **1**/Ph-I-d_5 with Et_2O were carried out. Qualitative standards of C_6H_6, C_6HD_5, C_6H_5D and C_6D_6 were run at the same time for verification of the GC-MS retention times and MS isotope patterns. The reaction of **1**/Ph-I with Et_2O-d_{10} resulted in formation of C_6H_5D, while the reaction of **1**/Ph-I-d_5 with Et_2O resulted in formation of C_6D_5H. The GC-MS analysis demonstrates the activated H had formed a bond to what was Ph-I. The use of deuterium labeled substrates for elucidation of a plausible mechanism is discussed in Chapter 4.

A second ether substrate successfully C-H activated was 1,4-dioxane. Addition of a 0.0525 M silylene solution to a 0.0235 M solution of Ph-I (3.17 mL/hr) resulted in 67 % C-H activation product and 17 % of OA, **Figure 2.3**. Banaszak Holl et al. reported using color buildup as a visual method for selecting the appropriate addition rate for the

Figure 2.3- C-H Activation of 1,4-dioxane



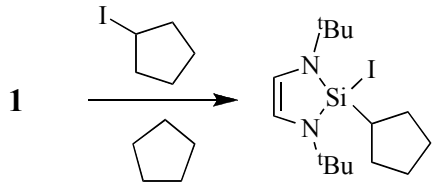
reactions of germylenes and stannylenes, but the colorless nature of **1** does not allow for monitoring color buildup as a method for optimizing the addition rate. Through trial and error the optimal rates were found to be addition of the silylene over 2 ½ to 4 hours. These ether C-H activation products could not be separated from the OA addition product using recrystallization or sublimation.

2.2.2- Silylene/Ph-I C-H Activation of Cycloalkanes

The inability to separate **2** away from the ether C-H activation products presented a unique challenge. To independently synthesize C-H activation products, a series of reactions were carried out with hydrocarbons, **1**, Ph-I, and alkyl iodides. The clean oxidative addition of C_6H_{11}-I and C_5H_9-I to **1** resulted in the independent synthesis of the expected **1**/Ph-I cyclohexane and cyclopentane C-H activation products.

West, Denk et al. has previously shown that OA of various halocarbons resulted in the formation of two types of products. In many instances, a mixture of the two types of products were observed as previously mentioned. One type of OA product can be described as a monomer, the insertion of **1** into a C-X bond forming compounds similar to **2**. The second type of OA product can be described as a dimer formed from the formal addition of two fragments, an X and C fragment, across a Si-Si bond. As shown below in **Figure 2.4**, OA of iodocyclopentane to **1** resulted in isolation of the monomer OA

Figure 2.4- Independent Synthesis of Cyclopentane C-H Activation Product



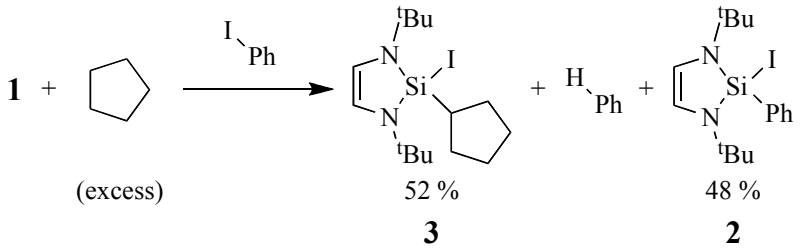
47.8 %

3

product **3**. Using vacuum distillation, analytically pure material was isolated and characterized for comparison to the products from the C-H activation of cyclopentane. The analogous procedure was also used with iodocyclohexane to independently synthesize the expected C-H activation product of cyclohexane.

While independently synthesizing the expected products for the C-H activation of cyclopentane and cyclohexane, the desired C-H activation reactions were carried out. Test reactions were carried out on a small scale by simple addition of **1**, the cyclic hydrocarbon and then Ph-I to a reaction vessel. With the expected C-H activation products independently characterized, the crude reaction mixtures were used for determining the ratio and percentage of C-H activation and OA products. Reactions using cyclohexane as the C-H activation substrate typically resulted in a 1:2 ratio of C-H activation to OA when reagents were added sequentially. Switching to a motor driven syringe addition of **1** in cyclohexane to solution of Ph-I in cyclohexane, typical ratios observed were ~3:1 for C-H activation to oxidative addition. When the C-H activation reaction of cyclopentane was carried out using motor driven synringes, a 0.162 M solution of **1** in cyclopentane was added to a 0.154 M solution of Ph-I in cyclopentane at a rate of 2.0 mL/hr. After removal of volatiles and analysis of the crude reaction mixture, the products were 52 % C-H activation and 48 % OA, **Figure 2.5**. With the C-H

Figure 2.5- C-H Activation of Cyclopentane Substrate



activation of cyclohexane, a 0.122 M solution of silylene in cyclohexane was added to a 0.112 M solution of Ph-I in cyclohexane at a rate of 3.17 mL/hr. Following removal of volatiles, 75 % C-H activation and 25 % OA was observed for the C-H activation of cyclohexane.

2.3- Attempted C-H activation of Benzylic and Allylic C-H Bonds

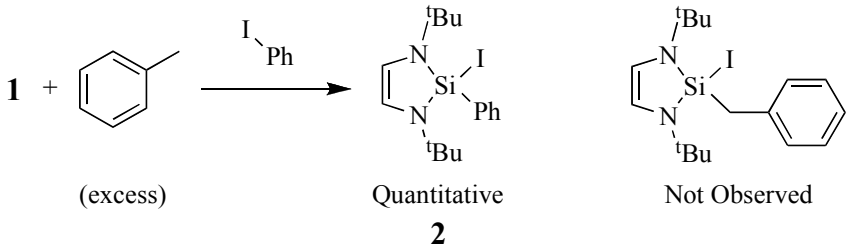
2.3.1- Attempted Activation of an Allylic C-H Bond

When using **1**/Ph-I to C-H activate diallylether, a mixture of compounds was obtained that could not be separated to determine if allylic C-H activation had occurred. The reactivity of π-bonds with silylenes and germylenes is known, thus the reaction of **1** or **21** with C-C π-bonds would have to be avoided for the desired allylic C-H activation to occur. Analysis of crude reactions by ^{1}H NMR spectra revealed many peaks between 5 and 7 ppm that could be attributed to terminal alkenes. Additionally, the ^{1}H and ^{13}C NMR spectra of the concentrated products were not helpful for interpreting if a silacyclopropane or other silacycloalkanes had been formed. The complicated crude reaction product mixture from the reaction of diallylether, coupled with the known reactivity of silylenes with π-bonds has resulted in no further attempts at allylic C-H activation using **1**/Ph-I or **21**/Ph-I.

2.3.2- Attempted Activation of a Benzylic C-H Bond

Tables of C-H hemolytic bond strengths list allylic and benzylic C-H bonds as weaker than the C-H bonds α to an oxygen atom of ethers. Combining the above knowledge with the potential for Hiyama type cross-coupling of benzylic C-Si bonds, an obvious motivational factor for attempting benzylic C-H activation with **1**/Ph-I existed. Proposing an electron transfer mechanism for the C-H activation of ethers and cycloalkanes should be consistent with observing C-H activation of the relatively weak benzylic C-H bond. Contrary to the desired result of benzylic C-H activation, **1** and Ph-I in toluene resulted in formation of the OA product rather than C-H activation, **Figure 2.6**.

Figure 2.6- OA Reaction in the Presence of C_6H_8 or C_6D_8



One interpretation of the lack of toluene reactivity is that a classical radical chain mechanism is not in effect for these C-H activation reactions. A second possible explanation could be formation of a benzylic radical is occurring, but the benzylic radical reverts back to toluene without forming a benzylic C-H activation product. For probing the formation of benzylic radicals, the reaction was carried out with a nominal 1:1 mixture of toluene and toluene-d_8. After the reaction had been allowed to sit for hours, analysis of the nominal 1:1 toluene mixture showed no distinguishable difference in the isotopic compositions. With the lack of any isotope crossover between the toluene molecules, a classical radical chain mechanism has been ruled out as the reaction

mechanism. If a classical radical chain mechanism was the mechanism, a weaker benzylic C-H bond should function as an easier C-H bond for activation than the stronger C-H bond of a hydrocarbon. From a practical perspective, the lack of toluene reactivity proved promising because an insert solvent had been found.

2.4- Summary of C-H Activation of Alkanes and Ethers with 1/Ph-I

Ethers and cyclic hydrocarbon substrates were successfully C-H activated with the use of the mixed reagent **1**/Ph-I. In addition to C-H activation it was observed that Ph-I, iodocyclopentane and iodocyclohexane formed a monomeric product when oxidatively adding to **1**. Analogous to the previous work of Banaszak Holl et al.,[1, 12-14] higher ratios of C-H activation products were obtained through the use of motor driven syringe additions. Attempts to expand the C-H activation reactions to include toluene and diallylether were unsuccessful. With the current reaction conditions being used, addition of the substrate to the silylene followed by addition of Ph-I, substrates containing an alkene or alkyne will react directly with **1** before a C-H activation reaction can occur. The lack of toluene reactivity is perplexing when considering C-H bond strengths. The C-H bonds activated by **1**/Ph-I have been the weakest C-H bonds in a substrate. When comparing C-H bond strengths of the substrates that do C-H activate and the benzylic C-H bond strength of toluene, the weak benzylic C-H bond of toluene was incorrectly presumed to function as an excellent C-H activation substrate. Upon successfully observing the desired C-H activation of ethers and cyclichydrocarbons, the C-H activation of amines was attempted and those results are in the following chapters.

2.5- Experimental Section

All manipulations were performed using dry solvents and air-free techniques. Tetrahydrofuran (THF), diethyl ether (Et_2O), cyclopentane, cyclohexane, 1,4–dioxane, toluene, benzene-d_6, Et_2O-d_{10} and THF-d_8 were degassed and dried over sodium benzophenone ketyl. Acetonitrile (CH_3CN) was dried over P_2O_5 and stored over 4 Å sieves. Aryl halides were passed through a plug of $MgSO_4$ and then degassed before use. $Si[N_2{}^tBu_2(CH)_2]$ (**1**)[15, 16] was synthesized according to literature procedures. GC-MS was performed using a HP 5890A GC connected to a Finnegan MS or a Shimadzu GC-17A connected to a GCMS-QP5000. A Razel syringe pump, model A-99, was used for syringe pump additions. ^1H and ^{13}C NMR spectra were acquired on Varian 500, 400, or 300 MHz instruments and referenced to residual solvent peaks. Mass Spectra (MS) were acquired on a VG (Micromass) 70-250-S Magnetic sector mass spectrometer. Time of flight (TOF) electro spray ionization (ESI) mass spectra were acquired on a MicroMass LCT operating in positive or negative ion mode. IR spectra were acquired on a Perkin Elmer Spectrum BX. Compounds **5** and **6** contained oxidative-addition product **2** as an impurity. We were unable to separate **2** from the mixture using fractional crystallization or sublimation. The C-H activation products were not stable towards column chromatography. Infrared spectra for all species containing the $^tBuNCHCHN^tBu$ backbone exhibited characteristic absorptions at roughly 3105, 2970, 2870, 1620 and 1590 cm^{-1}. Additional infrared data are provided in cases where specific functional groups of interest are present.

$[(CH)_2{}^tBu_2N_2]SiI(C_6H_5)$ (**2**). A 50 mL round bottom flask was charged with 126 mg (0.64 mmol, 1 equiv.) of **1** and 1.160 g (5.69 mmol, 8.9 equiv.) of iodobenzene (Ph-I) resulting in the formation of a gold-colored solution. After 1 hour, all volatiles were removed resulting in a golden oil. Upon exposure to dynamic vacuum for over 12 hours a white, feathery, crystalline solid formed. ^1H and ^{13}C NMR spectra are given for both benzene and chloroform solvents due to the benzene obscuring one of the carbon signals for **2** at 128 ppm. This is a revision of the original ^1H and ^{13}C assignments made for this molecule.[5] ^1H (C_6D_6) δ 8.05 (br, *o*-Ph, 2H), 7.09 (m, *m*,*p*-Ph, 3H), 5.91 (s, =C*H*, 2H), 1.15 (s, CH_3, 18H); ($CDCl_3$) δ 7.97 (d, $^3J_{H\text{-}H}$ = 4 Hz, *o*-Ph, 2H) 7.47 (m, *m*,*p*-Ph, 3H), 6.02 (s, =C*H* 2H), 1.21 (s, CH_3, 18H); ^{13}C (C_6D_6) δ 137.21 (*ipso*-Ph), 135.35 (*o*-Ph), 131.32 (Ph), 128 (Ph), 113.59 (CH=*C*H-N), 52.82 (^{t}Bu*C*-N), 30.53 (*C*H_3); ($CDCl_3$) δ 136.51 (*ipso*-Ph), 135.21 (*o*-Ph), 131.34 (Ph), 127.95 (Ph), 113.37 (*C*H-N), 52.95 (^{t}Bu*C*-N), 30.65 (*C*H_3); MS (EI) *m/z* (relative intensity): 400.1 (100), 161.0 (83.4), 273.2 (67.9), 287.9 (45.3), 286.9 (36.4), 344.0 (32.1), 401.1 (28.0), 329.0 (27.1), 217.1 (27.0); HRMS: 400.0832 predicted, 400.0831 found.

$[(CH)_2{}^tBu_2N_2]SiI(C_5H_9)$ (**3**). A 50 mL 2 neck round bottom flask was charged with 314 mg (1.54 mmol, 1.2 equiv.) of Ph-I and 10 mL of cyclopentane. A solution consisting of 248 mg (1.26 mmol, 1.0 equiv.) of **1** in 7.8 mL of cyclopentane was transferred to an airtight syringe. The solution containing **1** was added to the Ph-I solution at a rate of 2.0 mL/hr. Upon completion of the addition, the yellow solution was stirred for 1 hr and the volatiles were removed. This resulted in 450 mg of a golden oil containing a mixture of **3** (52%) and **2** (48%). Alternate method for synthesis of **3**: A 100 mL round bottom flask

was charged with 834 mg (4.25 mmol, 2.2 equiv.) of cyclopentyliodide and 10.263 g of cyclopentane. A solution containing 387 mg (1.97 mmol, 1 equiv.) of **1** dissolved in 2.5 mL of cyclopentane was added dropwise to the cyclopentyliodide solution using a Pasteur pipette. The reaction was stirred for 24 hr and all volatiles were removed. The golden oil was distilled *in vacuo* using a 90 °C oil bath resulting in 370 mg of an analytically pure colorless oil (47.8 % yield). ^{1}H NMR (C_6D_6) δ 5.80 (s, =C*H*, 2H), 2.0-1.86 (m, cy, 3H), 1.75-1.62 (m, cy, 2H), 1.62-1.49 (m, cy, 2H), 1.49-1.38 (m, cy, 2H), 1.26 (s, CH_3, 18H); ^{13}C NMR (C_6D_6) δ 114.0 (CH=*C*H-N), 52.4 (^{t}Bu*C*-N), 36.6 (CH_2-*C*H-Si), 30.9 (*C*H_3), 28.8 (*C*H_2), 27.0 (*C*H_2); MS (EI) *m/z* (relative intensity): 392.1 (100), 265.2 (48.9), 336.0 (39.6), 280.0 (37.8), 153.1 (31.4), 393.1 (26.4), 210.9 (25.0); CHN analysis – calculated for $C_{15}H_{29}N_2ISi$: C: 45.91, H: 7.45, N: 7.14; Found: C: 45.86, H: 7.27, N: 6.90.

$[(CH)_2{}^{t}Bu_2N_2]SiI(C_6H_{11})$ (**4**). A 100 mL two-necked round bottom flask was charged with 268 mg (1.31 mmol, 1.1 equiv.) of Ph-I and 15.020 g of cyclohexane. A solution consisting of 244 mg (1.24 mmol, 1 equiv.) of **1** in 10.2 mL of cyclohexane was transferred to an airtight syringe. The solution containing **1** was added to the solution containing Ph-I at a rate of 3.17 mL/hr. Upon completion of the addition, the yellow solution was stirred for 1 h and the volatiles were removed. The resulting golden oil contained a 3:1 mixture of **4** and **2**. Alternate method for synthesis of **4**: A 50 mL round bottom flask was charged with 727 mg (3.46 mmol, 2.2 equiv.) of cyclohexyldiodide and 10.35 g of cyclohexane. To this flask was added a solution of 310 mg (1.58 mmol, 1 equiv.) of **1** in 1.65 g of cyclohexane. The reaction was allowed to stir overnight before

removal of volatiles. The resulting golden oil was distilled onto an isopropyl alcohol/dry ice cooled probe *in vacuo* using a 90 °C oil bath. An analytically pure colorless oil was recovered (477 mg. 74.3 % yield). ^{1}H NMR (C_6D_6) δ 5.79 (s, =C*H*, 2H), 2.19 (pseudo-d, $^{3}J_{H\text{-}H}$ = 13.6 Hz, 2H), 1.70 (m, CH_2, 2H), 1.6-1.5 (m, CH_2, 2H), 1.28 (obscured-m, CH_2, 2H), 1.27 (s, CH_3, 18H) 1.15-1.05 (m, C*H* and CH_2, 3H); ^{13}C NMR (C_6D_6) δ 114.0 (CH=*C*H-N), 52.4 (^{t}Bu*C*-N), 37.3 (CH_2-*C*H-Si), 30.9 (*C*H_3), 28.5, 28.4, 27.1 (*C*H_2); MS (EI) *m/z* (relative intensity): 406.1 (100), 279.2 (55.5), 350.1 (37.4), 294.0 (33.3), 167.1 (29.8), 407.1 (28.0), 210.9 (26.3); CHN analysis – calculated for $C_{16}H_{31}N_2ISi$: C: 47.28, H: 7.69, N: 6.89; Found: C: 47.45, H: 7.66, N: 6.85.

$[(CH)_2{}^{t}Bu_2N_2]SiI(CH(CH_3)OCH_2CH_3)$ (**5**). A 100 mL round bottom flask was charged with 121 mg (0.593 mmol, 1.1 equiv.) of Ph-I and 25 mL Et_2O. A solution consisting of 103 mg (0.525 mmol, 1.0 equiv.) of **1** dissolved in 10.2 mL of Et_2O was transferred to an airtight syringe. The solution containing **1** was added to the Ph-I solution at a rate of 3.17 mL/hr. After addition of **1** was completed, volatiles were removed from the pale yellow solution. The resulting golden oil contained a mixture of **5** (76%) and **2** (15%). Spectroscopic data were obtained on this mixture. ^{1}H NMR (C_6D_6) δ 5.78 (d, =C*H*, $^{3}J_{H\text{-}H}$ = 4.4 Hz, 1H), 5.76 (d, $^{3}J_{H\text{-}H}$ = 4.4 Hz, 1H), 3.52 (q, $^{3}J_{H\text{-}H}$ = 7.3 Hz, C*H*, 1H), 3.45 (m, CH_2, 2H), 1.33 (d, $^{3}J_{H\text{-}H}$ = 7.3 Hz, CHCH_3, 3H), 1.32 (s, C(CH_3)$_3$, 9H), 1.26 (s, C(CH_3)$_3$, 9H), 1.10 (t, $^{3}J_{H\text{-}H}$ = 7.0 Hz, CH_2CH_3, 3H); ^{13}C NMR (C_6D_6) δ 113.9 (CH=*C*H-N), 113.6 (CH=*C*H-N), 73.3 (CH_3-*C*H(Si)-O) [$^{1}J_{C\text{-}Si}$ = 52 Hz], 67.6 (CH_3-*C*H_2-O), 52.5 ((CH_3)$_3$-*C*-N), 52.3 ((CH_3)$_3$-*C*-N), 30.7 (C-(*C*H_3)$_3$), 30.3 (C-(*C*H_3)$_3$), 16.9 (CH-*C*H_3), 15.8 (CH_2-*C*H_3); HRMS Calculated ($C_{14}H_{29}N_2OSiI$) 396.1094, Found 396.1089; MS (EI) *m/z*

(relative intensity): 396.2 (100 %), 157.1 (49.5 %) 196.2 (35.6 %), 211.0 (35.1 %), 213.2 (20.4 %), 267.1 (21.8 %), 267.1 (21.8 %), 269.0 (23.4 %), 269.3 (27.5 %), 283.1 (22.1 %), 284.1 (22.0 %).

$[(CH)_2{}^tBu_2N_2]SiI(C_4H_7O_2)$ (**6**). A 100 mL round bottom flask was charged with 120 mg (0.588 mmol, 1.1 equiv.) of Ph-I and 25 mL of 1,4–dioxane. A solution consisting of 103 mg (0.525 mmol, 1.0 equiv.) of **1** dissolved in 10.0 mL of 1,4–dioxane was transferred to an airtight syringe. The solution containing **1** was added to the Ph-I solution at a rate of 3.17 mL/hr. After addition of **1** was completed, the volatiles were removed. The resulting golden oil contained a mixture of **6** (67%) and **2** (17%). Spectroscopic data were obtained on this mixture. ^{1}H NMR (C_6D_6) δ 5.74 (d, $^3J_{H\text{-}H}$ = 4.0 Hz, =C*H*, 1H), 5.68 (d, $^3J_{H\text{-}H}$ = 4.0 Hz, =C*H*,1H), 3.96 (m, C*H* and CHCH_2, 2H), 3.76 (pseudo t, *J* = 11.2 Hz, CHCH_2, 1H), 3.48-3.38 (m, CH_2CH_2, 4H), 1.33 (s, 9H), 1.20 (s, 9H); ^{13}C NMR (C_6D_6) δ 114.3 (CH=*C*H-N), 113.6 (CH=*C*H-N), 75.7 (O-CH_2-*C*H(Si)-O) [$^1J_{C\text{-}Si}$ = 50 Hz], 69.5 (O-CH_2-*C*H_2-O), 67.9 (O-(Si)CH-*C*H_2-O), 67.1 (O-*C*H_2CH_2-O), 52.6 (^{t}Bu*C*-N), 52.5 (^{t}Bu*C*-N), 31.1 (*C*H_3), 30.7 (*C*H_3). HRMS Calculated ($C_{14}H_{27}N_2O_2SiI$) 410.0886, Found 410.0883; MS (EI) *m/z* (relative intensity): 410.3 (100 %), 105.1 (24.0 %) 127.1 (26.9 %), 143.1 (21.8 %), 144.1 (55.9 %), 161.1 (77.1 %), 171.1 (56.4 %), 211.0 (34.0 %), 217.2 (21.2 %), 273.1 (44.4 %), 287.1 (22.0 %), 288.1 (29.0 %), 298.1 (32.8 %), 354.2 (52.4 %).

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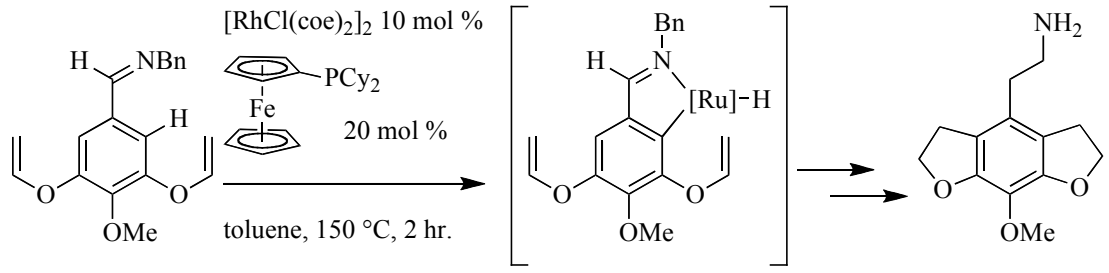
Chapter 3- Amines as Substrate in C-H Activations with Germylene/Ph-I or Silylene/Ph-I

3.1- Challenges with C-H Activation of Amines

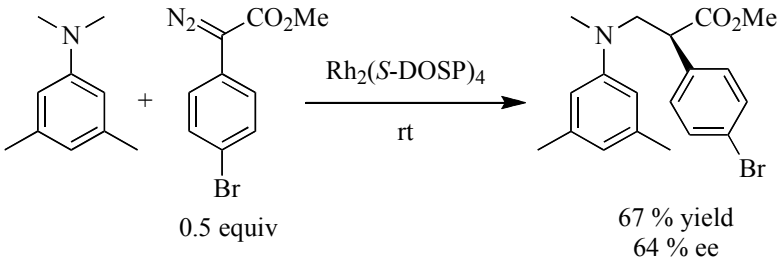
The C-H activation of amine substrates presents a unique challenge. Comparison of C-H bond strengths α to the oxygen of ethers and α to the nitrogen of amines establishes the amine C-H bond as a slightly weaker bond. A rational presumption based on the weaker C-H bond strengths present in amines is that amines should function as better substrates than ethers in C-H activation reactions. Though the bond strength rationale holds true, the Lewis basic character of amines presents a challenge for C-H activation. The transition metals typically used for the catalytic activation of C-H bonds are Lewis acidic. The combination of the Lewis basic amines with the Lewis acidic transition metal catalysts favors the formation of a Lewis acid-base complex. Formation of these Lewis acid-base complexes of amines and transition metals tend to disrupt catalytic cycles or the amine undergoes β-hydride elimination to form an imine. Typically, amine/imine C-H activation reactions found in the literature exploit the formation of a Lewis acid-base complex to purposefully direct the C-H activation reaction to a desired bond within close proximity of the Lewis basic nitrogen. Bergman, Ellman et al. have exploited nitrogen as a ligating group for forming Lewis acid-base complexes that will subsequently activate a C-H bond, resulting in the formation of metallocycles, see **Scheme 3.1**.[1, 2] Hartwig et al. exploited Lewis acid-base complex

Scheme 3.1- C-H Action Reaction in Synthesis of a Mescaline Analogue



formation for carrying out a hydroaminoalkylation that results in formation of a C-C bond at the carbon α to the nitrogen atom of an amine.[3] Davies et al. have been able to avoid the formation of Lewis acid-base complexes that disrupt catalytic cycles by the preferential formation of rhodium-carbeneoids.[4-9] An interesting aspect of selectivity reported by Davies et al. was the activation of the C-H's α to an aniline nitrogen atom as opposed to benzylic C-H bonds, see **Scheme 3.2**.[10]

Scheme 3.2- Selectivity of Rhodium-Carbenoid C-H Activation of an Aniline



3.2- Reactivity of Trialkylamines with Germylene/Ph-I

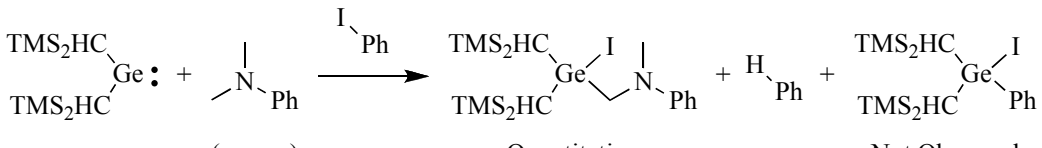
3.2.1- Activation of Tertiary Amines with Methyl C-H Bonds

Sara L. Scott made the initial discovery of amine C-H activation using $(TMS_2CH)_2Ge$ (**21**)/Ph-I. The initial screening of amines was carried out with compounds containing only methyl C-H bonds that were most likely to be activated.

Sara was able to demonstrate that motor driven syringe additions were not necessary with amine substrates for obtaining ≥90 % C-H activation.

The C-H activation of Me_2NPh with **21**/Ph-I was quantitative for the formation of the methyl C-H activation product. Typically, the C-H activation reactions were carried out by sequential addition of reagents to a reaction vessel. Quantitative C-H activation of Me_2NPh was observed when 301 mg of **21**, 70.5 mL Me_2NPh and then 163 mg of Ph-I combined in a reaction flask and left stirring until the solution was colorless. Removal of volatiles followed by analysis of the crude product mixture by ^1H NMR spectroscopy demonstrated no observable formation of **22**. By way of comparison, the **21**/Ph-I C-H activation of ethers requires motor driven syringe techniques for obtaining >75 % of a C-H activation product.

Figure 3.1- C-H Activation of N,N-dimethylaniline with **21**/Ph-I

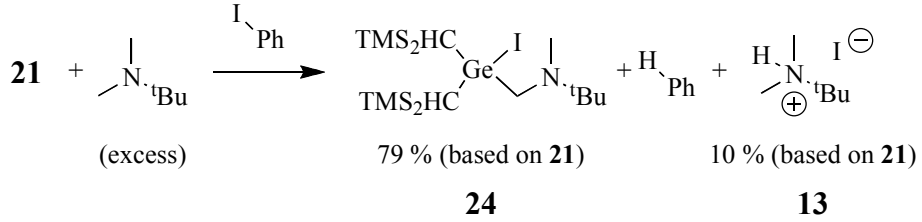


21 **23** **22**

Test reactions also demonstrated that Me_2N^tBu functioned as a better substrate than ethers for the C-H activation reactions using **21**/Ph-I. Unlike the reaction of Me_2NPh, analytically pure C-H activation product could not be obtained by removal of volatiles followed by filtration with pentane. Repeated attempts of simply adding the reagents together in the sequential order of **21**, amine and then Ph-I did not yield analytically pure material after re-crystallizations. Following repeated failures at isolating analytically pure material, the use of a motor driven syringe addition was used to increase the likelihood of isolating analytically pure C-H activation products. By

adding a 0.0197 M solution of **21** at a rate of 3.02 mL/hr. to a 0.0216 M solution of Ph-I, the C-H activation product **24** was obtained along with another compound. A ^{1}H NMR of the crude reaction revealed a 10:1 ratio of **24** to **22**, 91 % yield of **24**, along with the **13**, **Figure 3.2**. Following a pentane filtration of the crude reaction product, the unexpected product was isolated as a white solid. The unexpected product was characterized as the ammonium hydroiodide salt of Me_2N^tBu, $[Me_2N^tBuH]I$. The presence of the ammonium hydroiodide salt was verified by comparison with spectroscopic data of an independently synthesized sample of **13**.

Figure 3.2- C-H Activation of Me_2N^tBu with **21**/Ph-I

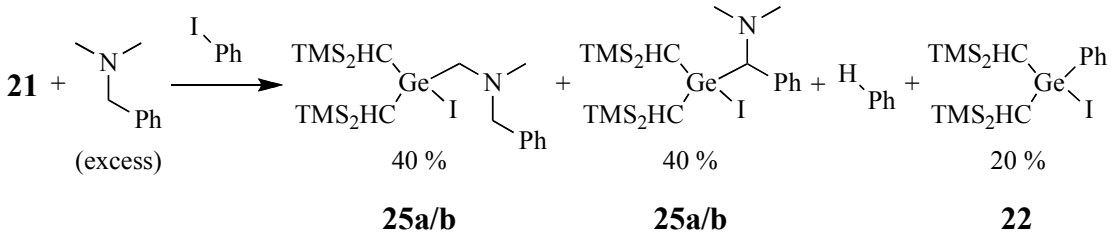


3.2.2- Selectivity of Germylene/Ph-I C-H Activation of Amines

The substrates Me_2NCH_2Ph and $Me_2NCH_2NMe_2$ were chosen as C-H activation substrates to establish the methyl vs. methylene and methyl vs. benzylic selectivity of amine substrates. The C-H activation of Me_2NCH_2Ph demonstrated a preference for the benzylic methylene C-H bond over the methyl C-H bond. Curiously, the substrate $Me_2NCH_2NMe_2$ formed a single C-H activation product and $[Me_2NCHNMe_2]I$.

Without the use of motor driven syringe additions the amine substrate Me_2NCH_2Ph afforded from 80 % to quantitative formation of the isomeric C-H activation products **25a** and **25b**, **Figure 3.3**. With various reaction concentrations a 1:1 mixture of methyl and methylene C-H activation was consistently observed. Accounting for the statistics of the two CH_3's and the single benzylic CH_2, the activation of the benzylic

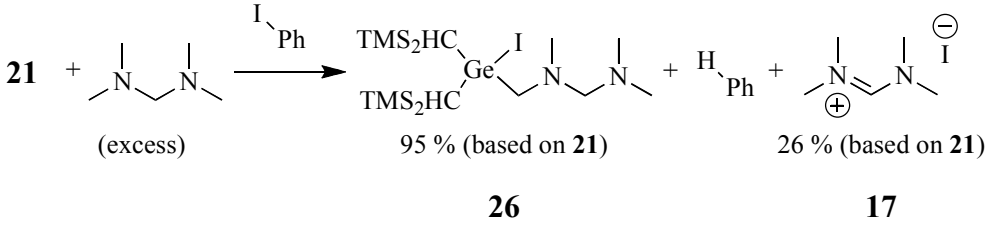
Figure 3.3- C-H Activation of Me_2NCH_2Ph with **21**/Ph-I



methylene was favored by a 3:1 ratio. Characterization of the compounds was carried out on the mixture of C-H activation isomers due to an inability to separate the isomers via re-crystallization.

Sara Scott's initial work on the C-H activation of $Me_2NCH_2NMe_2$ had been interpreted as demonstrating the presence of the methyl and methylene regioisomeric C-H activation products. The reaction of 171 mg (1.3 equiv.) of Ph-I, 20 mL of $Me_2NCH_2NMe_2$ and 248 mg (1.0 equiv.) of **21** resulted in 95 % yield of C-H activation product **26** and 26 % yield, based on **21**, of an unexpected salt, **Figure 3.4**. Contrary to the previous interpretation, the sole activation product containing a Ge-C bond derives from activation of the methyl, rather than the methylene, C-H bond. The 26 % yield, based on **21**, of the iminium iodide salt was unexpected. Mechanistic implications of the iminium iodide salt formation will be discussed in greater detail in chapter 4.

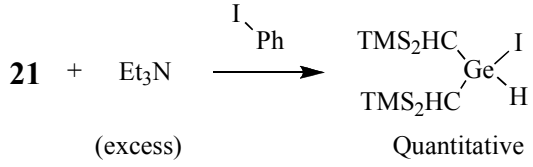
Figure 3.4- C-H Activation and Iminium Iodide Formation with **21**/Ph-I



3.2.3- A New Reaction of Germylene/Ph-I with Tertiary Amines

An unexpected non-C-H activation reaction was observed when attempting to C-H activate Et_3N with **21**/Ph-I. Characterization of the reaction product demonstrated an H and an I atom had added to **21**, see **Figure 3.5**. The addition of an H and I atom to **21** was observed with various tertiary amines that had alkyl chains two carbons or longer and C-H bonds at the α and β position to the amine nitrogen atom.

Figure 3.5- Formation of **27** from **21**/Ph-I and a Tertiary Alkyl Amine



27

Regardless of the reaction conditions used, **21**/Ph-I in Et_3N formed the product derived from net addition of an H atom and an I atom to **21**. When using comparable reaction conditions, the Et_3N reactions occurred in less time than the C-H activation reactions of Me_2NCH_2Ph and Me_2NPh. With Et_3N as the solvent the formation of **27** occurred quantitatively. The source of the H atom was believed to be coming from Et_3N and not the aryl halide. Using Et_3N-d_{15} as the solvent, the characteristic peak of the Ge-H was not observed with ^1H NMR.

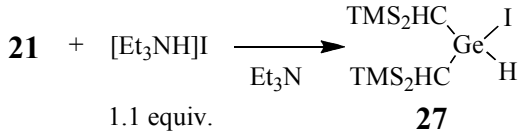
Formation of **27** was also observed when attempting to C-H activate Pr_3N and N-methylpiperdine. With Pr_3N as the solvent, the formation of **27** was quantitative. In N-methylpiperdine the major product formed was **27**, though formation of **27** does not occur quantitatively.

3.2.4- Germylene/Ph-I Reactions Forming Iodide Salts of the Amines

Formation of the $[Me_2N^tBuH]I$ salt was of immediate interest because the insertion of germylenes into C-H bonds of nitriles has been demonstrated to be catalyzed by salts.[11] A working hypothesis for the formation of **27** involves the formation of trace amounts of amine hydroiodide salts *in situ*. The direct reaction of a variety of amine hydroiodides salts with germylenes resulted in formation of **27**. The problem with this working hypothesis lies with how the corresponding amine hydroiodide salts are formed *in situ*.

Under a variety of reaction conditions an amine hydroiodide in the presence of **21** forms **27**. The reaction rate of amine hydroiodides with **21** are of a similar rate when compared to the reaction of **21**/Ph-I in Et_3N reaction, see **Figure 3.6**. A rational mechanism for the reaction of amine hydroiodides with **21** is presented in section 4.4.1.

Figure 3.6- Formation of **27** from **21** and R_3NHI

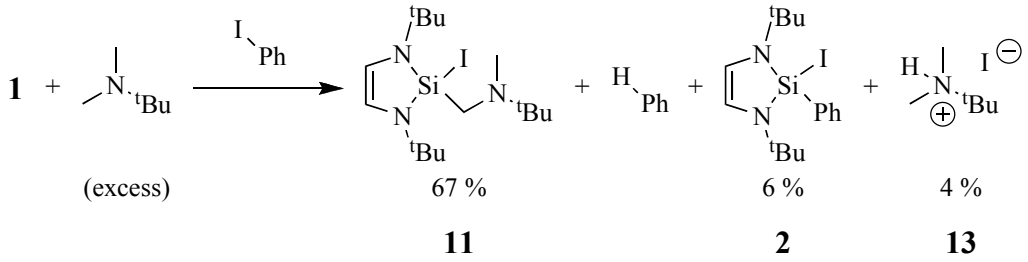


3.3- C-H Activation of Trialkylamines with Silylene/Ph-I

3.3.1- Activation of an Amine Substrate with Methyl C-H Bonds

The use of **1**/Ph-I resulted in C-H activation analogous to the observed **21**/Ph-I activation of Me_2N^tBu. The methyl group α to the nitrogen atom was selectively activated over the methyls of the *tert*-butyl. When using a motor driven syringe, addition of a 0.255 M solution of silylene, at a rate of 1.19 mL/hr, to a 0.217 M solution of Ph-I resulted in formation of the C-H activation product **11**, **Figure 3.7**. In addition to 67 %

Figure 3.7- C-H Activation of Me_2N^tBu with **1**/Ph-I



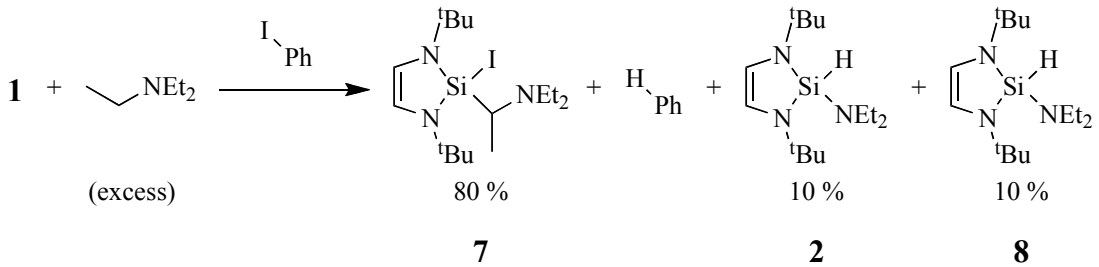
of **11**, the reaction also formed 6 % of **2** and 4 % of **13**. Successive re-crystallizations of the crude reaction product from pentane at -78 °C afforded analytically pure **11** in a 10 % isolated yield.

3.3.2- Successful Activation of Tertiary Alkyl Amines Forming a C-Si Bond

The initial purpose of running reactions with tertiary alkyl amine substrates such as Et_3N, Pr_3N and N-methylpiperdine was to establish the similar reactivity trend, and not a difference, in **1**/Ph-I and **21**/Ph-I reactivity. The **21**/Ph-I reactions with Et_3N, Pr_3N or N-methylpiperdine all formed the same product and the product did not contain a newly formed C-Ge. In direct contrast, **1**/Ph-I reactions with Et_3N, Pr_3N or N-methylpiperdine as the substrate all resulted in the major product containing a newly formed C-Si bond.

The reaction of **1**/Ph-I with Et_3N resulted in formation of three distinct products, **Figure 3.8**. The major product in all cases corresponded to activation of the C-H bond α

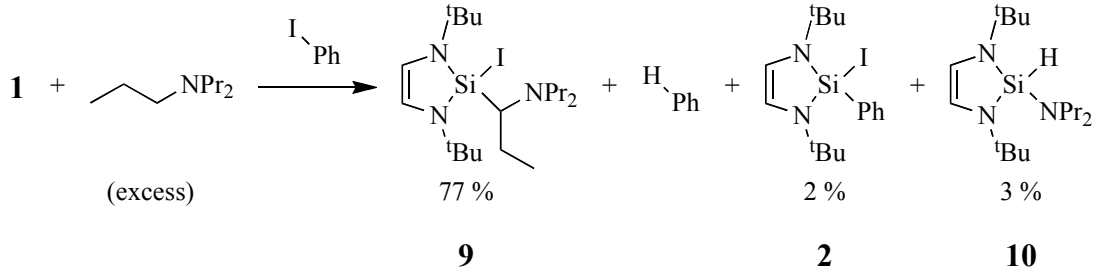
Figure 3.8- C-H Activation of Et_3N and Formation of a Silyl Hydrido Amide



to the nitrogen atom. When **1**, Et_3N and then Ph-I were added to a reaction vessel, the immediate appearance of a golden colored occurred. Volatiles could be removed immediately or the reaction allowed to stir for any desired amount of time. The typical ratio of C-H activation to **2** was better for C-H activation of amines than for the corresponding C-H activation of ethers with **1**/Ph-I. When using a motor driven syringe addition of a 0.0541 M solution of **1** to a 0.0233 M solution of Ph-I at a rate of 3.17 mL/hr. afforded 80 % C-H activation product **7**, 10 % of **2** and 10 % of a new Si-H containing product, **8**. The resulting C-H activation product demonstrates distinctingly diastereotopic methylene's in the ^1H NMR and ^{13}C NMR. An IR of the product mixture revealed the crude reaction product contained a Si-H bond. Subsequently, the Si-H containing product was identified as **8**. The independent synthesis of the **8** is discussed in greater detail in section 3.3.3.

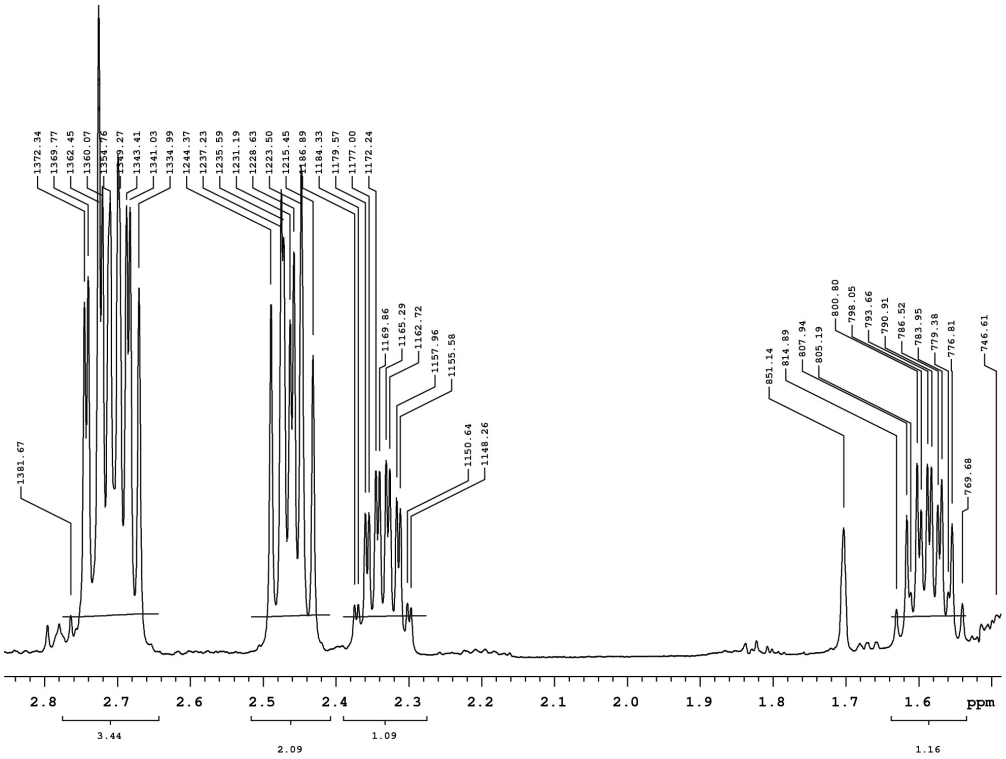
The C-H activation of Pr_3N with **1**/Ph-I demonstrated the above reaction of Et_3N was typical for **1**/Ph-I, rather than the formation of a silylene compound analgous to **27**. When using a motor driven syringe addition of a 0.0499 M solution of **1** to a 0.0239 M solution of Ph-I at a rate of 3.17 mL/hr. afforded 77 % C-H activation product **9**, 2 % **2**

Figure 3.9- C-H Activation of Pr_3N and Formation of a Silyl Hydrido Amide



and 3 % of a new silyl hydrido amide, **10**, after removal of volatiles, **Figure 3.9**. Like the **1**/Ph-I activation of Et_3N, the resulting C-H activation product of Pr_3N demonstrated

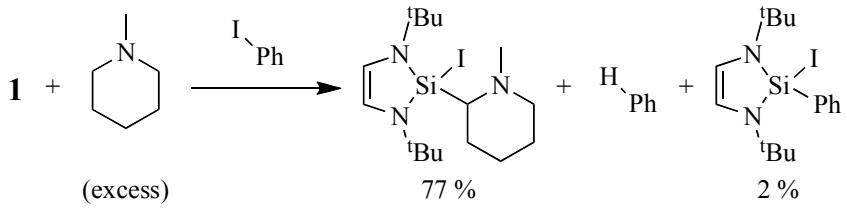
Figure 3.10- Diastereotopic CH_2's and CH_3's of **9**



distinctly diastereotopic methylene's in ^{1}H NMR, see **Figure 3.10**, and ^{13}C NMR. The rather high yield of **9** was surprising considering the steric bulk around the activated C-H bond α to nitrogen.

C-H activation of N-methylpiperdine was remarkable in that the product was isolable and suitable for single crystal x-ray analysis. A motor driven syringe addition of a 0.0412 M solution of **1** to a 0.0565 M Ph-I solution at a rate of 2.85 mL/hr. was used.

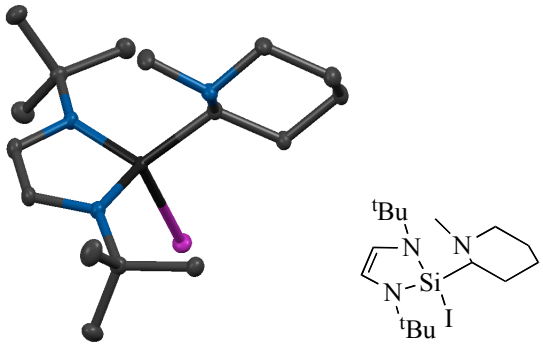
Figure 3.11- C-H Activation of N-methylpiperdine with **1**/Ph-I



Analysis of the crude reaction product showed 85 % C-H activation product **12** and less than 0.5 % **2**, **Figure 3.11**. The C-H activation product was a single regioisomer isomer that corresponded to activation of the methylene C-H, and not the methyl C-H bond, α to the nitrogen atom. After successive re-crystalizations, a 56 % yield of **12** was isolated and crystals were grown for single crystal X-ray analysis. Analysis of crude product mixtures did not show the presences of the corresponding amine hydroiodide salt or any Si-H containing compounds.

A single crystal X-ray structure analysis of **12** was carried out using crystals grown from slow evaporation of hexanes and the resulting X-ray structure published. The X-ray structure confirmed the structure derived from the assignments using ^{1}H, ^{13}C and 2-D NMR. The newly formed C-Si bond is exclusively at the methylene carbon α to the nitrogen atom. In the solid state the six-membered piperidine ring adopts a chair confirmation, with the newly formed C-Si bond at the carbon α to the nitrogen atom.[12]

Figure 3.12- X-ray Crystal Structure of **12**

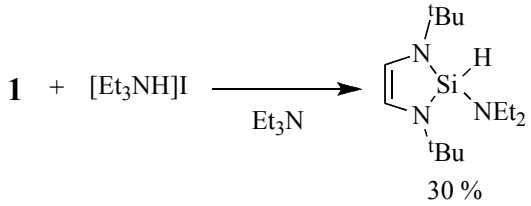


3.3.3- Independent Synthesis of Silyl Hydrido Amides

Formation of silyl hydrido amide products **8** and **10** was not anticipated, but a rationale for how compound **8** forms was developed. From the known germylene insertion reactions catalyzed by presence of salts such as $MgCl_2$, the presence of an

amine hyrdoiodide salt was theorized to play a part in formation of compounds **8** and **10**. As compound **8** lacks one of the ethyl groups from Et_3N, the simplest possible route for formation of **8** would be insertion of **1** into the N-H bond of Et_2NH. Attempts at synthesizing **8** from Et_2NH and **1** were not successful when using reaction times comparable to those of the C-H activation of amines with **1**/Ph-I. Addition of a secondary amine to **1** would be thermodynamically disfavored, as this would disrupt the aromatic nature of **1**. The aromatic character of **1** decreases the Lewis acidic character at the divalent silicon atom. A second unique feature previously noted was formation of an ammonium iodide salt for C-H activation reactions of Me_2N^tBu with **21**/Ph-I (**Figure 3.2**) and **1**/Ph-I (**Figure 3.7**). Attempts to form the compound derived from addition of H and I atom failed when using Et_3NHI as a source of H and I atoms, rather formation of silyl hydrido amide was observed with these reaction conditions, **Figure 3.13**.

Figure 3.13- Independent Synthesis of **8** with **1**, Et_3N and $[Et_3NH]I$

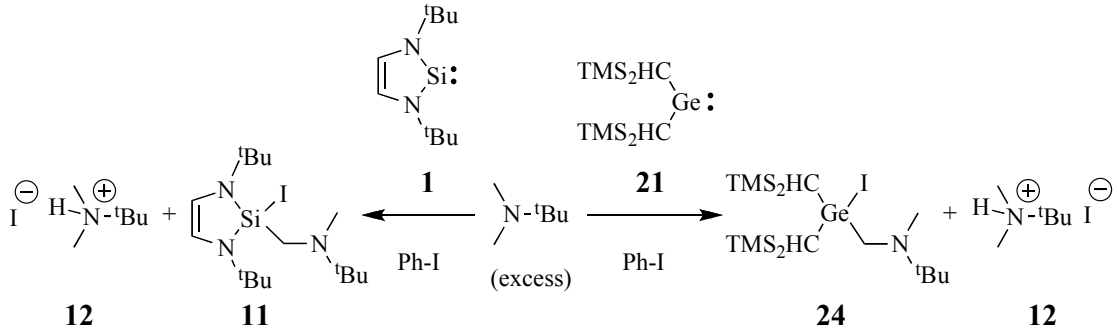


The independent synthesis of the silyl hydrido amide **10** was achieved in Pr_3N solvent in the presence of $[Pr_3NH]I$. The addition of 140 mg of $[Pr_3NH]I$ and 98 mg of silylene in 15 mL of Pr_3N was left to react for 24 hrs. to form **10**. After removal of volatiles and filtration with pentane, 81 % of the $[Pr_3NH]I$ salt was recovered along with an oil. The resulting oil did not contain **1, 2** or **9**. The ^1H NMR, ^{13}C NMR and GC-MS analysis were consistent with the oil containing a 23 % yield of **10**.

3.4- Summary of Silylene/Ph-I or Germylene/Ph-I C-H Activation of Amines

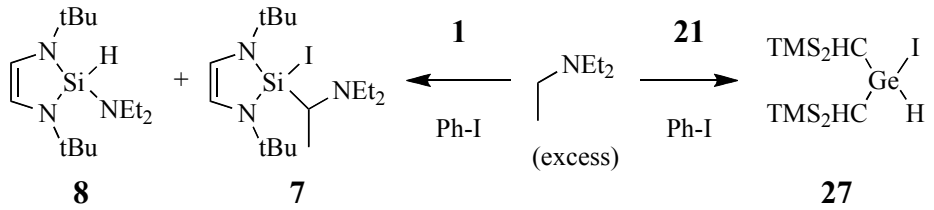
The C-H activation of tertiary amines has been achieved with **1**/Ph-I and **21**/Ph-I. The reactivity trends of tertiary amines varies between **1**/Ph-I and **21**/Ph-I. Amine substrates with only methyl C-H groups can be activated with either **1**/Ph-I and **21**/Ph-I to form similar C-H activation products, **see Figure 3.14**. When using motor driven slow additions with Me_2N^tBu as the activation substrate, the formation of $[Me_2N^tBuH]I$ was observed for both **1**/Ph-I and **21**/Ph-I along with the respective C-H activation products

Figure 3.14- Similar Reactivity of **1**/Ph-I and **21**/Ph-I with Amines



11 and **24**. Amines with C-H bonds α and β to a nitrogen atom, like Et_3N and N-methylpiperidine, produce vastly different products when using **21**/Ph-I and **1**/Ph-I, see **Figure 3.15**. Amine substrates with C-H bonds α and β to the amine nitrogen form C-H activation products containing Si-C bonds when using **1**/Ph-I. Additionally, the silyl hydrido amides **8** and **10** were observed to form with the amine substrates Et_3N and Pr_3N.

Figure 3.15- Dissimilar Reactivity of **1**/Ph-I and **21**/Ph-I with Amines



The net addition of an H and I atom to **21** was observed with the amine substrates Et_3N, Pr_3N and N-methylpiperidine. In addition, the amine substrate Me_2NCH_2Ph demonstrated a selectivity of 3:1 for the benzylic C-H bond over the methyl C-H bonds.

3.5- Experimental Section

All manipulations were performed using dry solvents and air-free techniques. *N*,*N*,*N*–triethylamine (Et_3N), *N*,*N*,*N*–tripropylamine (Pr_3N), *N*,*N*–dimethyl-*tert*-butylamine (Me_2N^tBu), *N*–methylpiperidine, *N*,*N*–dimethylaniline (Me_2NPh), *N*,*N*–dimethylbenzylamine (Me_2NCH_2Ph), *N*,*N*,*N*',*N*'–tetramethylmethanediamine ($Me_2NCH_2Me_2$), toluene, benzene-d_6, pentane and hexanes were degassed and dried over sodium benzophenone ketyl. Acetonitrile (CH_3CN) was dried over P_2O_5 and stored over 4 Å sieves. Aryl halides were passed through a plug of $MgSO_4$ and then degassed before use. $[(CH)_2{}^tBu_2N_2]Si$ (**1**)[13, 14] and $[(Me_3Si)_2CH]_2Ge$ (**15**)[15] were synthesized according to literature procedures. GC-MS was performed using a HP 5890A GC connected to a Finnegan MS or a Shimadzu GC-17A connected to a GCMS-QP5000. A Razel syringe pump, model A-99, was used for syringe pump additions. ^1H and ^{13}C NMR spectra were acquired on a Mercury 300, Inova 400, MR400, or Inova 500 Varian instruments and referenced to residual solvent peaks. Mass Spectra (MS) were acquired on a VG (Micromass) 70-250-S Magnetic sector mass spectrometer. Time of flight (TOF) electro spray ionization (ESI) mass spectra were acquired on a MicroMass LCT operating in positive or negative ion mode. IR spectra were acquired on a Perkin Elmer Spectrum BX. Compounds **7** and **9** contained oxidative-addition product **2** as an impurity. Separation of **2** from **8** or **9** using fractional crystallization or sublimation was not successful. The compounds were not stable towards chromatography. Infrared spectra

for all species containing the ^{t}BuNCH=CHN^{t}Bu backbone exhibited characteristic absorptions at roughly 3105, 2970, 2870, 1620 and 1590 cm^{-1}. Additional infrared data are provided in cases where specific functional groups of interest are present.

[(CH)$_2$^{t}Bu$_2$N$_2$]SiI[CH(CH$_3$)N(CH$_2$CH$_3$)$_2$] (**7**). A 100 mL round bottom flask was charged with 119 mg (0.583 mmol, 1.1 eq) of Ph-I and 25 mL of Et$_3$N. A solution consisting of 102 mg (0.519 mmol, 1.0 equiv.) of **1** dissolved in 9.6 ml of Et$_3$N was transferred to an airtight syringe. The solution containing **1** was added to the Ph-I solution at a rate of 3.17 mL/hr. After addition of **1** was completed, volatiles where removed. The resulting golden semi-solid contained a mixture of **7** (80%), **2** (10%) and **8** (10%). Spectroscopic data were obtained on this mixture. ^{1}H NMR (C$_6$D$_6$) δ 5.88 (d, $^{3}J_{H\text{-}H}$ = 4.4 Hz, =CH, 1H), 5.77 (d, $^{3}J_{H\text{-}H}$ = 4.4 Hz, =CH, 1H), 3.14 (q, $^{3}J_{H\text{-}H}$ = 7.3 Hz, C*H*, 1H), 2.63 (qd, ^{2}J$_{HH}$= 13.0 Hz, ^{3}J$_{H\text{-}H}$ = 7.2 Hz, C*H*$_2$, 2H), 2.26 (qd, ^{2}J$_{HH}$= 13.0 Hz, ^{3}J$_{H\text{-}H}$ = 7.2 Hz, C*H*$_2$, 2H), 1.38 (s, C*H*$_3$, 9H), 1.29 (d, ^{3}J$_{H\text{-}H}$ = 7.3 Hz, CHC*H*$_3$, 3H) 1.28 (s, C*H*$_3$, 9H), 0.90 (br t, 3$J_{H\text{-}H}$ = 7.2 Hz, CH$_2$C*H*$_3$, 6H); ^{13}C NMR (C$_6$D$_6$) δ 114.5 (CH=*C*H-N), 113.0 (CH=*C*H-N), 58.2 (*C*H, $^{1}J_{C\text{-}Si}$ = 48 Hz), 52.9 (^{t}Bu*C*-N), 52.3 (^{t}Bu*C*-N), 47.0 (CH$_3$*C*H$_2$N), 30.9 (C-(*C*H$_3$)$_3$), 30.2 (C-(*C*H$_3$)$_3$), 14.8 (CH$_2$*C*H$_3$), 8.0 (CH*C*H$_3$); HRMS Calculated (C$_{16}$H$_{34}$N$_3$SiI) 423.1567, Found 423.1578; MS (EI) *m/z* (relative intensity): 100.1 (100 %), 125.0 (6.5 %) 127.9 (6.7 %), 196.1 (7.3 %), 210.9 (7.1 %), 423.1 (5.1 %).

[(CH)$_2$^{t}Bu$_2$N$_2$]SiH[N(CH$_2$CH$_3$)$_2$] (**8**). This product is present in ~10% yield as indicated by ^{1}H NMR spectroscopy using the reaction conditions given for compound **7**. Synthesis of **8** was independently carried out by reaction of **1** with [HNEt$_3$]I. A 100 mL round

bottom flask was charged with [Et_3NH]I (148 mg, 0.646 mmol, 1.0 equiv.), **1** (121 mg, 0.616 mmol, 1.0 equiv.), and 15.94 g of Et_3N. The flask was capped and allowed to stir overnight. Removal of volatiles produced 239 mg of a white solid and an amber oil (154 mg). Filtration with pentane separated the white solid and amber oil. The white solid recovered was [$HNEt_3$]I. ^{1}H NMR spectroscopy indicated that ~30% of the amber oil was **8**. ^{1}H NMR (C_6D_6) δ 5.82 (s, *H*-C=C, 2H), 5.70 (br s, Si-*H*, 1H), 2.84 (q, $^3J_{H\text{-}H}$ = 7.1 Hz, CH_2, 4H), 1.25 (s, C(CH_3)$_3$, 18H), 0.99 (t, $^3J_{H\text{-}H}$ = 7.1 Hz, CH_2CH_3, 6H); ^{13}C NMR (C_6D_6) δ 111.8 (CH=*C*H-N), 51.0 (^{t}Bu*C*-N), 38.3 (NCH_2), 30.9 (C(*C*H_3)$_3$), 14.8 (CH_2CH_3); GC-MS *m/z* (relative intensity): 269.30 (53.02 %), 270.30 (11.27 %) 72.10 (100.00 %), 84.05 (24.95 %), 85.05 (72.22 %), 156.05 (23.21 %), 183.20 (14.81 %), 198.25 (24.20 %), 212.25 (24.15 %), 254.25 (26.04 %); IR (neat on NaCl plate) 2132 cm^{-1} (ν Si-H).

[$(CH)_2{}^t Bu_2N_2$]SiI[$CH(CH_2CH_3)N(CH_2CH_2CH_3)_2$] (**9**). A 100 mL round bottom flask was charged with 122 mg (0.598 mmol, 1.2 equiv.) of Ph-I and 25 mL of Pr_3N. A solution containing 102 mg (0.519 mmol, 1.9 equiv.) of **1** dissolved in 10.4 mL of Pr_3N was transferred to an airtight syringe. The solution containing **1** was added at a rate of 3.17 mL/hr to the Ph-I solution. After addition of **1** was completed, volatiles where removed from the pale yellow solution. The resulting golden oil was a mixture of **9** (77%), **2** (2%), and **10** (3%). Spectroscopic data were obtained on this mixture. ^{1}H NMR (C_6D_6) δ 5.83 (d, $^3J_{H\text{-}H}$ = 4.0 Hz, =C*H*, 1H), 5.76 (d, $^3J_{H\text{-}H}$ = 4.0 Hz, =C*H*, 1H), 2.76-2.68 (m, NCH_2 and N$CH$$CH_2$, 3H), 2.48 (m, N$CH_2$, 2H), 2.35 (dqd, NCHC$H_2$, $^2J_{H\text{-}H}$ = 14.2 Hz, $^3J_{H\text{-}H}$ = 7.2, 2.5 Hz, 1H), 1.60 (ddq, NCHCH_2, $^2J_{H\text{-}H}$ = 14.2 Hz, $^3J_{H\text{-}H}$ = 9.8, 7.2 Hz, 1H), 1.50-1.33

(m, $NCH_2CH_2CH_3$, 4H), 1.37 (s, $C(CH_3)_3$, 9H), 1.29 (s, $C(CH_3)_3$ 9H), 1.10 (t, $^3J_{H\text{-}H}$ = 7.2 Hz, $CHCH_2CH_3$, 3H), 0.81 (br t, $^3J_{H\text{-}H}$ = 7.4 Hz, $NCH_2CH_2CH_3$, 6H); ^{13}C NMR (C_6D_6) δ 114.3 (CH=*C*H-N), 113.5 (CH=*C*H-N), 64.1 (Si*C*H, $^1J_{C\text{-}Si}$ = 45 Hz), 56.2 (NCH_2), 53.3 (^{t}Bu*C*-N), 52.6 (^{t}Bu*C*-N), 30.8 ($C(CH_3)_3$), 30.3 ($C(CH_3)_3$), 23.2 ($CH_2CH_2CH_3$), 21.1 ($CHCH_2CH_3$), 16.0 ($CHCH_2CH_3$), 11.9 ($CH_2CH_2CH_3$); HRMS Calculated ($C_{19}H_{40}N_3SiI$) 465.2036, Found 465.2046; MS (EI) *m/z* (relative intensity): 196.2 (100 %), 84.0 (58.1 %) 84.1 (75.4 %), 112.1 (48.3 %), 125.1 (41.8 %), 141.2 (26.2 %) 142.2 (93.9 %), 161.1 (%), 181.1 (33.7 %), 335.3 (38.0 %), 450.0 (2.2 %), 465.3 (1.7 %).

$[(CH)_2{}^tBu_2N_2]SiH[N(CH_2CH_2CH_3)_2]$ (**10**): This product is present in ~3% yield as indicated by ^{1}H NMR spectroscopy using the reaction conditions given for compound **9**. Synthesis of **10** was independently carried out by reaction of **1** with $[HNPr_3]I$. A 100 mL round bottom flask was charged with 140 mg (0.516 mmol, 1.0 equiv.) of $[Pr_3NH]I$, 98 mg (0.499 mmol, 1 equiv.) of **1**, and 15 mL of Pr_3N. The solution was allowed to stir for 24 hours. Removal of volatiles afforded a white solid with a goldish colored oil. The white solid was removed via a filtration with pentane. 148 mg of a goldish colored oil was recovered, by ^{1}H NMR 23 % of the oil was **10**. The white solid remaining after filtration was 114 mg of $[HNPr_3]I$ (81 % recovery). ^{1}H NMR (C_6D_6) δ 5.83 (s, *H*-C=C, 2H), 5.73 (br s, Si-*H*, 1H), 2.77 (m, N-CH_2, 4H), 1.49 (m, CH_2-CH_3, 4H), 1.27 (s, $C(CH_3)_3$, 18H), 0.79 (t, ^{3}J = 7.2 Hz CH_2-CH_3), 6H); ^{13}C NMR (C_6D_6) δ 111.9 (CH=*C*H-N), 51.0 (^{t}Bu*C*-N), 47.9 (NCH_2), 30.9 ($C(CH_3)_3$), 23.2 ($CH_2CH_2CH_3$), 12.1 (CH_2CH_3); GC-MS *m/z* (relative intensity): 297.35 (49.34 %), 298.35 (11.70 %), 84.00 (36.55 %), 85.00 (100.00 %), 86.00 (17.03 %), 100.10 (91.56 %), 184.20 (25.25 %), 240.25 (20.03

%), 282.30 (18.75 %); IR (neat on NaCl plate) 2199 cm^{-1} (ν Si-H).

$[(CH)_2{}^tBu_2N_2]SiI[CH_2N(CH_3){}^tBu]$ (**11**). A 2 neck 100 mL round bottom flask was charged with 254 mg (1.24 mmol, 1.2 equiv.) of Ph-I and 7.750 g of $Me_2N{}^tBu$. A solution containing 200 mg (1.02 mmol, 1 equiv.) of **1** in 4 mL of $Me_2N{}^tBu$ was transferred to an airtight syringe. The solution containing **1** was added to the Ph-I solution at a rate of 1.19 mL/hr. After addition of **1** was completed, the solution was stirred for 16 h after which time all volatiles where removed. The crude material was composed of 6 % **2**, 67 % **11** and 4 % **13**. Crude material containing **11**, **2** and **13** was dissolved in 5 mL pentane and filtered yielding 17 mg of **13** (6 % yield based upon Ph-I) as a white solid. Analytically pure **11** was obtained as a white solid after three recrystallizations from pentane at –78 °C (45 mg, 10% yield based upon **1**). ^{1}H NMR (C_6D_6) δ 5.82 (s, =C*H*, 2H), 2.92 (s, CH_2, 2H), 2.20 (s, NCH_3, 3H) 1.38 (s, C(CH_3)$_3$, 18H), 0.89 (s, $NCH_2C(CH_3)_3$, 9H); ^{13}C NMR (C_6D_6) δ 113.4 (=*C*H), 54.8 (^{t}Bu*C*NCH_3), 52.7 (^{t}Bu*C*NSi), 52.5 (*C*H_2), 37.5 (*C*H_3N), 30.3 (SiNC(*C*H_3)$_3$), 25.4 ($CH_2NC(CH_3)_3$); MS (EI) *m/z* (relative intensity): 100.1 (100), 44.0 (45.1), 57.1 (17.2), 423.2 (14.3) ; HRMS: 423.1567 calculated, 423.1561 found; CHN analysis – calculated for $C_{16}H_{34}IN_3Si$: C: 45.38, H: 8.09, N: 9.92; Found: C: 45.67, H: 8.25, N: 9.68.

$[(CH)_2{}^tBu_2N_2]SiI[(CH(CH_2)_4)NCH_3]$ (**12**): A 100 mL round bottom flask was charged with 231 mg (1.13 mmol, 1.1 equiv.) of Ph-I and 20 mL of *N*–methylpiperidine. A solution containing 211 mg (1.07 mmol, 1 equiv.) of **1** in 26 mL of *N*–methylpiperidine was transferred to an airtight syringe. The solution containing **1** was added to the

solution containing Ph-I at a rate of 2.85 mL/hr. After addition of **1** the solution was colorless and appeared to contain a colloid. Upon removal of volatiles a pink colored solid remained. ^{1}H NMR spectroscopy revealed that the crude reaction mixture contained less than 0.5 % of **2** and 85 % of the desired C-H activation product. 20 mL of Et_2O was used for filtering the solution and all volatiles were subsequently removed yielding a pink solid. The solid was dissolved and filtered using 10 mL of hexanes and volatiles where subsequently removed yielding a slightly tan solid. Recrystallization from hexanes provided 265 mg (56.5 %) of an off-white solid. Material suitable for X-ray analysis was grown via slow evaporation of hexanes. ^{1}H NMR (C_6D_6) δ 5.82 (d, $^{3}J_{H-H}$ = 4.2 Hz, 1H, C*H*=CH), 5.78 (d, $^{3}J_{H-H}$ = 4.2 Hz, 1H, C*H*=CH), 2.67 (br d, $^{3}J_{H-H}$ = 11.2 Hz, 1H, CH_2), 2.41 (br d, $^{3}J_{H-H}$ = 13.2 Hz, 1H, CH_2), 2.26 (dd, $^{3}J_{H-H}$ = 12.8, 2.8 Hz, 1H, C*H*), 2.14 (s, 3H, CH_3), 1.79 – 1.64 (m, 3H), 1.58 – 1.25 (m, 2H), 1.38 (s, 9H, C(CH_3)$_3$), 1.08 (s, 9H, C(CH_3)$_3$)), 0.98 (m, 1H, CH_2); ^{13}C NMR (C_6D_6) δ 113.5 (=*C*H), 113.3 (=*C*H), 60.9 (N-*C*H_2), 60.9 (N-*C*H), 52.8 (^{t}Bu*C*-N), 52.1 (^{t}Bu*C*-N), 47.3 (N-*C*H_3), 31.0 (C-(*C*H_3)$_3$), 30.6 (*C*H_2), 30.4 (C-(*C*H_3)$_3$), 26,0 (*C*H_2), 25.8 (*C*H_2); HRMS (ESI with Na^+) Calculated ($C_{16}H_{33}IN_3Si^+$) 422.1489, Found 422.1471; MS (ESI) *m/z* (relative intensity) 326.2 (100 %), 191.1 (19.6 %) 327.2 (24.8 %), 409.3 (11.3 %), 422.1 (10.21 %); CHN analysis – calculated for $C_{16}H_{32}N_3ISi$: C: 45.60, H: 7.65, N: 9.97; Found: C: 45.88, H: 7.68, N: 9.88.

Structural Determination of [(CH)$_2$^{t}Bu$_2$N$_2$]SiI[(CH(CH$_2$)$_4$)NCH$_3$] (**12**). Colorless blocks of **12** were grown from hexanes at 20 °C. A crystal of dimensions 0.33 x 0.32 x 0.22 mm was cut from a larger mass and mounted on a Bruker SMART APEX CCD-based X-ray

diffractometer equipped with a low temperature device and fine focus Mo-target X-ray tube (λ = 0.71073 A) operated at 1500 W power (50 kV, 30 mA). The X-ray intensities were measured at 85(1) K; the detector was placed at a distance 5.055 cm from the crystal. A total of 4095 frames were collected with a scan width of 0.5° in ω and 0.45° in ϕ with an exposure time of 5 s/frame. The integration of the data yielded a total of 42226 reflections to a maximum 2θ value of 66.44° of which 7220 were independent and 7053 were greater than 2σ(I). The final cell constants were based on the xyz centroids of 9947 reflections above 10σ(I). Analysis of the data showed negligible decay during data collection; the data were processed with SADABS and corrected for absorption. The structure was solved and refined with the Bruker SHELXTL (version 6.12) software package, using the space group P1bar with Z = 2 for the formula $C_{16}H_{32}N_3SiI$. All non-hydrogen atoms were refined anisotropically with the hydrogen atoms placed in idealized positions. Additional details and a CIF file have been published.[12]

$[(Me_3Si)_2CH]_2GeI[(CH_2)N(CH_3)(Ph)]$ (**23**): A 100 mL flask was charged with 301 mg (0.796 mmol, 1.0 equiv.) of **21,** 163 mg (0.799 mmol, 1.0 equiv.) of Ph-I, and 70.5 mL of Me_2NPh. The contents were stirred for 72 h over which time the solution changed from orange-yellow to very pale yellow. The volatiles were removed to give yellow solid containing only **23** as indicated by ^{1}H NMR. ^{1}H NMR (C_6D_6) δ 7.20 (pseudo t, $^3J_{H-H}$ = 7.7 Hz, *m*-Ph, 2H), 6.87 (d, $^3J_{H-H}$ = 8.0 Hz, *o*-Ph, 2H), 6.78 (t, *p*-Ph, $^3J_{H-H}$ = 7.3 Hz 1H), 3.81 (s, C*H*$_2$, 2H), 3.00 (s, NC*H*$_3$, 3H), 0.64 (s, C*H*, 2H), 0.36 (s, Si(C*H*$_3$)$_3$, 18H), 0.23 (Si(C*H*$_3$)$_3$, 18H). ^{13}C NMR (C_6D_6): δ 152.7 (*ipso*-Ph), 129.4 (*m*-Ph), 119.0 (*p*-Ph), 115.9 (*o*-Ph), 53.1 (*C*H$_2$), 43.9 (N*C*H$_3$), 12.6 (*C*H), 4.2 (*C*H$_3$Si), 4.1 (*C*H$_3$Si). EI/MS: [M-

$CH_3]^+$ = 623.8 amu; CHN analysis – calculated for $C_{22}H_{48}GeINSi_4$: C: 41.39, H: 7.58 N: 2.19; Found C: 41.49, H: 7.70, N: 1.81.

Structural Determination of $[(Me_3Si)_2CH]_2Ge[I][(CH_2)N(CH_3)(Ph)]$ (**23**): Colorless plates were grown from a pentane solution at 22 °C. A crystal of dimensions 0.60 x 0.22 x 0.08 mm was mounted on a standard Bruker SMART CCD-based X-ray diffractometer equipped with a LT-2 low temperature device and normal focus Mo-target X-ray tube (λ = 0.71073 A) operated at 2000 W power (50 kV, 40 mA). The X-ray intensities were measured at 118(2) K; the detector was placed at a distance 4.950 cm from the crystal. A total of 2837 frames were collected with a scan width of 0.2° in ω and ϕ with an exposure time of 20 s/frame. The integration of the data yielded a total of 14401 reflections to a maximum 2θ value of 56.79° of which 7426 were independent and 6274 were greater than $2\sigma(I)$. The final cell constants were based on the xyz centroids of 4518 reflections above $10\sigma(I)$. Analysis of the data showed negligible decay during data collection; the data were processed with SADABS and corrected for absorption. The structure was solved and refined with the Bruker SHELXTL (version 5.10) software package, using the space group P1bar with Z = 2 for the formula $C_{22}H_{48}Si_4NGeI$. All non-hydrogen atoms were refined anisotropically with the hydrogen atoms placed in idealized positions. Full matrix least-squares refinement based on F^2 converged at R1 = 0.0311 and wR2 = 0.0808 [based on $I > 2\sigma(I)$], R1 = 0.0400 and wR2 = 0.0850 for all data. Additional details and a CIF file have been published.[12]

$[(Me_3Si)_2CH]_2GeI[CH_2N(CH_3)(C(CH_3)_3)]$ (**24**). A 100 mL flask was charged with **21** (351 mg, 0.897 mmol, 1 equiv.), Ph-I (210 mg, 1.03 mmol, 1.1 equiv.) and 12.5 mL of Me_2N^tBu. The contents were stirred for 37 h over which time the solution changed from orange-yellow to very pale yellow. The volatiles were removed and the solid recrystallized from Et_2O/acetonitrile (CH_3CN) to yield a fine, white powder (257 mg, 46% yield). ^1H NMR (C_6D_6) δ 3.11 (s, CH_2N, 2H), 2.36 (s, $CH_2N(CH_3)(C(CH_3)_3)$, 3H), 0.98 (s, $N(CH_3)(C(CH_3)_3)$, 9H), 0.66 (s, 2H, C*H*Si, 2H), 0.40 (s, $Si(CH_3)_3$, 18H), 0.32 (s, $Si(CH_3)_3$, 18H). ^{13}C NMR (C_6D_6) δ 4.34 ($SiCH_3$), 4.51 ($SiCH_3$), 12.19 ($CH(TMS)_3$), 25.84 ($(CH_3)_3$), 39.67 (NCH_3), 53.63 ($C(CH_3)_3$), 55.59 (CH_2). EI/MS: $[M\text{-}CH_3]^+$ = 603.9 amu.

$[(Me_3Si)_2CH]_2GeI[CH_2N(CH_3)(C(CH_3)_3)]$ (**24**) synthesized using high dilution conditions. A 100 mL flask was charged with 88 mg (0.431 mmol, 1.1 equiv.) of Ph-I and 20 mL of Me_2N^tBu. A 25 mL air tight syringe filled with 20 mL of a Me_2N^tBu solution containing 154 mg (0.393 mmol, 1.0 equiv.) of **21** was added to the Ph-I solution at an rate of 3.02 mL/h. After the addition was completed, the solution was stirred for 12 hours resulting in a colorless solution containing a white precipitate. Removal of volatiles resulted in formation of a white solid, containing a 1 : 10 ratio of **13** : **24** (ratio determined by ^1H NMR with $CDCl_3$ as the solvent). The $[HNMe_2{}^tBu]I$ salt (**13**) was isolated (9 mg, 10 % yield based on **21**) by filtration from pentane. 193 mg (79 % yield based on **21**) of **24** was isolated as a white solid from the filtrate by removal of volatiles.

$[(Me_3Si)_2CH]_2GeI[(PhCH)N(CH_3)_2]$ (**25a**) and $[(Me_3Si)_2CH]_2GeI[(PhCH_2)N(CH_2)(CH_3)]$ (**25b**): A 100 mL flask was charged with 124 mg (0.317 mmol, 1 equiv.) of **21**, 25 mL of Me_2NCH_2Ph, and 105 mg of Ph-I (0.515 mmol, 1.6 equiv.). Solution was left to stir until colorless. Volatiles removed under dynamic vacuum. ^{1}H NMR of crude reaction mixture showed 3 products present in a 2:2:1 ratio. 40 % **25a**, 40 % **25b** and 20 % of $[(Me_3Si)_2CH]_2GeI(Ph)$. We were unable to separate **25a** from **25b** and we were unable to obtain a ratio of **25a**:**25b** that was not 1:1. ^{1}H NMR (C_6D_6) δ 7.53 (d, $^3J_{H\text{-}H}$ = 7.0 Hz, 2H, *o*-Ph), 7.41 (d, $^3J_{H\text{-}H}$ = 7.1 Hz, 2H, *o*-Ph), 7.20 (t, $^3J_{H\text{-}H}$ = 7.7 Hz, 2H, *m*-Ph), 7.18 – 7.14 (m, 2H, *p*-Ph), 7.10 (t, $^3J_{H\text{-}H}$ = 7.2 Hz, 2H, *m*-Ph), 4.04 (s, 1H, NC*H,* **25a**), 3.60 (s, 2H, CH_2,, **25b**), 2.92 (s, 2H, CH_2, **25b**), 2.27 (s, 3H, CH_3, **25b**), 2.17 (s, 6H, CH_3, **25a**), 0.98 (s, 1H, C*H*(TMS)$_3$, **25a**), 0.59 (s, 2H, C*H*(TMS)$_3$, **25b**), 0.58 (s, 1H, C*H*(TMS)$_3$, **25a**), 0.46 (s, 9H, Si(CH_3)$_3$, **25a**), 0.40 (s, 9H, Si(CH_3)$_3$, **25a**), 0.39 (s, 18H, Si(CH_3)$_3$, **25b**), 0.29 (s, 18H, Si(CH_3)$_3$, **25b**), 0.25 (s, 9H, Si(CH_3)$_3$, **25a**), 0.10 (s, 9H, Si(CH_3)$_3$. **25a**); ^{13}C NMR (C_6D_6) δ 138.7 (*ipso*-Ph), 133.5 (*ipso*-Ph), 132. 5 (*o*-Ph – ^{1}H 7.53 ppm), 129.6 (*o*-Ph – ^{1}H 7.41 ppm), 128.5 (*m*-Ph – ^{1}H 7.20 ppm), 128.3 (*p*-Ph – ^{1}H 7.18-7.14 ppm), 127.8 (*p*-Ph – ^{1}H 7.18-7.14 ppm), 127.4 (*m*-Ph – ^{1}H 7.10 ppm), 69.0 (N*C*H. **25a**), 66.8 (*C*H_2, **25b**), 57.3 (CH_2, **25b**), 45.5 (CH_3, **25b**), 44.8 (CH_3. **25a**), 13.7 (*C*H(TMS)$_3$. **25a**), 13.4 (*C*H(TMS)$_3$. **25a**), 12.7 (*C*H(TMS)$_3$, **25b**), 4.9 (Si*C*H_3. **25a**), 4.8 (Si*C*H_3. **25a**), 4.6 (Si*C*H_3. **25a**), 4.4 (Si*C*H_3. **25a**), 4.2 (Si*C*H_3, **25b**), 4.1 (Si*C*H_3, **25b**). EI/MS: $[M\text{-}CH_3]^+$ = 638.0 amu; CHN analysis – calculated for $C_{23}H_{50}GeINSi_4$: C: 42.34, H: 7.72 N: 2.15; Found C: 42.45, H: 7.85, N: 1.84.

$[(Me_3Si)_2CH]_2GeI[CH_2N(CH_3)(CH_2N(CH_3)_2)]$ (**26**): A 100 mL flask was charged with 248 mg (0.634 mmol, 1 equiv.) of **21**, 20 mL of $Me_2NCH_2NMe_2$, and 171 mg (0.838 mmol, 1.3 equiv.) of Ph-I. The amber colored solution was allowed to stir for 12 hrs, at which time the reaction was colorless and contained a white precipitate. Removal of volatiles afforded a white oily solid. The white solid was removed via a filtration with pentane solvent. 374 mg (0.604 mmol, 95 % yield based on **21**) of a clear oil was recovered, corresponding to **26**. The white solid remaining after filtration was 39 mg of $[Me_2N{=}CH{-}NMe_2]I$ (0.171 mmol, 26 % yield based on **21**). ^{1}H NMR (C_6D_6) δ 2.90 (s, N-C*H*$_2$-N, 2H), 2.77 (s, Ge-C*H*$_2$-N, 2H), 2.56 (s, N-C*H*$_3$, 3H), 2.19 (s, N-(C*H*$_3$)$_2$, 6H), 0.63 (s, 2H, C*H*(TMS)$_2$), 0.40 (s, 18H, Si(C*H*$_3$)$_3$), 0.30 (s, 18H, Si(C*H*$_3$)$_3$); ^{13}C NMR (C_6D_6) δ 85.6 (N-*C*H$_2$-N), 55.3 (N-CH$_2$-Ge), 44.0 (N*C*H$_3$), 43.8 (N*C*H$_3$), 12.5 (*C*H(TMS)$_3$), 4.2 (Si*C*H$_3$), 4.1 (Si*C*H$_3$).

$[(Me_3Si)_2CH]_2Ge[H][I]$ (**27**): A 100 mL flask was charged with 350 mg (0.894 mmol, 1 equiv.) of **21**, 200 mg of Ph-I (0.983 mmol, 1.1 equiv.) and 18.5 mL of Et_3N. The contents were allowed to stir for 13 h, over which time the solution changed from orange-yellow to almost colorless, faint yellow to eventually a darker brownish yellow. Then the volatiles were pumped off under dynamic vacuum for 2 hours. Approximately an hour later the oil began to crystallize. Three successive recrystallizations out of THF/CH_3CN gave 0.065g white solid. ^{1}H NMR (C_6D_6): δ 0.17 (s, 18H, Si*Me*$_3$), 0.31 (s, 18H, Si*Me*$_3$), 0.38 (d, $^3J_{HH}$ = 2.8 Hz, 2H, GeC*H*Si), 5.17 (t, $^3J_{HH}$ = 2.8, 1H, Ge*H*). ^{13}C NMR (C_6D_6): δ 9.14 (Ge*C*HSi), 3.27 and 2.4 (Si(*C*H$_3$)$_3$). IR (cm^{-1}): 2031 *v* (Ge-H). EI/MS: $[M\text{-}CH_3]^+$

= 505.0 amu. CH analysis – calculated for $C_{14}H_{39}GeISi_4$: C 32.38, H 7.57; found: C 32.59, H 7.70.

Structural Determination of (**27**): Colorless blocks were grown from a Et_3N solution at 22 °C. A crystal of dimensions 0.38 x 0.32 x 0.20 mm was mounted the same as crystals **12** and **23**. The X-ray intensities were measured at 150(2) K; the detector was placed at a distance 4.950 cm from the crystal. A total of 3267 frames were collected with a scan width of 0.2° in ω and ϕ with an exposure time of 20 s/frame. The integration of the data yielded a total of 12948 reflections to a maximum 2θ value of 56.58° of which 5928 were independent and 5726 were greater than 2σ(I). The final cell constants were based on the xyz centroids of 5555 reflections above 10σ(I). Analysis of the data showed negligible decay during data collection; the data were processed with SADABS and corrected for absorption. The structure was solved and refined with the Bruker SHELXTL (version 5.10) software package, using the space group Cc with Z = 4 for the formula $C_{14}H_{39}Si_4GeI$. All non-hydrogen atoms were refined anisotropically with the hydrogen atoms placed in idealized positions. Full matrix least-squares refinement based on F^2 converged at R1 = 0.0189 and wR2 = 0.0502 [based on I > 2σ(I)], R1 = 0.0192 and wR2 = 0.0504 for all data. Additional details and a CIF file have been published.[12]

General procedure for independent preparation of [HNR_3]I salts.

4 mL of HI (aq) acid was added to a 20 mL scintillation vial, followed by 8 mL of R_3N. The solution was stirred for 30 minutes in a water bath. If a biphasic solution was not present after 30 minutes, an additional 2 mL of R_3N was added and solution allowed

to stir an additional 30 minutes. Volatiles where removed and the resulting solution was placed under vacuum to remove residual water and R_3N. A white solid soluble in $CDCl_3$ was obtained in all cases.

$[HN(CH_3)_2{}^tBu]I$ (**12**) : ^1H NMR ($CDCl_3$) δ 10.25 (br, N-*H*, 1H), 2.72 (s, N-C*H*$_3$, 6H), 1.51 (s, (C(C*H*$_3$)$_3$), 9H). ^{13}C NMR ($CDCl_3$) δ 63.1 (*C*-$(CH_3)_3$), 38.2 (N-*C*H_3), 25.1 (C-(*C*H_3)$_3$). MS (ESI) positive ion: 331.1; negative ion: 126.9.

$[HNMe(C_5H_{10})]I$ (**14**) : ^1H NMR δ ($CDCl_3$): 9.6 (br, N-H, 1H), 3.42 (d, $^3J_{H-H}$ = 10.8 Hz, N-C*H*$_2$, 2H), 3.00 (t, $^3J_{H-H}$ = 11.8 Hz, N-C*H*$_2$, 2H), 2.76 (s, N-C*H*$_3$, 3H), 2.14 (br d, $^3J_{H-H}$ = 12.8 Hz, NCH_2-C*H*$_2$-CH_2, 2H), 1.87 (br d, $^3J_{H-H}$ = 14.0 Hz, NCH_2-C*H*$_2$-C*H*$_2$, 3H), 1.52 (br d, $^3J_{H-H}$ = 12.4 Hz, NCH_2CH_2-C*H*$_2$, 1H); ^{13}C NMR ($CDCl_3$) δ 54.96 (N-*C*H_2), 44.08 (N-*C*H_3), 22.73 (NCH_2-*C*H_2), 20.99 (NCH_2CH_2-*C*H_2). MS (ESI) positive ion: 327.1 (100 %), 100.1 (34.5 %), 328.2 (13.4 %); negative ion: 126.9 (100 %).

$[HNEt_3]I$: ^1H NMR ($CDCl_3$) δ 10.06 (br, 1 H, *H*N), 3.19 (qd, $^3J_{H-H}$ = 7.4, 5.1 Hz, 6H, C*H*$_2$), 1.43 (br t,$^3J_{H-H}$ = 7.4 Hz, 9H, C*H*$_3$); ^{13}C NMR ($CDCl_3$) δ 46.3 (*C*H_2), 8.6 (*C*H_3); MS (ESI) positive ion: 331.2; negative ion: 126.9

$[HN{}^iPr_3]I$: ^1H NMR ($CDCl_3$) δ 10.14 (br, 1 H, *H*N), 3.01 (dt, $^3J_{H-H}$ = 12.3, 4.6 Hz, 6H, N-C*H*$_2$), 1.89 (m, 6H, C*H*$_2$-CH_3), 1.01 (t,$^3J_{H-H}$ = 7.4 Hz, 9H, C*H*$_3$); ^{13}C NMR ($CDCl_3$) δ

54.2 (N-*C*H_2), 16.8 (*C*H_2-CH_3), 11.2 (*C*H_3); MS (ESI) positive ion: 144.2; negative ion: 126.9.

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Chapter 4- Calculation of Primary and Aryl Isotope Effects and a Plausible Reaction Mechanism Accounting for Formation of Side Products

4.1- Previous Germylene/Ar-X C-H Activation Mechanistic Work

4.1.1- Rate Law Expression from Kinetic Measurements

A partial rate law expression was derived for the reaction of $(TMS_2HC)_2Ge$ (**21**)/Ph-Br with THF. Banaszak Holl et al. used pseudo first order conditions to determine the reaction order for the C-H activation of THF with **21**/Ph-Br. Using UV-vis as the method for monitoring the consumption of **21**, the kinetic traces were best fit with a linear regression using a plot of 1/Absorption vs. time, meaning the reaction demonstrated a second order dependence on **21**. The partial rate law expression derived by Banaszak Holl et al. is shown in **Figure 4.1**. When the kinetic experiment was repeated with **21**/Ph-Br-d_5 a change in reaction rate was observed, corresponding to a 2.28 times faster reaction of **21**/Ph-Br when compared with the **21**/Ph-Br-d_5 C-H activation of THF.

Figure 4.1- Rate Law Expression for C-H Activation Reaction

$$[\text{rate}] = k\,[\mathbf{21}]^2\,[\text{Ar-X}]^m\,[\text{R-H}]^n$$

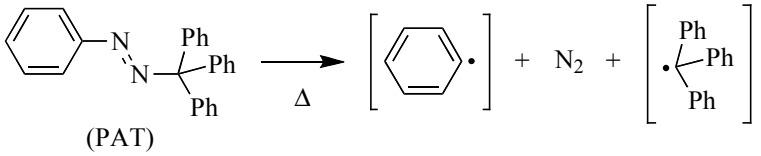
4.1.2- Primary Kinetic Isotope Effects

Banaszak Holl et al. have C-H activated deuterium labeled substrates for the purposes of calculating the primary kinetic isotope effect (KIE) and comparing the C-H activation reactions with aryl radicals abstracting H atoms. The fate of the activated H

was identified by identifying that reactions of $(TMS_2CH)_2Ge$ (**21**)/Ph-I or $(TMS_2N)_2Ge$ (**31**)/Ph-I with THF formed C_6H_6, while reactions of **21**/Ph-I or **31**/Ph-I with THF-d_8 formed C_6H_5D.[1]

Banaszak Holl et al. tested the hypothesis that an aryl radical was breaking the C-H bond at the RDS by comparing the KIE for H atom abstraction of **21**, **31** and phenyl-diazo-triphenylmethane (PAT), a compound that decomposes to form a phenyl radical upon heating to 60 °C or higher, see **Figure 4.2**.[2] The primary KIE's reported by

Figure 4.2- Thermal Decomposition of Phenyl-diazo-triphenylmethane (PAT)



(PAT)

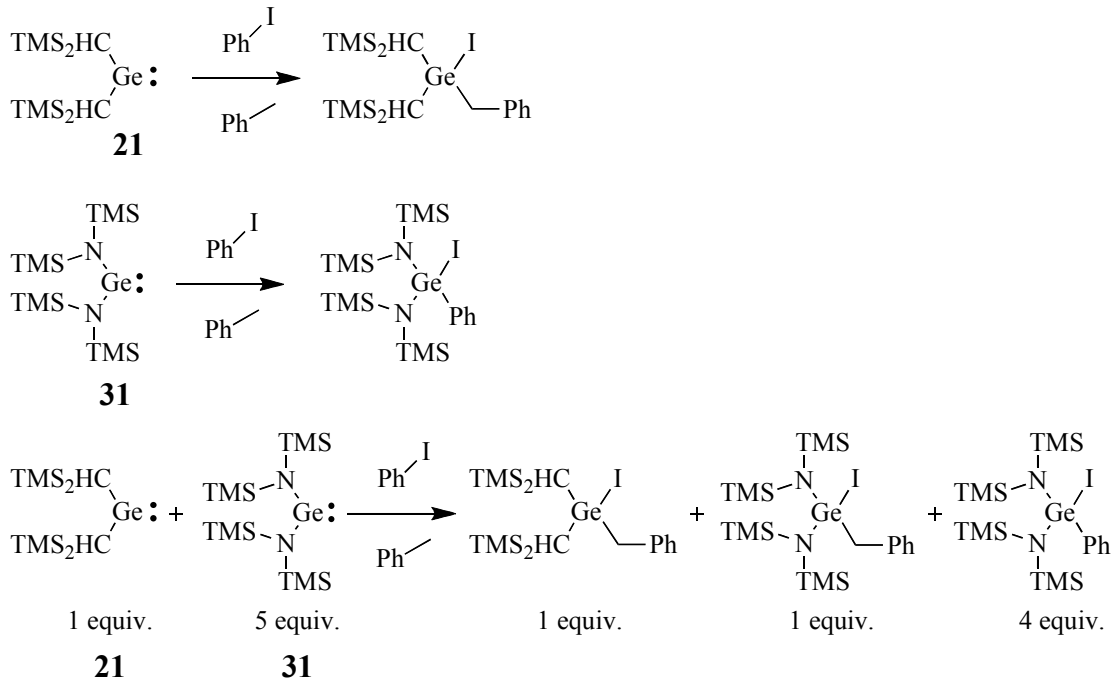
Banaszak Holl et al. for C-H abstraction of THF/THF-d_8, at 60 °C are: 4.3 ± 0.4 for PAT, 4.1 ± 0.2 for **31**/Ph-I and 5.0 ± 0.2 for **21**/Ph-I. These primary KIE's are relatively similar in magnitude, but the primary KIE's are statistically different across the collected data set. The data set for the H atom abstraction KIE's was interpreted as the C-H activation reactions not involving a solvated phenyl radical intermediate breaking the C-H bond at the RDS. Additionally, the lack of aryl-aryl, substrate-substrate or aryl-substrate radical coupled products further supported that radical intermediates remain within a solvent cage. Additionally, a phenyl radical as the intermediate breaking the C-H bond at the rate-determining step was tested by comparing the hydrogen atom abstraction KIE for **21**/Ph-I, **31**/Ph-I and PAT (a source of a phenyl radical) with a cumene/THF-d_8 mixture.[3] The difference in reactivity and difference KIE's of **21**/Ph-

I, **31**/Ph-I and PAT indicate a phenyl radical is not the active species that breaks the C-H bond at the rate-determining step.

4.1.3- Competition Reactions with Toluene as Substrate

A curious experimental observation made by Banaszak Holl et al. was the difference in reactivity of **21**/Ph-I and **31**/Ph-I with toluene as the potential C-H activation substrate. The benzylic C-H bond of toluene was activated with **21**/Ph-I, yet **31**/Ph-I did not form a C-H activation product with toluene. When 5 equivalents of **31**, 1 equivalent of **21** and then 6 equivalents of Ph-I where combined in toluene, 1 equivalent of the benzylic C-H activation product derived from **31** and 4 equivalents of the expected OA product of **31** were observed along with the benzylic C-H activation product derived from **21**, see **Scheme 4.1**. The change in reactivity of **31**/Ph-I with toluene due to the presence of **21** supports the reaction being second order with respect to the germylene.

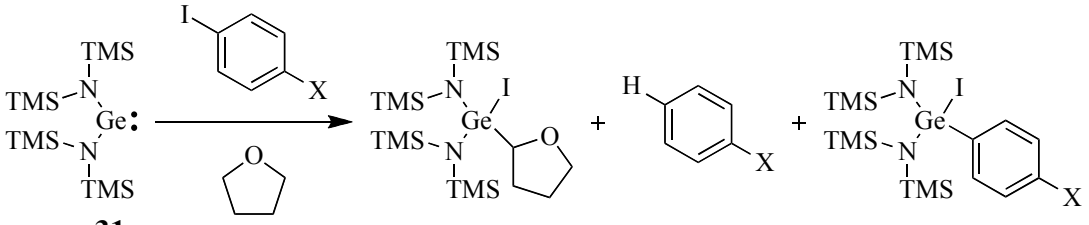
Scheme 4.1- Evidence for Second Order Dependence of Germylene



4.1.4- Hammett Plot: Affect of Substituted Aryl Halides

Jeff Bartolin used various *para* substituted aryl iodides for the purpose of constructing a Hammett plot. The Hammett plot was used for understanding more about the nature of the RDS. The reactions of **21**/Ph-I and **31**/Ph-I are known to produce two products: OA and C-H activation. Presuming the relative rate of C-H activation is directly proportional to the percentage of C-H activation product observed, the original reaction rate (K_o) and the reaction rate (K) were interpreted as the percentage of C-H activation product. Reactions of **31** with various *para* substituted aryl halides produced the data set for log (K/K_o) seen in **Table 4.1**.[4] The best linear fit of the data was observed using σ_I rather than σ_M, σ_R, σ_P or σ. The slope of the linear regression fit was 0.18, a ρ value of 0.18, which would be consistent with a negative charge build up on the aromatic ring. Additionally, the magnitude of $\rho<1$ would be consistent with the C-H activation reaction being relatively insensitive to electronic changes of the aryl halide.

Table 4.1- Data Set Used for Construction of Hammet Plot



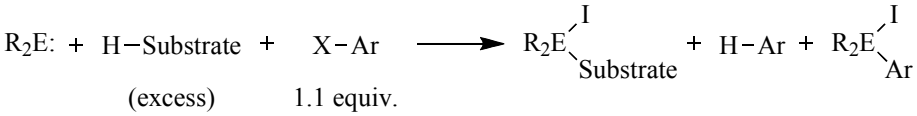
31

1-X-4-Iodobenzene	% of C-H Activation	log (K/K_o)	σ_I	σ_m	σ_p	σ_R
H	65	0.00	0.00	0.00	0.00	0.00
CH_3	67	0.01	0.01	-0.06	-0.14	-0.11
I	77	0.07	0.42	0.34	0.28	-0.16
Cl	83	0.11	0.47	0.37	0.24	-0.23
F	82	0.10	0.52	0.34	0.15	-0.32
CN	82	0.10	0.57	0.62	0.71	0.13

4.2- Primary Kinetic Isotope Effect for C-H Activation using 1/Ph-I

The primary KIE of the **1**/Ph-I based C-H activation of Et_2O was consistent with breaking of the C-H bond at or before the RDS. Using competition reaction conditions for the C-H activation of Et_2O/Et_2O-d_{10}, the experimentally determined primary KIE was calculated as 5.7 ± 0.1. The primary KIE for the **1**/Ph-I C-H activation reaction of Et_2O was of a similar magnitude to the primary KIE for hydrogen abstraction of THF/THF-d_8 using PAT, see **Table 4.2**.

Table 4.2- Primary KIE for C-H Activations with **1**/Ph-I, **21**/Ph-I and **31**/Ph-I



R_2E:	H-Substrate	Ar-X (Temp.)	KIE
$[H_2C_2{}^tBu_2N_2]Si$	Et_2O / Et_2O-d_{10}	C_6H_5I (rt)	5.7 ± 0.1
$[TMS_2HC]_2Ge$	THF / THF-d_8	C_6H_5I (60 °C)	5.0 ± 0.2
$[TMS_2N]_2Ge$	THF / THF-d_8	C_6H_5I (60 °C)	4.1 ± 0.2
PAT	THF / THF-d_8	(60 °C)	4.2 ± 0.2

The primary KIE was determined by calculating the Ph-H to Ph-D ratio from the reaction of **1**/Ph-I with a nominally 1:1 mixture of non-labeled and deuterium labeled substrate. Gas chromatography-mass spectroscopy (GC-MS) was used to separate Ph-H and Ph-D from other volatiles while providing the quantitative ratio of the compounds. To ensure accuracy of the MS data, standards of the labeled and non-labeled compounds were also analyzed with the same GC-MS instrument, and on the same day, used for calculating the KIE of a reaction. The KIE was calculated through curve fitting of the Ph-H and Ph-D reaction mixture to the MS of Ph-H and Ph-D standards. The calculated ratio of Ph-H to Ph-D was then corrected for the actual ratio of labeled and non-labeled

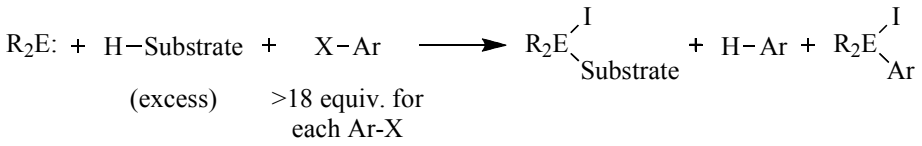
starting material present in the nominal 1:1 mixture. Each reaction was run as a minimum of three separate reactions, with each reaction analyzed by GC-MS a minimum of three times. Prior, during or after obtaining a data set the standard Ph-H and Ph-D samples were run to assure consistency of the calculated Ph-H to Ph-D ratio. When calculating the MS ratio of Ph-H to Ph-D, the normalization of the calculated curves was essential because the standard MS of Ph-H and Ph-D were normalized.

The calculated primary KIE is consistent with the activated C-H bond breaking at or before the RDS. The GC-MS analysis lacked any aryl-aryl, solvent-aryl or solvent-solvent radical coupled products. A lack of the aforementioned radical coupled products is consistent with a lack of long-lived solvated radical intermediates. Additionally, a single electron transfer (SET) mechanism would most likely involve short-lived radical intermediates, which would be consistent with a lack of detecting radical coupled products.

4.3- Isotope Effect from the Aryl Halide

Isotope labeling of aryl halides was used for calculating a KIE value for the aryl halide portion of the C-H activation reaction. As mentioned previously, a rate increase of 2.28 was observed for the C-H activation of THF with **21**/Ph-Br when compared to the corresponding **21**/Ph-Br-d_5 reaction. A set of experiments was carried out with labeled aryl halides for understanding the apparently large KIE arising from the aryl halide. Data collection for calculating the aryl KIE measurements were obtained with GC-MS, rather than the UV-vis kinetics analysis previously employed. The isotope labeled aryl halides used were 3-C_6H_4DBr, 4-C_6H_4DBr, C_6D_5I and C_6D_5Br. Reactions were run and analyzed

Table 4.3- Calculated Aryl KIE Values

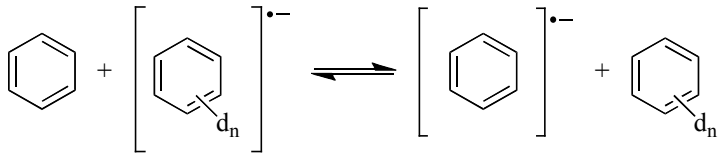


R_2E:	H-Substrate	X-Ar	KIE
$[H_2C_2{}^tBu_2N_2]Si$	Et_2O	C_6H_5I / C_6D_5I	1.3 ± 0.1
		C_6H_5I / 4-C_6H_4DI	1.1 ± 0.1
		C_6H_5I / 3-C_6H_4DI	1.1 ± 0.1
		C_6H_5Br / C_6D_5Br	1.3 ± 0.2
$[TMS_2HC]_2Ge$	THF	C_6H_5Br / C_6D_5Br	1.8 ± 0.1
	Et_2O	C_6H_5I / C_6D_5I	1.6 ± 0.1
		C_6H_5I / 4-C_6H_4DI	1.3 ± 0.1
		C_6H_5I / 3-C_6H_4DI	1.3 ± 0.1
		C_6H_5Br / C_6D_5Br	1.7 ± 0.2

using the same manner reported for the primary KIE data sets and a summary of the aryl halide KIE's are given in **Table 4.3**.

The origins of the aryl KIE are of interest for understanding what type of intermediates are formed along the reaction pathway. Aryl isotope effect values have been reported for the equilibrium ratios of aryl radical anions that are similar in magnitude to the isotope effect values measured for the C-H activation reactions.[5, 6] The reported aryl radical anion equilibrium isotope effects are summarized in **Table 4.4**.[5] One fault with drawing analogies based only on the equilibrium isotope values of the aromatic ring is the lack of a halide on the aromatic rings. Kochi et al. have shown that an aryl halide radical anion rapidly breaks down to the halide anion and aryl radical.[7] The equilibrium isotope effects are similar in magnitude to the calculated KIEs, an aryl

Table 4.4- Equilibrium Isotope Effect of Benzene Radical Anions

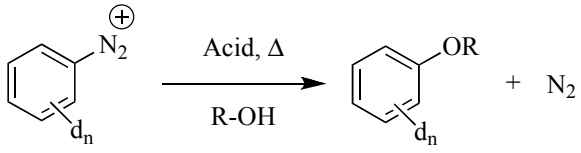


Ar-H	Ar-D	Equilibrium Isotope Effect
C_6H_6	C_6H_5D	1.16
	1,2-$C_6H_4D_2$	1.82
	1,4-$C_6H_4D_2$	1.79
	1,3,5-$C_6H_3D_3$	2.7
	C_6D_6	3.85

iodide or aryl bromide will not be in equilibrium with the corresponding aryl halide radical anion.

The thermal decomposition of diazobenzenes could provide a more realistic comparison of aryl KIE values. The C-H activation reaction breaks the Ar-X bond during the course of the reaction, similarly the Ar-N_2^+ bond is broken during the thermal decomposition of diazobenzenes. The published aryl KIE values for diazobenzenes

Table 4.5- KIE for the Thermal Decomposition of Diazobenzene



$ArHN_2^+$	$ArDN_2^+$	KIE
$C_6H_5N_2^+$	4-$C_6H_5DN_2^+$	1.02
	3,5-$C_6H_3D_2N_2^+$	1.18
	2,4,6-$C_6H_2D_3N_2^+$	1.52
	$C_6D_5N_2^+$	1.79
	2-$C_6H_4DN_2^+$	1.21

thermal decomposition are summarized in **Table 4.5**.[8] Initially the calculated aryl KIE's for the C-H activation seemed surprisingly large, but the magnitude of calculated aryl KIE's are consistent with the aryl C-X bond breaking at or before the rate-determining step (RDS).

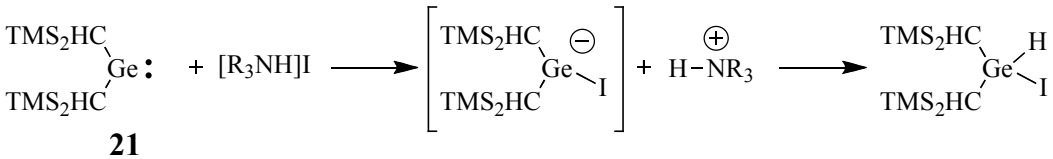
4.4- Role of Ammonium Iodide Salts in Reactions

*4.4.1- Fate of Ammonium Salts in Reactions with **21**/Ph-I*

The role of $[R_3NH]I$ type salts in reactions of **21**/Ph-I has been rationalized, but the mechanism of the $[R_3NH]I$ salt formations is not obvious. The observance of $[Me_2{}^tBuNH]I$ lead to the initial speculation of $[R_3NH]I$ salts being an intermediate in the formation of R_2GeHI. Two independent experimental conditions were found that resulted in formation of the R_2GeHI product. One method involves addition of **21**, the $[R_3NH]I$ salt and the corresponding amine in a reaction vessel. The second method involves addition of **21**, tertiary amine and Ph-I into a reaction vessel. The two independent methods forming the same product demonstrates $[R_3NH]I$ salts are kinetically competent intermediates in the formation of R_2GeHI from **21**/Ph-I and tertiary amines.

Two possible pathways have been considered as rational mechanisms for the formation of R_2GeHI when mixing $[R_3NH]I$ salts and **21** in amine solvents. One pathway, **Scheme 4.2**, involves the formation of a Lewis Acid-Base adduct from the complexation of iodide with the germylene. The newly formed germyl anion subsequently deprotonates $[R_3NH]^+$, thus forming R_2GeHI. A second pathway involves **21** first deprotonating $[R_3NH]^+$. The deprotonation results in formation of the Lewis Acidic intermediate $[R_2GeH]^+$, that upon complexation with iodide forms R_2GeHI. The

Scheme 4.2- A Proposed Mechanism for Formation of R_2GeHI



Lewis Acidic and Lewis Basic nature of **21** makes eliminating either pathway difficult. At this time, only speculative theories exist for how the $[R_3NH]I$ salts are formed *in situ* when **21** and Ph-I are combined with tertiary amines.

The lack of formation of C-H activation products when using $[R_3NH]I$ salts and **21** suggests the formation of $[R_3NH]I$ is not an intermediate along the mechanistic pathway for the C-H activation of tertiary amines with **21**/Ph-I. A mechanism that allows for formation of $[R_3NH]I$ from **21**/Ph-I and tertiary amines having α and β C-H bonds will help explain the formation of the non-C-H activation products.

*4.4.2- Role of Ammonium Salts in Reactions of **1**/Ph-I*

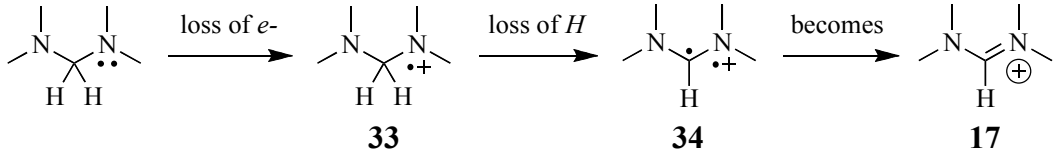
From results presented in chapter 3, the reactivity of **1**/Ph-I and **21**/Ph-I with tertiary amines was observed to be different in various instances. The isolation of a $[R_3NH]I$ salt only occurred for the C-H activation reactions of Me_2N^tBu. The role of the $[R_3NH]I$ salts would be expected to vary for reactions of **1**/Ph-I, as no R_2SiHI products have been identified for reactions involving tertiary amines and **1**/Ph-I. Combining a $[R_3NH]I$ salt, **1**, and a tertiary amine substrate in a reaction vessel resulted in the formation of $R_2SiH(NR'_2)$ type products, and a lack of R_2SiHI or C-H activation products. The two $R_2SiH(NR'_2)$ type products were independently synthesized by combining $[Et_3NH]I$ with **1** in Et_3N or $[Pr_3NH]I$ with **1** in Pr_3N. As was the case for reactions of **21**/Ph-I with tertiary amines, the *in situ* formation of a $[R_3NH]I$ salt would account for the formation of the formation of the $R_2SiH(NR'_2)$ side products. What can

be speculated is that in the case of **1**/Ph-I C-H activating tertiary amines, the reaction manifold that results in formation of $[R_3NH]I$ salts is disfavored due to the small ratio of $R_2SiH(NR'_2)$ type products formed.

4.4.3- Formation of the Iminium Iodide Salt $[Me_2NCHNMe_2]I$

The reaction of **21**/Ph-I with $Me_2NCH_2NMe_2$ resulted in formation of a single C-H activation product and a second compound, the salt $[Me_2NCHNMe_2]I$ (**17**). The preferred mechanism for justifying formation of **17** from the reaction of **21**/Ph-I with $Me_2NCH_2NMe_2$ involves a single electron transfer (SET) type mechanism. As shown in **Scheme 4.3**, formation of the radical cation of $Me_2NCH_2NMe_2$ (**33**) would result in direct

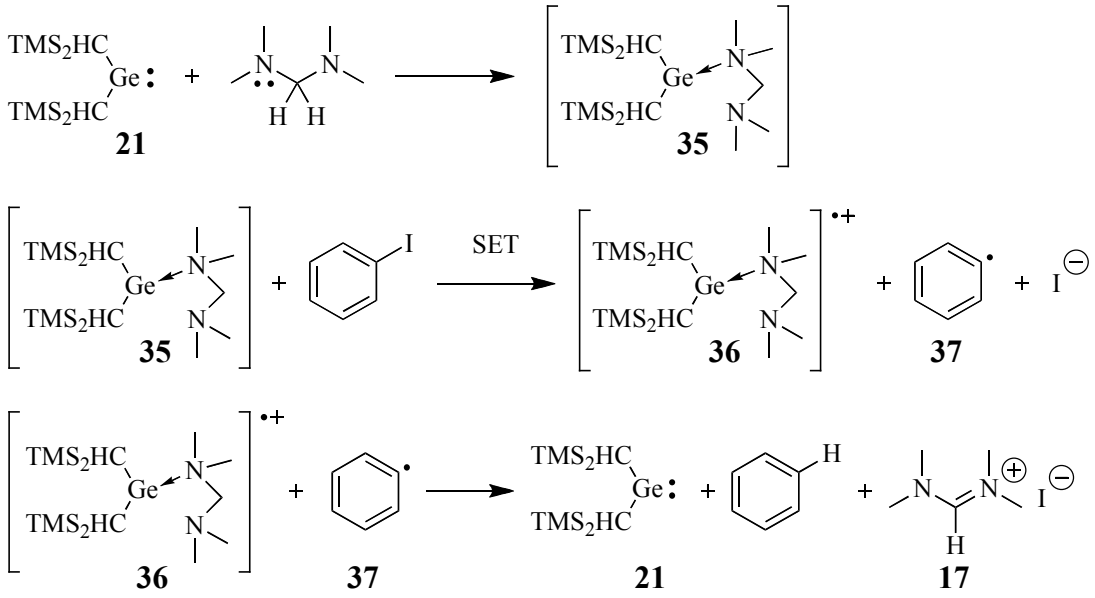
Scheme 4.3- Possible Mechanism for Formation of $[Me_2NCHNMe_2]I$



33 **34** **17**

formation of **17** via an H atom abstraction of **33** to form **34**, with **34** directly converting into **17**. The SET from a tertiary amine nitrogen is atypical under ambient conditions, leading to the presumption that a complex formed between **21** and the amine, compound **35**, would facilitate the SET. Invoking a SET transfer from **35** would form the cationic radical complex, compound **36**. The molecular orbit of the aryl halide most likely to accept the electron is the unoccupied π-orbital of aromatic ring. As stated previously, the transfer of an electron onto an aryl halide results in the rapid formation of the aryl radical, compound **37**, and the corresponding halide.[7] The abstraction of a methylene hydrogen by **37** forms **17**, an equivalent of benzene and would reform **21**, see **Scheme 4.4**. Slight adaptations to the mechanism shown below could provide a mechanism that accounts for the C-H activation and formation of various side products.

Scheme 4.4- Proposed Mechanism for Formation of $[Me_2NCHNMe_2]I$



4.5- Plausible Mechanism for C-H Activation Reactions of Amines

Previous mechanistic work by Banaszak Holl et al. on the C-H activation reaction was summarized in section 4.1. The key points to remember are (a) the reaction demonstrates a second order dependence on the divalent compound (b) primary KIE's were consistent with the C-H bond being broken at or before the rate determining step and (c) a solvated aryl radical intermediate is not breaking the C-H bond at the rate determining step. Additionally, C-H activation reactions using $([CH_2CTMS_2]_2)Sn$/Ph-I have formed products consistent with the addition of a phenyl radical and a Sn radical fragment across a C-C π-bond.[9] Furthermore, radical cyclizations are observed when $([CH_2CTMS_2]_2)Sn$ and aryl halides with homoallylic or homopropargyllic π-bonds on *ortho* groups are combined.

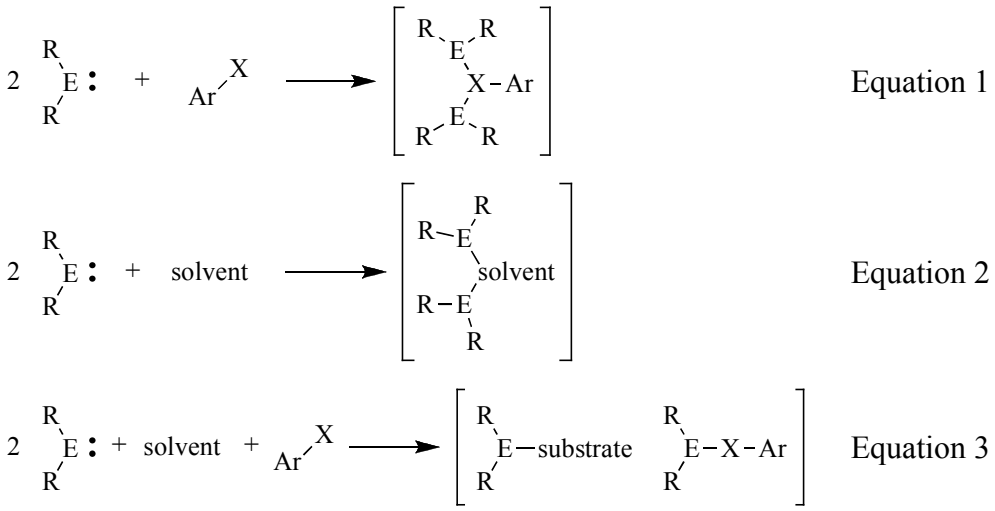
Extrapolating from the empirical results for the OA of silylenes with halocarbons, the presumption that C-H activation reactions involving **1**/Ph-I could be second order

with respect to the R_2E species, just like **21**/Ar-X reactions, appears to be a plausible presumption. Additionally the primary and secondary KIE's for the C-H activation reactions involving **1** and **21** are consistent with the C-H bond and the Ar-X bond breaking at or before the RDS.

The formation of side products provided insight to the type of intermediates formed in the reaction mechanism. The reactions of **21**/Ph-I with tertiary amines having C-H bonds α and β to the amine nitrogen forming R_2GeHI products can be accounted for with the *in situ* formation of $[R_3NH]I$ salts. For the **1**/Ph-I reactions, an *in situ* formation of $[R_3NH]I$ salts can account for the formation of the minor $R_2SiH(NR'_2)$ type products. The reactions of **1**/Ph-I and **21**/Ph-I with tertiary amines suggest $[R_3NH]I$ is formed during the course of the reaction, and the $[R_3NH]I$ compounds are not kinetically competent intermediates that lead to C-H activation products.

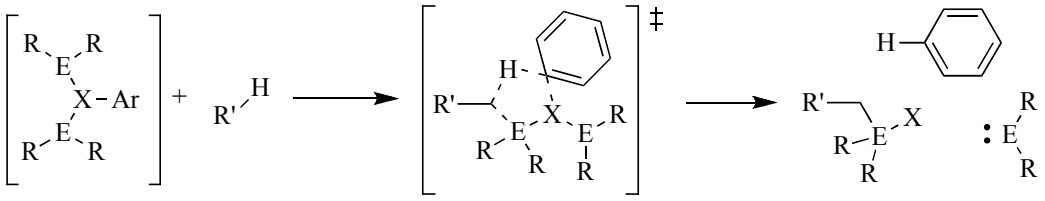
With slight adjustments to the mechanism shown in **Scheme 4.4** a rational mechanism can be derived that will account for the products formed and the essential mechanistic features. The proposed first step of the reaction is an equilibrium complexation step, see **Figure 4.3**. Three possible equilibrium complexations can be imagined: 2 equivalents of R_2E forming a complex with Ar-X (Equation 1), 2 equivalents of R_2E forming a complex with solvent (Equation 2) or one R_2E forming a complex with solvent and the second R_2E forming a complex with Ar-X (Equation 3). The three proposed activation complexes would all be second order with respect to R_2E.

Figure 4.3- Proposed Active Complexes of C-H Activation Mechanism



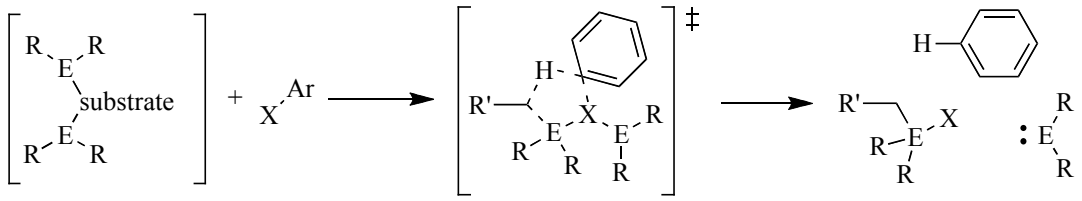
The complex shown in Equation 1 lacks the substrate that will be C-H activated. Formation of a transition state similar to the one shown in **Figure 4.4** would meet the criteria of the reaction being second order with respect to the R_2E, the C-H bond being broken at or before the transition state and the Ar-X bond breaking at or before the transition state.

Figure 4.4- R_2E-ArX Complex as Intermediate of C-H Activation Reactions



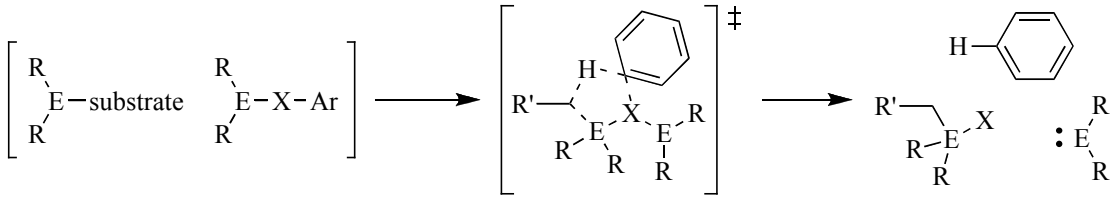
The active complex shown in Equation 2 lacks the Ar-X that is essential for observing the C-H activation reactions. When a molecule of Ar-X comes within proximity of the active complex, the reaction shown in **Figure 4.5** would lead the C-H activation reactions. The transition state structure is identical to the transition state structure from **Figure 4.4**.

Figure 4.5- R_2E-substrate Complex as Intermediate of C-H Activation Reactions



The third complexation reaction, Equation 3, requires two active complexes to come within proximity of each other. As shown in **Figure 4.6**, when the two complexes are in proximity and aligned, the identical transition state structure can occur.

Figure 4.6- Two Complexes Aligning Resulting in C-H Activation



All three proposed complexes can be used to rationalize the formation the C-H activation products. The formation of the oxidative addition (OA) product can be formed by the direct reaction of Ar-X with R_2E, a non-C-H activation reaction mechanism. As mentioned in section 1.7, shown for the OA of silylene in **Figure 1.6**, it is not unreasonable to presume the OA reaction is second order with respect to R_2E. The utility of forming an active complex like that of Equation 2 is the complexation of R_2E with an amine substrate is similar to the mechanism shown in **Scheme 4.4** for the formation of **17**. Diversion of the complex from Equation 2 to the SET mechanism of **Scheme 4.4** would account for formation of C-H activation products and formation **17**. The proposed reaction mechanism is first formation of an active complex, like the three different complexation reactions shown in **Figure 4.3**. The proposed transition state structure is

based on the following points: (a) the rate law for the reaction is second order with respect to R_2E (b) the C-H bond is broken at or before the RDS and (c) the Ar-X bond is broken at or before the RDS. To achieve this type of transition state, an SET occurs from the active complex to Ar-X, which will rapidly become the corresponding halide anion and aryl radical if no other reaction pathways are immediately available. The incipient aryl radical abstracts an H atom, while the halide anion and C of the activated C-H bond combine with R_2E. This results in formation of the C-H activation product and an equivalent of Ar-H.

4.6- Experimental Section

All manipulations were performed using dry solvents and air-free techniques. Tetrahydrofuran (THF), diethyl ether (Et_2O), toluene, benzene-d_6, Et_2O-d_{10} and THF-d_8 were degassed and dried over sodium benzophenone ketyl. Aryl halides were passed were passed through a plug of $MgSO_4$ and then degassed prior to use. $[(CH)_2{}^tBu_2N_2]Si$ (**1**)[10, 11] and $[TMS_2HC]_2Ge$ (**15**)[12] were synthesized according to literature procedures. GC-MS was performed using a HP 5890A GC connected to a Finnegan MS or a Shimadzu GC-17A connected to a GCMS-QP5000. ^1H and ^{13}C NMR spectra were acquired on Varian 500, 400, or 300 MHz instruments and referenced to residual solvent peaks. Mass Spectra (MS) were acquired on a VG (Micromass) 70-250-S Magnetic sector mass spectrometer. Time of flight (TOF) electro spray ionization (ESI) mass spectra were acquired on a MicroMass LCT operating in positive or negative ion mode.

4-C_6H_4DI: To a 250 mL flask was added Mg powder (481 mg, 19.79 mmol, 1.3 equiv.), 100 mL of dry degassed THF and a crystal I_2 to activate the Mg surface. After heating to

a gentle reflux, a solution 1,4-$C_6H_4I_2$ (5.209 g, 15.79 mmol, 1.0 equiv.) dissolved in 10 mL of THF was added drop wise over 15 minutes. After 18 hrs the reaction was quenched by slowly adding 0.75 mL of "100 %" D_2O (2.6 equiv.). The magnesium salts were filtered away from the THF solution and then dissolved in minimal amount of water. The aqueous solution was extracted with three times with 15 mL of hexanes. Organic fractions were combined, including the filtered THF solution and dried over $MgSO_4$. Volatiles were distilled away from the aryl iodide, leaving a yellow colored liquid. The resulting yellow liquid was chromatagraphed on silica gel using 100 % hexanes, like fractions were combined and concentrated. 0.893 g (4.36 mmol, 28 % yield) of 4-C_6H_4DI was isolated as a colorless liquid. ^{1}H NMR ($CDCl_3$) d 7.70 (d, $^3J_{H-H}$ = 7.8 Hz, 2H), 7.10 (d, $^3J_{H-H}$ = 7.8 Hz 1H); ^{13}C NMR ($CDCl_3$) d 139.3, 137.5, 130.1; GC-MS *m/z* (relative intensity): 77.05 (11.55 %), 78.05 (99.68 %), 79.05 (6.93 %), 204.00 (7.18 %), 205.05 (100.00 %), 206.05 (6.60 %); C_6H_5I sample *m/z* (relative intensity): 77.05 (63.75 %), 78.05 (4.48.00 %), 79.05 (0.14 %), 204.00 (100 %), 205.00 (6.33 %), 206.00 (0.19 %);

3-C_6H_4DI: A similar prodcedure to the synthesis of 4-C_6H_4DI was used. ^{1}H NMR ($CDCl_3$) d 7.72 (m, 2H), 7.35 (dd, $^3J_{H-H}$ = 7.2 Hz, $^4J_{H-H}$ = 1.2 Hz, 1H), 7.12 (t, $^3J_{H-H}$ = 7.3 Hz, 1H); ^{13}C NMR ($CDCl_3$) d 137.7, 137.6, 130.5, 127.6; GC-MS *m/z* (relative intensity): 77.05 (16.77 %), 78.05 (100.00 %), 79.05 (6.88 %), 204.00 (10.29 %), 205.00 (88.68 %), 206.00 (5.75 %);

Measurement of primary kinetic isotope effects:

Primary isotope effect for reaction of **21** or $Ge[N(SiMe_3)_3]_2$ (**31**) with Ph-I/THF. A vial was charged with THF (0.50 mL, 6.17 mmol), THF-d_8 (0.50 mL, 6.61 mmol), and **21** (22 mg, 0.056 mmol). Ph-I (9.0 μL, 0.064 mmol) was added and the contents mixed. After completion of the reaction at 20 °C, as monitored by color and ^{1}H NMR spectroscopy, all volatiles were transferred. GC-MS was used for separating the volatiles into a THF fraction and a benzene fraction and the ratio of C_6H_6/C_6H_5D was determined using MS data. An analogous procedure was used for **31**. The k_H/k_D ratio was determined to be 6.5 ± 0.2 for **21** and 5.6 ± 0.2 for **31**. The primary isotope effect for **21**/PhCl/THF was measured in a similar fashion with the exception that the sealed vial containing the mixture was heated for 1 week at 70 °C. Over this time period the reaction color varied from orange to brown to green to colorless. The k_H/k_D ratio was determined to be 5.2 ± 0.2.

*Primary isotope effect for reaction of **1**/Ph-I/Et_2O/Et_2O-d_{10}.*

A 1 dram GCMS vial was charged with **1** (16 mg, 0.081 mmol), Et_2O (0.5 mL, 4.76 mmol), Et_2O-d_{10} (0.5 mL, 4.76 mmol), and Ph-I (20 mL, 0.18 mmol). The solution immediately turned a golden color upon addition of Ph-I. Vials where capped immediately after addition of Ph-I and shaken to ensure complete mixing. GC-MS analysis was used to determine the ratio of C_6H_6/C_6H_5D. The k_H/k_D ratio was measured to be 5.7 ± 0.1.

*Measurement of order in **21** and kinetic measurement of $k_{Ph\text{-}Br}/k_{Ph\text{-}Br\text{-}d5}$ ratio.*

A 0.025 M stock solution (**A**) was prepared by dissolving **21** (225 mg, 0.575 mmol) in THF (20.070 g, 22.51 mL). A dilution was made by extracting 0.813 g of stock solution

A (9.1 mg **21**, 0.023 mmol) and adding THF to give a total weight of 2.711g and a final concentration of 0.0076 M for stock solution **B**. A concentration of **21** in THF suitable for UV-vis spectroscopy was obtained by taking 0.550 g **B** (1.88 mg **21**, 0.0048 mmol), and diluting it with THF to give 3.483 g (3.91 mL). The final concentration of **21** in THF is 0.0012 M. The sample was placed in a quartz cuvette capable of being sealed by a Teflon stopcock. The initial spectrum of **21** in THF was obtained. The sample was returned to the dry box, where Ph-Br (10.0 μL, 0.092 mmol, 19.2 equiv.) were added. Spectra were acquired for 32 minutes, until the absorption at 420 nm was barely visible. The reaction mixture was then transferred to a flask and volatiles were removed. ^{1}H NMR spectroscopy revealed only the formation of C-H activation product. No trace of oxidative addition product was observed. A second order plot of the data resulted in the best fit ($R^2 = 0.992$). Zero order, first order and third order plots gave R^2 values of 0.587, 0.888, and 0.975, respectively. Additionally, the zero, first, and third order plots exhibited systematic, consistent deviation from linearity across the full data set.

This reaction was also performed using C_6D_5Br instead of C_6H_5Br. A 0.0013 M solution of **21** in THF was prepared by taking 0.675 g of solution **B** (2.3 mg **21**, 0.0059 mmol) and diluting with THF to a final weight of 4.085 g (4.59 mL). To this solution in the quartz cuvette was added C_6D_5Br (10.0 μL, 0.092 mmol, 15.6 equiv.), and the reaction was monitored via UV-vis spectroscopy for over 1 hour. Once again, ^{1}H NMR spectroscopy indicated only C-H activation product was formed. A second order plot gave the best fit to the data ($R^2 = 0.994$). The $k_{Ph\text{-}Br}/k_{Ph\text{-}Br\text{-}d5}$ ratio measured kinetically was 2.3.

Measurement of isotope effects arising from deuteration of the aromatic ring of the aryl halide using GC-MS analysis of the resulting ratio of benzenes.

a) Measurement of the $k_{Ph\text{-}Br}/k_{Ph\text{-}Br\text{-}d5}$ ratio for **21**/THF. A stock solution of **21** was prepared by adding 192 mg of **21** to 20 mL of THF. 1.0 mL of the stock solution of **21** and 75 μL of C_6H_5Br/C_6D_5Br were added to a 1 dram GC-MS vial. The vial was capped and left at room temperature until colorless (2 1/2 days). Employing a 70 °C hold for 2 min followed by a 70-250 °C ramp at 20 °C/min using a DB-5 equivalent column, the C_6H_6/C_6HD_5 mixture was separated from the other materials present and analyzed by mass spectrometry. All reactions were repeated in quadruplicate and each sample was injected on the GC-MS in triplicate to generate the data presented in **Table 4.3**. For all methods (a, b, and c), the exact ratio of deuterated to non-deuterated aryl halide present in the initial reaction mixture was determined by an independent MS measurement of the prepared stock solution containing a nominal 1 : 1 ratio of the aryl halides.

b) Measurement of ratios for $Ge[CH(SiMe_3)_2]_2$ (**21**)/Et_2O. A stock solution of **21** was prepared by adding 33 mg **21** to 16.0 mL Et_2O. 1.0 mL of the stock solution of **21** and 25 μL of C_6H_5Br/C_6D_5Br (20 equiv. of each aryl halide) were added to a 1 dram GC-MS vial. The vial was capped and left at room temperature until colorless (this time varies with aryl halide). Employing a 40 °C hold for 2.5 min followed by a 40-200 °C ramp at 20 °C/min using a DB-5 equivalent column, the C_6H_6/C_6HD_5 mixture was separated from the other materials present and analyzed by mass spectrometry. All reactions were repeated in quadruplicate and each sample was injected on the GC-MS in quadruplicate to generate the data of **Table 4.3**. All other ratios reported for **21** in Et_2O were collected using a similar method.

c) Measurement of ratios for **1**/Et_2O. A stock solution of **1** was prepared by adding 16 mg **1** to 16.0 mL Et_2O. 1.0 mL of the stock solution of **1** and the amount of a stock solution of C_6H_5Br/C_6D_5Br required to give 20 equiv. of each aryl halide were added to a 1 dram GC-MS vial. The vial was capped and left at room temperature until colorless (this time varies with aryl halide). Employing a 40 °C hold for 2.5 min followed by a 40-200 °C ramp at 20 °C/min using a DB-5 equivalent column, the C_6H_6/C_6HD_5 mixture was separated from the other materials present and analyzed by mass spectrometry. All reactions were repeated in quadruplicate and each sample was injected on the GC-MS in quadruplicate to generate the data presented in **Table 4.3**. All other ratios reported for **1** in Et_2O were collected using a analogous method.

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Chapter 5- Summary and Direction of C-H Activation with Germylenes and Silylenes

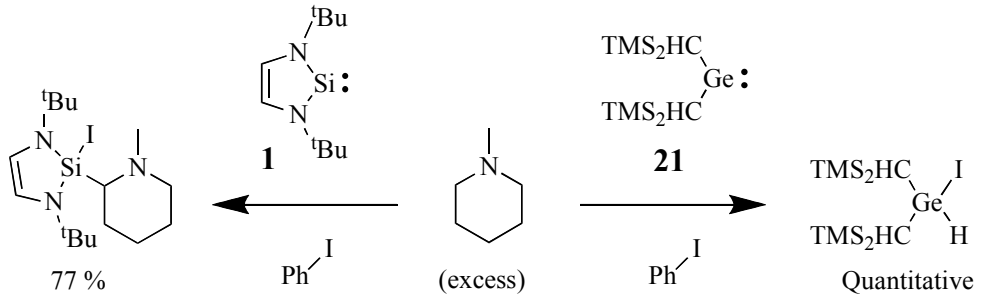
5.1- Conclusions on C-H Activation Chemistry of Silylenes and Germylenes

The germylene aryl halide C-H activation chemistry first reported by Banaszak Holl et al.[1] has proven to be more than a unique case of germylene reactivity. Subsequent publications have demonstrated the C-H activation of alkanes, ethers, alkenes and alkynes are feasible with stannylenes/Ar-I.[2, 3] Chapters 2 and 3 contain a summary of the new silylene/Ph-I C-H activation chemistry that has been achieved with alkane, ether and amine substrates. Contributions of this work to C-H activation chemistry are (a) tertiary amines can be C-H activated with $[(CH)_2{}^tBu_2N_2]Si$ (**1**)/Ph-I or $(TMS_2HC)_2Ge$ (**21**)/Ph-I (b) demonstrating that side products (non-C-H activation products) of the amine C-H activation reactions are formed from $[R_3NH]I$ salts reacting with **1** or **21** in the corresponding R_3N solvent and (c) measuring a kinetic isotope effect (KIE) from the aryl halide that is consistent with the aryl-halide bond breaking at or before the rate-determining step (RDS).

The reactions with amine substrates broadened the functional group compatibility of the C-H activation chemistry. In addition to expanding the scope of useable substrates, the amines demonstrated there are many aspects of the chemistry that not are understood. Either **1** or **21** can be used in combination with an aryl halide for the C-H activation of amines that have methyl C-H bonds only. When attempting to C-H activate amines

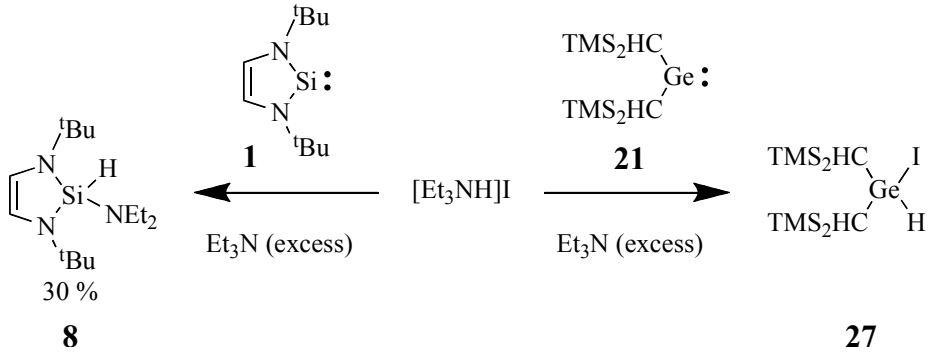
containing more than methyl C-H bonds, the choice of **1** or **21** dictates if a C-H activation product will be observed. Amines with α methylenes or methines and β C-H bonds will form C-H activation products with **1**/Ph-I. The use of **21**/Ph-I with tertiary amines possessing α and β C-H bonds results in the formation of R_2GeHI. Examples of the differing reactivity of **1**/Ph-I and **21**/Ph-I is demonstrated by the reactions carried out in N-methylpiperdine, see **Scheme 5.1**.

Scheme 5.1- Reactions of N-methylpiperidine with **1**/Ph-I and **21**/Ph-I



The formation of various side products of the amine C-H activation reactions can be rationalized by the formation of $[R_3NH]I$ *in situ*. Numerous side products of the C-H activation reactions were identified and independently synthesized by reacting **1** or **21** with a $[R_3NH]I$ salt in the corresponding R_3N solvent, see **Scheme 5.2**. The direct

Scheme 5.2- Reaction of $[Et_3NH]I$ with **1** and **21**



reaction of **21** with $[Et_3NH]I$ in Et_3N forms the R_2GeHI product in a kinetically competent reaction. Additionally, reacting **1** and a $[Et_3NH]I$ in Et_3N forms the $R_2SiH(NEt_2)$ compound. Elucidating that $[R_3NH]I$ was playing a roll in the formation of side products occurred after isolating a trace solid from the C-H activation reactions of Me_2N^tBu, the solid was identified as $[Me_2{}^tBuNH]I$.

A third contribution of this work has been the measurement of the aryl KIE. Initial measurements of the aryl KIE produced a surprisingly large value of 2.28. Additional aryl KIE measurements and comparison with known reactions demonstrated the measured aryl KIE's were within the range of previously reported aryl KIE's. Two examples of aryl KIE's are the aryl radical anion equilibrium and the thermal decomposition of aryl diazonium salts. The reported aryl KIE's and the measure aryl KIE's were all within a similar range. Based on the C-H activation reactions breaking a C-X bond during the course of the reaction and the known rapid breakdown of radical anions of aryl halides, the aryl diazonium salt aryl KIE's were interpreted as a more logical comparision. From this comparision, the aryl KIE's measured have been interpreted as supporting the cleavage of the aryl C-X bond at or before the rate-determining step (RDS).

5.2- Directions for Continued Work on C-H Activation Reactions

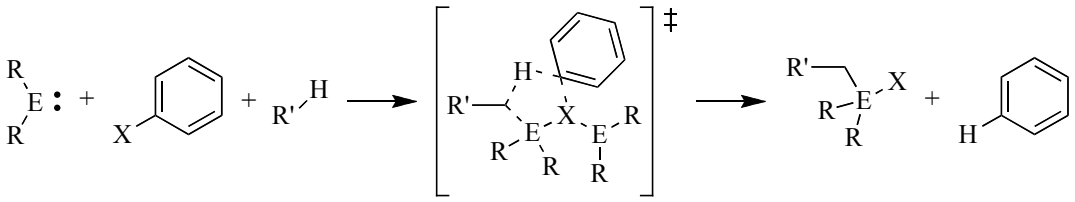
5.2.1- Additional Mechanistic Studies

The continued work on the C-H activation reaction mechanism provides a better understanding of specific parts of the reaction mechanism. In chapter 4 a summary of previous and new results on the reaction mechanism are given. A subtle frequently glossed over point exists within the rate law expression and the experiments used for

deriving the rate law expression. The rate law expression was derived from reaction conditions that were pseudo first order for the substrate and the aryl halide. From the derived rate law expression using pseudo first order conditions of the aryl halide, the reaction has been presumed to be first order with respect to the aryl halide. Knowing if the reaction is indeed first order with respect to the aryl halide, a significant step will be made in validating one presumption that has been made regarding the rate law expression.

To achieve the type of transition state depicted in **Scheme 5.3** an SET is proposed. The active complex transfers an electron to Ar-X, which will rapidly become the corresponding halide anion and aryl radical if no other reaction pathways are immediately available. The incipient aryl radical abstracts an H atom from the solvent cage (represented as R-H) surrounding the activated complex, while the halide anion and carbon of the activated C-H bond combine with R_2E. This results in formation of the observed C-H activation product and the equivalent of Ar-H.

Scheme 5.3- Proposed Transition State of Rate Determining Step



Another valuable set of mechanistic experiments to carry out is determination of the activation parameters. Calculating the $\Delta S^{\ddagger}$ for the C-H activation reaction helps establish how accurate **Scheme 5.3** is as a valid proposal of aligning four molecules at the RDS. Fortunately the germylenes and stannylenes that have been used to date possess a

UV-vis spectroscopic handle that allows for monitoring the reaction kinetics at various temperatures.

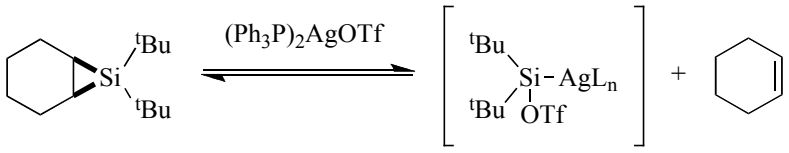
5.2.2- Continued Development of the C-H Activation Reaction

The conditions used for the C-H activation reactions presented throughout these chapters are not very attractive for large-scale reactions. Running a reaction that requires +500 equivalents of a valuable intermediate is of little interest for large-scale reactions. In addition to using +500 equivalents of the C-H activation substrate, the reaction requires stoichiometric quantities of a reagent that is taxing to purify and isolate. The above sentences highlight two areas for continued development that would make the C-H activation reactions more appealing for synthetic applications.

One area of further study is pushing the limits of the reaction towards stoichiometric amounts of the C-H activation substrate. Two options for using fewer equivalents of the C-H activation substrate have been discovered. Work on the C-H activation of amines revealed Me_4Si was a terrible substrate to C-H activate, the major product of attempts at C-H activating Me_4Si was oxidative addition. With Me_4Si present as a solvent, $PhNMe_2$ was successfully C-H activated with **21**/Ph-I.[4] During the course of the experimental work presented in Chapter 2 attempts at C-H activating toluene with **1**/Ph-I were a complete failure, the reaction product was oxidative addition. Failure to C-H activate toluene with **1**/Ph-I revealed an inert substrate that has been used as a solvent for C-H activation reactions using **1**/Ph-I. What remains to be discovered is how close to stoichiometric amounts of the C-H activation substrate can be used before oxidative addition becomes the major product.

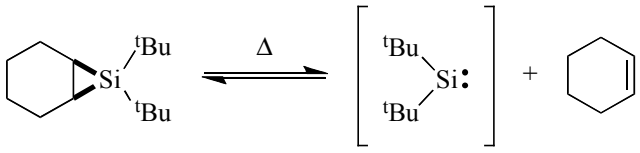
A second area for continued development is finding alternate methods of forming the divalent group 14 compounds used for these C-H activation reactions. The current germylenes, stannylenes and silylene used for the C-H activation reactions require much care and attention to successfully isolate the pure divalent compounds. The *in situ* formation of the divalent species would eliminate the time consuming and tedious isolation procedures. Looking over the work of Woerpel et al., the thermoloysis of silacyclopropanes in the presence of transition metals is proposed to form a silver coordinated silylanol *in situ*, see **Scheme 5.4**.[5] Removal of the transition metal, and its associated ligands, from the thermoloysis of silacyclopropanes, the *in situ* formation of a

Scheme 5.4- Proposed Intermediate of Silcyclopropane Transfer Reactions



silylene could be achieved, see **Scheme 5.5**. Converting from the use of isolated divalent reagents that are handled under glove box conditions to a reagent which can be dispensed from a bottle is not only more synthetically appealing, but also provides a more convenient and rapid way of obtaining large quantities of a silylene.

Scheme 5.5- Proposed Method for *in situ* Formation of Silylene



A concerted effort in the areas of (a) finding the reaction order for the aryl halide and/or substrate (b) reaction conditions requiring few equivalents, or even stoichiometric

amounts, of the C-H activation substrate and (c) generation of silylenes, germylenes or stannylenes *in situ* from benchtop reagents will help establish the C-H activation chemistry as a more viable synthetic methodology. The work presented within this dissertation and futures efforts will play a key role in advancing the understanding of how the C-H activation reaction is occurring. Additionally, an open-ended basic science question arises from this work. Stannylenes, germeylenes and a silylene are all capable of activating C-H bonds of various substrates when an aryl halide is present, surely a carbene can be discovered to C-H activate ethers, hydrocarbons or amines in the presence of an aryl halide or pseudo halide.

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