

Recyclable Palladium(0)-Catalyzed Addition of Silylstannanes to Terminal Alkynes in Ionic Liquids

By Ivan W. Hemeon

A thesis submitted to the Chemistry Department and the Faculty of
Graduate Studies in partial fulfillment of the requirements for a
Master of Science degree in Applied Science

April 25, 2003



Saint Mary's University

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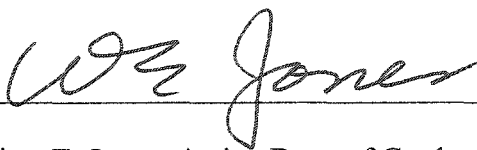
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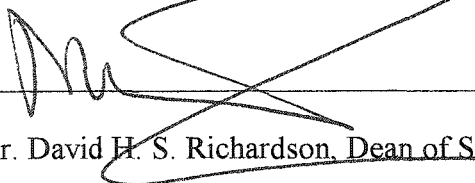
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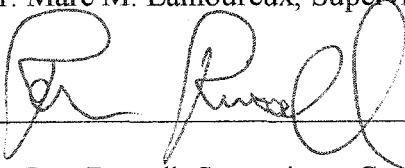
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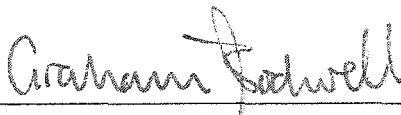
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Abstract

Recyclable Palladium(0)-Catalyzed Addition of Silylstannanes to Terminal Alkynes in Ionic Liquids

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April 25, 2003

Ionic liquids have been used as solvents for many different organic reactions, often providing rate enhancements, selectivity improvements, and affording better yields compared to conventional solvents. In this study, the palladium(0)-catalyzed addition of trimethyl(tributylstannyl)silane and diphenylmethyl(tributylstannyl)silane to terminal alkynes is investigated using two different ionic liquids, 1-*n*-butyl-3-methylimidazolium hexafluorophosphate and 1-*n*-butyl-3-methylimidazolium tetrafluoroborate, under biphasic conditions using diethyl ether as a co-solvent. Five terminal alkynes were used, phenylacetylene, 1-decyne, 5-hexyn-1-ol, 5-hexyn-1-ol THP ether, and 6-chlorohexyne. In general, reactions between the silylstannanes and alkynes proceeded efficiently in both ionic liquids to give quantitative or near quantitative yields of their addition products as a single isomer.

Ionic liquids have gained much popularity of late due to their ability to immobilize transition metal catalysts, allowing them to be recycled due to the nonvolatile nature of ionic liquids. The tetrakis(triphenylphosphine)palladium(0) catalyst used in these silylstannation reactions was immobilized in both ionic liquids and shown to be extensively recyclable without loss of activity. Ionic liquid/catalyst systems were recycled ten times in the reaction of phenylacetylene with trimethyl(tributylstannyl)silane.

Quotations

“Do not worry about tomorrow; for tomorrow will take care of itself. Each day has enough trouble of its own.”

Matthew 6:34

“The most exciting phrase to hear in science, the one that heralds the most discoveries, is not ‘Eureka!’, but ‘That’s funny...’”

Isaac Asimov

“If I lived back in the wild west days, instead of carrying a six-gun in my holster, I'd carry a soldering iron. That way, if some smart-aleck cowboy said something like ‘Hey, look. He's carrying a soldering iron!’ and started laughing, and everybody else started laughing, I could just say, ‘That's right, it's a soldering iron. The soldering iron of justice.’ Then everybody would get real quiet and ashamed, because they had made fun of the soldering iron of justice, and I could probably hit them up for a free drink.”

Jack Handy's Deep Thoughts

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I would like to acknowledge several individuals and organizations that aided me in my academic career, which led to the production of this thesis. Firstly, I would like to thank Dr. Rob Singer. As my senior supervisor, he has provided insight, suggestions, opportunities, and support during my time under his wing. It was difficult to top his taking me to Australia during his sabbatical where I performed research for my Honours thesis. I think we may have come close after a successful two years during the Masters program – several publications, conferences, and awards later. As I learned long ago, Rob's motto of "work hard, play harder" always pays off.

I would like to thank the Natural Sciences and Engineering Research Council for financial support, as well as Saint Mary's University for support. I would like to acknowledge Dr. Don Hooper, Dr. Mike Lumsden, and Dr. Bob Berno at the Atlantic Regional Magnetic Resonance Centre at Dalhousie University for acquiring those all-important NMR spectra on my behalf. I would also like to thank the SMU Chemistry departmental technicians Darlene Goucher and Elizabeth McLeod for getting equipment and supplies for me, regardless of when I approached them.

Working in a university research lab is a far less enjoyable experience without lab mates, people to bounce ideas off of, people to clean your glassware, people to help you change vacuum pump oil, and sometimes just to have around to rant and rave with. So thanks to everyone who I've worked with over the years who have helped make the lab a better place to be, most recently and perhaps most importantly (for sanity's sake) Gavin Beck and Steve Dickson. What we need is a Caesar and a 'gar! Write that down...

Thanks to my parents (and my other parents, the out-laws... I mean, in-laws) for all the support over the years and though you may not have understood much of what I was saying or doing, you still urged me on, knowing the end result would be the best one. And last, but certainly not least, thanks to my loving wife Leah for being so supportive, especially during the end days (mood swings, turning the apartment into a library, etc.). Now it's my turn to be supportive as we begin a new phase in our lives. Vancouver, here we come!

List of Abbreviations

acac	acetylacetone
[bbim]	1,3-di- <i>n</i> -butylimidazolium
[bmim]	1- <i>n</i> -butyl-3-methylimidazolium
br	broad
Bu	butyl
dba	dibenzylideneacetone
DMAP	4-(<i>N,N</i> -dimethylamino)pyridine
DMF	<i>N,N</i> -dimethylformamide
emim	1-ethyl-3-methylimidazolium
Et ₂ O	diethyl ether
GC	gas chromatography
ICP-MS	inductively coupled plasma mass spectrometry
LDA	lithium diisopropylamide
OAc	acetate
OTf	trifluoromethanesulfonate
m	multiplet
Me	methyl
NMP	<i>N</i> -methylpyrrolidinone
NMR	nuclear magnetic resonance
NTf ₂	bis(trifluoromethanesulfonyl)imide
s	singlet
ScCO ₂	supercritical carbon dioxide
t	triplet
TBAF	tetrabutylammonium fluoride
TEM	transmission electron microscopy
THF	tetrahydrofuran
THP	tetrahydropyran-2-yl
TsOH	<i>p</i> -toluenesulfonic acid
XAFS	X-ray absorption fine structure

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1.0 Introduction

1.1 Ionic Liquids

1.1.1 Identifying Ionic Liquids

Ionic liquids are interesting materials due to their uncommon properties. Many ionic compounds are solids at room temperature and do not reach their liquid phases until much higher temperatures are reached. Sodium chloride, for example, has a melting point of 801 °C.¹ Most of the compounds that are liquids at room temperature are of a molecular, uncharged nature composed of only one species. As well, compounds that are liquids at room temperature have relatively low molecular weights and/or have few intermolecular attractions to hold them in a solid phase. Ionic liquids are unique in that they are compounds composed of ions, having both cationic and anionic species, and are liquids at room temperature despite the fact that they are salts. This is counter-intuitive; however, when the relative sizes of the cations and anions of common ionic liquids are considered, it can be seen that the cation is often a large organic species while the anion is often a non-coordinating species. The charges of both cation and anion are often spread out over the species so as not to become a point charge. Coupled with the sizes of the ionic species, these facts make it seem more reasonable that ionic liquids are in fact liquids at room temperature.

Studies by several groups indicate that packing inefficiency between the cation and anion is mainly responsible for the existence of ionic compounds that are liquids at room temperature.² Melting points of ionic compounds are generally governed by electrostatic interactions, whereas those of organic compounds are generally influenced

by intermolecular hydrogen bonding. Both of these factors help determine the strength of the crystal lattice. Many ionic liquids contain anions that are poorly basic and cannot hydrogen bond efficiently, inhibiting crystal lattice formation. However, the cations of common ionic liquids are often based on aromatic molecules that can stack to form stable lattices.³ All of these factors make it difficult to predict which combinations of cation and anion will lead to ionic compounds that are liquids at room temperature.^{4,5}

Ionic liquids have been known for many years. One of the first ionic liquids, discovered in 1914, was ethylammonium nitrate [EtNH₃][NO₃]. This was found to have a melting point of 12 °C.⁶ This compound was formed by reaction of ethylamine with concentrated nitric acid, but its report attracted little interest at the time. It was the salts containing chloroaluminate anions that first saw extensive use by chemists. Ionic compounds such as AlCl₃-NaCl eutectics and pyridinium hydrochloride were used mainly in high temperature electrochemical applications throughout the mid-20th century.⁷ One of the first totally organic ionic compounds used as a solvent for kinetic studies and electrochemical reactions was tetra-*n*-hexylammonium benzoate, which was developed in 1967.⁸ Until the late 1970s, room temperature ionic liquids had not reached a general audience. This was remedied when the groups of Osteryoung and Wilkes “rediscovered” them. These groups managed to synthesize the first chloroaluminate salts that were liquids at room temperature; although, research was still restricted mainly to their electrochemical applications.⁹

In the early 1980’s the first *N,N'*-dialkylimidazolium chloroaluminate salts were synthesized and shown to be liquids at room temperature.¹⁰ The groups of Seddon and Hussey then began to use room-temperature ionic liquids as solvents for investigations of

transition metal complexes through electrochemical and spectroscopic methods. These ionic liquids proved to be ideal solvents for such investigations due to their abilities to stabilize a number of species that normally exist only transiently in such molecular solvents as acetonitrile and water in addition to their anhydrous, aprotic natures.¹¹

The first reaction performed in these chloroaluminate ionic liquids was a Friedel-Crafts reaction that used the ionic liquid both as a solvent and a catalyst, taking advantage of the Lewis acidic nature of the ionic liquid.¹² This and other early studies showed that ionic liquids could be used as solvents for organic reactions, potentially with novel results. Catalytic reactions were also performed in chloroaluminate ionic liquids. Chauvin et al. used them to dissolve nickel catalysts and investigated the ionic liquid/catalyst solution for the dimerization of propene,¹³ while Osteryoung et al. studied ethylene polymerization in acidic chloroaluminate ionic liquids using Ziegler-Natta catalysts.¹⁴

Although these chloroaluminate-based ionic liquids were useful, they were extremely sensitive to water and oxygen, thus limiting their usefulness. In 1992, a major breakthrough occurred when Wilkes and Zaworotko synthesized a series of air- and moisture-stable ionic liquids containing tetrafluoroborate $[\text{BF}_4]$ and hexafluorophosphate $[\text{PF}_6]$ anions.^{15,16} These ionic liquids tolerated being mixed with a wider variety of molecules, being much less acidic than chloroaluminate-based ionic liquids, allowing ionic liquid use in a much wider range of applications. Based on these studies it was apparent that many combinations of cations and anions could potentially afford room temperature ionic liquids.

Several cations are available on which to base an ionic liquid. These consist of quaternized nitrogen or phosphorus atoms with branched or lengthy alkyl chains to prevent close-packing of cation and anion, forcing the compound to remain as a liquid at room temperature. Tetraalkylphosphonium and *N*-alkylpyridinium cations have been used to synthesize some ionic liquids; however, tetraalkylammonium cations are more common and *N,N'*-dialkylimidazolium cations are the most common (Figure 1).¹⁷ Salts of dialkylimidazolium cations have a wide array of physico-chemical properties. They are easily prepared and many different groups can be placed on the nitrogen atoms of the imidazole ring to afford ionic liquids with different properties. They also tend to interact weakly with anions and are more thermally stable than tetraalkylammonium cations.¹⁸

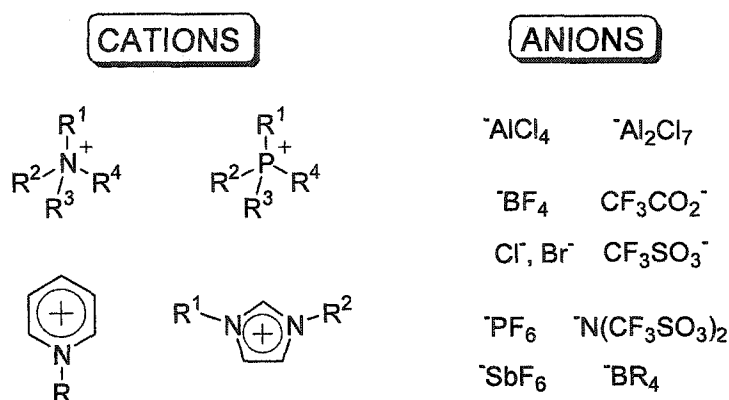


Figure 1. Cations and anions that compose common ionic liquids

Although the length and nature of the alkyl groups on the imidazolium cation have some influence over the physical properties of the ionic liquids, the nature of the anion has far more. Two main types of anions are available: (1) water- and air-sensitive and (2) water-stable. Of the first kind, the chloroaluminate anions are most widely

known. These anions not only form room-temperature liquids when complexed with dialkylimidazolium cations, they afford liquids with tunable Lewis acidity. Typically formed by the reaction of aluminum chloride AlCl_3 with dialkylimidazolium chloride salts, these ionic liquids can be Lewis basic if less than one equivalent of AlCl_3 is added (the predominant species being Lewis basic Cl^-), Lewis neutral if exactly one equivalent is added (the predominant species being Lewis neutral AlCl_4^-), and Lewis acidic if more than one equivalent is added (the predominant species being Lewis acidic Al_2Cl_7^-).¹¹ These liquids can be made mildly acidic by adding a slight excess of AlCl_3 or strongly acidic by adding a two-fold excess of AlCl_3 . These ionic liquids decompose rapidly in the presence of water. As such, they are rather tedious to work with as great care must be taken to exclude water from all reagents to be introduced into the ionic liquid, including its components.

With the discovery of the moisture stable imidazolium-based ionic liquids in 1992 came the development of many more stable anions. As stated earlier, the anions BF_4^- and PF_6^- were among the first to be used to generate moisture-stable ionic liquids based on imidazolium cations. These two anions are both non-coordinating and are fairly stable thermally, but interestingly enough liquids based on BF_4^- are miscible with water, while those based on PF_6^- are immiscible with water. This has led to the classification of moisture stable ionic liquids into two groups: (1) water-soluble ionic liquids and (2) so-called “hydrophobic” ionic liquids. It has been shown that the hydrophobic ionic liquids are in fact hygroscopic (as are most imidazolium-based salts), having a point at which they become saturated with water and form a second phase.¹⁹ These two anions make up the most commonly used moisture stable ionic liquids; however, several others exist.

Nitrate, trifluoroacetate, and trifluoromethanesulfonate (triflate), chloride and bromide anions all form water-miscible imidazolium-based ionic liquids. Bis(trifluoromethanesulfonyl)amide (NTf_2^-), hexafluoroantimonate, and tetraalkylborate anions all form water-immiscible imidazolium-based ionic liquids.¹⁸

As more studies are published regarding the water solubilities of different ionic liquids, it is becoming apparent that there is more to determining water miscibility than simple examination of the ionic species present. The commonly used ionic liquid 1-*n*-butyl-3-methylimidazolium tetrafluoroborate [bmim] BF_4 is widely thought to be miscible with water. Below 0 °C, however, the solubility decreases.²⁰ As well, when the alkyl chain on the methylimidazolium ring has more than six carbons, the tetrafluoroborate salt becomes water immiscible.²¹ The commonly used ionic liquid [bmim] PF_6 is water immiscible while the PF_6^- salt of 1,3-dimethylimidazolium is water soluble.¹⁸ It is therefore misleading to classify PF_6^- as a water immiscible anion and BF_4^- as a water miscible anion. Ionic liquids should therefore be classified on the basis of individual cation/anion combinations.

Studies by several groups have shown that water hydrogen bonds to the anion, existing in a free state rather than self-aggregating. This suggests that the “hydrophobic” anions are poorly basic and cannot hydrogen bond to water efficiently, although since even “hydrophobic” ionic liquids are hygroscopic it seems that these anions can hydrogen bond to some extent.²² It is also this lack of hydrogen bonding ability that contributes to these compounds being liquids at room temperature. As well, cations with large alkyl groups such as 1-dodecyl-3-methylimidazolium are immiscible with water, likely as a

result of the hydrophobic nature of the long alkyl chains, even when associated with anions normally thought to give water miscible ionic liquids such as triflate.³

There also exists a limited number of examples of a unique type of ionic liquid, a zwitterionic ionic liquid, in which the cation and anion are part of the same molecule. In these species, the counterions are covalently linked and there are no separate counterions. One zwitterionic ionic liquid has an alkylsulfonate bound to the imidazolium ring, and another has a sulfonamide bound to the imidazolium ring (Figure 2).²³

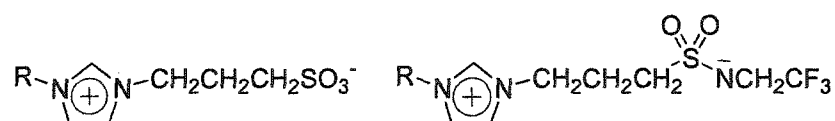


Figure 2. Zwitterionic species representing potential zwitterionic ionic liquids

It may not be proper to call these compounds “ionic liquids” as they have relatively high melting points – the sulfonate-containing species melts at 150 °C. They do however show that it may be possible to synthesize zwitterionic ionic liquids based on such structures. These compounds have unique characteristics in that they present very high ion densities but their ions cannot migrate and therefore act as excellent ion conductive matrices in which only added ions can migrate.²³

1.1.2 Preparation of Imidazolium-Based Ionic Liquids

As the use of ionic liquids becomes more widespread, an increasing number of chemical companies are selling various commonly used ionic liquids. The commercial

availability of ionic liquids may be attractive to a novice user wishing to accomplish a synthetic step using them for one or two steps rather than using a more conventional solvent, allowing the chemist to use the ionic liquid without having to become an “ionic liquid chemist.” However, the high cost of these commercially available ionic liquids is likely a deterrent to their more widespread use. For example, 5 g of [bmim]PF₆ cost \$93, 5 g of [bmim]BF₄ cost \$95, and 5 g of [bmim]Cl cost \$40 from Aldrich in the 2003-2004 catalogue.

The syntheses of most ionic liquids are relatively straightforward and can be performed for a significantly smaller cost compared to that of purchasing ionic liquids directly from a supplier. For example, 1 L of 1-methylimidazole cost \$251, 1 L of 1-chlorobutane cost \$88, and 500 g of 60% HPF₆ cost \$70 from Aldrich in the 2003-2004 catalogue, allowing [bmim]PF₆ to be synthesized for less than 5% of the cost of its purchase, based on raw material price. Imidazolium-based ionic liquids are commonly generated through metathesis reactions or acid/base reactions between an imidazolium halide and a salt or acid that contains the desired anion (Figure 3).

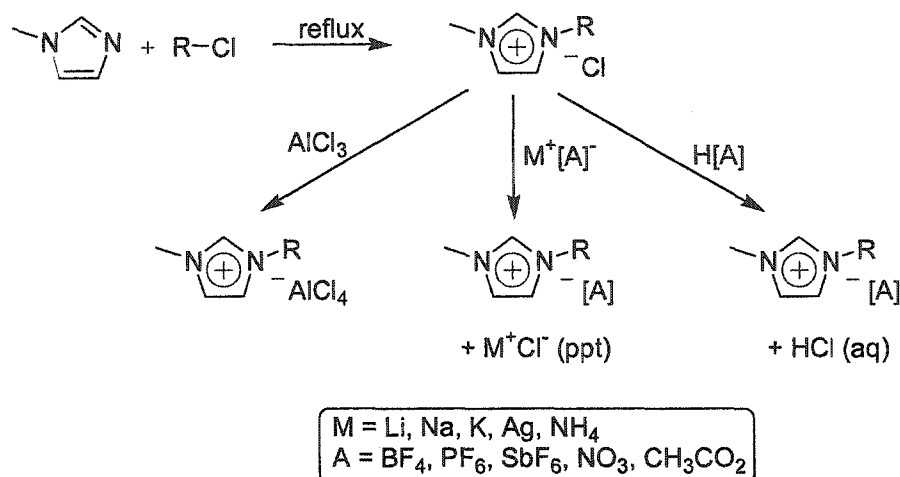


Figure 3. Synthetic routes to N,N'-dialkylimidazolium ionic liquids

The synthesis of the imidazolium halide simply involves refluxing 1-methylimidazole with the appropriate alkyl halide such as 1-chlorobutane. The imidazolium chloride salt forms a second layer that is easily purified by washing with several portions of ethyl acetate.²⁴ If an alkyl group other than methyl is desired in the 1 position, imidazole can be used as the starting material. This can be deprotonated under a variety of conditions, using sodium metal, sodium ethoxide,³ or sodium hydride.²⁵ The resulting anion can then be reacted with two equivalents of the appropriate alkyl halide to obtain a symmetrical imidazolium salt. Reaction with one equivalent of one alkyl halide followed by reflux with a second alkyl halide results in the generation of a nonsymmetrical imidazolium salt. Alternative synthetic methods for imidazolium halides have been developed that do not entail such long reaction times or such high excesses of alkyl halide in the interests of making ionic liquid syntheses more environmentally sound. Varma and Namboodiri have been investigating imidazolium halide synthesis

using sonication at temperatures far lower than reflux²⁶ and using microwaves to generate products with reaction times of less than two minutes.²⁷

There are three types of reactions that can be performed with the imidazolium halide to exchange the halide for another anion: acid/base reactions, metathesis reactions, and direct combination. Although the acid/base method was used to generate one of the first ionic liquids (ethylammonium nitrate from ethylamine and nitric acid⁶), metathesis methods were commonly used to generate ionic liquids during most of their history. Only recently have acid/base methods seen increased usage. Direct combination is a specialized synthetic pathway used when the imidazolium halide is treated with a Lewis acid, generating the ionic liquid as the only product.

Metathesis involves taking two salts and swapping their ionic components. For example, a common method for the preparation of [bmim]BF₄ is to suspend [bmim]Cl and NaBF₄ in acetone with stirring. After an extended reaction period, the ions exchange to give NaCl as a precipitate, leaving [bmim]BF₄ dissolved in acetone. The inorganic salt is removed by filtration and the solvent evaporated from the filtrate, leaving the ionic liquid behind.²⁸ A number of salts have been used in metathesis reactions with imidazolium halides, including Li⁺, Na⁺, K⁺, and NH₄⁺ salts of BF₄⁻ and PF₆⁻. Silver(I) salts of these anions have also been used with water as the solvent. The precipitated AgCl that forms has an extremely low solubility in water and can be removed by filtration.⁹

Purification of these ionic liquid products can be difficult since residual salt by-product or unreacted imidazolium halide can be present. This can be problematic since free halide anions are known to interfere with transition metal catalyzed reactions and

also increase the viscosity of ionic liquids.¹⁸ The metathesis reactions performed with alkali metal salts often do not go to completion, as evidenced by Seddon et al. in a study his group performed to determine which method of preparation yielded the cleanest ionic liquid. As determined by ion-selective electrodes, the chloride content of ionic liquids formed by metathesis reactions between imidazolium chlorides and sodium salts was high while the sodium content was very low, indicating that the chloride was from unreacted imidazolium chloride.²⁹ Removal of this unreacted starting material is easier to accomplish with water immiscible ionic liquids as they can be washed repeatedly with water in attempts to extract the imidazolium chloride. This does result in some ionic liquid loss as they are slightly soluble in water. Purification of water miscible ionic liquids is more difficult. Sometimes they can be dissolved in dichloromethane and washed with water, but this also results in some ionic liquid loss. The study by Seddon et al. also showed that metathesis reactions involving silver(I) salts provided products with the least amount of halide contaminant, likely stemming from the insolubility of silver(I) chloride in water, but was also very costly due to the expense of the silver salts.

Acid/base synthesis of ionic liquids is much more simple. It involves the reaction of an acid such as HBF_4 or HPF_6 as an anion source with an imidazolium chloride as a base. Performed in water, these reactions generally proceed to completion with the production of HCl . With water miscible ionic liquids, the HCl is removed by heating under vacuum resulting in near quantitative yields of product. These ionic liquids can also be dissolved in dichloromethane and washed with water, but this results in loss of some yield.³⁰ With water immiscible ionic liquids, the product can be washed successively with water until the washings are pH neutral, resulting in a slightly

decreased yield.²⁴ With the acid/base method there is no need for tedious filtration of finely-divided metal halide salts and little cause for worry about incomplete reaction. The study performed by Seddon et al. showed that this method provided ionic liquids that were virtually halide-free, containing similar trace amounts to ionic liquids generated from metatheses with silver(I) salts.²⁹ Since this method is less expensive than using silver(I) salts, it seems superior.

Direct combination of the imidazolium halide with a Lewis acid results in an ionic liquid with no by-products. The Lewis acid abstracts the halide base to form an anionic species associating with the imidazolium cation. Drawbacks with these types of ionic liquids are that they are often water-sensitive and are often Lewis acidic themselves. The best known Lewis acid used to generate ionic liquids from imidazolium chlorides is aluminum trichloride AlCl_3 , generating an $^-\text{AlCl}_4$ anion. As mentioned earlier, the predominant aluminum species in the ionic liquid is dependent on the amount of AlCl_3 added. Since $^-\text{AlCl}_4$ is Lewis neutral, if less than one equivalent of AlCl_3 is added the ionic liquid will be Lewis basic due to excess chloride being present. At exactly one equivalent of AlCl_3 , the ionic liquid will be Lewis neutral. With more than one equivalent of AlCl_3 added, it begins to react with $^-\text{AlCl}_4$ to produce complex anions such as $^-\text{Al}_2\text{Cl}_7$, which are Lewis acidic. Thus these types of ionic liquids have tunable Lewis acidities that can be taken advantage of for various applications. Other less commonly-used Lewis acids include BCl_3 , CuCl , and SnCl_2 .⁹

1.1.3 Novel Properties of Ionic Liquids

Ionic liquids have several unique properties that are absent in conventional molecular solvents. Being ionic, they can provide a unique solvent environment that may be able to better stabilize transition states or intermediates of reactions compared to conventional solvents, thus influencing rate, yield, and selectivity of various reactions. Many ionic liquids contain non-coordinating anions and as such ionic liquids form a new class of solvent: polar, aprotic, and non-coordinating. They can therefore dissolve a wide variety of organic, inorganic, and organometallic reagents, bringing together novel combinations of reactants in the same phase.³¹

Ionic liquids have generally been accepted to be polar in nature simply because they are composed of ions, the thinking being that if a molecule with a large dipole moment (such as dimethylformamide or water) can be polar, then species that actually have formal positive and negative charges on them should be extremely polar. This claim often attracts debate, especially considering the interesting solvent miscibility properties of ionic liquids.³² Most, if not all, ionic liquids form a biphasic mixture with non-polar solvents such as hexane and toluene and even slightly polar solvents such as diethyl ether. Solvents of intermediate polarity have interesting solubilities; ethyl acetate forms a second phase when mixed with [bmim]PF₆ but is miscible with [bmim]BF₄ while THF has the opposite effect, being miscible with [bmim]PF₆ but not with [bmim]BF₄. Halogenated solvents such as dichloromethane and chloroform seem to be miscible with most ionic liquids, while acetonitrile (a fairly polar solvent) has been used as a recrystallization solvent for ionic liquids that melt slightly above room temperature.

Perhaps unexpectedly, water (the most polar solvent) does not dissolve in [bmim]PF₆ and is only miscible with [bmim]BF₄ above 5 °C. These differing solvent miscibilities have been described as a useful property of ionic liquids, since reactions can be performed in them and the products can be extracted using the appropriate organic solvent. This also opens up possibilities for biphasic and even triphasic reactions containing organic, aqueous, and ionic liquid phases.³³

Several studies have been undertaken to assess the actual polarity of ionic liquids. Most of them have used solvatochromic dyes to measure solvent-solute interactions.^{34,35} The wavelength absorption bands of these dyes change depending on the magnitude of solvent interactions, registering effects from solvent dipolarity, hydrogen bonding, and Lewis acidity.¹⁷ These studies have shown that ionic liquids have polarities in the vicinity of short-chain primary alcohols, putting them near the top of the solvent polarity chart. Studies using the *endo/exo* ratios of Diels-Alder adducts as a measure of polarity confirm the findings of the solvatochromic dye studies, as more polar media increase the amount of *endo* product formed.³⁶

Perhaps the most intriguing property of ionic liquids is that being ionic in nature, they possess no measurable vapour pressure. This has many positive implications. This means that ionic liquids could be a safe alternative to toxic, noxious, volatile solvents used on a regular basis in laboratories worldwide. Coupled with the non-flammable nature of ionic liquids, this makes them a very safe solvent alternative. This also has environmental benefits. Since ionic liquids don't evaporate, they cannot contaminate the atmosphere as other more volatile solvents do. This property also allows ionic liquid usage to have economic and efficiency-oriented benefits. Since the solvent does not

evaporate, it can simply be washed clean of any contaminants after a reaction has been performed in it and re-used. This is an attractive property for many chemists given the potential high cost of purchasing ionic liquids. The nonvolatility of ionic liquids coupled with their ability to dissolve inorganic and organometallic reagents has made these systems extremely useful for catalytic reactions since a potentially expensive catalyst can be immobilized/dissolved in the ionic liquid, used for a reaction, and after the products are removed from the system the catalyst can often be re-used.³¹

Most ionic liquids are also very thermally stable. Most have wide liquid temperature ranges; [bmim]BF₄ for example melts at -81 °C and doesn't decompose until over 300 °C.²⁰ This wide temperature range allows extensive kinetic studies to be performed in ionic liquids. The large electrochemical window of ionic liquids coupled with their wide thermal operating range makes them excellent candidates for electrochemical applications.¹⁸ It has been suggested that some ionic liquids are less stable than others. For example, PF₆ based ionic liquids have been reported to decompose to generate phosphate and HF in the presence of water at elevated temperatures below 100 °C.²⁰ The thermal stability of most ionic liquids, along with their lack of vapour pressure, allows distillation to be used for isolating relatively volatile products of reactions performed in them rather than using volatile solvents for extraction; azeotrope formation is not a concern with ionic liquids.⁹

Gases are very soluble in ionic liquids. This has great implications for reactions in which one of the reagents is a gas, such as catalytic hydrogenations, carbonylations, hydroformylations, and alkene polymerization involving low molecular weight substrates.³¹ In addition to this, supercritical carbon dioxide is highly soluble in many

ionic liquids but does form a second phase after a certain point. Great attention is being paid to the use of supercritical CO₂ for extracting products from reactions performed in ionic liquids as a more environmentally-friendly alternative to using volatile organic solvents for such purposes.^{37,38,39,40}

Ionic liquids are being included in many lists as possible alternatives to conventional organic solvents and as possible components for “greener” chemistry. In fact, an entire issue of the journal *Green Chemistry* has been dedicated to articles dealing with ionic liquid research (volume 4, issue 2, 2002). There is, however, a great lack of knowledge regarding the toxicity of ionic liquids and their potential environmental impacts. It is naive to state that, because they are nonvolatile, ionic liquids cannot contaminate the environment and can be contained. Invariably they will find their way into the environment through “mechanical losses” or partial dissolution in an aqueous or organic phase during product extraction.³¹ Work in these areas is now beginning to proceed. One study has at last measured LD₅₀ values for the ionic liquid 3-hexyloxymethyl-1-methylimidazolium tetrafluoroborate and found them to be 1400 mg/kg in male Wistar rats, concluding that these ionic liquids can be safely used.⁴¹ Far more toxicity studies are required, though, since LD₅₀ values only describe acute toxicity as opposed to chronic toxicity. Work is proceeding on development of ionic liquids that contain imidazolium alkyl chains that are potentially easily biodegradable.⁴² These studies have also shown that [bmim]PF₆ is also biodegradable to a certain extent, measuring the amount of CO₂ produced by wastewater microorganisms incubated with the compound to be tested in an aerobic aqueous solution. Models are also under development to aid in sustainable ionic liquid development.⁴³ These models are based on

structure-activity relationship studies of various ionic liquids that correlate structure with environmental and health concerns such as release, spatiotemporal range, bioaccumulation, and biological activity to determine the magnitude of risks involved when using ionic liquids. These studies have also led to the proposal of a possible metabolic degradation pathway for imidazolium-based ionic liquids involving oxidation of the N-alkyl chains by cytochrome P₄₅₀ in the endoplasmic reticulum of any cell. Once oxidized to contain a hydroxy functionality, the alkyl chain can be further processed metabolically and enter the same degradation pathway as fatty acids, leaving imidazole behind.

Ionic liquids have also attracted criticism due to their incorporation of halogenated components that are hydrolytically or thermally unstable such as AlCl_4^- and PF_6^- anions that can release toxic and corrosive HF and HCl into the environment. Although there are several ionic liquids that do not contain halogens, they often have melting points above 40 °C and/or are unstable in aqueous solutions or at higher temperatures (e.g. 80 °C). Work is proceeding on the development of halogen-free anions such as octylsulfate to generate ionic liquids such as $[\text{bmim}][n\text{-C}_8\text{H}_{17}\text{OSO}_3]$ that are liquids at room temperature and stable at high temperatures. The aforementioned ionic liquid has been successfully used as a solvent for rhodium-catalyzed hydroformylations of alkenes.⁴⁴ Some have argued that the use of ionic liquids as green solvents is somewhat of a paradox since volatile organic solvents are frequently used to extract products from them. While it is true that many processes involving ionic liquids are not completely “green,” in many cases these processes are “greener” than they were. The ionic liquid may be replacing an environmentally unacceptable solvent, lowering

safety risks and environmental concerns. Products of organic reactions could be extracted using supercritical CO₂, a more environmentally benign solvent than the commonly used volatile organic solvents.³¹

1.2 Uses of Ionic Liquids

1.2.1 As Solvents for Non-Transition Metal-Catalyzed Reactions

For many years after their discovery, ionic liquids were used primarily as electrolyte sources for batteries and other electrochemical applications. It was the late 1980s before the potential for use of ionic liquids as solvents for organic reactions was realized. It was thought, and later proved true, that ionic liquids could offer several benefits as solvents. Most notable of these were the potential for rate enhancements by stabilizing charged transition states and improving chemo- and regioselectivities in comparison with other solvents.¹⁸ In addition, ionic liquids offered the potential to increase the “greenness” of chemical reactions by allowing easy solvent recovery and reuse due to their nonvolatile nature. Since the late 1980s, many different types of organic reactions have been performed in ionic liquids, often with benefits over using conventional solvents, and several reviews have been published on the subject.^{17,18,45,46}

As the most commonly used ionic liquids at the time contained anions based on AlCl₃, the first applications of ionic liquids as solvents were toward reactions requiring Lewis acid catalysis. Since these ionic liquids had tunable Lewis acidities, they were perfect solvents for Friedel-Crafts alkylation and acylation reactions. The first alkylation reactions were performed with benzene and different alkyl chlorides which gave products

in good yields, but gave mixtures of many different isomers of Friedel-Crafts products containing variable numbers of alkyl groups.¹² Acylation reactions on simple aromatic compounds with acetyl chloride proceeded with much better results, providing yields similar to those reported in the literature with excellent regioselectivities.⁴⁷ Acylation reactions on ferrocene also proceeded with differing selectivities and yields depending on the acid chloride/anhydride used and the amount.⁴⁸

The Diels-Alder cycloaddition reaction between 1,3-dienes and dienophiles (electron-poor alkenes) was also one of the earliest reactions to be performed in ionic liquids. They were performed first in chloroaluminate-based ionic liquids since many Diels-Alder reactions are Lewis acid-catalyzed. The reaction between cyclopentadiene and methyl acrylate proceeded with enhanced rate and *endo*-selectivity compared to conventional solvents.⁴⁹ The same reaction was performed in several air-stable ionic liquids, also giving high *endo*-selectivity. The reason for this increase in ionic liquids has been attributed to increased solvation of the transition state leading to the *endo* isomer over that leading to the *exo* isomer (Figure 4).⁵⁰

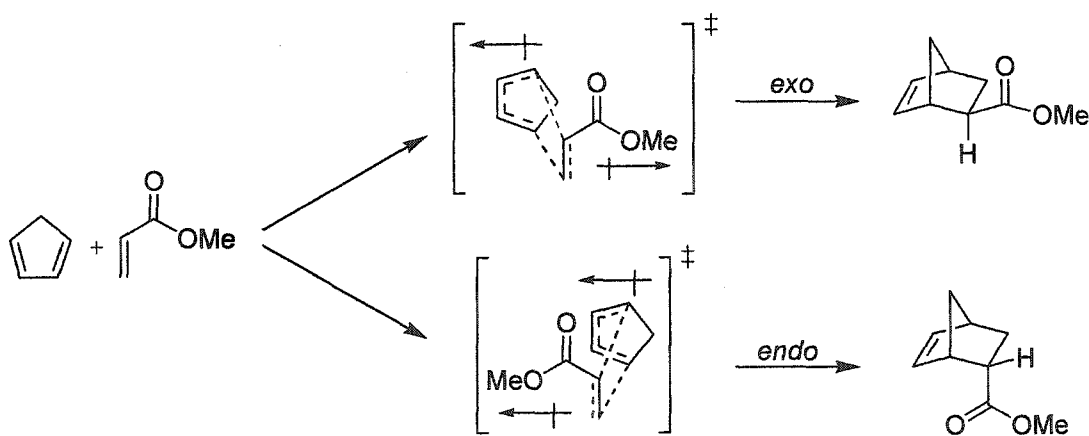


Figure 4. Transition states leading to the formation of *endo* and *exo* isomers in the Diels-Alder reaction

The transition state leading to the formation of *endo* isomer has the dipole moments of the diene and dienophile aligned, increasing the overall dipole moment of the transition state allowing it to be solvated by ionic liquids and thus allowing faster formation of the *endo* isomer. The transition state leading to the *exo* isomer has the dipole moments of the reactants pointing in opposite directions, giving the transition state a smaller dipole moment.

The Diels-Alder reaction was then performed in a wider array of air-stable ionic liquids between various dienes and dienophiles, most of which gave enhanced yields and *endo*-selectivity, providing a viable alternative to toxic and explosive lithium perchlorate/diethyl ether mixtures. In the case of isoprene reacting with but-3-en-2-one in [bmim]PF₆, a catalytic amount of zinc iodide was added to promote the reaction which increased the product yield from 11% to 98%.⁵¹ The seldom-used trialkylphosphonium tosylate ionic liquid was also used for Diels-Alder reactions of isoprene with various dienophiles showing high regioselectivity without Lewis acid addition.⁵² Ionic liquids themselves have also been used as catalysts for Diels-Alder reactions, an air-stable ionic liquid being used in dichloromethane in 20 mol%. When performed at low temperatures, the reaction did not proceed without the addition of ionic liquid.⁵³

The Diels-Alder reaction between cyclopentadiene and methyl acrylate has been used as a probe to measure the polarity of ionic liquids (as stated earlier) since the *endo/exo* ratio of the Diels-Alder adduct increases with increasing polarity of the solvent.³⁶ The ionic liquid [bmim]PF₆ has also been used as an additive for the Diels-Alder reaction conducted using microwave irradiation in 1,2-dichloroethane. Addition of

the ionic liquid causes an increase in the dielectric constant of the medium over that of 1,2-dichloroethane, allowing the microwave energy to be efficiently transmitted through an ionic conduction mechanism. This solvent system afforded a rate enhancement for the intra- and intermolecular hetero-Diels-Alder reactions.⁵⁴ Air-stable ionic liquids have also been used as solvents for 1,3-dipolar cycloaddition reactions using different dipolarophiles to give rate enhancements and improved yields.⁵⁵

Different types of condensation reactions have been performed under different conditions in ionic liquids. The benzoin condensation, a self-condensation reaction undergone by benzaldehyde to form benzoin, was performed in an N-alkylthiazolium tetrafluoroborate ionic liquid (similar to imidazolium in that a sulfur atom replaces one of the nitrogen atoms). This was promoted by a catalytic amount of triethylamine, albeit very slowly as the reaction proceeded in 80% yield after a week.⁵⁶ The authors believed that the triethylamine removed the weakly acidic proton on the carbon between the heteroatoms on the thiazolium ring to give a carbene and that this was the active condensation promoter, but provided no evidence to this effect. Other types of condensation reactions have given better performances; the condensation of substituted benzyl alcohols, generally veratryl alcohol (3,4-dimethoxybenzyl alcohol), was performed in a tetraalkylammonium ionic liquid.⁵⁷ The reaction was catalyzed by phosphoric acid to give cyclotrimeratrylenes in good yields. The ionic liquid was reusable, but after five cycles yield decreases were observed due to buildup of by-products. The three-component Biginelli condensation between β -dicarbonyl compounds, aldehydes, and urea to form 3,4-dihydropyrimidin-2(1*H*)-ones was performed neat with a catalytic amount of [bmim]BF₄ or [bmim]PF₆. Less than 1 mol%

of ionic liquid was able to give a rate enhancement and afford products in near quantitative yields. The reaction did not proceed without the addition of the ionic liquid, but little speculation was made regarding the role of the ionic liquid.⁵⁸

Several reactions involving the replacement of the oxygen atom of carbonyl compounds have also been performed in ionic liquids. Heterocyclic compounds (benzoxazines) have been prepared from the reaction of benzaldehyde with 2-aminobenzyl alcohol in several air-stable ionic liquids.⁵⁹ These reactions generate a new heterocyclic six-membered ring containing the nitrogen atom of the amino group and an oxygen atom, either from the benzyl alcohol or the carbonyl of the aldehyde. These reactions proceed in quantitative yields and the ionic liquid can be recovered and reused with no ill effects. Alkene-generating Wittig reactions between stabilized phosphorane ylides and various aldehydes have been performed in [bmim]BF₄ with good yields.⁶⁰ The reaction gives an alkene resulting from the exchange of the carbonyl oxygen of the aldehyde with the organic group doubly-bound to the phosphorus atom of the ylide, in addition to triphenylphosphine oxide Ph₃PO. The separation of the alkene from the by-product has often been troublesome, but the ionic liquid holds the Ph₃PO by-product while allowing the selective extraction of the alkene with diethyl ether. The Ph₃PO can be removed using another solvent such as toluene and the ionic liquid reused. The authors demonstrated the utility of ionic liquid recycling by showing that different aldehydes could be used in successive ionic liquid cycles without ill effects (most authors perform recycling studies using the same reagents successively). Base-promoted Knoevenagel and Robinson annulation reactions have also been performed in an air-stable ionic liquid. These reactions use enolate chemistry to replace carbonyl oxygen

atoms with carbon atoms and afforded products in good yields in the ionic liquid that was recyclable.⁶¹

Oxidation reactions have been successfully performed in ionic liquids. The air-stable ionic liquid [bmim]BF₄ has been used as an extractive aid in the MnO₂ oxidation of the allylic ether moiety of codeine methyl ether to a 1,3-diene system, generating thebaine (Figure 5).⁶²

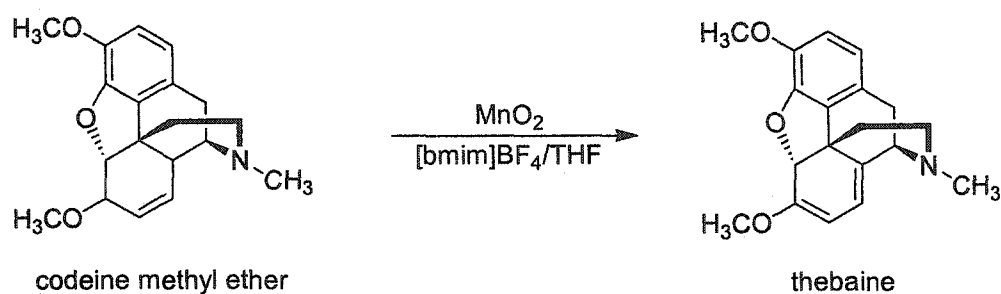


Figure 5. Oxidation of codeine methyl ether to thebaine using MnO₂ in ionic liquids

The oxidation generally proceeds to good conversion levels in conventional solvents, but separation of the products from the large excess of MnO₂ and associated impurities is extremely difficult. The ionic liquid immobilized the MnO₂ and impurities after reaction, allowing complete and selective extraction of the oxidized product. Another type of oxidation performed in [bmim]BF₄ and [bmim]PF₆ is the epoxidation of electrophilic alkenes. This reaction proceeds using the hydrogen peroxide oxidant in slight excess to give epoxides with a rate enhancement over using water as a solvent. This procedure also gave no epoxide hydrolysis products.⁶³

Reductions of aldehydes and ketones have also been performed in ionic liquids. Common aldehydes and ketones have been reduced to alcohols with sodium borohydride

in [bmim]PF₆ in good yields and the ionic liquid was recyclable.⁶⁴ Trialkylboranes have also been used for the same purpose in air-stable ionic liquids, although only one alkyl group of the trialkylborane was utilized, requiring equimolar quantities of trialkylborane and aldehyde.⁶⁵ The reactions proceeded at room temperature, but went much faster at 100 °C. Alcohols were generated in quantitative yields and the ionic liquid was able to be recycled. In an interesting application of ionic liquids, ketones were reduced in [bmim]PF₆ using immobilized baker's yeast.⁶⁶ These reactions proceeded with good yields and high enantiomeric excesses, showing the potential for whole-cell transformation reactions in ionic liquids.

Alkylations of carbonyl compounds using relatively non-basic organometallic reagents have been performed in ionic liquids. Tetraallylstannane was reacted with several aldehydes to prepare homoallylic alcohols in [bmim]BF₄ and [bmim]PF₆ with good yields.⁶⁷ All four allyl groups from the tin atom were transferred and although the yields were not improved over those obtained when using methanol as a solvent, the ionic liquid was recycled without loss of activity. The same reagent was added to Weinreb amides (Figure 6) and *N*-protected α -aminoaldehydes, generating *N*-protected allylketones and *N*-protected homoallylic alcohols.⁶⁸

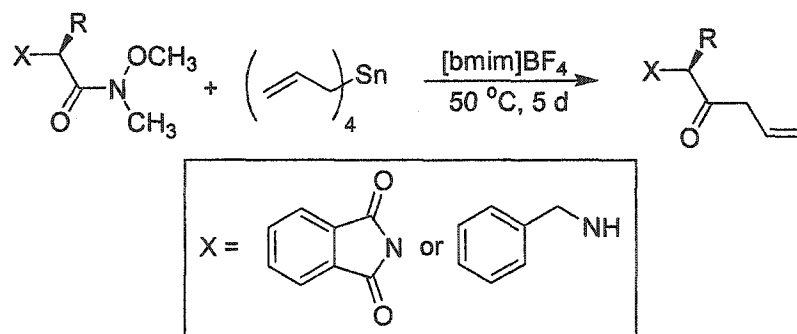


Figure 6. Allylation of Weinreb amides with tetraallylstannane

As with additions to simple alkyl or aromatic aldehydes, the yields obtained from the ionic liquids showed no improvement over those obtained from methanol. Allylation of aldehydes and ketones was also carried out in air-stable ionic liquids using allyldiisopropoxyborane, generating homoallylic alcohols in good yields and giving greater diastereofacial selectivity than in conventional solvents. The ionic liquid could be reused, providing the same product yields and selectivities.⁶⁹ The Reformatsky reaction involving the generation of an organozinc reagent from zinc and an α -halo ester followed by addition of the ester to an aldehyde to give an alcohol has been performed in various air-stable ionic liquids. As well, the generation of alkynylzinc reagents from zinc salts and terminal alkynes followed by their addition to aldehydes to give propargylic alcohols has been accomplished.⁷⁰ In another type of alkylation reaction, vinylboronic esters and acids have been used to transfer substituted vinyl groups to phenylselenenyl chloride, generating vinylselenides stereospecifically; the ionic liquid could be recycled.⁷¹

Rearrangements have been shown to take place in ionic liquids. The Beckmann rearrangement of ketoximes to lactams and amides proceeded to good yield in various air-stable ionic liquids, enhanced by the addition of PCl_5 .⁷² The Fries rearrangement of

various phenyl benzoates was accomplished in a chloroaluminate ionic liquid. This Lewis acid-catalyzed migration of the benzoyl group to another position on the phenyl ring to generate *o*- and *p*-hydroxybenzophenones benefited from a rate enhancement and products were obtained in high selectivity (*ortho* vs. *para*) depending on the substrate.⁷³ In addition to these types of rearrangements, several studies regarding alkane cracking and isomerization in ionic liquids have been undertaken. Isomerization and cracking of paraffins, cracking of alkanes and cycloalkanes, catalytic cracking of polyethylene, and alkylations of isobutene with olefins have all been investigated in chloroaluminate ionic liquids.¹⁸

Ether cleavages have been performed in ionic liquids, providing a general method for the cleavage of both cyclic and acyclic ethers. Symmetric ethers were acylatively cleaved in a halogenoaluminate ionic liquid derived from [emim]I/AlCl₃. In the presence of benzoyl chloride, acyclic ethers were cleaved to give an alkyl benzoate and an alkyl iodide while cyclic ethers were cleaved to give an ω -iodobenzoate ester.⁷⁴ Ethers have also been cleaved in a novel ionic liquid generated from the reaction of 1-methylimidazole and two equivalents of anhydrous HBr, giving a 3-methylimidazolium cation and a mixture of ⁻Br, ⁻HBr₂, and ⁻H₂Br₃ anions.⁷⁵ The cleavage of acyclic ethers afforded alcohols and alkyl bromides while the cleavage of cyclic ethers afforded ω -bromoalcohols with rate enhancements. In some instances, however, dibrominated compounds were isolated due to high temperatures used to distill products from the ionic liquid.

Ionic liquids have been used in a number of other reactions commonly performed by organic chemists. Esterification reactions between acetic acid and various alcohols

were performed in chloroaluminate ionic liquids in order to take advantage of the Lewis acidity of the medium.⁷⁶ Yields of acetate esters were higher than obtained when using sulfuric acid as a solvent. As well, the ionic liquid was recycled on several occasions, something not normally done with the air- and moisture-sensitive chloroaluminate ionic liquids. Air-stable ionic liquids have been used for the generation of tetrahydropyran-2-yl (THP) ethers from alcohols and 3,4-dihydro-2*H*-pyran with different acid catalysts.⁷⁷ The reactions proceeded to nearly quantitative yields with short reaction times, generally less than ten minutes. The ionic liquid containing the acid catalyst was also recycled extensively, requiring the addition of fresh catalyst periodically. Electrophilic nitration of aromatic molecules has been achieved in different air-stable ionic liquids with different nitrating agents.⁷⁸ While some nitrating agents reacted with the ionic liquids, others afforded nitrated products in good yields and the ionic liquids were recyclable. Bromination reactions of alkenes and alkynes have been shown to proceed stereospecifically in various air-stable ionic liquids using only bromine and the alkene/alkyne as reactants.⁷⁹ These reactions proceed in nearly quantitative yields very quickly and the ionic liquid can be reused. Nucleophilic displacement reactions were performed in [bmim]PF₆, generating phenylacetonitrile from the reaction between cyanide and benzyl chloride. The phenylacetonitrile could then be cycloalkylated with 1,4-dibromobutane in the presence of potassium hydroxide, adding a cyclopentyl ring to the benzylic position.⁸⁰ Indole and 2-naphthol were selectively *N*- and *O*-alkylated in [bmim]PF₆ and [bmim]BF₄ with alkyl halides in the presence of potassium hydroxide, comprising another type of nucleophilic displacement reaction.⁸¹ The ionic liquids could be recycled simply by filtering off potassium halides and unreacted potassium hydroxide.

Since many different types of standard organic reactions can be performed in ionic liquids, often with rate, selectivity, and yield enhancements coupled with solvent recyclability, one would expect to see ionic liquid use in more synthetic pathways. It seems as though the use of ionic liquids as solvents is still in embryonic stages as most of the reactions carried out in them are not for the purpose of obtaining products for subsequent use, but simply to see if the reactions can be done in ionic liquids and to determine their effects. One example of a synthetic route to a pharmaceutical compound has been published that uses an ionic liquid as a solvent for both steps of the two-step synthesis.⁸² The synthesis of Pravastatin, a non-steroidal anti-inflammatory drug, was synthesized in two steps (Figure 7).

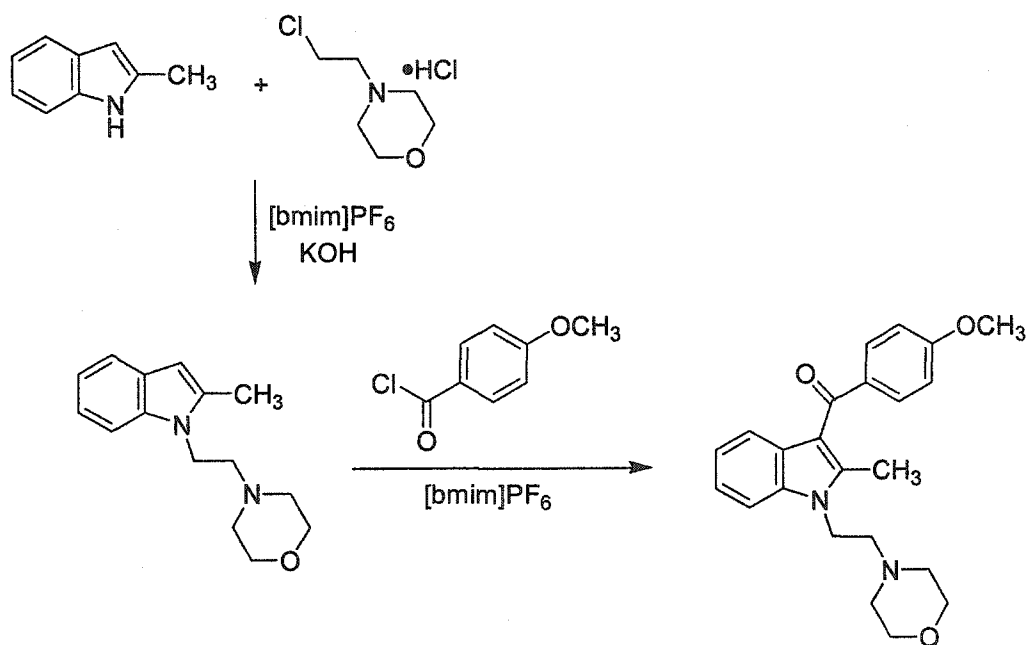


Figure 7. Synthesis of Pravastatin in $[bmim]PF_6$ ⁸²

The synthesis started with an *N*-alkylation of 2-methylindole with 1-(*N*-morpholino)-2-chloroethane hydrochloride in [bmim]PF₆ using solid sodium hydroxide as a base, giving quantitative yields of the alkylated product; the ionic liquid was recycled. The second step involved a Friedel-Crafts acylation at the 3-position of the indole ring using 4-methoxybenzoyl chloride. This reaction was performed in a chloroaluminate ionic liquid, but resulted in the formation of by-products due to the high acidity. The reaction was also performed in [bmim]PF₆, giving near quantitative yields of Pravadoline without the production of by-products and without the addition of Lewis acid. Pravadoline was isolated in 90-94% overall yield and the ionic liquid was recycled, showing the utility of ionic liquids for replacing conventional solvents in many standard synthetic pathways.

1.2.2 As Solvents for Transition Metal-Catalyzed Reactions

Since the discovery that ionic liquids could be used as solvents for organic reactions, many have been investigated for rate, yield, and selectivity enhancements. Soon after this discovery, it was recognized that ionic liquids could also be used as solvents for reactions catalyzed by transition metals. Many reactions mediated by transition metal catalysts proceed *via* mechanisms involving charged active species that could be stabilized by the ionic nature of the solvent, enhancing the rate of reaction and possibly selectivity. As well, the non-coordinating nature of the anions on which common ionic liquids are based allows coordination of unsaturated molecules to active metal centers rather than having to compete with solvent molecules.¹⁸

In addition to these benefits, ionic liquids can also be used to recycle catalysts. Since ionic liquids are nonvolatile, they themselves can be recovered. In many transition metal-catalyzed reactions, it is often the case that the catalyst remains in the ionic liquid phase after product removal and can be reused along with the ionic liquid. Often the catalysts are not leached out by non-polar or moderately-polar extractive solvents, presumably due to their ionic nature. This allows the dissolution of many metal species without necessitating syntheses of specialized ligands. In some cases metal complexes are removed by polar reaction products; this can be avoided by using ionic ligands on the metal. It has been suggested that ionic liquids would be better thought of as polymeric liquid supports rather than solvents, immobilizing catalysts rather than actually dissolving them as ionic liquids are believed to be highly ordered liquids.³³ Ionic liquids also combine the benefits of homogeneous and heterogeneous catalyses. They allow dissolution/immobilization of many catalysts, giving each metallic center the possibility of being catalytically active, increasing catalytic density and turnover frequencies, while allowing easy separation of products and catalyst.³²

The first reaction performed in an ionic liquid using a homogeneous transition-metal catalyst was a platinum-catalyzed hydrogenation of various alkenes in a tetraalkylammonium chlorostannate ionic liquid, $[R_4N][SnCl_3]$, in 1972.⁸³ The melting point of this ionic liquid was relatively high, 78 °C, and the reaction rate was relatively low, limiting the utility of the reaction. It did, however, show that homogeneous transition metal catalysis was possible in ionic liquids. These results were largely overlooked for the next two decades until several groups began investigating the area in the 1990s, made easier by the discovery of air- and moisture-stable ionic liquids.³¹ Since

that time many different transition metals have been immobilized in ionic liquids for different purposes and many have been recyclable with little to no loss in activity; several recent reviews comprehensively cover many of these.^{9,18,31,32,33,84,85,86}

Alkene hydrogenation reactions are among the first transition-metal catalyzed reactions performed in ionic liquids. Rhodium complexes have been dissolved in [bmim]BF₄ and [bmim]PF₆ for the hydrogenation of cyclohexene, producing cyclohexane with large turnover numbers.⁸⁷ When products were removed from the ionic liquid, 98% of the rhodium species remained in the ionic liquid. Rhodium-catalyzed hydroformylation of 1-octene was used as a probe to determine the utility of the “greener” ionic liquid 1-*n*-butyl-3-methylimidazolium octylsulfate under biphasic conditions.⁴⁴ Although the selectivity of the process for generating *n*-nonanal vs. branched nonanals was relatively low, the activity of the catalyst was higher than in BF₄ and PF₆ ionic liquids. Due to its lack of halogens, this ionic liquid is considered to be “greener” than other halogen-containing ionic liquids such as [bmim]BF₄ and [bmim]PF₆.

Ruthenium complexes are much more commonly employed in ionic liquids for hydrogenation reactions. Asymmetric hydrogenation of 2-arylacrylic acids was performed with a ruthenium catalyst in [bmim]BF₄ to give quantitative conversions to the aryl alkane, as was obtained with molecular solvents; however, the enantioselectivity of the reaction was higher in the ionic liquid.⁸⁸ The products were easily separated from the ionic liquid/catalyst, which was reused without loss of activity. Studies were undertaken to determine the effects of hydrogen concentration in the ionic liquid and concluded that hydrogen concentration in the ionic liquid is the important kinetic parameter rather than hydrogen pressure in the gas phase for rhodium(I)- and ruthenium(II)-catalyzed

asymmetric hydrogenations.⁸⁹ Studies have also been performed investigating the use of supercritical CO₂ as an extractant to remove products from [bmim]PF₆ after ruthenium-catalyzed asymmetric hydrogenation of several substituted acrylic acids. This allowed extensive reuse of the ionic liquid/catalyst system to provide quantitative yields of hydrogenated product with very high enantioselectivities.⁹⁰ Biphasic ruthenium-catalyzed hydrogenations of 1-hexene were performed in the uncommon ionic liquid resulting from the mixture of [bmim]Cl with zinc chloride, ZnCl₂.⁹¹ This ionic liquid is solid at room temperature, allowing reactions to be performed at higher temperatures then cooled and the products can simply be decanted from the solid ionic liquid/catalyst phase with no catalyst leaching. These reactions gave similar results to those obtained when using [bmim]BF₄ as a solvent.

Arenes have also been hydrogenated in ionic liquids with ruthenium catalysts. Perhydrogenated alkanes have been isolated from [bmim]BF₄ in good yields with good turnover numbers; however, these data were no better than those obtained when using water as a solvent. The advantage of the ionic liquid was that it could be reused repeatedly for the catalytic hydrogenation of different arenes.⁹² Ruthenium catalysts have also been used in ionic liquids that selectively hydrogenate the arene moiety of compounds containing both arene and alkene functionalities.⁹³ Olefin metathesis has been performed in [bmim]PF₆ using Grubb's ruthenium catalyst. Not much yield improvement was made using the ionic liquid over using dichloromethane as a solvent, however.⁹⁴ As well, the catalyst successively lost activity on recycling. An interestingly different ruthenium-catalyzed reaction performed in various air-stable ionic liquids is the selective oxidation of alcohols to aldehydes and ketones.⁹⁵ No over-oxidation was

observed, but yields obtained were similar to those from using conventional solvents. It was discovered through these studies, however, that bubbling oxygen through the ionic liquid was better than using an oxygen blanket due to the low solubility of oxygen in the ionic liquid.

Lanthanide catalysts, most commonly scandium trifluoromethanesulfonate $\text{Sc}(\text{OTf})_3$, have seen much use in ionic liquids for different applications. The mild Lewis acidity of microencapsulated $\text{Sc}(\text{OTf})_3$ was taken advantage of to promote the aza-Diels-Alder reaction between imines and Danishefsky's diene (1-methoxy-3-(trimethylsilyl)oxybuta-1,3-diene). This reaction was carried out in several air-stable ionic liquids, generating the corresponding 5,6-dihydro-4-pyridones (after loss of the trimethylsilyl group) in very good yields. Most important, however, is that the reaction did not proceed without the Lewis acid catalyst and this was recyclable with excellent recovery of the ionic liquid/catalyst system and no loss in activity.⁹⁶ The same catalyst was used in extremely small amounts by another group for normal Diels-Alder reactions between various dienes and dienophiles in air-stable ionic liquids. Even at 0.1 mol% $\text{Sc}(\text{OTf})_3$ the system provided excellent rate enhancements in $[\text{bmim}]\text{PF}_6$ compared to dichloromethane, often with excellent yields and *endo*-selectivity. The system was also extensively recycled without loss of activity.⁹⁷

Friedel-Crafts alkylations of aromatics with various alkenes proceeded quantitatively in hydrophobic ionic liquids at room temperature in the presence of $\text{Sc}(\text{OTf})_3$.⁹⁸ These reactions did not proceed in hydrophilic ionic liquid nor in the conventional solvents tested. The authors noted that the catalyst dissolved in the hydrophilic ionic liquids but was only suspended in the hydrophobic ionic liquids. The

system was recyclable without activity loss. Claisen rearrangements followed by cyclizations of allyl aryl ethers to give 2-methyl-2,3-dihydrobenzo[*b*]furan derivatives have been performed in air-stable ionic liquids catalyzed by $\text{Sc}(\text{OTf})_3$.⁹⁹ The system provided good yields, was stable at high temperatures (200°C), and was recyclable. The reaction did not proceed without the Lewis acid catalyst. The three-component synthesis of α -amino phosphonate esters (important molecules in the pharmaceutical industry) from aniline, diethyl phosphonate, and various aromatic aldehydes has been accomplished in air-stable ionic liquids in the presence of various lanthanide trifluoromethanesulfonate catalysts.¹⁰⁰ This reaction proceeded quantitatively, giving better yields in ionic liquid solvents than in dichloromethane, and was recyclable without loss of activity. $\text{Sc}(\text{OTf})_3$ has been used in the tin- and indium-mediated allylation of aldehydes and ketones in $[\text{bmim}]\text{PF}_6$ and $[\text{bmim}]\text{BF}_4$ to increase the rate and selectivity of the reaction.¹⁰¹ As with the reaction of tetraallylstannane in ionic liquids without Lewis acid catalysts, products were isolated in good yields, giving better stereoselectivities over conventional solvents. The catalyst did increase the rate and yield of the reaction over the uncatalyzed reaction and the ionic liquid/catalyst system was recyclable without activity loss.

Zinc catalysts have been used in ionic liquids for different applications. Hydroamination reactions involving the zinc(II)-mediated addition of an N-H bond across unsaturated systems have been performed in biphasic systems involving air-stable ionic liquids to give quantitative yields of products with much higher rates than obtained when using a homogeneous toluene solution of the catalyst.¹⁰² Zinc iodide has been used in $[\text{bmim}]\text{BF}_4$ and $[\text{bmim}]\text{PF}_6$ to promote the Diels-Alder reaction between various

dienophiles and heterocyclic dienes such as furan, thiophene, and *t*-butoxycarbonylpyrrole.¹⁰³ This catalyst allowed the reaction to proceed in good yields with *endo*-selectivity.

Oxidation reactions have been performed in ionic liquids mediated by different catalysts. A cobalt catalyst, Co(acac)₂, was used to oxidize ethylbenzene to acetophenone and 1-phenylethanol in 2,3-dimethyl-1-*n*-hexylimidazolium tetrafluoroborate [C₆dmim]BF₄ to good yields.¹⁰⁴ The expensive and toxic osmium catalyst OsO₄ has been immobilized in ionic liquids for the dihydroxylation of alkenes. When used in [emim]BF₄, the catalyst provided excellent yields of dihydroxylated products and was recyclable without loss of activity.¹⁰⁵ The same reactions were also performed in [bmim]BF₄ using 4-dimethylaminopyridine DMAP as an agent to form a zwitterionic OsO₄-DMAP complex, which would likely be less volatile than OsO₄ and would remain in the ionic liquid during product extraction.¹⁰⁶ It was found that upon recycling the ionic liquid/catalyst system without DMAP, activity was successively lost suggesting that the catalyst was leaching out after each cycle. Adding DMAP formed a more polar complex, preventing leaching and providing an ionic liquid/catalyst system that did not lose activity on recycling.

Epoxidation reactions have been carried out in ionic liquids using different catalysts. Jacobsen's chiral manganese-based epoxidation catalyst (salen)Mn has been immobilized in [bmim]PF₆ to generate epoxides from alkenes enantioselectively in good to excellent yields.¹⁰⁷ The ionic liquid conferred rate enhancements to the reaction and the catalyst system was recyclable; however, yield and enantioselectivity slowly decreased. Methyltrioxorhenium was used as a catalyst in [emim]BF₄ in the presence of

urea and hydrogen peroxide to generate epoxides from a number of alkenes in a highly enantioselective fashion in quantitative yields.¹⁰⁸ A chiral chromium catalyst, (salen)Cr, similar to Jacobsen's manganese-based epoxidation catalyst, was immobilized in various air-stable ionic liquids for asymmetric epoxide ring-openings with trimethylsilylazide TMSN₃.¹⁰⁹ The hydrophobic ionic liquids provided the desired azido silyl ethers in good yields and enantioselectivities, comparable to those obtained using conventional solvents, but the ionic liquid/catalyst system was recyclable.

Another example of transition metal catalysts immobilized in ionic liquids are nickel-based catalysts. Different nickel catalysts have been used for alkene oligomerization/dimerization reactions. The dimerization/oligomerization of ethene was achieved in chloroaluminate ionic liquids under biphasic conditions, giving mainly but-1-ene, but-2-enes, and hexenes.¹¹⁰ Cationic nickel complexes were used in air-stable hexafluorophosphate-based ionic liquids to generate higher α -olefins selectively with improved turnover numbers compared to conventional solvents.¹¹¹ Nickel-catalyzed hydrovinylation of styrene (dimerization of styrene and ethene) was accomplished in several air-stable ionic liquids using high-pressure CO₂ to activate the nickel catalyst.¹¹² This led to moderate activation of the catalyst, providing good yields of dimerized products with good selectivity. The authors found that the catalyst decomposed upon successive recycling; this was avoided if the ionic liquid/catalyst system was employed in a continuous flow reactor. Michael additions of acetylacetone to methyl vinyl ketone have been catalyzed by [bmim]BF₄-immobilized Ni(acac)₂.¹¹³ Better yields of the 1,4-addition product were obtained from [bmim]BF₄ than from dioxane or under solventless conditions and the ionic liquid/catalyst system was extensively recycled without loss of

activity. As well, $\text{Ni}(\text{acac})_2$ was used to catalyze the oxidation of substituted benzaldehydes to benzoic acids in $[\text{bmim}]\text{PF}_6$ using an oxygen blanket.¹¹⁴ The yields were not as high as those obtained from perfluorinated solvents, possibly due to the low solubility of oxygen in $[\text{bmim}]\text{PF}_6$. The system was recycled without activity loss.

In addition to reactions catalyzed by transition metals, many enzyme-mediated reactions have been performed in ionic liquids. Many of the enzymes used in ionic liquids were ones known to operate well under anhydrous conditions. Although, given the exceedingly large role that tertiary protein structure plays in the function and activity of an enzyme and given the large roles that solvents play in aiding the folding of proteins into their active conformations, it is fascinating to see that enzymes work at all in ionic liquids. Many different classes of enzymes have been used successfully in ionic liquids, some with rate and selectivity enhancements, including proteases, galactosidases, lipases, and esterases. Ionic liquids increase the stability of many enzymes and allow their reuse. Several reviews have been published regarding the use of enzymes in ionic liquids.^{31,45,85,115,116}

1.2.2.1 As Solvents for Palladium-Catalyzed Reactions

As outlined in the above section, many different transition metal catalysts have been immobilized in ionic liquids for different purposes. It seems, however, that palladium catalysis is the subject of a rather large number of publications regarding their use in ionic liquids, perhaps due to their wide array of possible applications. Commonly, palladium catalysts have been used to mediate coupling reactions between various types

of unsaturated systems, forming new carbon-carbon bonds. Depending on the type of substrate used in the coupling, the reaction generally has a specific name. Ionic liquids have been used in many palladium-catalyzed reactions, affording the same benefits as for other transition metal-catalyzed reactions; namely, easy catalyst/product separation and catalyst recyclability.⁸⁵

The Heck reaction is perhaps the most investigated palladium-catalyzed reaction in ionic liquids judging from the number of publications on the subject. The Heck reaction generally involves the palladium-mediated coupling of aryl halides with alkenes to yield arylated alkenes. The reaction was performed in several air-stable ionic liquids between iodobenzene and ethyl acrylate in the presence of a base (triethylamine or sodium bicarbonate) and palladium(II) acetate $\text{Pd}(\text{OAc})_2$ to yield the coupled products in quantitative yields (Figure 8).¹¹⁷

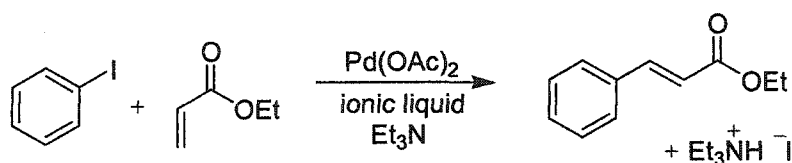


Figure 8. Palladium-catalyzed Heck reaction in ionic liquids

Several group 15 ligands were added to the reaction mixture to determine their effects on reaction rate and it was found that addition of triphenylphosphine provided a system that gave quantitative yields of coupled products in one hour in $[\text{bmim}]\text{PF}_6$ and was extensively recycled. The products were extracted with cyclohexane and the triethylammonium iodide byproduct was extracted with water. The Heck reaction was

also performed with other aryl halides with ethyl acrylate as well as with styrene in [bmim]Br and [bmim]BF₄, giving good yields and excellent selectivity toward the *trans*-isomeric products.¹¹⁸ Other aryl halides and alkenes have also been used in [bmim]PF₆ giving moderate yields compared to using *N,N*-dimethylformamide DMF as solvent.¹¹⁹ When Heck reactions were performed in non-imidazolium-based ionic liquids, careful drying was necessary as water lowered catalyst turnover numbers. Higher catalytic activity was observed in these ionic liquids compared to conventional organic solvents but early palladium black precipitation inhibited efficient catalyst recycling.¹²⁰

Heck reactions were performed in non-imidazolium-based ionic liquids using a novel palladium-benzothiazole carbene complex to catalyze the coupling of aryl halides with α -substituted¹²¹ and β -substituted acrylates¹²² giving good yields of coupled products. The ionic liquid/catalyst system could be recycled but was very limited due to buildup of ionic byproducts (e.g. NaBr). Electron-rich olefins such as butyl vinyl ether were coupled with aryl halides under Heck conditions in [bmim]BF₄ giving only one of two possible products at high rates in near quantitative yields. The product obtained from the reaction in [bmim]BF₄ results from α -arylation of the olefin and is formed *via* an ionic pathway while the other possible (but unobserved) product results from β -arylation of the olefin and is formed *via* a neutral pathway. Conventional solvents gave mixtures of the two products, suggesting that the ionic liquid stabilized the ionic pathway so as to provide only one product isomer.¹²³

Less commonly employed reaction conditions have been investigated regarding the Heck reaction in ionic liquids. Ultrasound was used to promote the palladium-catalyzed reaction in ionic liquids [bbim]Br and [bbim]BF₄ between aryl iodides and

various acrylates, styrene, and phenylacetylene at sonicator temperatures (generally 45-50 °C as sonication heats the sonicator bath), providing the coupled products in good yields and short reaction times.¹²⁴ These reactions did not proceed in conventional solvents such as DMF and *N*-methylpyrrolidinone (NMP) nor in the absence of ultrasound at ambient temperatures. Heck reactions in [bmim]PF₆ have also been accelerated using microwave irradiation giving good yields of coupled products in short reaction times; the use of microwave irradiation also resulted in high temperatures. The ionic liquid/catalyst was recyclable without loss of activity.¹²⁵ Heck reactions have also been performed in [bmim]PF₆ using the heterogeneous catalyst Pd/C.¹²⁶ These reactions do not require the use of a trialkyl or triarylphosphine and do not produce palladium black. Upon filtering the ionic liquid/catalyst mixture after use, no palladium was detected in the ionic liquid by inductively-coupled plasma mass spectrometry (ICP-MS), indicating no dissolution of the catalyst. The ionic liquid/catalyst system was recyclable but required periodic water washes to remove ionic byproducts that slowly decreased yields. Heck reactions were also performed in [bmim]PF₆ using silica-supported palladium complex catalysts, displaying higher activities than in DMF.¹²⁷ After filtering the silica-supported palladium catalyst from the ionic liquid after use, the ionic liquid was able to catalyze the Heck reaction without addition of fresh catalyst, indicating that some palladium had dissolved in the ionic liquid.

The Suzuki cross-coupling reaction is similar to the Heck reaction in that it involves palladium-catalyzed coupling of an aryl halide to another molecule but uses arylboronic acids instead of olefins to generate biaryls. These reactions have been accomplished in [bmim]BF₄ between phenylboronic acid and different aryl halides,

producing biaryls in good yields in only 10 minutes at 110 °C (Figure 9). These reactions could be conducted in air and the ionic liquid/catalyst system was recyclable without loss of activity.¹²⁸

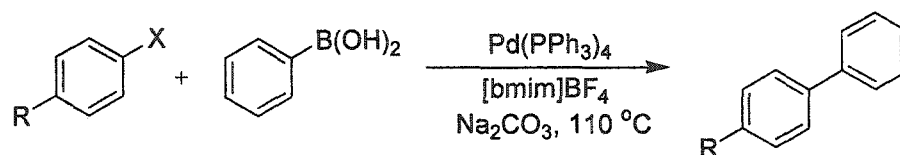


Figure 9. Palladium-catalyzed Suzuki cross-coupling in [bmim]BF₄

Suzuki reactions were performed in [bbim]BF₄ with methanol using ultrasound to promote the reaction with fast reaction times at ambient temperature.¹²⁹ Excellent yields were obtained generally in less than one hour. Reactions did not proceed at room temperature in the absence of ionic liquid or ultrasound, as when similar techniques were employed for the Heck reaction in ionic liquids. As well, by-product formation was noted when the reactions were performed in air, which was suppressed by performing the reactions under argon. The Suzuki coupling has been performed with the iodoarene bound to a solid phase resin in [bmim]BF₄/DMF mixtures.¹³⁰ The reactions proceeded to give good yields at high temperatures, showing that ionic liquids can be used for solid-phase reactions. The ionic liquid could be reused; however, the catalyst was not recyclable due to palladium black precipitation.

The Stille coupling is another palladium-catalyzed cross coupling reaction that has been performed in ionic liquids.¹³¹ This reaction involves coupling of a vinyl- or arylstannane with a vinyl or aryl halide (Figure 10).

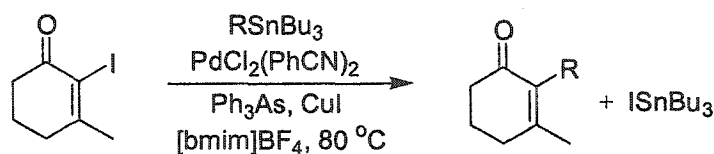


Figure 10. Palladium-catalyzed Stille couplings in [bmim]BF₄

Studies with different halogenated and tin-containing compounds showed different palladium catalyst preferences in [bmim]BF₄. Aryl bromides coupled with aryl stannanes most efficiently using Pd(PPh₃)₄ while aryl iodides coupled most efficiently with PdCl₂(PhCN)₂. Both systems were recyclable without loss of activity. The ionic liquid/catalyst system could even be reused after being left standing for weeks without special air or moisture exclusion techniques.

Palladium-catalyzed allylic alkylation reactions have been performed in ionic liquids. Soft carbon nucleophiles, stabilized carbanions, generated from compounds containing protons that are easily removed to give enolates (such as dimethyl malonate) can be added to allylic acetates mediated by palladium. These reactions proceed to good yields, but when triphenylphosphine was used to form the catalyst precursor from Pd(OAc)₂ significant leaching of palladium occurred, preventing efficient recycling of the ionic liquid/catalyst system. Using *m*-sulfonated triphenylphosphine instead, the complex remained in the ionic liquid and was recyclable without loss of activity.¹³² These reactions have been performed enantioselectively using palladium(0)-ferrocenyl complexes in [bmim]PF₆, giving higher yields and enantiomeric excesses than THF.¹³³ The ionic liquid/catalyst system was cleaned between cycles using a complex procedure

involving dissolution in ethyl acetate, washing with water, and drying over MgSO_4 . This resulted in poorer yields upon recycling but gave similar enantiomeric excesses. The use of other palladium(0)-ferrocenyl complexes provided similar results.¹³⁴

Other palladium-catalyzed reactions have been performed in ionic liquids. Selective hydrodimerization reactions of 1,3-butadiene have been performed in $[\text{bmim}]\text{BF}_4$ using palladium(II) catalysts to give 1,3,6-octatriene and 2,7-octadien-1-ol selectively, depending on the reaction conditions.¹³⁵ The ionic liquid/catalyst system was recyclable without loss of activity. Hydroesterifications of styrenes were performed in a $[\text{bmim}]\text{BF}_4$ /isopropanol/cyclohexane solvent system using palladium(II) catalysts to give the corresponding 2-arylpropionic esters in good yields with excellent selectivities.¹³⁶ The catalyst could not be recycled, however, due to decomposition. Carbonylation of aryl halides and alcohols in the presence of a base to produce aromatic esters has been accomplished in $[\text{bmim}]\text{BF}_4$ and $[\text{bmim}]\text{PF}_6$ with palladium(II) catalysts.¹³⁷ Good yields were obtained, but recyclability was limited due to palladium black precipitation. Oxidation of styrene to acetophenone has been achieved selectively using PdCl_2 in $[\text{bmim}]\text{BF}_4$ and $[\text{bmim}]\text{PF}_6$ to give good yields using only a small excess of hydrogen peroxide as the oxidant.¹³⁸ The reaction did not proceed in the absence of palladium. Heterogeneous palladium catalysts have also been used in ionic liquids with D_2O to replace the protons on the imidazolium ring with deuterium atoms.¹³⁹ Using deuterated alkyl halides, fully deuterated imidazolium-based ionic liquids can be generated for use in various applications.

1.2.3 For Novel Applications

As ionic liquids have been shown to have great potential to act as solvents for a number of organic reactions, both catalyzed and non-catalyzed, they have also been investigated for use in a number of applications other than as reaction media. Due to their miscibility with some solvents but not with others, ionic liquids have been used in several applications acting as selective extractants. As outlined in the above section, ionic liquids often immobilize transition metal catalysts, allowing easy separation of product and catalyst through either distillation or through extraction with an immiscible solvent. They have also been used to remove large excesses of inorganic reagents; for example, in the MnO_2 oxidation of allylic ethers as outlined in Section 1.2.1 and shown in Figure 5 $[\text{bmim}]\text{BF}_4$ was able to immobilize excess MnO_2 after the oxidation was performed in THF, allowing products to be isolated in quantitative yields by extraction with diethyl ether. In conventional solvents, MnO_2 is removed from the reaction mixture by filtration but this leaves products adsorbed on the MnO_2 particles. Several studies have shown ionic liquids to be immiscible with a number of reagents and organic solvents, showing the potential for ionic liquids to replace conventional molecular solvents in liquid-liquid separations.^{24,140,141} Chloroaluminate ionic liquids have shown promise for the extraction of sulfur-containing compounds from Diesel fuel, removing almost all of the sulfur-containing compounds after five cycles of the fuel through ionic liquids.¹⁴² The sulfur-saturated ionic liquid could potentially be regenerated by extracting with light alkanes or supercritical CO_2 , allowing the isolation of the sulfur-containing

compounds for their conversion to more environmentally-friendly compounds, and the ionic liquid could then be reused.

Ionic liquids have also been synthesized with cations specially designed to remove toxic metal anions from contaminated water samples. Imidazolium-based cations have been synthesized with *N*-alkyl substituents containing urea and thiourea groups for the purpose of binding to and complexing mercury(II) and cadmium(II) ions. These ionic liquids have PF_6^- anions and are immiscible with water. They have been shown to be capable of removing metal ions, mercury(II) especially, from contaminated water samples (Figure 11).^{143,144}

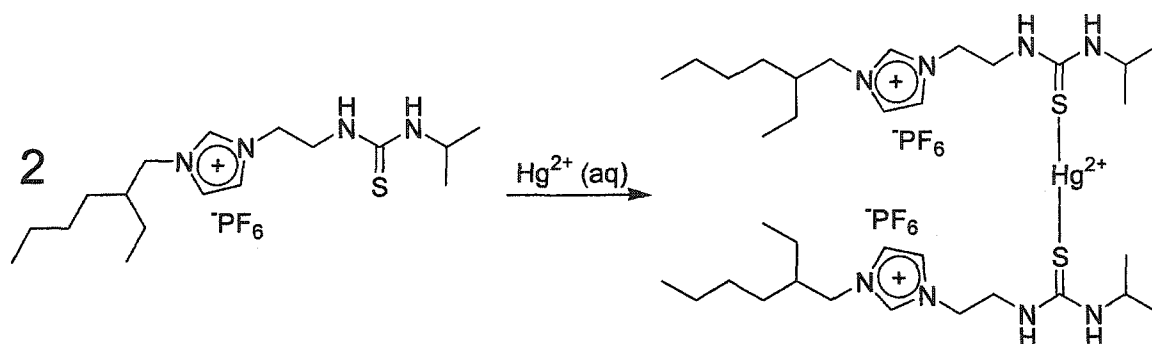


Figure 11. Removal of mercury(II) ions from water samples using water-immiscible functionalized ionic liquids

Ionic liquids have also been demonstrated to remove alkali metals from water samples using crown ethers. Various water-immiscible ionic liquids were mixed with water samples containing strontium nitrate. With the addition of a crown ether, dicyclohexyl-18-crown-6 (known to form a strong complex with Sr^{2+}), the concentration of strontium was 1,000 to 10,000-fold higher in the ionic liquid phase than in the aqueous phase depending on the ionic liquid used. Without the crown ether the strontium concentration

was approximately twice as large in the aqueous phase as in the ionic liquid. The same results were obtained when toluene and chloroform were used with crown ethers.¹⁴⁵ Later studies indicated that a cation exchange process may be responsible for the partitioning of the metal-crown ether M^+CE^{2+} complex wherein the imidazolium cation partitions into the aqueous phase as the M^+CE^{2+} complex partitions into the ionic liquid phase, eventually causing the ionic liquid to become miscible with water.¹⁴⁶ Another study investigated the effects of varying the imidazolium *N*-alkyl chain length of various PF_6^- ionic liquids regarding the partitioning of metal-crown ether complexes.¹⁴⁷ In general, extraction efficiency decreased with increasing chain length. The studies also showed that potassium was the easiest metal ion to extract, not surprising since it fits best into the crown ether used.

The novel properties of ionic liquids have been taken advantage of in other applications besides selective extraction. Supercritical CO_2 has been shown to act as a switch to separate ionic liquids from organic compounds with which they are miscible under normal circumstances. Methanol/[bmim] PF_6 solutions have been induced to separate into triphasic mixtures in the presence of supercritical CO_2 . The lower layer is rich in ionic liquid and the upper methanol-rich phase can be induced to merge with the middle supercritical CO_2 layer to provide a methanol-rich, ionic liquid-free phase.³⁸ The phase behaviour in such mixtures is quite complex and is not yet fully understood, although it has been attributed to a lowering of the dielectric constant of the solvent mixture when CO_2 is added as compared to that of pure methanol, causing it to become less soluble in the ionic liquid and more soluble in supercritical CO_2 . Ionic liquids, being thermally stable, have also been explored as potential stationary phases for gas

chromatography. The ionic liquids [bmim]PF₆ and [bmim]Cl were investigated and appeared to have a dual nature, acting as non-polar stationary phases when separating non-polar analytes, but acting highly interactively and retentively when used to separate molecules with strong proton donor and acceptor groups. The nature of the anion was shown to be important as the chloride salt interacted more strongly with proton donor and acceptor molecules while the PF₆ salt interacted more strongly with non-polar substrates. Thus, ionic liquids may offer advantages in separation science.¹⁴⁸ Ionic liquids have been used to dissolve large polymeric materials such as cellulose. Cellulose, a linear polymer of glucose monomers, is a major renewable resource that is currently processed using environmentally harsh conditions. Dissolution in an ionic liquid would increase the amount of control available over the processing methodology. This was shown to be possible with several air-stable ionic liquids, those containing coordinating ions such as [bmim]Cl proving to be the best; a 25% w/w solution of cellulose was prepared in this ionic liquid using microwave pulses.¹⁴⁹

Ionic liquids have been used in even more unorthodox applications. Dialkylimidazolium tetrafluoroborates were examined as potential lubricants for the contact of several metals since most of the lubricants used in industries are not applicable to a wide variety of materials. Ionic liquids showed excellent friction reduction, antiwear performance, and a high load-carrying capacity, performing better than two widely used fluorine-containing lubricants phosphazene and perfluoropolyether. Coupled with their thermal stabilities and low volatilities, ionic liquids make attractive, although expensive, alternatives to conventional liquid lubricants.¹⁵⁰ Ionic liquids have also been tested as antimicrobial agents. Studies have shown that ionic liquids have antimicrobial activity,

which increases in potency as the length of the imidazolium alkyl chains increase (similar to the commonly-used antimicrobial agent benzalkonium chloride). This has implications for whole-cell biotransformations carried out in ionic liquids.¹⁵¹

1.3 Silylstannanes

Silylstannanes are highly synthetically useful reagents but are not as common as one might expect, given their potential in synthesis. As the name suggests, silylstannanes are organometallic compounds in which a triorganotin moiety is joined to a triorganosilyl moiety through a silicon-tin bond. This covalent bond is not very polarized since both tin and silicon are in group four on the periodic table, the same group as carbon. The steric environment around each metal atom can be varied to determine which would be more open to nucleophilic attack.^{152,153}

Silylstannanes were first prepared in the 1960s but were not used in many applications.^{154,155} It was not until the 1980s that silylstannanes saw use in organic synthesis where they were shown to be capable of incorporating both the triorganosilyl and triorganotin moieties into organic products to afford bifunctional organic dianion equivalents.^{153,156} Since that time, silylstannane use has increased in different applications, but they are not yet commonplace.

Silylstannanes are relatively easily synthesized. This is generally done by generating a triorganotin anion through various methods followed by quenching with a chlorotriorganosilane. The products can be purified by distillation as they are thermally stable and although they have been reported to be air- and moisture-stable they are

generally handled and stored under inert atmospheres. The toxicity of silylstannanes is relatively unexplored. Given the relative toxicity of organotin reagents, however, silylstannanes should be used with caution. Triorganotin moieties are known to be rather toxic, although as the size of the alkyl group increases the toxicity decreases.¹⁵⁷

Three methods are commonly employed to generate a triorganotin anion (Figure 12). The first involves a metal-halogen exchange between a triorganotin chloride and lithium metal (or another group 1 metal) to generate a triorganotin lithium species and lithium chloride. A problem with this method is that as the triorganotin lithium species is generated, it can attack unreacted triorganotin chloride to generate an unreactive hexaorganodistannane byproduct. The second involves cleavage of a hexaorganodistannane with *n*-butyllithium, generating the desired triorganotin lithium species and a relatively inert tetraorganostannane, or with lithium metal to generate two equivalents of triorganotin lithium species. The third method is the highest-yielding, involving deprotonation of a triorganotin hydride with a strong base such as lithium diisopropylamide (LDA) to generate the lithium triorganotin species along with the volatile diisopropylamine byproduct. These reactions are generally performed below room temperature, but the quench with a chlorotriorganosilane can be performed near room temperature (Figure 12). The reaction then proceeds quickly to give the silylstannane product along with precipitated lithium chloride, which can be removed by filtration, and the product distilled.¹⁵⁸ As well, trimethyl(tributylstannyl)silane ($\text{Bu}_3\text{SnSiMe}_3$) is commercially available.

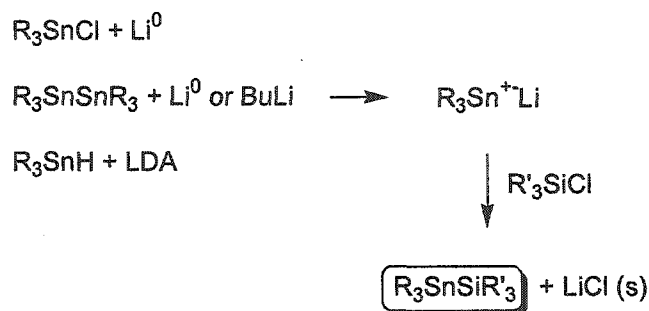


Figure 12. Synthetic routes to silylstannanes

Perhaps the most useful reaction silylstannanes undergo is the palladium-catalyzed addition to unsaturated systems. This was first accomplished in the late 1980s when two research groups investigated the potential to add variably substituted silylstannanes to a number of terminal alkynes. This resulted in the generation of terminally-silylated, internally-stannylated *cis*-bismetallated alkenes (Figure 13).^{153,156} Products were generally isolated in good to excellent yields after variable reaction times.

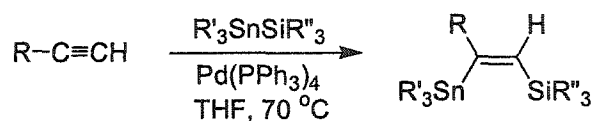


Figure 13. Palladium-catalyzed addition of silylstannanes to terminal alkynes

These reactions proceeded with remarkable regio- and stereoselectivities, always affording the *cis*-bismetallated alkene containing the triorganosilyl moiety on the terminal carbon and the triorganotin moiety on the internal carbon. When additions were attempted with internal alkynes, however, regiochemical scrambling occurred.^{159,160}

The palladium-catalyzed addition of silylstannanes across alkenes is rather limited in scope with many such reactions being unsuccessful. The reaction has only been successfully performed with ethene and bicyclic norbornene systems resulting in excellent yields of the silylstannylated alkanes.¹⁶¹ Silylstannanes have been added across allenes to give very good yields of products in a highly regio- and stereoselective fashion. Using a $\text{Pd}_2(\text{dba})_4$ catalyst in toluene at room temperature, variously substituted terminal allenes were inserted into the tin-silicon bond of different silylstannanes to afford 1-triorganostannyl-2-triorganosilylalk-2-ene products as (*E*)-isomers. Other solvents and catalysts provided poorer yields.¹⁶²

The products resulting from the addition of silylstannanes to terminal alkynes can be used in a variety of applications given that these silylstannylated alkenes have two reactive centers with differing reactivities. These compounds can be selectively protodesilylated or protodestannylated by using different reaction conditions. The trialkylsilyl group can be replaced with a proton using tetrabutylammonium fluoride (TBAF) to generate 2-stannylalkenes (which works especially well with dimethylphenylsilyl derivatives).¹⁶³ The trialkylstannyl group can be replaced with a proton by treating with hydriodic acid to give the corresponding (*E*)-1-silylalkene (Figure 14).¹⁶⁰

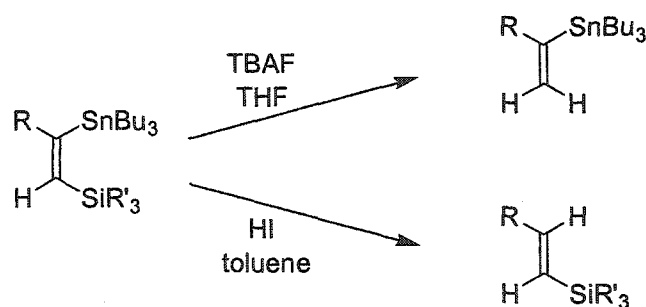


Figure 14. Protodesilylation vs. protodestannylation of silylstannation products¹⁶⁰

The trialkyltin moiety can be replaced with a suitable electrophile *via* tin-lithium exchange. If the silylstannation product is treated with an alkylolithium reagent such as BuLi, tin-lithium exchange will occur to generate a β -silylvinyllithium species, which can be used to form various substituted vinylsilanes when treated with the appropriate electrophile.¹⁶⁰ Since the products of silylstannation reactions are vinyl stannanes, they can be used in palladium-catalyzed Stille couplings with aryl and vinyl halides to generate 2-arylated or 2-vinylated 1-silylalkenes.¹⁵⁹

Silylstannanes have seen use in more varied applications as well. They have been coupled with vinyl halides using palladium catalysis, generating vinylstannanes that have been used in Stille-type intramolecular cyclization reactions with vinyl triflates.¹⁶⁴ Silylstannanes have been added to 1,6-enynes (compounds containing an alkyne and an alkene moiety in the same molecule), the products of which cyclize to give 5-membered rings bearing trialkylstannylmethyl and *exo*-methylenylsilane moieties.¹⁶⁵ They have also been added to internal alkynes (with limited success) that were cyclized to give 5-membered lactone products containing trialkyltin and trialkylsilyl moieties.¹⁶⁶ They have also been shown to undergo 1,4-addition to α,β -unsaturated carbonyl compounds to generate 3-stannylated silyl enol ether products that can be hydrolyzed to give 3-stannylated ketones.^{152,167}

Most of the synthetic utility of silylstannanes results from their palladium-catalyzed addition to unsaturated systems such as terminal alkynes. Major drawbacks to their more widespread use are the inherent toxicity of the tin-containing compounds and the expense of the palladium catalysts.

1.4 Objectives

Several reactions involving transition metal catalysts have been performed in ionic liquids. These catalysts have often contained organic ligands and thus are organometallic reagents. Few reactions have been performed in ionic liquids involving organometallic reagents that are not part of a transition metal complex. This may be a result of the relatively high basicity of many organometallic reagents such as alkyllithium reagents, being problematic due to the relatively high acidity of the proton on carbon 2 of the imidazolium ring on which most commonly-used ionic liquids are based. Reagents such as tetraallylstannane have been used to add allyl groups to carbonyl compounds⁶⁷ and alkylzinc reagents have also been added to aldehydes in Reformatsky reactions, although these reactions were performed in non-imidazolium-based ionic liquids for the most part.⁵⁹

Many palladium-catalyzed reactions have been performed in ionic liquids, some of which have proceeded with rate, yield, and selectivity enhancements. In many cases the palladium catalyst was recyclable with little to no loss in activity. Many of these reactions provide similar types of products, coupling aryl halides with molecules such as acrylates in the Heck reaction, boronic acids in the Suzuki coupling, and vinyl stannanes in the Stille coupling.

The objectives of this research focused on successfully performing palladium-catalyzed addition reactions of silylstannanes to terminal alkynes in imidazolium-based air-stable ionic liquids. An array of alkynes, silylstannanes, and ionic liquids were to be employed to investigate the scope of the reaction. Investigations focused on yield

enhancements and the possibility of rate enhancements resulting from the use of ionic liquid solvents rather than THF. Another large area of focus was the potential recyclability of the ionic liquid/palladium catalyst systems.

2.0 Results and Discussion

2.1 Silylstannation Reactions in Ionic Liquids

There are many possibilities when choosing the conditions for any reaction in organic chemistry, especially when developing new methodology. For the initial attempts at adding silylstannanes to terminal alkynes in ionic liquids, optimal reaction conditions used in the conventional solvent THF were employed. Phenylacetylene was chosen as the first alkyne to use as it has been shown to be particularly active in silylstannation reactions, requiring only three hours to react to completion in refluxing THF while other alkynes required more than a day.¹⁵³ The silylstannane used was trimethyl(tributylstannyl)silane ($\text{Bu}_3\text{SnSiMe}_3$). This is a commonly used silylstannane for many applications, being less toxic and volatile and more stable toward hydrolysis than the structurally simpler trimethyl(trimethylstannyl)silane. Its synthesis is relatively straightforward using inexpensive chlorotrimethylsilane. It is also the only commercially available silylstannane. The catalyst chosen was tetrakis(triphenylphosphine)palladium(0) ($\text{Pd}(\text{PPh}_3)_4$); this catalyst has been shown to be the significantly more active in the addition of silylstannanes to terminal alkynes when tested against several palladium(0) and palladium(II) catalysts as well as molybdenum-, rhodium-, and platinum-containing catalysts.^{153,156} The first ionic liquid used was $[\text{bmim}]\text{PF}_6$. This ionic liquid is one of the most (if not the most) commonly used ionic liquids. It is commercially available but can easily be prepared and purified for a much smaller cost (Figure 3, Section 1.1.2), is immiscible with a number of organic solvents and with water, is relatively thermally-stable, and has been shown to function well in

other palladium-catalyzed reactions. The [bmim]PF₆ used in these reactions was prepared *via* the acid/base neutralization method. The precursor [bmim]Cl was prepared by refluxing 1-methylimidazole with excess chlorobutane and was purified by washing repeatedly with ethyl acetate followed by heating under vacuum. This was then dissolved in water and stirred with an aqueous solution of HPF₆. The ionic liquid product precipitated as a second layer and was purified by repeated water washes followed by heating under vacuum.²⁴

The first addition of Bu₃SnSiMe₃ to phenylacetylene was carried out under nitrogen using the silylstannane in slight excess (1.2 equivalents) in neat [bmim]PF₆ (1 mL) that had been dried by heating under vacuum at 70 °C for 4 h. 5 mol% Pd(PPh₃)₄ had been added to the dry ionic liquid in an argon glove box, providing a yellow suspension on stirring. Once the silylstannane and alkyne were injected *via* needles and syringes the reaction was heated in a 70 °C oil bath using a temperature-controlled hotplate; the reaction proceeded under a stream of nitrogen as the reaction vessel was sealed with a rubber septum. Aliquots were periodically removed from the reaction and analyzed for the presence of unreacted alkyne using a gas chromatograph equipped with a flame ionization detector (GC-FID).

The first reaction was devoid of alkyne after 18 h; however, only a 66% isolated yield was obtained. It was observed during the reaction (as well as in a second reaction being performed using 5-hexyn-1-ol instead of phenylacetylene) that droplets of clear liquid were condensing on the walls of the reaction vessel, indicating that the reagents were evaporating out of the palladium-containing ionic liquid but were not present in large enough quantities to run back down into the ionic liquid. Thus, the reactions

appeared complete by GC-FID but had not actually proceeded to completion. To combat this problem, all subsequent reactions were conducted under biphasic conditions using freshly dried and distilled diethyl ether Et₂O. The reaction was repeated under biphasic conditions, heating it in a 70 °C oil bath after fitting the flask with a dry reflux condensor to provide the product in excellent yield.

Reactions were initially performed with two other alkynes to investigate the scope and functional group tolerance of the reaction. 5-Hexyn-1-ol contained a hydroxyl group and 1-decyne had a long alkyl chain. Both alkynes were inserted into the tin-silicon bond of Bu₃SnSiMe₃ in the same manner as aromatic phenylacetylene to provide good yields of the coupled products.¹⁶⁸ In addition to these alkynes, two others were synthesized from 5-hexyn-1-ol to investigate a wider scope of functional groups. The tetrahydropyran-2-yl (THP) ether was synthesized from 5-hexyn-1-ol with 3,4-dihydro-2H-pyran and a catalytic amount of *p*-toluenesulfonic acid (TsOH) in dichloromethane (Figure 15) to generate an alkyne containing an ether/acetal moiety.¹⁶⁹

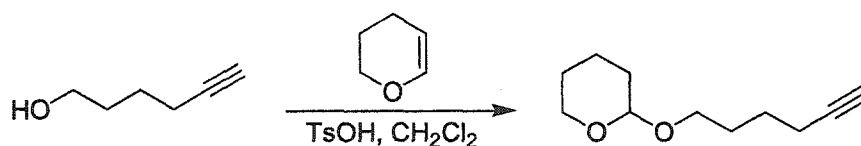


Figure 15. Synthesis of 5-hexyn-1-ol THP ether

5-Hexyn-1-ol was used also to generate 6-chlorohex-1-yne by refluxing with freshly distilled thionyl chloride in dry pyridine overnight, followed by quenching with water,

extraction with diethyl ether, and purification *via* flash chromatography (Figure 16).¹⁷⁰ This gave an alkyne containing a halogen.

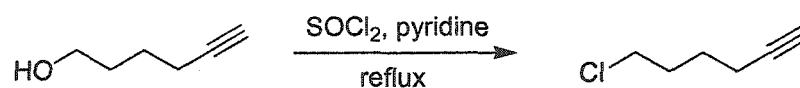


Figure 16. Synthesis of 6-chlorohex-1-yne from 5-hexyn-1-ol

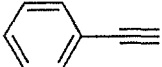
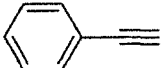
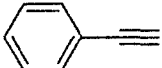
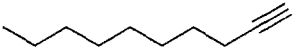
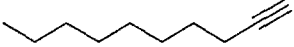
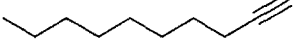
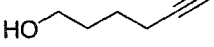
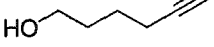
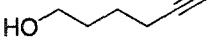
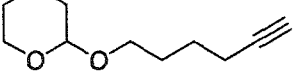
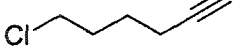
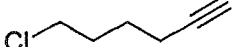
A second ionic liquid, [bmim]BF₄, was investigated as a catalyst immobilization agent/solvent for reactions involving Bu₃SnSiMe₃. This ionic liquid is water-miscible, whereas [bmim]PF₆ is immiscible with water. The ionic liquid [bmim]BF₄ was prepared in a similar manner as [bmim]PF₆, using the acid/base neutralization method. This ionic liquid is also commercially available but is much less costly when prepared in the lab. An aqueous solution of HBF₄ was added to an aqueous solution of [bmim]Cl and stirred for 3 d to ensure complete reaction. After this time, the water was removed under reduced pressure and the resulting ionic liquid was heated under vacuum.³⁰ A water wash was not feasible since the ionic liquid is miscible with water.

Reactions were performed in these two ionic liquids, [bmim]PF₆ and [bmim]BF₄, under biphasic conditions with Et₂O as a co-solvent, heating in a 70 °C oil bath. In general, 5 mol% Pd(PPh₃)₄ was used; however, catalyst loadings of 1 mol% were used on occasion to probe the robustness of the system. The results of additions of Bu₃SnSiMe₃ to the five alkynes, phenylacetylene, 5-hexyn-1-ol, 1-decyne, 5-hexyn-1-ol THP ether,

and 6-chlorohex-1-yne, under different conditions are presented in Table 1. The reactions were run until the absence of alkyne was determined by GC-FID analysis.

Table 1. Results of the addition of Bu₃SnSiMe₃ to five alkynes in [bmim]PF₆/Et₂O and [bmim]BF₄/Et₂O

$$\text{R}-\text{C}\equiv\text{CH} \xrightarrow[\substack{\text{ionic liquid}/\text{Et}_2\text{O} \\ 70\text{ }^\circ\text{C oil bath}}]{\substack{\text{Bu}_3\text{SnSiMe}_3 \\ \text{Pd(PPh}_3)_4}} \text{Bu}_3\text{Sn}-\text{C}(\text{R})=\text{CH}-\text{SiMe}_3$$

Entry	Alkyne	Ionic liquid	Pd (mol %)	Reaction time (h)	Yield (%) ^a
1		[bmim]PF ₆	5	36	100 (100)
2		[bmim]PF ₆	1	17	97 (99)
3		[bmim]BF ₄	5	36	100 (100)
4		[bmim]PF ₆	5	15	99 (97)
5		[bmim]PF ₆	1	72	99 (100)
6		[bmim]BF ₄	5	120	100 (82)
7		[bmim]PF ₆	5	18	100 (89)
8		[bmim]PF ₆	1	24	100 (87)
9		[bmim]BF ₄	5	24	97 (61)
10		[bmim]PF ₆	5	84	100 (99)
11		[bmim]PF ₆	5	120	100 (68)
12		[bmim]PF ₆	1	144	90 (22)

Reaction conditions: 1 mmol alkyne, 1.2 mmol Bu₃SnSiMe₃, 1.0 mL ionic liquid, 5.0 mL Et₂O, 70 °C oil bath

^aGC yield based on disappearance of alkyne (isolated yield in brackets)

As can be seen from the results presented in Table 1, nearly all of the reactions proceeded to give quantitative yields of the addition product as assessed by GC-FID

analysis for the disappearance of alkyne (assuming only one reaction product). These findings were generally supported by high isolated yields. As has been observed in other studies where THF was used as a solvent, the addition of silylstannanes to terminal alkynes is tolerant of a variety of functional groups. This also appears to be true using ionic liquids under biphasic conditions. The use of ionic liquids allowed facile product isolation and separation from the catalyst as the upper Et₂O layer was decanted, which contained the addition product as well as unreacted silylstannane. The lower ionic liquid phase, which contained the palladium catalyst, was washed repeatedly with ether (8 x 8 mL, generally) in order to ensure complete extraction of addition products. The final washings were analyzed by GC-FID and were always devoid of products or starting materials, indicating complete extraction. The products were then separated from excess silylstannane using flash chromatography to afford the products in yields presented in brackets in Table 1.

All reactions proceeded to give only a single product isomer. Four isomers are possible, one with tin on the terminal carbon and silicon on the internal carbon, another with tin on the internal carbon and silicon on the terminal carbon, and each of these could be *cis* or *trans* alkenes. Each of the regio- and stereoisomers would likely give different retention times by GC-FID, different elution rates during flash chromatography, and different response factors (R_f) by thin-layer chromatography (TLC); only one product was observed from each of these chromatographic techniques. With the aid of proton nuclear magnetic resonance spectroscopy, ¹H NMR, the isomeric form of the products were confirmed to be the *cis*-bismetallated adducts with the tin on the internal carbon and the silicon on the terminal carbon as shown in the figure above Table 1. Tin has ten

naturally occurring isotopes of varying relative abundances, giving tin-containing compounds characteristic spectra when analyzed *via* mass spectrometry. Two isotopes of tin have nuclear spin values of $\frac{1}{2}$ and are present in high enough abundances to be suitable for NMR studies, ^{117}Sn and ^{119}Sn .¹⁷¹ The coupling of the tin atom to the vinylic proton of the alkyne addition product produces satellites on the ^1H NMR spectrum; the coupling constants of these satellites indicate the isomeric form of the groups contributing to the tin-proton coupling. The value of the coupling constants from the tin satellites are known to be around 100 Hz for *cis*-coupling as well as for geminal coupling. Geminal coupling would result if the tin was on the terminal carbon, the same as the vinylic proton, while *cis*-coupling would result if the tin was on the internal carbon but the silicon was in the *trans* position on the alkene. *Trans*-coupling between tin and vinylic protons is known to occur with coupling constants around 180 Hz, resulting from tin being on the internal carbon and silicon being in the *cis* position on the alkene.¹⁵³ The tin-vinylic proton coupling constants of all products isolated from these reactions were between 160-184 Hz as measured from the ^1H NMR spectra of the products, indicating that the products were *cis*-bismetallated, internally-stannylated, terminally-silylated alkenes. The satellites resulting from ^{117}Sn and ^{119}Sn were both observable at 250 MHz and even at 60 MHz (Figure 17).

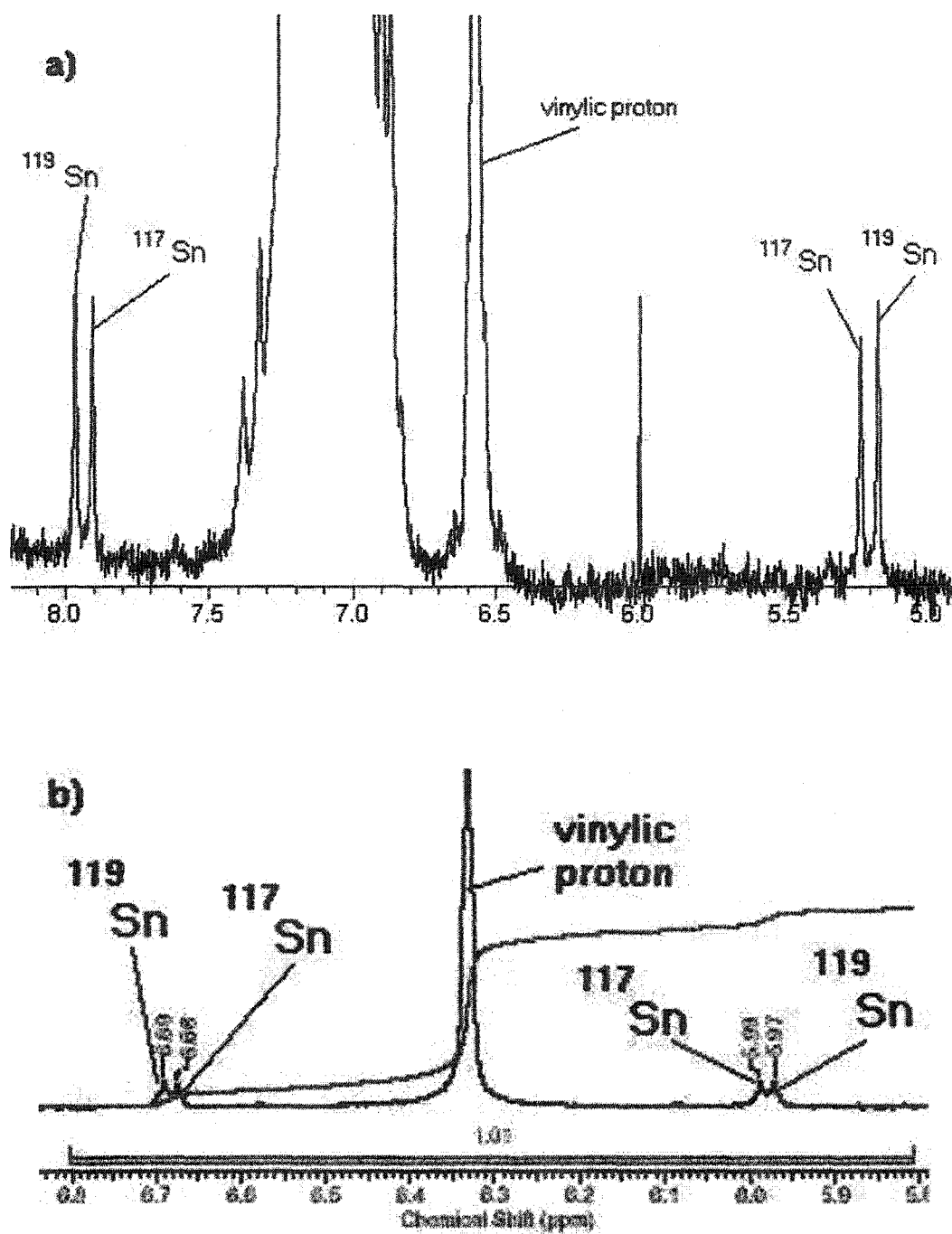


Figure 17. Examples of the ^{117}Sn and ^{119}Sn satellites resulting from coupling to the vinyllic proton of the addition product a) between phenylacetylene and $\text{Bu}_3\text{SnSiMe}_3$ at 60 MHz and b) between 6-chlorohex-1-yne and $\text{Bu}_3\text{SnSiMe}_3$ at 250 MHz

The isolated yields of adducts from the five alkynes compared very well to literature values from reactions performed in refluxing THF, generally equaling or surpassing previously obtained results. The times required for the reaction to proceed are rather lengthy; however, this is typical of these types of reactions. A 91% yield of the adduct between phenylacetylene and $\text{Bu}_3\text{SnSiMe}_3$ had previously been obtained using refluxing THF as a solvent.¹⁵³ 99-100% yields of the adduct were obtained using the ionic liquid/ Et_2O solvent system (Table 1, Entries 1-3). The reaction performed in refluxing THF was complete after 3 hours while that in the ionic liquid required 17 hours to proceed to completion, indicating that the reaction proceeds much slower in the ionic liquid. It may be, however, that satisfactory amounts of product may be formed in the ionic liquid after shorter reaction times to make the process attractive to operators of continuous flow systems. Reactions performed with non-aromatic alkynes proceeded with somewhat more promising reaction times compared to literature results. The coupling of 1-decyne with $\text{Bu}_3\text{SnSiMe}_3$ afforded quantitative yields of product after 15 hours in $[\text{bmim}]\text{PF}_6/\text{Et}_2\text{O}$ (Table 1, Entry 4) while the product of 1-hexyne with the same silylstannane was obtained in 52% yield after 20 hours when the reaction was performed without solvent at 80 °C.¹⁵⁶ An 89% yield of the adduct between 5-hexyn-1-ol and $\text{Bu}_3\text{SnSiMe}_3$ was obtained from $[\text{bmim}]\text{PF}_6/\text{Et}_2\text{O}$ after 18 hours (Table 1, Entry 7) while a comparable yield, 88%, was obtained from the reaction of 4-pentyn-1-ol with the same silylstannane after refluxing in THF for 72 hours.¹⁵³ The results for the final two alkynes provided little improvement over literature reports. The adduct of the 5-hexyn-1-ol THP ether and $\text{Bu}_3\text{SnSiMe}_3$ was obtained in quantitative yield after 84 hours in $[\text{bmim}]\text{PF}_6/\text{Et}_2\text{O}$ (Table 1, Entry 10) while that of a 3-butyne-1-ol THP ether with the

same silylstannane was obtained in 91% yield after refluxing in THF for only 48 hours.¹⁵³ 6-Chlorohex-1-yne afforded its $\text{Bu}_3\text{SnSiMe}_3$ coupling product in only 68% yield after heating in $[\text{bmim}]\text{PF}_6/\text{Et}_2\text{O}$ for 120 hours (Table 1, Entry 11) while the adduct from 5-chloropentyne was reported to undergo coupling with the same silylstannane in 80% after 72 hours in refluxing THF.¹⁵³ The result for the chloroalkyne does not appear to be as good as those obtained with other alkynes regardless of the solvent system chosen for their reaction, indicating that chloroalkynes may be less reactive than other alkynes. This is not likely the case since an 87% isolated yield was obtained from the reaction between chloropentyne and another silylstannane.¹⁵³ It has been shown in this work and previous studies that chloride functional groups are tolerated in these reactions despite their adducts not being obtained in >90% yields. In addition, 6-chlorohex-1-yne was observed to be significantly more volatile than the other alkynes used and may have simply evaporated during the course of the 5-d reaction.

Reactions between all alkynes except 5-hexyn-1-ol THP ether were performed with 5 mol% and 1 mol% $\text{Pd}(\text{PPh}_3)_4$ in $[\text{bmim}]\text{PF}_6/\text{Et}_2\text{O}$. Using 5 mol% palladium became standard procedure for the majority of these reactions but results of reactions using only 1 mol% palladium were promising. In general, reactions performed using 1 mol% palladium required longer reaction times to proceed to completion than those using 5 mol% palladium. These results are not unexpected as it only makes sense that reactions proceed slower when smaller amounts of catalysts are used. Interestingly, the reaction of phenylacetylene proceeded faster at lower catalyst loadings than at higher, providing excellent yields of product after only 17 hours at 1 mol% palladium (Table 1, Entry 2) as compared to the 36 hours required with 5 mol% palladium (Table 1, Entry 1). Reactions

of 1-decyne (Table 1, Entries 5 vs. 4) and 5-hexyn-1-ol (Table 1, Entries 8 vs. 7) required longer reaction times at lower catalyst loadings to reach the same yields obtained at higher catalyst loadings. The reaction of 6-chlorohex-1-yne proceeded very poorly at 1 mol% palladium when comparing isolated yields (Table 1, Entries 12 vs. 11), perhaps resulting from the high volatility of the alkyne and having less palladium species in the ionic liquid phase. These results show that the addition of alkynes to $\text{Bu}_3\text{SnSiMe}_3$ can be performed at lower catalyst loadings but require longer reaction times. It should be noted that the ionic liquid/catalyst mixtures were clear yellow solutions with 1 mol% $\text{Pd}(\text{PPh}_3)_4$ while those with 5 mol% $\text{Pd}(\text{PPh}_3)_4$ were cloudy yellow suspensions until heated with the other reaction components in the 70 °C oil bath and remained clear upon cooling. It may be that optimal catalyst activity lies somewhere between 1 and 5 mol%.

The results of the palladium-catalyzed addition of different alkynes to $\text{Bu}_3\text{SnSiMe}_3$ in two different ionic liquids were promising, showing that not only could the reaction proceed in ionic liquids but also that in some cases it proceeded with better results than in THF. A second silylstannane was synthesized to further probe the scope of these reactions in ionic liquids. Dimethylphenyl(tributylstannyl)silane ($\text{Bu}_3\text{SnSiMe}_2\text{Ph}$) was synthesized by deprotonating tributyltin hydride with lithium diisopropylamide LDA in THF at -10 °C to generate a tributyltin lithium species, which was then quenched with chlorodimethylphenylsilane at 0 °C (Figure 18). The resulting mixture was stirred at room temperature for an hour, after which time the solvent was evaporated and the precipitated lithium chloride was filtered off. The silylstannane was purified *via* vacuum distillation. This dimethylphenylsilylstannane has been used in

addition reactions with alkynes as the addition products have been shown to be more readily protodesilylated than their trimethylsilyl counterparts.¹⁶³

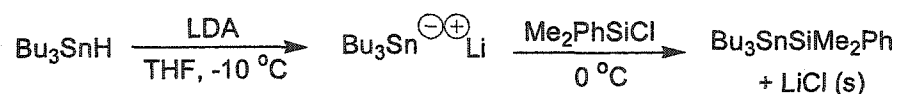
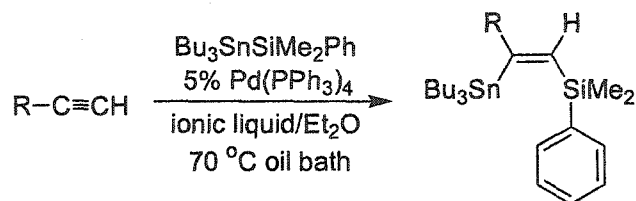
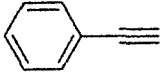
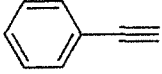
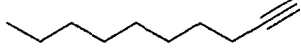
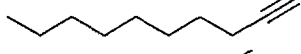
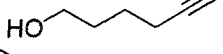
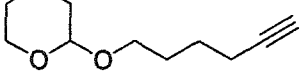


Figure 18. Synthesis of Bu₃SnSiMe₂Ph

Reactions were carried out between Bu₃SnSiMe₂Ph and the four alkynes that provided acceptable results from studies with Bu₃SnSiMe₃. 6-Chlorohex-1-yne was not used with the new silylstannane as it was too volatile to provide meaningful results. The reactions with Bu₃SnSiMe₂Ph were carried out in the same manner as before, using 1.2 equivalents of silylstannane in a biphasic mixture of ionic liquid and dry Et₂O heating in a 70 °C oil bath. All reactions with this silylstannane were carried out using 5 mol% Pd(PPh₃)₄. The results of these reactions are presented in Table 2.

Table 2. Results of the addition of Bu₃SnSiMe₂Ph to four alkynes in [bmim]PF₆/Et₂O and [bmim]BF₄/Et₂O in the presence of 5 mol% Pd(PPh₃)₄



Entry	Alkyne	Ionic liquid	Reaction time (h)	Yield (%) ^a
1		[bmim]PF ₆	96	100 (98)
2		[bmim]BF ₄	96	100 (97)
3		[bmim]PF ₆	108	100 (78)
4		[bmim]BF ₄	144	95 (62)
5		[bmim]PF ₆	19	100 (62)
6		[bmim]PF ₆	168	100 (83)

Reaction conditions: 1 mmol alkyne, 1.2 mmol Bu₃SnSiMe₂Ph, 0.05 mmol Pd(PPh₃)₄, 1.0 mL ionic liquid, 5.0 mL Et₂O, 70 °C oil bath

^aGC yield based on disappearance of alkyne (isolated yield in brackets)

The reactions with Bu₃SnSiMe₂Ph were monitored by GC-FID and continued until no more alkyne was present. Products were isolated by washing the ionic liquid layer repeatedly with Et₂O. The final washing was always devoid of products and starting materials as determined by GC-FID. It can be seen from the results presented in Table 2 that the isolated yields generally corresponded with the results of the GC analyses showing absence of alkyne, indicating complete reactions. The products all had the same regio- and stereochemistries as those obtained from reactions with Bu₃SnSiMe₃. The values of the tin-vinyl proton coupling constants were all between 156-185 Hz,

verifying that the products were *cis*-bismetallated containing the tin on the internal carbon atom and the silicon on the terminal carbon atom of the alkene, as depicted in the figure above Table 2.¹⁶³ This indicates that increasing the steric bulk around the silicon atom has no effect on the regio- or stereochemistry of the reaction.

As with results obtained from the coupling of the trimethylsilylstannane with various alkynes, the results obtained from the coupling of $\text{Bu}_3\text{SnSiMe}_2\text{Ph}$ with various alkynes gave similar results as reactions performed in refluxing THF as reported in the literature.¹⁶³ When using phenylacetylene as the alkyne, an excellent yield (98%) was obtained after 96 hours of heating in $[\text{bmim}]\text{PF}_6/\text{Et}_2\text{O}$ in a 70 °C oil bath (Table 2, Entry 1). In refluxing THF, the same alkyne gave a 95% yield after only three hours, not unlike the reaction performed with the same alkyne and the trimethylsilylstannane in refluxing THF. Again, other alkynes proceeded to completion with much longer reaction times in refluxing THF. From $[\text{bmim}]\text{PF}_6/\text{Et}_2\text{O}$, 1-decyne afforded a 78% yield of coupled product after 108 hours (Table 2, Entry 3) which compares very well to the 80% yield afforded by 1-hexyne after 120 hours in refluxing THF. 5-Hexyn-1-ol provided the poor isolated yield of 62%, but showed no more alkyne by GC-FID after only 19 hours in $[\text{bmim}]\text{PF}_6/\text{Et}_2\text{O}$ (Table 2, Entry 5). An 81% yield of the adduct from 4-butyne-1-ol was obtained after 120 hours in refluxing THF. It may be that the GC-FID was not as responsive to 5-hexyn-1-ol as to other alkynes, showing complete absence of alkyne prematurely; thus, the reaction in the ionic liquid may have provided a higher isolated yield if allowed to proceed longer. The 5-hexyn-1-ol THP ether provided more acceptable results, giving its adduct in 83% yield after the lengthy 168 hour reaction time, similar to the 82% yield obtained from 4-butyne-1-ol THP ether from refluxing THF after

120 hours. When the reaction times and yields of adducts obtained using $\text{Bu}_3\text{SnSiMe}_2\text{Ph}$ are compared to those from using the trimethylsilylstannane, it can be seen that these reaction times are longer and the isolated yields are slightly lower. This is a trend observed when using refluxing THF as a solvent and thus is not attributable to the ionic liquids. The reactions involving the larger, bulkier $\text{Bu}_3\text{SnSiMe}_2\text{Ph}$ simply require more time to proceed. It can be assumed then that if lower catalyst loadings were used that the reactions would proceed even slower.

Comparing results from the same reaction performed in different ionic liquids, it can be seen that $[\text{bmim}]\text{BF}_4$ generally provides products in lower yields with longer reaction times over those performed in $[\text{bmim}]\text{PF}_6$. Phenylacetylene coupled with both silylstannanes equally well in both ionic liquids but is uniquely reactive¹⁵³ and thus no conclusions can be drawn from reactions performed with this alkyne regarding activity in different ionic liquids. 1-Decyne coupled with $\text{Bu}_3\text{SnSiMe}_3$ much faster and in higher yield in $[\text{bmim}]\text{PF}_6/\text{Et}_2\text{O}$, giving a 97% isolated yield after 15 hours (Table 1, Entry 4) compared to the 82% isolated yield obtained after 120 hours in $[\text{bmim}]\text{BF}_4/\text{Et}_2\text{O}$ (Table 1, Entry 6). Similar results were obtained with $\text{Bu}_3\text{SnSiMe}_2\text{Ph}$ as 1-decyne gave a 78% isolated yield after 108 hours in $[\text{bmim}]\text{PF}_6/\text{Et}_2\text{O}$ (Table 2, Entry 3) but gave only a 62% isolated yield after 144 hours in $[\text{bmim}]\text{BF}_4/\text{Et}_2\text{O}$ (Table 2, Entry 4). 5-Hexyn-1-ol also gave lower a yield in $[\text{bmim}]\text{BF}_4/\text{Et}_2\text{O}$, giving a 61% isolated yield after 24 hours of coupling with $\text{Bu}_3\text{SnSiMe}_3$ as compared with the 89% isolated yield obtained after 18 hours in $[\text{bmim}]\text{PF}_6/\text{Et}_2\text{O}$. It appears by these results that the reaction in $[\text{bmim}]\text{BF}_4$ occurs at a slower rate than in $[\text{bmim}]\text{PF}_6$. It also seems as though $[\text{bmim}]\text{BF}_4$ may be

giving problems regarding product isolation, since GC-FID analyses show absence of alkyne yet isolated yields are still lower than those from [bmim]PF₆.

The reasons for slower reaction rates in [bmim]BF₄ do not immediately present themselves. The only obvious difference between the two ionic liquids is the miscibility of [bmim]BF₄ with water. On the surface the lower reaction rates may be due to the increased viscosity of the ionic liquids. While this may be a reason for the lower reaction rates of some alkynes compared to their rates in THF, it is likely not a contributing factor in the explanation of the lower reaction rates in [bmim]BF₄. It is known that residual chloride impurities in ionic liquids resulting from their inefficient preparation increase their viscosities. Some transition metal-catalyzed reactions are also inhibited by excess halide present as the halide coordinates to the metal center, generally lowering the rate of reaction.¹⁸ Studies have been performed on the different methods commonly used to prepare ionic liquids, analyzing the products for halide content, described earlier in Section 1.1.2. Although metathesis with a silver(I) salt affords the cleanest ionic liquids (i.e. most halide-free), the much cheaper acid/base neutralization method affords ionic liquids with halide levels almost as low.²⁹ As the methods used to generate the ionic liquids employed in these studies involved acid/base neutralization, it is unlikely that the viscosity of [bmim]BF₄ has been so increased over that of [bmim]PF₆ to cause it to afford slower reaction rates in these silylstannations. As well, it is known that viscosities of ionic liquids are markedly decreased when almost any organic substrate is added to them, including reagents and co-solvents. In addition, the viscosities of several ionic liquids have been measured by different research groups and although they do not all agree on an exact value, they show that the viscosity of [bmim]PF₆ ranges from being twice as high

as that of [bmim]BF₄ to having equal value.²⁰ It is thus unlikely that viscosity plays a role in the different rates of silylstannation reactions observed in these two ionic liquids.

It may be that the “hydrophobic” nature of [bmim]PF₆ allows it to support the palladium-catalyzed addition of silylstannanes to alkynes with a higher rate than the hydrophilic [bmim]BF₄. Being hydrophobic, it is intuitive that [bmim]PF₆ would have a lower water content than [bmim]BF₄. Although the ionic liquids were dried by heating under vacuum for several hours prior to use, studies have shown that this cannot remove all water from ionic liquids. As described in Section 1.1.1, all imidazolium-based ionic liquids are in fact hygroscopic, absorbing a certain amount of water from the atmosphere which hydrogen bonds to the anion of the ionic liquid. The so-called “hydrophobic” ionic liquids simply do not absorb as much moisture as the hydrophilic ionic liquids and form a second phase with excess water. Thus, [bmim]PF₆ contains a certain amount of bound water even after heating under vacuum for several hours. It has been shown, however, that [bmim]BF₄ contains significantly more water than [bmim]PF₆. Rogers et al. have shown that after heating under vacuum at 70 °C for 4 hours [bmim]PF₆ contained 590 ppm water while [bmim]BF₄ contained 4530 ppm water, about 7.5 times the amount.²⁰ It is impossible to determine how much water is present in [bmim]BF₄ by simple visual inspection since it is miscible with water. Thus, if the [bmim]BF₄ to be used contains a large amount of water it will require longer to dry under vacuum. When THF is dried using potassium metal it is nearly devoid of water; thus, the presence of bound water in both ionic liquids could be responsible for the longer reaction times necessary compared to those observed in THF. The higher water content of [bmim]BF₄ could also be responsible for its lower rate of reaction compared to [bmim]PF₆. The

presence of water in ionic liquids has been known to impede the progress of some palladium-catalyzed reactions.^{120,133} Indeed, the initial reaction performed in [bmim]BF₄ had been done after the ionic liquid was heating under vacuum for only 3 hours. This reaction showed mainly decomposition products of Bu₃SnSiMe₃, which has been reported as being moisture-sensitive.

It may also be that the products of silylstannation reactions are more soluble in [bmim]BF₄ than in [bmim]PF₆. The reaction cycle under biphasic conditions is envisioned to be one involving starting materials, silylstannane and alkyne, dissolved in the upper Et₂O phase from which they dissolve into the lower palladium-containing ionic liquid phase. Here they undergo coupling to give the silylstannylated alkene product, which then moves into the upper Et₂O phase, driving the reaction forward (Figure 19).¹⁰² This forward drive of the reaction may give rise to slightly higher isolated yields in some cases over reactions performed in THF. On the other hand, if the products are more soluble in [bmim]BF₄ than in [bmim]PF₆ or if the starting materials are not as soluble in [bmim]BF₄ as compared to [bmim]PF₆, then the reaction would proceed slower in [bmim]BF₄ as it would take longer for products to leave the ionic liquid phase and/or for starting materials to enter the same phase as the palladium catalyst. The starting materials and products are all quite soluble in Et₂O as evidenced by their easy separation from the ionic liquids and the palladium catalyst remains immobilized in the ionic liquid phase and is likely not leached into the Et₂O phase during product extraction, evidenced by several researchers.^{18,31} The most likely possibility of these is that the reaction products are more soluble in the [bmim]BF₄ layer and reside in this phase longer,

impeding higher reaction rates. It is likely that the catalytic reaction occurs in the ionic liquid layer itself since the palladium catalyst resides there.

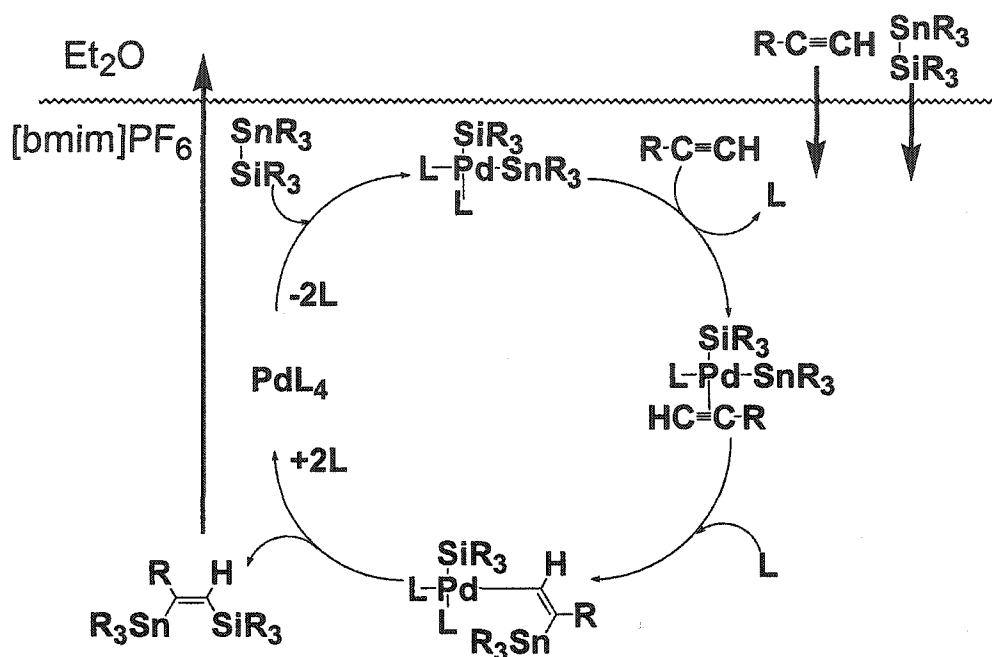


Figure 19. Proposed reaction sequence and mechanism for palladium-catalyzed silylstannane additions to terminal alkynes in ionic liquid/ Et_2O biphasic systems

The mechanism of the catalytic cycle shown in Figure 19 is based on experimental evidence, on the proposed mechanism of the closely related bis-silylation of unsaturated molecules,¹⁶⁰ and on a theoretical study using ab initio Hartree-Fock calculations to determine energies of steps involved in the reaction between a hypothetical silylstannane H_3SnSiH_3 catalyzed by the hypothetical catalyst $\text{Pd}(\text{PH}_3)_2$.¹⁷² After dissolution of the alkyne and silylstannane into the ionic liquid phase, the first step in the reaction is oxidative addition of the silylstannane across palladium(0) in the form of PdL_2 . Coordination of the alkyne follows next (not competed for by the ionic liquid due to its non-coordinating nature), the internal end of which is inserted into the

palladium-tin bond; this is presumed to be the rate determining step based on calculations. Reductive elimination then follows to generate the *cis*-bismetallated, terminally silylated, internally stannylated alkene and regenerate the palladium(0) catalyst. The product then dissolves into the upper Et₂O phase.

The reactivities of different alkynes used toward insertion into silylstannanes generally follow trends already outlined in studies performed in THF. Chenard et al. have concluded that efficient addition of alkynes to silylstannanes is limited to terminal alkynes with smaller substituents due to steric considerations. This group states that unreactive alkynes are generally those that are poor ligands for palladium due to steric bulk.¹⁵³ This may explain the lower yields obtained when using 5-hexyn-1-ol and 6-chlorohex-1-yne. Phenylacetylene provided excellent yields in relatively short reaction times under many different conditions, but this is known to be a particularly active alkyne toward silylstannation reactions, possibly stemming from the aromaticity of its substituent. Relatively high yields were obtained from using the 5-hexyn-1-ol THP ether and 1-decyne, both of which contain the largest substituents. It may be that these alkynes were the least volatile and provided higher yields, as it was observed that 6-chlorohex-1-yne possessed a relatively high volatility. Steric bulk may explain the slightly lower yields and longer reaction times observed when using the bulkier Bu₃SnSiMe₂Ph as opposed to the smaller Bu₃SnSiMe₃. All five alkynes did, however, yield their coupling products, showing a small cross-section of the functional group tolerance of this reaction.

As mentioned earlier, studies had previously been performed regarding the choice of catalyst for these reactions. The palladium(0) catalyst Pd(PPh₃)₄ had been shown to provide significantly better yields than all other catalysts tried in THF.^{153,156} It was

decided to investigate the use of a palladium(II) catalyst in a [bmim]PF₆/Et₂O system to determine if catalyst selectivity were different in ionic liquids. Bis(acetonitrile)palladium(II) chloride, (CH₃CN)₂PdCl₂, was used in 5 mol% for the coupling of phenylacetylene with Bu₃SnSiMe₃. After 24 hours at room temperature in [bmim]PF₆/Et₂O, very little reaction had occurred. The reaction was then heated to 70 °C for 48 hours, which also resulted in very little product formation. A fair amount of unreacted silylstannane was present as was a large amount of hexabutyliditin Bu₃SnSnBu₃. This by-product has been observed by other researchers when using unreactive alkynes. The silylstannane Me₃SnSiMe₃ is known to undergo a palladium-catalyzed disproportionation reaction when attempts are made to couple it with unreactive alkynes. The products of the disproportionation of Me₃SnSiMe₃ are the hexamethyldistannane Me₃SnSnMe₃ and the hexamethyldisilane Me₃SiSiMe₃.¹⁵³ Thus we were unable to improve on the original catalyst selection of Pd(PPh₃)₄.

The reactions between Bu₃SnSiMe₃ and various alkynes were investigated for possible rate enhancements resulting from the use of ionic liquids. Many transition metal-catalyzed and uncatalyzed reactions report rate enhancements due to the use of ionic liquids. From simple observations of the long reaction times required in ionic liquids it is apparent that there is no rate enhancement resulting from the use of ionic liquids; in fact, there is likely a rate decrease when compared to reactions performed in THF. The Pd(PPh₃)₄-catalyzed reaction between phenylacetylene and Bu₃SnSiMe₃ has been shown to proceed in THF at room temperature to quantitative yields.¹⁵³ When the same reaction was allowed to proceed in [bmim]PF₆ without any Et₂O, no reaction had occurred after 18 h. After the addition of Et₂O the reaction was heated in a 70 °C oil

bath, after which time complete reaction was observed overnight, showing that the catalyst had not decomposed but that the reaction required heating to proceed in the ionic liquid. The ionic liquid was light yellow in colour after the reaction was complete with no precipitation of palladium black, indicating no decomposition of the catalyst. The same reaction was performed in refluxing THF and this was complete after 3 hours. In THF at room temperature the reaction ran to completion overnight. Although the reactions proceeded at higher rates in THF as compared to ionic liquids, the colour of the solvent in both cases (refluxing and at room temperature) quickly changed from the initial orange colour to black, indicating that palladium black had precipitated. Thus, the reactions performed in ionic liquids may have lower rates, but the catalyst appears to be much more stable and amenable to potential reuse. In addition, the reactions performed in ionic liquid/Et₂O biphasic systems were placed in a 70 °C oil bath but may not have actually reached this temperature. 70 °C was chosen as the bath temperature because the boiling point of THF is 66-69 °C and comparison was desired; however, the boiling point of Et₂O (35 °C) is much lower. The lower ionic liquid phase may have reached slightly higher temperatures, but would have been regulated somewhat by the low boiling point of Et₂O which would lower the rates of reactions performed in these systems when compared to those performed in refluxing THF.

2.2 Recyclability Studies

Ionic liquids provide several benefits as solvents for transition metal-catalyzed reactions compared to other molecular solvents, including facilitating product isolation,

separation of catalyst, and potentially increasing reaction rate. Their most important benefit, however, may be the potential to recycle the catalyst. This is especially attractive for reactions that use expensive catalysts, such as the palladium-catalyzed coupling of silylstannanes with alkynes.

As ionic liquids are being touted as “greener solvents” for doing chemistry with less negative environmental impact, it is important to show that they can be reused without loss of activity for the reactions they support. The silylstannylation of alkynes is an excellent example of a “greener” reaction as it proceeds with total “atom economy” in that every atom of the starting materials is incorporated into the product with no by-product or waste formation.¹⁷³ If the ionic liquid/catalyst support system can be recycled, this would enhance the “green” potential of this reaction.

Many groups have successfully recycled catalysts contained in ionic liquids without activity losses while others have had less promising results. In some cases, the ionic liquid/catalyst system was purified between reaction cycles using complex extraction/washing procedures. In the enantioselective allylation of carbonyl compounds with palladium(0) complexes the ionic liquid was dissolved in ethyl acetate, washed with water, and dried over magnesium sulfate, after which the ethyl acetate was evaporated. Although the recovered ionic liquid still contained the catalyst, activity decreases were large.^{133,134} Other groups noticed that the presence of water lowered the activity of palladium catalysts and extremely careful drying procedures were necessary in order to avoid catalyst activity loss, noting as well that added water severely detracted from the catalyst's turnover number.¹²⁰ Other groups found that the presence of water had little to no effect on the efficiency and recyclability of their ionic liquid/palladium catalyst

systems. Suzuki couplings have been performed without precautions to exclude air and water with no loss of catalytic activity,¹²⁸ although it was observed that the use of an argon atmosphere decreased by-product formation.¹²⁹ One group found it necessary to wash their ionic liquid/Pd/C catalyst systems with water during successive Heck reactions to remove ionic by-products that lowered activity, after which activity returned to normal.¹²⁶ Most groups found, however, that simply washing the ionic liquid/catalyst system repeatedly with an extractive solvent such as Et₂O to remove products allowed recyclability without leaching of the palladium catalyst.^{117,119,129,131,}

The method used in these recyclability studies of the ionic liquid/Pd(PPh₃)₄ systems for the addition of silylstannanes to alkynes was relatively simple. After the first reaction was performed, the products were extracted using dry Et₂O (8 x 8 mL) *via* needle and syringe under nitrogen to exclude moisture due to the possibility of catalyst deactivation and/or silylstannane hydrolysis in subsequent reactions. After the final washing, fresh silylstannane, alkyne, and Et₂O were injected and the reaction was allowed to proceed again (Figure 20).

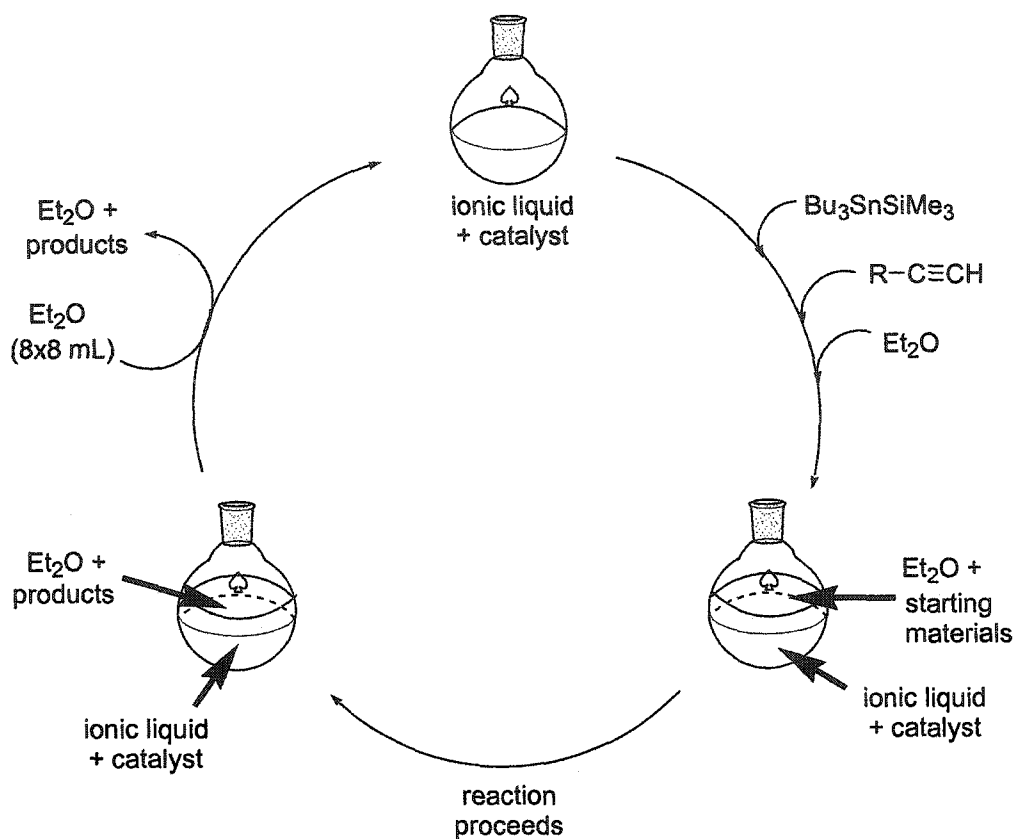


Figure 20. Pathway used to recycle ionic liquid/ $\text{Pd}(\text{PPh}_3)_4$ in silyl stannane couplings

Many studies were performed regarding the recyclability of the ionic liquid/catalyst system. The most extensive studies used phenylacetylene as the alkyne with $\text{Bu}_3\text{SnSiMe}_3$. These reactions were performed in both $[\text{bmim}]\text{PF}_6$ and $[\text{bmim}]\text{BF}_4$ ionic liquids containing 5 mol% $\text{Pd}(\text{PPh}_3)_4$. Reactions were generally run for 48 hours under biphasic conditions heating in a 70 °C oil bath; all reactions proceeded to completion by GC-FID (100% disappearance of alkyne). We have reported that this reaction in $[\text{bmim}]\text{PF}_6$ was able to be performed four times in the same system without loss of activity.¹⁶⁸ These ionic liquid/catalyst systems were then shown to be recyclable ten times without loss of activity, the results of which are presented in Figure 21.

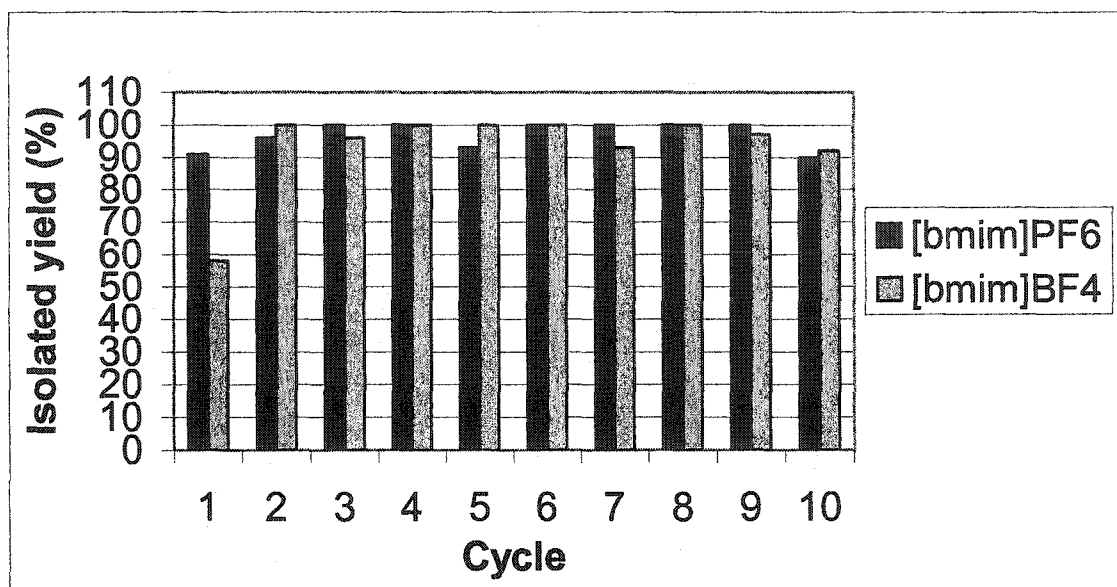


Figure 21. Recyclability of 5% Pd(PPh₃)₄ in [bmim]PF₆ and [bmim]BF₄ in the reaction of phenylacetylene with Bu₃SnSiMe₃

Recyclability studies were also performed in both ionic liquids for the coupling of Bu₃SnSiMe₂Ph and phenylacetylene in the presence of 5 mol% Pd(PPh₃)₄. The reactions were performed in the same manner as those using the trimethylsilylstannane except that reactions were generally performed for 72 hours as opposed to 48 hours due to the lower reaction rate of the dimethylphenylsilylstannane. All reactions were monitored by GC-FID and were complete before products were isolated (100% disappearance of alkyne). These studies were not as extensive as those performed with the trimethylsilylstannane due to the limited availability of the dimethylphenylsilylstannane but were extensive enough to demonstrate that the catalytic system is likely as recyclable with either silylstannane. The results of these studies are presented in Figure 22.

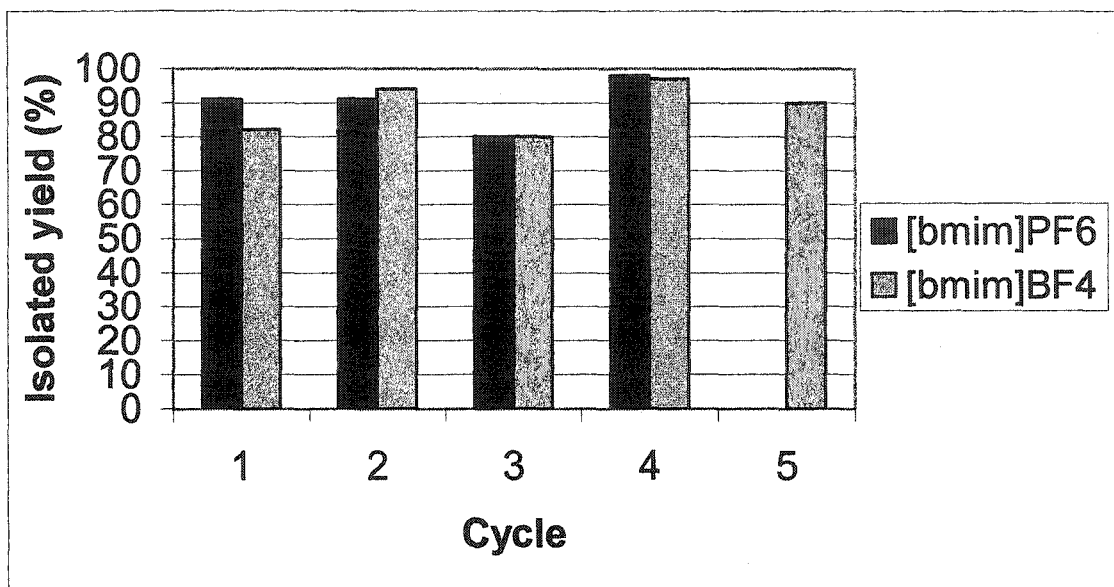


Figure 22. Recyclability of 5% $\text{Pd}(\text{PPh}_3)_4$ in $[\text{bmim}]\text{PF}_6$ and $[\text{bmim}]\text{BF}_4$ in the reaction of phenylacetylene with $\text{Bu}_3\text{SnSiMe}_2\text{Ph}$

It can be seen from the results presented in Figures 21 and 22 that the ionic liquid/catalyst systems are very amenable to recycling. Reactions performed with $\text{Bu}_3\text{SnSiMe}_3$ were repeated ten times in the same ionic liquid/catalyst system, generally affording isolated yields above 90% regardless of the identity of the ionic liquid. Reactions performed with $\text{Bu}_3\text{SnSiMe}_2\text{Ph}$ were also recyclable as the $[\text{bmim}]\text{PF}_6$ /palladium system was recycled four times and the $[\text{bmim}]\text{BF}_4$ /palladium system was recycled five times, producing isolated yields above 80% in all cases. It is likely that the ionic liquid/catalyst systems used with $\text{Bu}_3\text{SnSiMe}_2\text{Ph}$ would be as extensively recyclable as those used with $\text{Bu}_3\text{SnSiMe}_3$ as there is little difference in the reactivities of these two silylstannanes. There was no obvious evidence of palladium leaching during product extraction, although neither the ionic liquids nor their extracts were analyzed for palladium content between cycles.

The ionic liquid/catalyst systems appear to be very robust systems, being amenable to recycling even with less reactive alkynes. Recycling of ionic liquid/catalyst systems using 1-decyne and 5-hexyn-1-ol were also accomplished without loss of catalyst activity in both ionic liquids. Reactions performed with 1 mol% Pd(PPh₃)₄ were also shown to be recyclable, supporting the possibility that palladium leaching is not occurring during product isolation. In fact, many combinations of ionic liquid, alkyne, silylstannane, and palladium content were shown to be recyclable (Table 3).

Table 3. Results of recyclability studies on various alkyne/ionic liquid/palladium content reactions

<i>Cycle</i>	<i>Alkyne</i>	<i>Bu₃SnSiR₃</i>	<i>Pd</i> (mol %)	<i>Ionic liquid</i>	<i>Reaction time (h)</i>	<i>Yield^a</i>
1	Phenylacetylene	R ₃ =Me ₃	1	[bmim]PF ₆	20	100 (78)
2	Phenylacetylene	R ₃ =Me ₃	1	[bmim]PF ₆	17	99 (99)
1	1-Decyne	R ₃ =Me ₃	5	[bmim]PF ₆	15	99 (97)
2	1-Decyne	R ₃ =Me ₃	5	[bmim]PF ₆	72	100 (>95)
1	1-Decyne	R ₃ =Me ₃	1	[bmim]PF ₆	72	99 (99)
2	1-Decyne	R ₃ =Me ₃	1	[bmim]PF ₆	336	100 (>95)
1	1-Decyne	R ₃ =Me ₂ Ph	5	[bmim]BF ₄	144	95 (62)
2	1-Decyne	R ₃ =Me ₂ Ph	5	[bmim]BF ₄	144	85 (44)
1	5-Hexyn-1-ol	R ₃ =Me ₃	5	[bmim]PF ₆	18	100 (89)
2	5-Hexyn-1-ol	R ₃ =Me ₃	5	[bmim]PF ₆	16	100 (46)
1	1-Decyne	R ₃ =Me ₂ Ph	5	[bmim]PF ₆	108	100 (78)
2	5-Hexyn-1-ol ^b	R ₃ =Me ₂ Ph	5	[bmim]PF ₆	24	100 (38)
1	5-Hexyn-1-ol	R ₃ =Me ₂ Ph	5	[bmim]PF ₆	19	100 (62)
2	1-Decyne ^c	R ₃ =Me ₂ Ph	5	[bmim]PF ₆	120	100 (43)

Reaction conditions: 1 mmol alkyne, 1.2 mmol Bu₃SnSiMe₂Ph, 0.05/0.01 mmol

Pd(PPh₃)₄, 1.0 mL ionic liquid, 5.0 mL Et₂O, 70 °C oil bath

^aGC-FID yield based on disappearance of alkyne (isolated yield in brackets)

^b5-Hexyn-1-ol used in [bmim]PF₆ previously used with 1-decyne

^c1-Decyne used in [bmim]PF₆ previously used with 5-hexyn-1-ol

In general, successive reactions performed using the same ionic liquid/catalyst system were performed immediately after workup of the previous reaction. On occasion, however, subsequent reactions were not performed until the next day. In one instance,

the subsequent reaction was not performed until 10 d after products from the previous reaction were isolated. The flask containing the ionic liquid/catalyst system was sealed with a septum but no other moisture or atmosphere exclusion techniques were employed. When the subsequent reaction was performed, no loss in catalytic activity was observed. Many studies investigating recyclability of transition metal catalysts examine the ionic liquid/catalyst systems using only the same reaction performed in them previously, as most of our studies have done. Few researchers perform reactions in recycled ionic liquid/catalyst systems using different reagents than had been used in previous reactions.⁹² On several occasions, ionic liquid/catalyst systems that had been used for reactions involving 1-decyne or 5-hexyn-1-ol were reused in subsequent reactions with the opposite alkyne. No loss in catalytic activity was observed, suggesting that these ionic liquid/catalyst systems are not just reusable for reactions that had previously been performed in them but that they can be used for a number of applications.

An interesting result obtained from these studies is the lag time required for the first reaction to proceed. For most of the recyclability studies, the first reaction generally required a longer reaction time to proceed to completion than did subsequent reactions performed in the same ionic liquid/catalyst system. This effect is most pronounced in the very low isolated yield (<60%) from the reaction between phenylacetylene and $\text{Bu}_3\text{SnSiMe}_3$ in $[\text{bmim}]\text{BF}_4/\text{Et}_2\text{O}$ system as compared to the quantitative yields isolated from subsequent reactions. After 144 hours in the 70 °C oil bath, only ~85% of the phenylacetylene had been reacted as measured by GC-FID and the reaction was worked up at that point to afford a 58% isolated yield. On the subsequent reaction, however, quantitative GC and isolated yields were obtained after only 36 hours. This lag time may

indicate that $\text{Pd}(\text{PPh}_3)_4$ is not the active palladium species during catalysis and that the active species requires time to be generated.

Other groups working with palladium-catalyzed reactions in imidazolium-based ionic liquids have observed lag times. These groups often pre-heat the ionic liquid/catalyst system with only some or none of the reagents present for a “catalyst activation period” during which time the active species is presumably generated,^{127,128,130} some noticing a drop in initial rate if the reagents were preheated without the ionic liquid.¹³² These effects were often ascribed to the generation of some other active palladium species, most probably an imidazolylidene carbene complex. The proton on carbon 2 of the imidazolium ring is mildly acidic and can be removed under the right conditions to generate a carbene.¹⁷⁴ Indeed, palladium-imidazolylidene complexes have been prepared independently from research concerned with ionic liquids and are quite active in many palladium-catalyzed reactions, including Heck reactions^{175,176} as well as many others.¹⁷⁷ These complexes show excellent stabilities and turnover numbers compared to other palladium catalysts, acting as non-participative ligands in catalytic processes. The donation of electron density from the imidazolium nitrogen atoms to the carbene carbon enhances its nucleophilicity and compensates for electron flow to the metal. Imidazolylidene ligands are described as pure donor ligands and appear to coordinate more strongly to metal centers than tertiary phosphines, undergoing little or no dissociation from the metal in solution.¹⁷⁸

Experimental studies have confirmed a density functional theory analysis done on the oxidative addition of the C-H bond of *N,N*-dimethylimidazolium across the platinum(0) complex $\text{Pt}(\text{PPh}_3)_4$. These studies have shown that this reaction is

exothermic, resulting in the isolation of a platinum-imidazolylidene complex, although calculations showed that the same reaction across $\text{Pd(PPh}_3)_4$ was slightly endothermic.¹⁷⁹ However, palladium-imidazolylidene complexes have been observed, isolated, and characterized from Suzuki^{129,180} and Heck¹¹⁸ reactions performed in imidazolium-based ionic liquids.

During investigations into the Heck reaction in imidazolium-based ionic liquids, Xu et al. observed that the reaction proceeded much faster in [bmim]Br than in [bmim]BF₄.¹¹⁸ When palladium(II) acetate Pd(OAc)_2 was heated in [bmim]Br, the ionic liquid changed colour from brown to red to yellow within a few minutes, a similar colour observed in ionic liquid systems used in these silylstannation studies. Other groups investigating palladium catalysis in ionic liquids have also observed yellow catalytically active solutions.¹²⁷ Extraction of the ionic liquid resulted in the isolation of a mixture of palladium-imidazolylidene complexes. When examined by NMR, some of these complexes appeared to be dimeric while most were monomeric isomers containing two bromide ligands and two imidazolylidene carbene ligands. The formation of these complexes was not observed under similar conditions in [bmim]BF₄, indicating that the halide was necessary to deprotonate the imidazolium species and generate the carbene. Since these types of palladium-carbene complexes were known to be very active in Heck reactions, it was presumed that their formation in [bmim]Br was responsible for its higher activity. When these isolated catalysts were used instead of Pd(OAc)_2 for Heck reactions, they showed high activity in [bmim]Br but not in [bmim]BF₄, indicating their transformation into some less active species in this ionic liquid.

When investigating the Suzuki coupling catalyzed by $\text{Pd}(\text{PPh}_3)_4$ in $[\text{bmim}]\text{BF}_4$, Mathews et al. added halide anions *via* NaCl to their ionic liquid in an attempt to prevent catalyst decomposition.¹⁸⁰ When it was observed that the catalyst did not decompose after the addition of halide, the system was further investigated and it was discovered that a palladium-imidazolylidene complex was forming (Figure 23). This complex was even observed in some samples of $[\text{bmim}]\text{BF}_4$ without added halide. It was later determined that residual halide from the preparation of the ionic liquid *via* metathesis reaction with NaBF_4 was causing the carbene to form and after further purification the ionic liquid ceased to afford the carbene complex without added halide. The palladium-imidazolylidene complex was isolated and characterized and was shown to be extremely active and recyclable in subsequent Suzuki reactions.

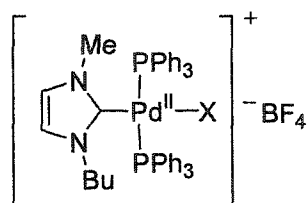


Figure 23. Palladium-imidazolylidene complex isolated by Mathews et al. during $\text{Pd}(\text{PPh}_3)_4$ -catalyzed Suzuki reactions in impure $[\text{bmim}]\text{BF}_4$

Another possible active palladium species may be palladium nanoclusters. Deshmukh et al. observed the formation of and isolated a bis-(imidazolylidene)-palladium complex from Heck catalysts $\text{Pd}(\text{OAc})_2$ and $\text{PdCl}_2/\text{NaOAc}$ in $[\text{bbim}]\text{Br}$ and $[\text{bbim}]\text{BF}_4$ under sonicating conditions.¹²⁴ After a Heck reaction was performed in $[\text{bbim}]\text{BF}_4$ under sonicating conditions, however, the remaining ionic liquid/catalyst mixture was analyzed by transmission electron microscopy (TEM), which showed the

presence of palladium nanoclusters (Figure 24). These clusters were stable even after storage for a week.

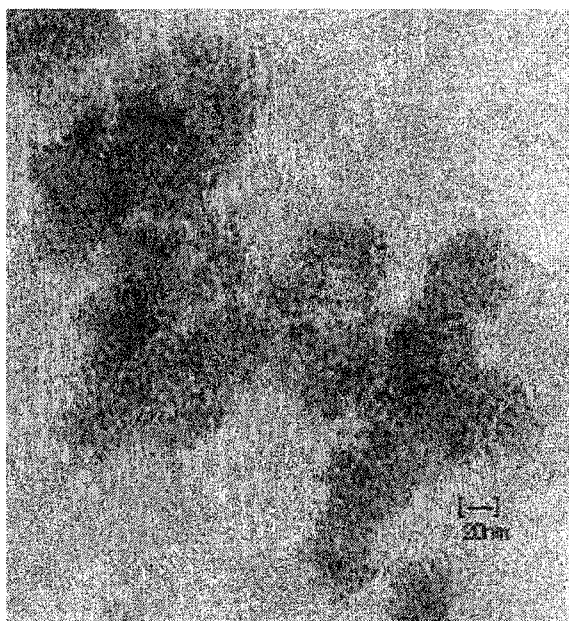


Figure 24. TEM image of palladium nanoclusters formed during a Heck reaction in [bbim]BF₄¹²⁴

A study performed during the Heck reaction in different imidazolium-based ionic liquids used X-ray absorption fine structure (XAFS) analysis to characterize the palladium species present.¹⁸¹ This study showed that bis-(carbene) complexes formed in ionic liquids with halide anions such as [bmim]Cl, but in tetrafluoroborate-based ionic liquids palladium nanoclusters were the predominant species. The study showed that the addition of triphenylphosphine increased the induction time of the reaction while the active palladium species formed and also decreased the rate, but increased the stability of the palladium catalyst with respect to palladium black formation, showing higher recyclability. In addition, neither palladium-carbene complexes nor palladium

nanoclusters were observed to form in non-imidazolium based ionic liquid or in C2-substituted imidazolium-based ionic liquids.

It appears as though more investigations are necessary to determine the active palladium species present in such reactions in imidazolium-based ionic liquids. It is possible that a carbene complex forms during silylstannane reactions, generated from anions from HF resulting from the thermal decomposition of the hexafluorophosphate anion and giving rise to the higher activity of [bmim]PF₆ over [bmim]BF₄. It could also be that palladium nanoclusters are the active catalysts. Whatever it is, it seems clear that it is not Pd(PPh₃)₄ and that imidazolium-based ionic liquids stabilize it more toward recyclability as palladium black precipitation is often observed from such reactions in non-imidazolium-based ionic liquids. These findings also support comments made by many researchers regarding the not-so-benign nature of ionic liquids in the reactions they support.^{118,129,135,180}

2.3 Attempted Tandem Silylstannation-Stille Coupling Reactions

Vinylstannanes have been shown to be active in palladium-catalyzed Stille coupling reactions with different halide-containing unsaturated systems such as haloarenes and vinyl halides. Since the addition of silylstannanes to alkynes yield vinylstannanes, it was conceivable that tandem silylstannation-Stille coupling reactions could be performed, generating the vinylstannane from a palladium-catalyzed silylstannation reaction followed by addition of a haloarene to generate the Stille product in one pot. Although Stille couplings have already been shown to proceed in ionic

liquids under different conditions,¹³¹ the *in situ* generation of the vinylstannane may provide a benefit for the reaction.

The first part of the tandem silylstannation-Stille reaction was a coupling of an equimolar amount of phenylacetylene with $\text{Bu}_3\text{SnSiMe}_3$ under biphasic conditions in $[\text{bmim}]\text{PF}_6/\text{Et}_2\text{O}$ in the presence of 1 mol% $\text{Pd}(\text{PPh}_3)_4$, heated in a 70 °C oil bath. This afforded the normal silylstannylated product in quantitative yield by GC-FID after 1 d (evidenced by the disappearance of the phenylacetylene peak). An equimolar amount of freshly distilled bromobenzene was injected into the reaction, which continued to heat under nitrogen in the 70 °C oil bath. Bromobenzene was chosen as the aryl halide based on the previous study of Stille reactions in ionic liquids that suggested bromobenzene to be the aryl halide of choice when using $\text{Pd}(\text{PPh}_3)_4$ as a catalyst. The reaction was monitored by GC-FID and after 14 d there appeared to be no remaining vinylstannane. The products were extracted with Et_2O as normal and purified *via* flash chromatography to yield the Stille product in 29% yield (Figure 25).

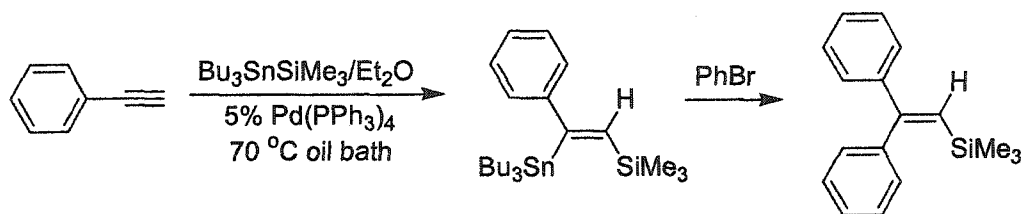


Figure 25. Tandem silylstannation-Stille coupling mediated by $\text{Pd}(\text{PPh}_3)_4$ in $[\text{bmim}]\text{PF}_6/\text{Et}_2\text{O}$

This reaction was repeated with 5 mol% $\text{Pd}(\text{PPh}_3)_4$ and provided a similarly low yield of 34% after 51 d heating in the 70 °C oil bath. In order to determine if the reaction

would proceed better in a conventional solvent or if an unreactive combination of reagents was chosen, these reactions were performed in refluxing THF. The vinylstannane was generated in quantitative yield by GC-FID after only 3 hours; it was observed that the THF was black at this point, indicating the precipitation of large amounts of palladium black. After the addition of bromobenzene, however, the reaction failed to provide better yields of the Stille product than the ionic liquid. The reactions were also performed in THF at room temperature, the vinylstannane being quantitatively generated overnight. This temperature also failed to afford improved yields of the Stille product. These results indicate that the slow rate of Stille coupling and the poor yields obtained are not due to the use of the ionic liquid but are more than likely due to the use of an unreactive combination of reagents.

Although the previous study performed on the Stille reaction in ionic liquids showed that bromobenzene was the aryl halide of choice when using $\text{Pd}(\text{PPh}_3)_4$, the study also showed that vinylstannanes do not proceed to give good yields using this palladium catalyst.¹³¹ Arylstannanes such as PhSnBu_3 provide far better yields with bromobenzene and $\text{Pd}(\text{PPh}_3)_4$ than vinylstannanes and are much more widely used for such applications. The study showed that vinylstannanes may react better with palladium(II) catalysts such as $\text{PdCl}_2(\text{PhCN})_2$ and with iodoarenes. Since palladium(II) catalysts did not afford vinylstannanes from the reaction between phenylacetylene and $\text{Bu}_3\text{SnSiMe}_3$, it was unavoidable to use an unreactive combination of reagents that did not provide Stille products in high rates or yields.

Mitchell et al. have succeeded in performing Stille couplings with the vinylstannanes generated from additions of alkynes to silylstannanes.¹⁵⁶ They use

palladium(II) catalysts for the Stille coupling that are known to better catalyze such reactions, however. The use of a palladium(II) catalyst for the tandem silylstannation-Stille reactions in ionic liquids is not feasible since it will not yield the vinylstannane in the first place. As well, Mitchell et al. have not performed tandem silylstannation-Stille reactions. They have avoided the catalyst selection problem by isolating the vinylstannane from one reaction and performing the Stille coupling in a separate reaction vessel. This is therefore an avenue that could be open to further exploration, perhaps using different sources of palladium.

3.0 Conclusions

Ionic liquids have been known for a long period of time, but have only recently been explored regarding their applications as solvents for organic transformations. In the early investigations of the potential utility of ionic liquids as solvents, they were often regarded as curiosities, interesting solvents composed entirely of ions that happen to give rate, selectivity, and yield enhancements when compared to conventional molecular solvents. Since that time, the use of ionic liquids appears to be growing exponentially since it was demonstrated that transition metal catalysts could be immobilized in ionic liquids and recycled, often providing some kind of enhancement over conventional solvents.

Ionic liquids have emerged along with a select few other classes of compounds as potential “green solvents” in which more environmentally friendly chemistry could be conducted. This is due in large part to their nonvolatility and their ability to be recycled, especially when containing expensive, rare, or toxic catalysts. It is important not to get caught up in their potential applications as green solvents too early. Many fundamental facts about ionic liquids and their behaviour are still missing from the literature, such as how they can be disposed of if need be and what will happen if they somehow escape into the ecosystem. There is still a large amount of basic frontline research that must be conducted on ionic liquids if they are to be adopted worldwide as an environmentally friendly solvent alternative. Part of this basic research is to determine the limits to which reactions can be pushed in ionic liquids.

This work has shown that silylstannanes can be used efficiently in ionic liquids. It has added to the growing number of palladium-catalyzed reactions shown to be possible in ionic liquids. The atom-economical addition of silylstannanes to terminal alkynes has been shown to proceed cleanly in ionic liquids, providing good to excellent yields in acceptable reaction times. Two different silylstannanes were used, trimethyl(tributylstannyl)silane and dimethylphenyl(tributylstannyl)silane. Five different terminal alkynes were used, phenylacetylene (the most reactive), 1-decyne, 5-hexyn-1-ol, 5-hexyn-1-ol THP ether, and 6-chlorohex-1-yne. Two different ionic liquids were used, 1-*n*-butyl-3-methylimidazolium hexafluorophosphate and 1-*n*-butyl-3-methylimidazolium tetrafluoroborate, which were shown to provide better product yields under biphasic conditions with diethyl ether as a co-solvent. The reactions were shown to be best catalyzed by tetrakis(triphenylphosphine)palladium(0), affording little to no yield with a palladium(II) catalyst. Although no rate enhancement was observed in ionic liquids as compared to using tetrahydrofuran as a solvent, the reactions still proceeded to give only one out of a possible four product isomers. These reactions have been shown to proceed in the presence of 5 mol% palladium and also in the presence of 1 mol% palladium (albeit slightly slower at this catalyst loading).

The ionic liquid/catalyst systems were also shown to be considerably recyclable, both affording quantitative yields of the addition product between phenylacetylene and $\text{Bu}_3\text{SnSiMe}_3$ after ten cycles. All of the other alkynes and silylstannanes were shown to be recyclable, as well.

There are many future directions for this project. The ionic liquid/catalyst mixtures were shown to be recyclable and it was assumed that no palladium was being

leached into the ether extracts during product isolation between cycles; however, studies could be done to determine whether this is actually true. The ether extracts could be analyzed for palladium content by inductively coupled plasma mass spectrometry between cycles. In addition, it appears as though $\text{Pd}(\text{PPh}_3)_4$ is not the active catalyst species during these reactions. It is possible that the actual catalytic species is a palladium-imidazolyliene carbene complex, or it could be in the form of palladium nanoclusters. X-ray absorption fine structure analysis of silylstannation reactions performed in ionic liquids could be undertaken to identify the active palladium species. The ionic liquid could be heated with diethyl ether and $\text{Pd}(\text{PPh}_3)_4$ without the addition of alkyne or silylstannane to determine if preactivation is necessary or if it provides better yields. The ionic liquid could also be extracted in attempts to isolate the active palladium catalyst.

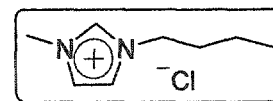
These reactions could be performed with a wider array of silylstannanes and alkynes. Internal alkynes could be used to assess any possible selectivity influences of the ionic liquid on the regiochemical outcome of the reactions. Different catalysts could be used to develop the not-so-successful tandem silylstannation-Stille coupling. Other “hydrophobic” and non-imidazolium based ionic liquids could also be used to determine their effects on these reactions.

4.0 Experimental

General

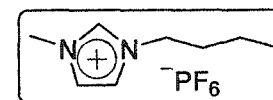
Synthesis and reactions of silylstannanes were performed in oven-dried glassware that was cooled under vacuum and released to a nitrogen atmosphere. THF and Et₂O that were used in the synthesis and reactions of silylstannanes were dried and distilled from potassium/benzophenone immediately prior to use. Dichloromethane was dried and distilled over calcium hydride. Pyridine and diisopropylamine were dried over and distilled onto potassium hydroxide pellets. Thionyl chloride was distilled from quinoline. Ionic liquids,^{24,131} Bu₃SnSiMe₂Ph,^{158,163} 6-chlorohex-1-yne,¹⁷⁰ and 5-hexyn-1-ol THP ether¹⁶⁹ were synthesized and purified before use. All other reagents were used as received. Column chromatography was performed using Kieselgel 60, 230-400 mesh silica gel. Thin-layer chromatography was performed using aluminium-backed plates coated with Kieselgel 60 F254; plates were visualized under ultraviolet lamp and/or using 5% phosphomolybdic acid in ethanol. Silylstannation reactions were heated on a Mirak Thermolyne temperature controlled hotplate. Low temperatures for silylstannane syntheses were maintained by an FTS Systems cooling apparatus. Gas chromatography was performed using a Varian 3800 gas chromatograph equipped with a flame ionization detector. Nuclear magnetic resonance spectra were recorded on a Bruker 250 MHz spectrometer at the Atlantic Regional Magnetic Resonance Centre; spectra were recorded using CDCl₃ solutions and chemical shifts are reported in ppm referenced to tetramethylsilane unless otherwise stated. The 60 MHz spectrum shown in Figure 17a was recorded on a Varian EM360L spectrometer equipped with an Anasazi FT-NMR probe, recorded using a CDCl₃ solution and referenced to tetramethylsilane.

1-n-Butyl-3-methylimidazolium chloride: 1-Methylimidazole (40 mL, 0.50 mol) and 1-chlorobutane (90 mL, 0.86 mol) were



refluxed for 18 h, after which time excess 1-chlorobutane was decanted off of the newly-formed viscous tan-coloured lower layer. This lower layer was washed with ethyl acetate (EtOAc, 3 x 100 mL) then heated under vacuum at 80 °C for 6 h. An off-white solid formed upon cooling (81.43 g, 0.466 mol, 93%). ^1H NMR: δ 0.75 (t, 3H, N-CH₂CH₂CH₂CH₃, $^3J=7.3$ Hz), 1.17 (sextet, 2H, N-CH₂CH₂CH₂CH₃, $^3J=7.3$ Hz), 1.70 (quintet, 2H, N-CH₂CH₂CH₂CH₃, $^3J=7.3$ Hz), 3.93 (s, 3H, N-CH₃), 4.14 (t, 2H, N-CH₂CH₂CH₂CH₃, $^3J=7.3$ Hz), 7.41 (br s, 1H, H4/H5), 7.58 (br s, 1H, H4/H5), 10.36 (s, 1H, H2). ^{13}C NMR: δ 13.3, 19.3, 32.0, 36.4, 49.5, 122.0, 123.7, 137.5.

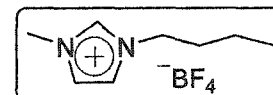
1-n-Butyl-3-methylimidazolium hexafluorophosphate: [bmim]Cl (87.95 g, 0.504 mol) was dissolved in water (150 mL) and cooled



in an ice bath. A 60% aqueous solution of HPF₆ (74.5 mL, 0.506 mol) was added dropwise over 20 min as a lower tan-coloured layer formed exothermically. The mixture was stirred for 24 h, after which time the upper aqueous phase was decanted. The lower ionic liquid phase was washed with water (10 x 100 mL) after which the washings were pH neutral. After heating under vacuum at 70 °C for 6 h the ionic liquid was obtained as a clear tan oil (96.26 g, 0.339 mol, 67%). ^1H NMR (*acetone-d₆*): δ 0.94 (t, 3H, N-CH₂CH₂CH₂CH₃, $^3J=7.3$ Hz), 1.38 (sextet, 2H, N-CH₂CH₂CH₂CH₃, $^3J=7.3$ Hz), 1.92 (quintet, 2H, N-CH₂CH₂CH₂CH₃, $^3J=7.3$ Hz), 4.03 (s, 3H, N-CH₃), 4.34 (t, 2H, N-

$\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_3$, $^3J=7.3$ Hz), 7.67 (br s, 1H, H4/H5), 7.72 (br s, 1H, H4/H5), 8.91 (s, 1H, H2). ^{13}C NMR (*acetone-d*₆): δ 13.7, 19.9, 32.7, 36.6, 50.2, 123.4, 124.8, 137.3.

1-n-Butyl-3-methylimidazolium tetrafluoroborate: [bmim]Cl

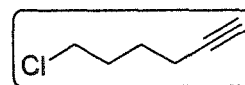


(30.76 g, 0.176 mol) was dissolved in water (150 mL) to which a 48% aqueous solution of HBF_4 (23.0 mL, 0.176 mol) was added. The solution stirred for 72 h after which time the water was evaporated under reduced pressure. Heating under vacuum at 70 °C for 6 h afforded the ionic liquid as a clear tan oil (38.87 g, 0.172 mol, 98%). ^1H NMR (*acetone-d*₆): δ 0.93 (t, 3H, $\text{N-CH}_2\text{CH}_2\text{CH}_2\text{CH}_3$, $^3J=7.3$ Hz), 1.37 (sextet, 2H, $\text{N-CH}_2\text{CH}_2\text{CH}_2\text{CH}_3$, $^3J=7.3$ Hz), 1.91 (quintet, 2H, $\text{N-CH}_2\text{CH}_2\text{CH}_2\text{CH}_3$, $^3J=7.32$ Hz), 4.03 (s, 3H, N-CH_3), 4.34 (t, 2H, $\text{N-CH}_2\text{CH}_2\text{CH}_2\text{CH}_3$, $^3J=7.3$ Hz), 7.69 (br s, 1H, H4/H5), 7.75 (br s, 1H, H4/H5), 9.01 (s, 1H, H2). ^{13}C NMR (*acetone-d*₆): δ 13.7, 19.9, 32.8, 36.5, 50.1, 123.4, 124.7, 137.6.

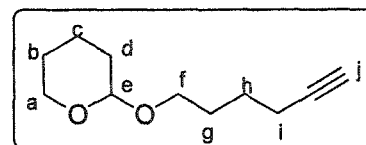
Dimethylphenyl(tributylstannyl)silane: Dry THF (50 mL) was injected into a dry flask followed by freshly distilled diisopropylamine (3.08 mL, 22.0 mmol). This was cooled to -10 °C and a 1.6 M hexanes solution of butyllithium (13.75 mL, 22.0 mmol) was injected dropwise. After stirring for 10 min, Bu_3SnH (5.38 mL, 20.0 mmol) was injected dropwise. This stirred at 0 °C for 45 min., after which time chlorodimethylphenylsilane (3.69 mL, 22.0 mmol) was injected dropwise. The solution was allowed to warm to room temperature and stir for 1 h, after which time GC-FID analysis of a water-quenched aliquot showed almost complete reaction. The solvent was evaporated under reduced pressure and the resulting cloudy white oil was filtered through celite and washed with

Et₂O. After evaporating the Et₂O under reduced pressure, the yellow oil was purified *via* short-path distillation under vacuum, the product coming over at 160-165 °C as a clear colourless oil (5.93 g, 13.9 mmol, 70%). ¹H NMR: δ 0.54 (s, 6H, Si(CH₃)₂), 0.85-0.92 (m, 15H, Sn(CH₂CH₂CH₂CH₃)₃), 1.23-1.49 (m, 12H, Sn(CH₂CH₂CH₂CH₃)₃), 7.34-7.51 (m, 5H, ArH). ¹³C NMR: δ 0.2, 8.3, 13.8, 27.7, 30.3, 128.0, 128.5, 133.7, 141.5.

6-Chlorohex-1-yne: 5-Hexyn-1-ol (1.00 mL, 9.1 mmol) was injected into a flask containing dry Et₂O (15 mL) followed by dry pyridine (0.74 mL, 9.1 mmol) and stirred in an ice bath for 30 min. Thionyl chloride (0.80 mL, 11.0 mmol) was injected dropwise; the flask was fitted with a dry condensor and the cloudy white mixture heated to reflux under nitrogen overnight. GC-FID analysis confirmed complete reaction, at which time the brown solution was poured into water (50 mL). The mixture was extracted with Et₂O (30 mL). The Et₂O layer was washed with water (2 x 50 mL), dried over anhydrous MgSO₄, filtered and concentrated to afford a dark oil. This was purified *via* flash chromatography (10:1 hexanes/EtOAc) to afford the product as a volatile clear light brown oil (0.436 g, 3.7 mmol, 41%). ¹H NMR: δ 1.68 (quintet, 2H, H4/H5, ³J=6.5 Hz), 1.91 (quintet, 2H, H4/H5, ³J=6.5 Hz), 1.97 (t, 1H, H1, ⁴J=2.6 Hz), 2.25 (dt, 2H, H3, ³J=6.5 Hz, ⁴J=2.6 Hz), 3.57 (t, 2H, H6, ³J=6.5 Hz). ¹³C NMR: δ 17.7, 25.6, 31.4, 44.5, 68.9, 83.7.

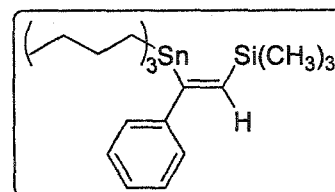


(±)-5-Hexyn-1-ol, THP ether: *p*-Toluenesulfonic acid (0.13 g, 0.68 mmol) was dissolved in dry dichloromethane (10 mL). 5-Hexyn-1-ol (1.50 mL, 13.6 mmol) was injected to the solution, followed by



3,4-dihydro-2H-pyran (2.50 mL, 27.4 mmol). The pink solution was stirred at room temperature and turned dark green after 10 min. When the reaction was complete by TLC analysis, the solvent was evaporated and the resulting dark green oil was purified *via* flash chromatography (10:1 hexanes/EtOAc), affording the product as a clear colourless oil (2.10 g, 11.5 mmol, 85%). $^1\text{H NMR}$: δ 1.48-1.80 (m, 10H, H_b , H_c , H_d , H_g , H_h), 1.91 (s, 1H, H_j), 2.23 (t, 2H, H_i), 3.37-3.51, 3.71-3.87 (m, 4H, H_a , H_f), 4.56 (t, 1H, H_e). $^{13}\text{C NMR}$: δ 18.4, 19.8, 25.6, 25.7, 29.0, 30.9, 62.5, 67.1, 68.6, 84.6, 99.0.

(Z)-1-Phenyl-1-(tributylstannyl)-2-(trimethylsilyl)ethane
(representative procedure for silylstannation of terminal
alkynes): Ionic liquid (1.0 mL) was heated in a dry flask

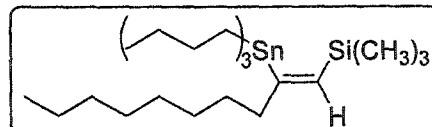


under vacuum at 70 °C for 4 h. After releasing the vacuum to nitrogen, the flask was transferred to an argon glove box where $\text{Pd}(\text{PPh}_3)_4$ (0.058 g, 0.05 mmol for 5%, 0.012 g, 0.01 mmol for 1%) was weighed and added. After stirring to suspend the palladium, the reaction vessel was removed from the glove box. $\text{Bu}_3\text{SnSiMe}_3$ (0.42 mL, 1.2 mmol) was injected *via* needle and syringe, followed by phenylacetylene (0.11 mL, 1.0 mmol) and dry Et_2O (5.0 mL). A dry reflux condensor was connected and the reaction was heated under nitrogen in a 70 °C oil bath for 36 h. Once the reaction was complete by GC-FID, the reaction was cooled and the upper Et_2O phase was removed *via* needle and syringe. The ionic liquid was washed with dry Et_2O (8 x 8 mL) under nitrogen using needles and syringes. The Et_2O extracts were combined and solvent was evaporated under reduced pressure. The resulting oil was purified *via* flash chromatography (hexanes) to afford the product as a clear colourless oil (0.46 g, 0.99 mmol, 99%). $^1\text{H NMR}$: δ 0.32 (s, 9H,

Si(CH₃)₃), 0.98-1.10 (m, 15H, Sn(CH₂CH₂CH₂CH₃)₃), 1.34-1.65 (m, 12H, Sn(CH₂CH₂CH₂CH₃)₃), 6.71 (s, 1H, C=C-H, ^{sat}J_{SnH}=160, 168 Hz), 7.13-7.16 (m, 2H, ArH), 7.26-7.32 (m, 1H, ArH), 7.38-7.41 (m, 2H, ArH). ¹³C NMR: δ 0.3, 12.1, 13.8, 27.5, 29.2, 125.6, 126.0, 128.0, 148.5, 152.0, 166.2.

(Z)-2-(Tributylstannyl)-1-(trimethylsilyl)dec-1-ene:

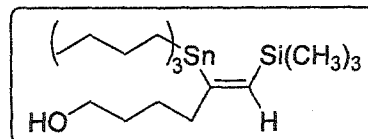
Prepared as above, clear yellow oil (0.484 g, 0.97



mmol, 97%). ¹H NMR: δ 0.09 (s, 9H, Si(CH₃)₃), 0.79-1.58 (m, 42H, SnBu₃, C₇H₁₅CH₂-C=C), 2.20-2.33 (m, 2H, C₇H₁₅CH₂-C=C), 6.32 (s, 1H, C=C-H, ^{sat}J_{SnH}=176, 184 Hz). ¹³C NMR: δ 0.4, 8.0, 11.4, 13.8, 14.3, 22.8, 27.7, 29.4, 29.7, 30.2, 30.5, 32.1, 47.8, 143.3, 166.0.

(Z)-5-(Tributylstannyl)-6-(trimethylsilyl)hex-5-en-1-ol:

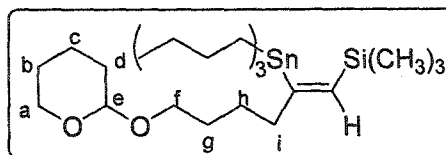
Prepared as above, cloudy white oil (0.412 g, 0.89 mmol,



89%). ¹H NMR: δ 0.09 (s, 9H, Si(CH₃)₃), 0.87-0.99 (m, 15H, Sn(CH₂CH₂CH₂CH₃)₃), 1.25-1.68 (m, 17H, Sn(CH₂CH₂CH₂CH₃)₃, HOCH₂CH₂CH₂CH₂-C=C), 2.30 (t, 2H, HOCH₂CH₂CH₂CH₂-C=C), 3.64 (m, 2H, HOCH₂CH₂CH₂CH₂-C=C), 6.34 (s, 1H, C=C-H, ^{sat}J_{SnH}=172, 180 Hz). ¹³C NMR: δ 0.2, 11.2, 13.6, 25.9, 27.5, 29.2, 32.3, 47.1, 62.9, 143.7, 165.1.

(±)-(Z)-5-(Tributylstannyl)-6-(trimethylsilyl)hex-5-

en-1-ol, THP ether: Prepared as above, clear colourless oil (0.538 g, 0.99 mmol, 99%). ¹H NMR:



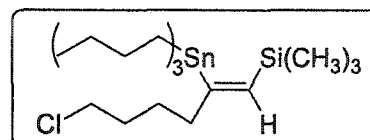
δ 0.08 (s, 9H, Si(CH₃)₃), 0.86-0.95 (m, 15H, Sn(CH₂CH₂CH₂CH₃)₃), 1.27-1.65 (m, 22H, Sn(CH₂CH₂CH₂CH₃)₃, H_b, H_c, H_d, H_g, H_h), 2.29 (t, 2H, H_i), 3.30-3.90 (m, 4H, H_a, H_f), 4.58 (t, 1H, H_e), 6.33 (s, 1H, C=C-H, ^{sat}*J*_{SnH}=175, 183 Hz). ¹³C NMR: δ 0.22, 11.2, 13.6, 19.6, 25.5, 26.6, 27.5, 29.2, 29.3, 30.8, 47.5, 62.3, 67.6, 98.9, 143.7, 165.5.

(Z)-6-Chloro-2-(tributylstannyl)-1-(trimethylsilyl)hex-1-

ene: Prepared as above, clear colourless oil (0.327 g, 0.68

mmol, 68%). ¹H NMR: δ 0.09 (s, 9H, Si(CH₃)₃), 0.86-

0.96 (m, 15H, Sn(CH₂CH₂CH₂CH₃)₃), 1.24-1.50, 1.71-1.77 (m, 16H, Sn(CH₂CH₂CH₂CH₃)₃, ClCH₂CH₂CH₂CH₂-C=C), 2.28 (t, 2H, ClCH₂CH₂CH₂CH₂-C=C, ³*J*=6.7 Hz), 3.52 (t, 2H, ClCH₂CH₂CH₂CH₂-C=C, ³*J*=6.7 Hz), 6.33 (s, 1H, C=C-H, ^{sat}*J*_{SnH}=172, 180 Hz). ¹³C NMR: δ 0.2, 11.2, 13.7, 27.0, 27.5, 29.2, 32.1, 45.0, 46.6, 144.1, 164.8.



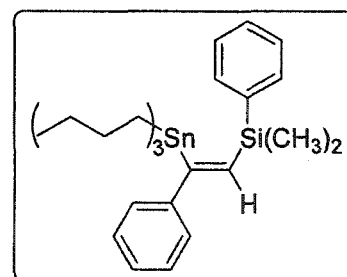
(Z)-2-(Dimethylphenylsilyl)-1-phenyl-1-

(tributylstannyl)ethene: Prepared as above using

Bu₃SnSiMe₂Ph (0.510 g, 1.2 mmol) instead of Bu₃SnSiMe₃,

product obtained as a clear colourless oil (0.516 g, 0.98

mmol, 98%). ¹H NMR: δ 0.11 (s, 6H, Si(CH₃)₂), 0.33-0.50 (m, 15H, Sn(CH₂CH₂CH₂CH₃)₃), 0.78-0.99 (m, 12H, Sn(CH₂CH₂CH₂CH₃)₃), 6.41 (s, 1H, C=C-H, ^{sat}*J*_{SnH}=156, 164 Hz), 6.70-7.04, 7.24-7.28 (m, 10H, ArH). ¹³C NMR: δ 0.5, 12.0, 13.7, 27.4, 29.1, 125.8, 126.0, 127.9, 128.1, 129.1, 134.2, 139.6, 146.0, 152.0, 169.0.



(Z)-1-(Dimethylphenylsilyl)-2-(tributylstannyl)dec-1-

ene: Prepared as above, clear colourless oil (0.439 g,

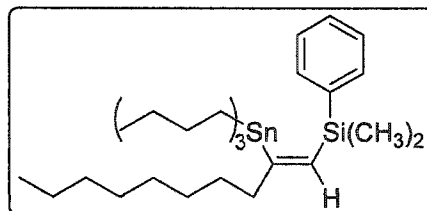
0.78 mmol, 78%). ^1H NMR: δ 0.34 (s, 6H,

$\text{Si}(\text{CH}_3)_2$), 0.73-0.88, 1.18-1.41 (m, 42H, SnBu_3 , $\text{C}_7\text{H}_{15}\text{CH}_2\text{-C=C}$), 2.29-2.35 (m, 2H,

$\text{C}_7\text{H}_{15}\text{CH}_2\text{-C=C}$), 6.50 (s, 1H, C=C-H , $^{\text{sat}}J_{\text{SnH}}=170$, 176 Hz), 7.30-7.35 (m, 3H, ArH),

7.49-7.54 (m, 2H, ArH). ^{13}C NMR: δ -0.6, 11.1, 13.7, 14.2, 22.7, 27.5, 28.0, 29.2, 29.4,

29.6, 31.0, 31.9, 47.8, 127.7, 128.8, 134.0, 140.1, 140.7, 168.9.



(Z)-6-(Dimethylphenylsilyl)-5-(tributylstannyl)hex-5-en-1-

ol: Prepared as above, cloudy oil (0.325 g, 0.62 mmol,

62%). ^1H NMR: δ 0.36 (s, 6H, $\text{Si}(\text{CH}_3)_2$), 0.81-0.90 (m,

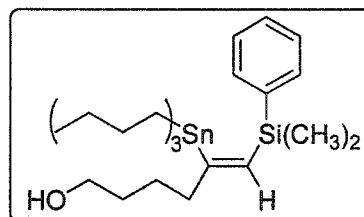
15H, $\text{Sn}(\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_3)_3$), 1.19-1.64 (m, 17H,

$\text{Sn}(\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_3)_3$, $\text{HOCH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{-C=C}$), 2.37 (t, 2H, $\text{HOCH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{-}$

C=C), 3.65-3.67 (m, 2H, $\text{HOCH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{-C=C}$), 6.53 (s, 1H, C=C-H , $^{\text{sat}}J_{\text{SnH}}=170$,

178 Hz), 7.31-7.55 (m, 5H, ArH). ^{13}C NMR: δ -0.4, 11.4, 13.8, 26.2, 27.6, 29.5, 32.6,

47.4, 63.0, 127.9, 129.0, 134.4, 139.6, 141.5, 168.4.



(\pm) -*(Z)*-6-(Dimethylphenylsilyl)-5-

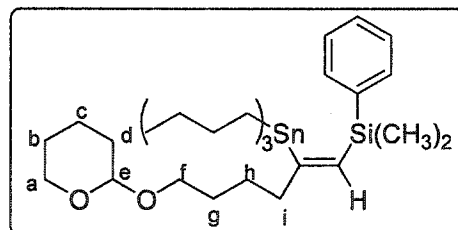
(tributylstannyl)hex-5-en-1-ol, THP ether:

Prepared as above, clear colourless oil (0.492 g,

0.83 mmol, 83%). ^1H NMR: δ 0.36 (s, 6H,

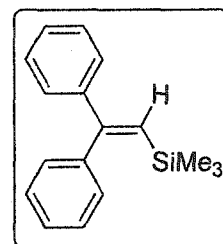
$\text{Si}(\text{CH}_3)_2$), 0.77-0.93 (m, 15H, $\text{Sn}(\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_3)_3$), 1.18-1.72 (m, 22H,

$\text{Sn}(\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_3)_3$, H_b , H_c , H_d , H_g , H_h), 2.37 (t, 2H, H_i), 3.38-3.90 (m, 4H, H_a , H_f),



4.58 (t, 1H, H_e), 6.53 (s, 1H, C=C-H, ^{sat}J_{SnH}=177, 185 Hz), 7.26-7.55 (m, 5H, ArH). ¹³C NMR: δ -0.5, 11.2, 13.8, 19.8, 25.7, 26.7, 27.6, 29.3, 29.5, 30.9, 47.6, 62.3, 67.5, 98.9, 127.8, 128.9, 134.1, 140.0, 141.2, 168.6.

1,1-Diphenyl-2-trimethylsilyl-ethene: [bmim]PF₆ (1.0 mL) was heated under vacuum at 65 °C for 5 h. After cooling and releasing to a nitrogen atmosphere, the ionic liquid was placed in an argon glove box where Pd(PPh₃)₄ (0.012 g, 0.01 mmol, 1%) was weighed and



added. After stirring to dissolve the catalyst, the reaction vessel was sealed with a septum and removed from the glove box. Phenylacetylene (0.11 mL, 1.0 mmol) was injected, followed by Bu₃SnSiMe₃ (0.35 mL, 1.0 mmol) and dry Et₂O (5.0 mL). After fitting with a dry reflux condensor, the reaction was placed in a 70 °C oil bath and heated under nitrogen. After 1 d, GC-FID analysis indicated complete reaction to the vinylstannane. Freshly distilled bromobenzene (0.105 mL, 1.0 mmol) was injected and heating of the mixture was continued. After 14 d, no vinylstannane was observed by GC-FID. The reaction was cooled and the upper Et₂O phase decanted. The ionic liquid was washed with Et₂O (7 x 10 mL); the GC-FID trace of the last extract was devoid of signals attributable to products or starting materials. The solvent was evaporated under reduced pressure to give a dark oil which was purified *via* flash chromatography (hexanes), affording the product as a clear colourless oil (0.073 g, 0.29 mmol, 29%). ¹H NMR: δ 0.12 (s, 9H, Si(CH₃)₃), 6.52 (s, 1H, C=C-H), 7.40-7.60 (m, 10H, ArH). ¹³C NMR: δ -0.4, 127.2, 127.3, 127.6, 127.9, 128.0, 129.7 (insufficient number of scans).

5.0 References

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