Highly Electrophilic Phosphorus(V) Cations as Robust Lewis Acids in Catalysis and Frustrated Lewis Pair Chemistry

by

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A thesis submitted in conformity with the requirements for the degree of Doctor of Philosophy
Department of Chemistry
University of Toronto

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Abstract

Catalysts are critical to the production of desirable chemicals and materials that are used to manufacture goods which are essential to our modern economy. Efforts to decrease our reliance on precious metal catalysts has led to the proliferation of main group species and the development of the chemistry of frustrated Lewis pairs (FLPs). While the literature is dominated with reports of strong Lewis acids based on Group 13 elements (e.g. Al, B), Group 15, namely phosphorus-based Lewis acids, are emerging as viable alternatives.

The graduate work presented in this thesis expands the scope of phosphorus-based Lewis acids to encompass more robust, yet reactive species for applications in catalysis and FLP chemistry, allowing access to unprecedented reactivity for electrophilic phosphorous cations (EPCs). The first chapter of this thesis details the exploration of fluoro pyridiniumphosphonium mono- and dications as efficient Lewis acid catalysts for a range of Lewis acid-catalyzed organic transformations. Following is the second chapter, which explores the synthesis of more robust EPCs and their applications in catalysis and as initiators for the Mukaiyama-Aldol condensation reaction. In the third chapter, P₃-trimethylated tricationic species, accessed from the well-known triphos ligands, are synthesized and their catalytic capabilities are explored in reductive amination reactions. As
well, preliminary results are presented wherein C-F bond activation and functionalization are also realized with these robust EPCs.

The application of phosphorus(V)-based Lewis acids is then expanded to encompass FLP chemistry, wherein the last chapter discloses the synthesis and reactivity of rare all-phosphorus based FLPs. The reactivity of these FLPs has been exploited in E-H (E = Si, B, C, H) bond activation reactions. Initial attempts to develop related N/P FLPs have also been discussed.
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I didn’t grow up wanting to be a scientist, but I was fortunate enough to be raised in a family where I was encouraged to pursue my dreams – “the world is your oyster”, my parents used to say. Thus, it was through my experiences, my curiosity, my thirst for knowledge and my passion for helping others that I encountered the people who have shaped me into the scientist I am today. Firstly, thank you to my parents – Margo and Ian Bayne – for showing me what unconditional love is, for believing in me and my wild dreams, and for providing me with a platform upon which I could build my success. As well, thank you to my younger brother Andrew for being such a great listener, supporter and motivator, and for picking up my phone calls no matter the time of day.

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<tr>
<td>FIA</td>
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<tr>
<td>FLP</td>
<td>frustrated Lewis pair</td>
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GOF goodness of fit
h hour
Hz Hertz, s⁻¹
HOMO highest occupied molecular orbital
HRMS high resolution mass spectrometry
i ipso
iPr isopropyl, (CH₃)₂CH
nᵣₓᵧ n-bond scalar coupling constant between X and Y atoms
K Kelvin
kcal kilocalories, 10³ cal
KHMDMS potassium bis(trimethylsilyl)amide
kJ kilojoule, 10³ J
LA Lewis acid
LB Lewis base
LUMO lowest unoccupied molecular orbital
m meta
m multiplet
Me methyl, CH₃
MeOTf methyl trifluoromethanesulfonate
Mes mesityl
MHz megahertz, 10⁶ Hz
mg milligram, 10⁻³ g
mL milliliter, 10⁻³ L
mmol millimole, 10⁻³ mol
MP2 Møller-Plesset perturbation theory, second order
MS mass spectrometry
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<td>m/z</td>
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<td>N-heterocyclic phosphonium</td>
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<td>phenyl</td>
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<tr>
<td>pH</td>
<td>measure of acidity and basicity (potential hydrogen)</td>
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<td>PMHS</td>
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<td>tertiary phosphine</td>
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<td>tol</td>
<td>toluene</td>
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<td>rBu</td>
<td>tert-butyl, (CH$_3$)$_3$C</td>
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Chapter 1

Introduction

1.1 Green Chemistry Revolution

Since the 1970’s when Norman Borlaug was awarded the Nobel Peace Prize for his work on developing new plant strains, which formed the basis for the Green Revolution, the world’s population has almost doubled.\(^1\) Unfortunately, along with this population increase has come an increasing strain on oil production and consumption (and other fossil fuel resources), deforestation, and greenhouse gas emissions. In this regard, the dominance of humankind has been so impactful and detrimental, that we are driving Earth out of its current geologic epoch into the “Anthropocene”\(^2\). In other words, with such a large influence on Earth’s processes and functions, humankind is poised to be responsible for the growth or destruction of our planet.

One of the largest environmental concerns is climate change. While the Montreal Protocol successfully eliminated the large majority of ozone-depleting substances from the participating 24 countries,\(^3\) our world today is beginning to feel the effects of this approaching environmental catastrophe. According to Canada’s Climate Changing Report, Earth’s warming over the 20\(^{th}\) century is largely due to human activities, and Canada’s rate of warming is about twice the global rate.\(^4\) Therefore, if viable, sustainable and effective strategies to mitigate growing environmental concerns surrounding climate change are not implemented soon, future generations will suffer.

The battle against climate change and the reduction of greenhouse gas emissions relies on the knowledge and resources of scientists around the world; and, if it is not controlled, greenhouse gas emission will lead to irreversible climate change.\(^5-7\) In this regard, Green Chemistry is at the forefront of chemical research, and governments are reliant upon chemists to produce solutions to reduce emissions, develop cleaner and more efficient energy sources, and to advocate for the responsible use of our limited natural resources.

Green Chemistry takes a bottom-up approach to chemical synthesis and calls for more sustainable chemical processes and Earth-friendly products that will prevent the release of new pollution. One strategy to mitigate some of the concerns associated with climate change, is catalysis – one of the twelve principles of Green Chemistry.\(^8\) As Ron Breslow said, “no subject so pervades modern
chemistry as that of catalysis”, and to some extent, he is correct: the field of catalysis has transformed the chemical landscape, creating more efficient and less wasteful processes. Catalysis is the action of “a substance that increases the rate of a reaction by providing an alternative path with less energetic requirement”. These substances – catalysts – are both reactants and products in a given reaction, and thus, substoichiometric amounts of catalysts are used. In the context of Green Chemistry, catalysis describes the design of more efficient chemical products and processes that reduce or eliminate the use and generation of hazardous substances. Catalysts are critical to the production of desirable chemicals and materials that are used to manufacture goods which are the basis of our modern economy. From pharmaceuticals and polymers to agrochemicals and electronics, these advances of civilization depend on effective catalyst technologies. However, at the same time, manufacturing and production technologies are under increasing scrutiny with respect to their impact on the environment. While catalysis can offer increased efficiencies and lower production costs, these technologies – largely based on precious metals in either homogeneous or heterogeneous catalysis – can also come with their own environmental concerns.

To begin to offer disruptive catalyst technologies, there has been much effort in recent years within the organometallic chemistry field to uncover catalysts based on earth-abundant elements (e.g. Fe, Co, Ni). While generally less studied, the use of main group species for catalysis has garnered increasing attention in the last decade, and most notably, has prompted the development of technologies for metal-free hydrogenation reactions.

In this regard, the work outlined in this thesis will highlight some of the advances in main group catalysis, aiming for more sustainable, less toxic, and less expensive homogeneous catalysts. In particular, the development of more stable and robust phosphorous-based compounds as Lewis acid catalysts and initiators for a variety of industrially-relevant processes (e.g. hydrosilylation, hydrodefluorination) will be described. As well, applications of robust phosphorus-based salts in Frustrated Lewis pair chemistry will be discussed.

1.2 Lewis Acid and Base Pairs

In 1923, Gilbert Lewis classified the reactivity of molecules according to electron accepting and donating abilities, which would later be defined as Lewis acids and bases, respectively. Since
In one of the earlier reports, Brown et al. studied different B/N coordination compounds and observed the formation of a classical Lewis acid/base adduct between BX₃ (X = H, F) and 2,6-lutidine (Scheme 1-1, top). However, reaction of BMMe₃ (Me = CH₃) and 2,6-lutidine did not form an adduct as predicted, presumably due to the increased steric bulk around the boron Lewis acidic centre, which prevented the efficient overlap of frontier molecular orbitals required to form a dative bond (Scheme 1-1, bottom). Unknowingly at the time, this observation would lead to a historic discovery almost six decades later.

Scheme 1-1. Lewis acid and base adduct formation (top) and interaction (bottom) with 2,6-lutidine as the Lewis base and borane Lewis acids.

In 1950, another unexpected result was reported by Wittig and co-workers, wherein the combination of triphenylboron, BPh₃ and [Na][CPh₃] resulted in the ring opening reaction of THF. Shortly thereafter, reaction of BPh₃ with PPh₃ and benzyne generated a 1,2-phosphonium borate zwitterion because the rigid backbone imparted by the phenyl rings precludes adduct formation between this acid/base pair. In 1966, Tochtermann et al. harnessed the reactivity of bulky Lewis acid/base pairs and used the unquenched reactive combination of [Na][CPh₃] and BPh₃ to polymerize butadiene and facilitate a 1,6-addition of the C/B pair to acenaphthylene.
The cleavage of cyclic ethers such as THF, 2,5-dihydrofuran, coumarin and dioxane were also reported with the bulky trityl anion \([\text{CPh}_3]^−\) and the appropriate Lewis acid (Scheme 1-2).

![Scheme 1-2](image)

**Scheme 1-2.** Reactivity of a C/B Lewis base/acid pair.

More recently, some research groups have expanded the reactivity of bulky Lewis acid and base pairs and have shown that judicious choice of the substituents can significantly alter the nature of the unquenched reactivity. In one example, a phosphorus ylide Lewis base was shown to attack the *para*-position of a pentafluorophenyl ring of the Lewis acid B(C₆F₅)₃ in the absence of an additional substrate.²⁶-²⁸

In 2006, these sterically-encumbered, yet reactive Lewis acid/base pairs would be deemed “frustrated Lewis pairs” (FLPs) and their chemistry would transform the landscape of inorganic chemistry.²⁹ In this seminal report, *para*-attack of a nucleophilic phosphine Lewis base was shown to generate a zwitterionic phosphonium-borate, Mes₂PH(C₆F₄)BF(C₆F₅)₂, which readily reacts with Me₂SiHCl to give Mes₂PH(C₆F₄)BH(C₆F₅)₂. Subsequently, this compound was shown to undergo stoichiometric loss of H₂ upon heating above 100 °C, and remarkably, the corresponding phosphine-borane reacts with H₂ at ambient temperature regenerating the phosphonium-borate species (Scheme 1-3).

![Scheme 1-3](image)

**Scheme 1-3.** First example of reversible metal-free H₂ activation.
1.3 Frustrated Lewis Pair (FLP) Chemistry

Since the discovery of the first metal-free system to reversibly activate H\textsubscript{2} in 2006\textsuperscript{29} many research groups have developed simple combinations of sterically-encumbered electron donors and acceptors to activate a variety of small molecules.\textsuperscript{30, 31} Most notable are the systems capable of effecting reduction chemistry with H\textsubscript{2}, wherein different combinations of Lewis acids and bases have been used to affect the reduction of polar substrates,\textsuperscript{32, 33} such as imines,\textsuperscript{34} anilines,\textsuperscript{35} silylenol-ethers,\textsuperscript{36} olefins,\textsuperscript{37} polyaromatics,\textsuperscript{38} alkynes\textsuperscript{39} and ketones.\textsuperscript{40-42} More recently, asymmetric hydrogenation reactions have also been developed for different polar substrates.\textsuperscript{43-49}

For many years, the most widely used Lewis acid in FLP chemistry was the electrophilic borane B(C\textsubscript{6}F\textsubscript{5})\textsubscript{3}; however, there have been several research groups who have broadened the scope of Lewis acids beyond simple boranes.\textsuperscript{50} In this regard, other Group 13 Lewis acids including borenium cations have been shown to affect H\textsubscript{2} activation and hydrogenation catalysis.\textsuperscript{51-54} Moving to Group 14, electrophilic carbon-based Lewis acids have also been used in FLP chemistry to catalyze transfer hydrogenation and hydrosilylation reactions of aldimines.\textsuperscript{55} Similarly, H\textsubscript{2} activation with FLPs is not limited to the use of phosphine Lewis bases; other examples of Lewis bases include NHCs,\textsuperscript{56, 57} and pyridine,\textsuperscript{58, 59} acridine and quinoline derivatives.\textsuperscript{60}

In addition to applications in catalysis, FLPs have been used as acid-base pairs to capture a range of small molecules. For example, FLPs have also been shown to react with N-sulfinyltolylamines (p-tol)NSO and act as a SO-transfer reagent to other molecules,\textsuperscript{61} to capture SO\textsubscript{2}, N\textsubscript{2}O, NO, CO,\textsuperscript{62} and to facilitate CO reduction.\textsuperscript{63, 64} Given the growing global warming and climate change concerns, developing efficient methods for CO\textsubscript{2} capture and usage is at the forefront of modern chemical research. To this end, perhaps one of the most impactful applications of FLP chemistry beyond hydrogenation catalysis is their reactivity with CO\textsubscript{2}. In this regard, the ability of FLPs to capture CO\textsubscript{2}\textsuperscript{62, 65} and effect hydroboration\textsuperscript{66, 67} and reduction to methanol\textsuperscript{68} highlights the potential of these systems to have a significant long-term global impact.

The reactivity of FLPs towards organic molecules has expanded the scope of C-H activation reactions beyond traditional metal catalysts. In a major advance, Fontaine and coworkers used the intramolecular FLP 1-tetramethylpiperidine-2-BH\textsubscript{2}-C\textsubscript{6}H\textsubscript{4} to catalyze the borylation of different heterocycles \textit{via} C-H activation.\textsuperscript{69} Radical-based systems and single-electron transfer have also been exploited in C-H,\textsuperscript{70} Sn-H and other small molecule activation reactions.\textsuperscript{71, 72} In addition to
main group FLPs, transition-metal based FLP systems have also been used to capture small molecules, and in some cases, demonstrate behavior analogous to main group donor/acceptor combinations.\textsuperscript{50} Moreover, some research groups have begun to create analogies between hydrogenase enzymes and FLPs, wherein mechanisms of catalysis mimic those reported for FLPs.\textsuperscript{73, 74} More recently, FLPs have also been exploited in polymers and materials chemistry to prepare lactone-derived polymers,\textsuperscript{75} cyanamide oligomers\textsuperscript{76} and acrylate and vinyl polymers.\textsuperscript{77} Moreover, CO\textsubscript{2} reduction on indium oxide nanocrystals is also believed to proceed through an FLP-type mechanism with Lewis basic hydroxide and Lewis acidic indium sites.\textsuperscript{78} Similarly, CeO\textsubscript{2} has recently been shown to activate CO\textsubscript{2} to generate cyclic carbonates via a solid-state FLP-type mechanism.\textsuperscript{79}

Overall, the development of FLP chemistry has showcased the potential for main group chemists to have a lasting impact on the world. Through reduced catalyst and production purification costs, lower toxicity and distinct functional group tolerances, main group-based FLPs can be part of the solution to reduce our reliance upon metal-based systems and subsequently, our environmental footprint.

1.4 Main Group Lewis Acids

The utilization of Lewis acids is one of the most versatile ways to facilitate catalysis, and many industrially-relevant reactions rely upon the use of Lewis acid catalysts. While the most common Lewis acids employed in catalysis are based on metals, such as lithium, boron, zinc, aluminum, magnesium and titanium, efforts to develop more sustainable and “green” alternatives remains at the forefront of chemical research.\textsuperscript{80}

1.4.1 Group 13 Lewis Acids

Group 13 compounds have been known for their electron-deficient properties long before the inception of FLPs in 2006. In their neutral state, compounds with Group 13 centres have 6 bonding electrons and an empty p-orbital, which make them an ideal platform for reactivity with electron donors. Unfortunately, upon their inception, boron trihalides proved to be too hydrolytically sensitive, and thus, led to the development of more sterically-bulky boranes, namely perfluoroalkyl and perfluoroaryl boranes.\textsuperscript{81, 82} Although the synthesis of B(C\textsubscript{6}F\textsubscript{5})\textsubscript{3} was first reported in the early 1960’s,\textsuperscript{83} the remarkable properties and reactivity of this electrophilic borane were not exploited
until much later\textsuperscript{84} when the electron-withdrawing character of the C\textsubscript{6}F\textsubscript{5} substituents was used to synthesize an iminoborane\textsuperscript{85} and pentafluorophenyl-xenon compounds.\textsuperscript{86, 87} After these findings but preceding the development of FLPs, Lewis acidic boranes found applications in hydroboration\textsuperscript{88} and olefin polymerization reactions.\textsuperscript{89} B(C\textsubscript{6}F\textsubscript{5})\textsubscript{3} was also shown to be an efficient Lewis acid catalyst for a wide variety of organic transformations, namely H-H and Si-H activation.\textsuperscript{90}

While aluminum Lewis acids are less prevalent in the FLP literature, the applications of aluminum Lewis acids are widespread in organic catalysis. Perhaps the most notable uses of aluminum Lewis acids include methylaluminoxane (MAO) as a co-catalyst for Ziegler-Natta olefin polymerization reactions,\textsuperscript{91} and AlCl\textsubscript{3} as a catalyst for Friedel-Crafts alkylation\textsuperscript{92} and Diels-Alder reactions.\textsuperscript{93} AlCl\textsubscript{3} and EtAlCl\textsubscript{2} have also been used as hydroxysilylation catalysts with alkyne\textsuperscript{94} and allene substrates.\textsuperscript{94} Moreover, the Lewis acidic cationic aluminum species [Et\textsubscript{2}Al]\textsuperscript{+} has been shown to be a potent catalyst for the electrophilic ethenation of benzene, polymerization of cyclohexene oxide, the oligomerization of ethene\textsuperscript{95} and the deoxygenation reduction of CO\textsubscript{2}.\textsuperscript{96} Roesky \textit{et al.} have also reported a well-defined aluminum dihydride that behaves like a transition metal catalyst in hydroboration and dehydrocoupling reactions (Figure 1-1).\textsuperscript{97, 98}

Moving down the group, the B(C\textsubscript{6}F\textsubscript{5})\textsubscript{3}-analogue with gallium – Ga(C\textsubscript{6}F\textsubscript{5})\textsubscript{3} – has been prepared\textsuperscript{99} and was shown to catalyze the hydrogenation of an imine with H\textsubscript{2} in the presence of a phosphine Lewis base.\textsuperscript{100} Less Lewis acidic Ga species have also been used in FLP chemistry to capture CS\textsubscript{2} and to facilitate H\textsubscript{2} transfer from ammonia-borane to an imine (Figure 1-1).\textsuperscript{101} Moreover, Prakash \textit{et al.} have studied the use of Ga(OTf)\textsubscript{3} as a robust and efficient catalyst for Friedel-Crafts alkylation, hydroxyalkylation and acylation reactions.\textsuperscript{102} While less prevalent in the literature, there are some examples of indium Lewis acids. In one rare example, In(C\textsubscript{6}F\textsubscript{5})\textsubscript{3} was shown to

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{Figure1.png}
\caption{Examples of Group 13 Lewis acids.}
\end{figure}
reversibly split H₂, in conjunction with phosphine donors. In a different vein, the Gabbaï group has reported examples of supramolecular bifunctional indium Lewis acids for molecular recognition and coordination polymer synthesis. Indium oxide surfaces have also been used to reduce CO₂, presumably via a FLP-type mechanism. As well, our group published an indium-silylamide FLP, In(N(SiMe₃)₂Cl₂)(THF)ₙ, capable of catalyzing the conversion of aryl and alkylsilylimines to their corresponding ureas under CO₂.

1.4.2 Group 14 Lewis Acids

Initially thought to be too unstable to isolate or utilize, the field of carbocation chemistry rapidly began to develop after Olah’s observation of the first long-lived alkyl cation salt, tert-butyl hexafluoroantimonate in 1962. In an early example of carbocations in catalysis, Mukaiyama et al. reported the use of trityl perchlorate as an activator for glycosylation reactions, and as a catalyst for aldol-type reactions. However, after these initial reports, researchers published experimental and computational data which challenged the role of the carbocation in the catalytic cycle. After much debate, a seminal report was published in 2014 by Bah and Franzen which demonstrated the catalytic abilities of carbocations in the Diels-Alder reaction. In addition to their use in FLP reduction chemistry, air-stable carbocations have been used as catalysts for the hydrothiolation of alkenes.

Unlike carbocation chemistry, the analogous silicon chemistry sparked years of fierce debate over the nature of the “free” trisubstituted silylium ion. The larger atomic radius of silicon prevents effective overlap to carbon atoms, resulting in longer and weaker C-Si bonds compared to C-C bonds. As well, while carbenium ions are stabilized by conjugation and hyperconjugation, the three-coordinate silicon atom instead prefers to bind even weak nucleophiles, such as solvent molecules, arenes and counteranions. In this regard, while Lambert, Reed and coworkers published the synthesis of trialkylsilylium cations bound to solvent or anions, respectively, it wasn’t until 2002 that evidence of a free silylium ion was reported. Nonetheless, the “free” nature of the silylium cation was deemed to not be a requirement for catalysis and [Et₃Si(tol)][B(C₆F₅)₄] was shown to be an active Lewis acid catalyst for a wide variety of organic transformations, such as the hydrodefluorination of fluoroalkanes, reduction of amines, and Mukaiyama-Aldol and Diels-Alder reactions. In addition to solvent
stabilized-silylium catalysts, different Lewis acid reactivity has been achieved with mesityl-\textsuperscript{129}, naphthyl\textsuperscript{130} and ferrocenyl-stabilized\textsuperscript{131,132} silylium cations (Figure 1-2).

![Silylium Cation Structures](image)

**Figure 1-2.** Examples of intramolecularly-stabilized silylium cations.

1.4.3 Group 15 Lewis Acids

Pnictogen compounds can behave as both two-electron donors and two-electron acceptors\textsuperscript{133}. Given the greater electronegativity of Group 15 species, the electron-donating properties of pnictine derivatives have largely dominated the literature as prototypical ligands in the coordination chemistry of transition metals. However, despite the available lone pair of electrons, there are several examples of Group 15 Lewis acids in the literature. Unlike traditional Group 13 or Group 14 Lewis acids which derive their Lewis acidity from an empty p-orbital or a vacant coordination site, Group 15 species rely upon the energy and accessibility of a π* or a σ* anti-bonding orbital.

While earlier reports have demonstrated N-centered electrophilic behavior\textsuperscript{134-136}, it wasn’t until 2017 that the first example of a donor-acceptor interaction of a stable N-based nitrenium Lewis acids was reported (Figure 1-3).\textsuperscript{137} Shortly thereafter, our group reported cyclic (alkyl)(amino)nitrenium\textsuperscript{138} and cyclic (amino)(aryl)nitrenium\textsuperscript{139} cations which formed stable adducts with neutral Lewis bases. Simple nitrogen Lewis acids derived from diazonium cations have also been reported and form adducts with a series of Lewis bases (Figure 1-3).\textsuperscript{140}
Counterions have been omitted for clarity.

While examples of arsenic Lewis acids are rare, antimony(V) compounds are well represented in the literature as electron acceptors. In this regard, antimony fluorides have long been known as reactive “superacids” capable of protonating robust hydrocarbons.142,143 The size, electropositivity and atomic orbital polarizability of antimony results in Lewis acidic compounds with high fluoride affinities. For instance, early experimental work showed that the fluoride ion affinity (FIA) of SbF$_5$ was about 50% greater than BF$_3$ (ca. 150 kJ/mol).145 This FIA has been exploited by the Gabbai group over the last decade, wherein intramolecular stibonium-borane cation [o-(Ph$_2$MeSb)(Mes$_2$B)C$_6$H$_4$]$^+$ (Figure 1-3)146, a palladium147 or platinum148 complex with a pendant antimony ligand, a 9-anthryltriphenylstibonium cation149 and a neutral organoantimony(V) compound150 have all been used to complex fluoride ions at the Sb centre. More recently, highly electrophilic stibonium(V) salt [(C$_6$F$_5$)$_4$Sb][B(C$_6$F$_5$)$_4$] was synthesized and this robust Lewis acid was shown to polymerize THF and catalyze the hydrodefluorination of fluoroalkanes.151

The acceptor properties of the pnictogens has also been expanded to Bi.152 It is noteworthy that while bismuth Lewis acids are less stable in water, combinations of bismuth Lewis acids and basic ligands have been used in asymmetric catalysis in aqueous media.153

1.5 Phosphorus as a Lewis Acid

1.5.1 History of Phosphorus

About 50 years after Brand’s accidental discovery of phosphorus in 1669, Professor Johann Thomas Hensing showed that phosphorus was also present in the human brain. Shortly thereafter, early medicines containing elemental phosphorus were sold, but it wasn’t until decades later that researchers discovered minerals contained phosphorus.154
Phosphorus is an essential mineral that is required for healthy cellular function. In the human body, phosphorus is a major structural component of bone and cell membranes, and is essential to energy production in the form of adenosine triphosphate (ATP). Phosphorus plays a key role in the structural stability of nucleic acids, DNA and RNA, as the backbone of these structures contain two phosphate groups per pair of nucleic bases. As well, several enzymes, hormones and signaling pathways depend on the phosphorylation reaction. Phosphorus found in phosphates represents one of the most important buffer systems, helping to regulate the body’s pH. In biological systems, phosphorus is found as $[\text{PO}_4]^{3-}$, and approximately 85% of the body’s phosphorus is found in bones and teeth.

The primary use of phosphorus in industry is the manufacturing of fertilizers. Other applications include baking powder, flame retardants, and light emitting diodes. Phosphates are also ingredients in some detergents; however, the detection of high phosphate levels in natural water supplies has led to a reduction of phosphorus concentrations in some countries due to the detrimental effects of eutrophication. In the chemical sciences, organophosphorus compounds have become ubiquitous ligands in organometallic chemistry. Organophosphorus compounds can have an oxidation state ranging from -3 to +5 at the phosphorus centre, which offers a diverse platform for chemical reactivity. While phosphine ligands are traditionally known for their strong $\sigma$-donor and weak $\pi$-acceptor properties, trends exploring the umpolung in reactivity are surfacing. In addition to the oxidation state, the steric environment around the phosphorus centre of tricoordinate phosphines can be tuned and subsequently described using the Tolman cone angle.

The versatility and tunability of organophosphorus compounds has led to the widespread use of phosphines in coordination complexes as Lewis bases, and more recently, as metal-free entities in homogenous catalysis as Lewis bases and acids.

### 1.5.2 Phosphorus Lewis Acids

While the use of phosphorus compounds as electron acceptors was not fully understood nor exploited until the 21st century, the Lewis acidic nature of these P(III) and P(V)-based species was present in the early literature. One of the first examples of Lewis acidic phosphorus compounds was reported by Dimroth and Hoffmann in 1964, wherein a divalent phosphienenium cation was synthesized. Trigonal planar phosphorus cations have also attracted considerable attention. In 1989, Burford and coworkers synthesized dithia- and diselena-diphosphete dications. In a
similar vein, several examples of oxophosphonium cations have been synthesized and shown to form stable adducts with Lewis basic donors.\textsuperscript{165,166}

One decade later, Burford \textit{et al.} reported an unprecedented “\textit{coordination chemistry umpolung}” between a gallane Lewis base and phosphorus(III) Lewis acid,\textsuperscript{167} and after this report, the development of N-heterocyclic phosphonium (NHP) cations dominated the literature.\textsuperscript{168} Ragogna and coworkers reported the formation of an adduct between a unique bifunctional Lewis acidic NHP cation and $N,N$-dimethylaminopyridine (DMAP).\textsuperscript{169} It was later shown that some phosphenium cations are substantially more Lewis acidic than the main group Lewis acids BF$_3$, BCl$_3$, AlCl$_3$, SbF$_5$.\textsuperscript{170} In one seminal report, Kinjo and coworkers exploited the electrophilicity of NHPs for the catalytic $N$-formylation of amine derivatives with CO$_2$ with a 1,3,2-diaza phospholene pre-catalyst.\textsuperscript{171} The same pre-catalyst was also shown to affect catalytic hydroboration of aliphatic and aromatic aldehydes and ketones,\textsuperscript{172} and transfer hydrogenation of N=N double bonds with ammonia-borane.\textsuperscript{173} Similarly, regio- and chemoselective hydroboration of pyridines was achieved with a NHP triflate salt.\textsuperscript{174} It is noteworthy that Speed and coworkers reported a related hydroboration reaction with an \textit{in situ} generated NHP cation.\textsuperscript{175}

More recently, in 2012, Radosevich \textit{et al.} reported the first redox P(III)/P(V) catalytic cycle to affect the reduction of azobenzene.\textsuperscript{176} This strategy (\textit{i.e.} 2-electron redox cycling) was recently expanded and now includes phosphacycles capable of catalytic intermolecular reductive C-N cross coupling of nitroarenes and boronic acids,\textsuperscript{177} C(sp$^2$)-H amination,\textsuperscript{178} and deoxygenative N-N bond forming heterocyclization\textsuperscript{179} and O-atom transfer.\textsuperscript{180} As well, the Radosevich group has exploited the use of geometrically-constrained electrophilic tricoordinate phosphorus compounds in hydroboration catalysis,\textsuperscript{181} and E-H oxidative addition reactions.\textsuperscript{182}

Another strategy used to employ Lewis acidity at phosphorus(III) has been the inclusion of additional positive charges in the molecule. To this end, Burford \textit{et al.} have studied the properties and reactivity of P(III) acceptors, wherein bipyridine-stabilized phosphorus polycations were shown to activate strong E-H (E = H, C, P) bonds (Figure 1-4).\textsuperscript{141} In a related sense, two-coordinate phosphorus(III)-based dicationic salts were shown to activate E-H bonds (E = B, Si, C).\textsuperscript{183,184} More recently, our group developed P(III) dications featuring bipyridine or terpyridine ligands which were shown to effect the hydrodefluorination of primary, secondary and tertiary alkyl C-F
bonds (Figure 1-4). The reactivity of these species was later expanded to C-C bond formation strategies via the allylation of C-F bonds.

![Chemical structures](image)

**Figure 1-4.** Examples of P(III) Lewis acidic cations (ArCl = 3,5-Cl2-C6H3).

Unlike P(III) compounds, P(V) species are more easily recognized as Lewis acids. Perhaps the most notable example is the Wittig reagent, wherein the electrophilic P(V) nature of these ylide reagents has been exploited for the conversion of aldehydes and ketones to alkenes. In a similar vein, pentacoordinate phosphoranes with electron-withdrawing substituents were recognized to be Lewis acids in the 1960s. The Lewis acidity of these species is believed to be derived from the low-lying σ* orbital oriented opposite the polar P-EWG (EWG = electron-withdrawing group) bond. Indeed, these types of compounds have been shown to form a variety of Lewis acid/base adducts and six-coordinate species derived from bi- and tridentate ligands.

In an early example, Cavell et al. reported the insertion of CO2 into a pentacoordinate amidophosphorane CH3(CF3)3PN(CH3)2 (Scheme 1-4, top). Later, Schmutzler et al. treated PF5 with a N-trimethylsilylimidazole base and observed the formation of a Lewis acid-base adduct (Scheme 1-4, middle). Interestingly, almost two decades later, our group reported a related CO2 sequestration reaction with a ring-strained amidofluorophosphorane (Scheme 1-4, bottom). In all cases, the P(V) centre behaved as the Lewis acidic site, either binding Lewis basic N or O atoms.
The Lewis acidity of phosphorus(V) species was later enhanced by the formation of phosphonium cations, wherein the tetracoordinate configuration around phosphorus is believed to produce a more accessible and lower-energy LUMO. One of the most promising advances in this area was realized in 2006 when Terada and coworkers reported the first Diels-Alder reaction catalyzed by a phosphonium salt. In fact, this is the first publication where a tetracoordinate phosphorous species is explicitly proposed as catalyst (Figure 1-5). In this report, electron-deficient aryloxyphosphonium cations were shown to be active Lewis acid catalysts for the Diels-Alder reaction. The key to successful catalysis was believed to be the donor-acceptor interaction between the Lewis base and the σ* P-EWG anti-bonding orbital of the P(V) centre.

Since this initial report, phosphonium salts have been used to catalyze a wide variety of organic reactions. Some of the first examples include the addition to polar unsaturates and the cyanosilylation of aldehydes and ketones, and C-C, C-O and C-N bond forming reactions.
Quaternary phosphonium salts derive considerable Lewis acidic character from their capacity to accept electron density into their (P-X) antibonding orbitals. Therefore, in the case where the X-groups are strongly electron-withdrawing, the hypervalent bond formed by reaction between the phosphonium salt and the substrate is stabilized, resulting in enhanced Lewis acidic at phosphorus (Scheme 1-5).\textsuperscript{196}

![Scheme 1-5. Activation of a basic substrate by coordination to phosphorus.]

This hypothesis was supported experimentally in 2013, wherein Stephan \textit{et al.} synthesized the highly electrophilic cation (EPC) salt [(C\textsubscript{6}F\textsubscript{5})\textsubscript{3}PF][B(C\textsubscript{6}F\textsubscript{5})\textsubscript{4}] which was shown to effect the hydrodefluorination of fluoroalkanes in the presence of Et\textsubscript{3}SiH.\textsuperscript{197} This was the first example of C-F bond activation with a phosphonium salt, and highlights the need for strongly electron-withdrawing groups around phosphorus. Remarkably, this EPC was shown to be a viable Lewis acid catalyst for a variety of organic transformations.\textsuperscript{198} However, [(C\textsubscript{6}F\textsubscript{5})\textsubscript{3}PF][B(C\textsubscript{6}F\textsubscript{5})\textsubscript{4}] demonstrated limited stability in the presence of external Lewis bases, which limits applications in FLP chemistry. Since this seminal report, our group has developed several derivatives of EPCs with the goal of increasing stability and tunability. Some efforts included: P-X bonds to less electronegative elements (X = Cl, Br, OAr)\textsuperscript{199,200} or aryl substituents,\textsuperscript{201,202} inclusion of additional positive charges with cationic substituents\textsuperscript{203,204} or pendant phosphonium centres.\textsuperscript{205-207} In most cases, decreasing the electronegativity of substituents increases the robustness of the catalysts, but diminishes the reactivity. While advances have been made towards active catalysts, more work must be done to develop the optimal system – one capable of catalyzing a desired reaction without the need for strict air- and moisture-free reaction conditions – for applications beyond the research laboratory.

Overall, the early literature indicated the Lewis acidity of P(III) and P(V) species in coordination chemistry. While several older studies have exploited this Lewis acidity for small molecule capture, it has been more recent developments that have focused attention on the potential of P-based Lewis acids in catalysis and FLP chemistry. To date, the literature contains examples of
P(III) and P(V) mono-, di- and tricationic species which have demonstrated Lewis acidic properties. These examples highlight this area as an emerging trend in the larger efforts to further develop metal-free catalysis. It is also clear that P-based Lewis acid catalysis is still in its infancy; there is no doubt that this field will continue to rapidly develop and remain a fertile area for development for many years to come.

1.6 Scope of thesis

The objective of this graduate work was to synthesize more robust, yet reactive Lewis acid catalysts based upon phosphorus for applications in Lewis acid catalysis and FLP chemistry. The goal was to build upon previous work completed by Dr. Chris Caputo and further modulate the structure of electrophilic phosphonium cations to improve the stability, selectivity and reactivity of these P-based Lewis acids.

To this end, Chapter 2 focuses on the development of a family of Lewis acid phosphorus(V) cationic species with a fluoro pyridiniumphosphonium framework. This framework was chosen due to its availability, ease of handling and versatility, with inspiration from previous work completed by post-doctoral fellow Dr. Michael Holthausen. To this end, we report the synthesis of a range of mono- and dicationic phosphorus cations with different counterions. In most cases, oxidation with XeF$_2$ and subsequent fluoride abstraction afforded the desired fluorophosphonium species. While FLP chemistry of the monocations was limited, the Lewis acidity of these phosphorus(V) salts was probed computationally and experimentally. When weakly coordinating anions such as [B(C$_6$F$_5$)$_4$]$^-$ were incorporated into the molecule, fluoro pyridiniumphosphonium salts were shown to be active Lewis acid catalysts for the Friedel-Crafts dimerization of 1,1-diphenylethylene, the hydrodefluorination of 1-fluoropentane, the hydrosilylation of $\alpha$-methylstyrene, the dehydrocoupling of phenol and Et$_3$SiH and the hydrodeoxygenation of benzophenone. The experimental work completed in this chapter was done exclusively by this author with insightful discussions with post-doctoral fellow Dr. Michael Holthausen. The computations in this chapter were completed by fellow graduate student James LaFortune.

The work presented in Chapter 3 builds upon Chapter 2, with the goal of developing more robust phosphonium(V) cations. In this chapter, we synthesize air-stable phosphonium salts with cyclopropenium and pyridinium scaffolds, wherein Lewis acidity is derived from the inclusion of a second positive charge rather than strongly electron-withdrawing groups such as fluoride. In the
first part of the chapter, we probe the relative Lewis acidities of these compounds experimentally and computationally. In this regard, we report the use of these robust phosphonium salts as initiators for a Mukaiyama-aldol condensation reaction. In the latter half of the chapter, we report the synthesis of a phenoxy-substituted phosphonium dication, which was shown to be a robust and active Lewis acid catalyst. As well, the phenoxyphosphonium dication was shown to be an active catalyst for the double hydroarylation of alkynes and arylamines, and the substrate scope and mechanism is reported herein. The work completed in the first half of the chapter was done in collaboration with graduate student Alejandro G. Barrado and Prof. Manuel Alcarazo, wherein Mr. Barrado completed the syntheses and reactivity studies with the cyclopropenium-substituted phosphonium salts. For the latter half, the catalytic reactions, mechanistic investigation and substrate scope were completed by fellow graduate student James LaFortune. All computational investigations throughout this chapter were completed by post-doctoral fellow Dr. Timothy Johnstone.

The work presented in Chapter 4 continues to address shortcomings of previous systems reported in this thesis and in the literature pertaining to air- and moisture-stability. In this chapter we target polyphosphorus cations as a strategy to obtain robust yet sufficiently Lewis acidic species. The compounds synthesized in this chapter are based on well-known triphos ligands, and conversion to the corresponding Lewis acids has been achieved through simple methylation reactions. The reported P$_3$-trimethylated tricationic species were shown to be active Lewis acid catalysts for a series of organic reactions, despite the lack of strongly electron-withdrawing groups. The remarkable air- and moisture-stability of these compounds was exploited in reductive amination reactions. In this case, the C$_3$-symmetric variant was chosen as the active catalyst and different aldehydes and anilines were successfully converted to their condensation product. As well, the P$_3$-trimethylated tricationic species were shown to effect C-F bond activation, and preliminary results are reported at the end of this chapter. The reductive amination work in this chapter was completed in collaboration with recent graduate Dr. Valerio Fasano and fellow graduate student Kevin Szkop. The C-F chemistry reported in the latter half of the chapter was completed in collaboration with fellow graduate student Kevin Szkop and undergraduate volunteer Piers St-Onge. Calculations were completed by post-doctoral fellow Dr. John De Backere. Work in this area is ongoing.

Chapter 5 explores the synthesis of a 1,2-diphosphonium dication and its reactivity in FLP chemistry. The Lewis acidic nature of this compound was probed computationally and
experimentally. Interestingly, the 1,2-diphosphonium dication was shown to be more hydridophilic than strong silylium cations and electrophilic boranes. In this regard, the FLP combination of the 1,2-diphosphonium dication and PrBu₃ or PPh₃ Lewis bases were used to affect E-H (E = Si, B, C, H) bond activations. Similarly, 1-diphenylphosphino-8-N,N-dimethylamino naphthalene was synthesized and preliminary oxidation reactions are reported. The experimental work completed in the early part of this chapter was done in collaboration with post-doctoral fellow Dr. Michael Holthausen and Dr. Ian Mallov, whereas the computational investigation was completed by Dr. Roman Dobrovetsky. The remaining experimental work completed in this chapter was completed by the author, with insightful discussions with and guidance from Dr. Michael Holthausen.

*Portions of each chapter have been published, as stated below:*


1.7 References


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Chapter 2
Pyridiniumphosphonium Dications as Highly Electrophilic Lewis Acids

2.1 Introduction

Metal-free catalysis is an emerging alternative to conventional transition metal catalyst technologies. Among the various metal-free strategies, catalysts based on main-group species have garnered significant attention in the past decade. Indeed, many research groups have studied electrophilic phosphorus compounds and their applications in stoichiometric and catalytic reactions. For instance, dicoordinate P(III) phosphonium cations have been shown to activate C-C, C-H, and P-P bonds, and form Lewis acid-base adducts with nucleophilic amidines and 4-N,N-dimethylaminopyridine. Similarly, PF₅ phosphoranes have formed Lewis acid-base adducts with bases such as N-trimethylsilyl imidazole and pyrazole derivatives. Moreover, the synergistic use of tetracoordinate P(V) phosphonium salts and B-Lewis acid have been used to capture fluoride ions in sensor applications, and to facilitate addition to polar unsaturates.

2.1.1 Phosphorus(V) Lewis Acidic Dications

While the initial report of C-F bond activation by electrophilic phosphonium cation (EPC) [(C₆F₅)₃PF][B(C₆F₅)₄] spearheaded the development of phosphorus(V) Lewis acid catalysis, the need for strongly electron-withdrawing groups (e.g. C₆F₅) limited potential structural variations at the time. In this regard, our group targeted the new fluorophosphonium dication [(SIMes)PFPh₂][B(C₆F₅)₄]₂, which is highly electrophilic as a result of the increased formal charge. This dication proved to be more soluble in polar organic solvents and more Lewis acidic than [(C₆F₅)₃PF][B(C₆F₅)₄], and was shown to be an active Lewis acid catalyst for a range of organic transformations, including C-F bond activation. Since this report, several dicationic phosphorus(V) species have been synthesized and their Lewis acidity has been probed computationally and experimentally (Figure 2-1).
2.1.2 Lewis Acid-Catalyzed Reactions

The Lewis acidity of \([\text{B(C}_6\text{F}_5\text{)}_3\text{PF}][\text{B(C}_6\text{F}_5\text{)}_4]\) and the dicationic phosphorus(V) species shown in Figure 2-1 has been suggested to originate from the low-lying σ* anti-bonding orbital opposite the polar P-X bond. This inherent reactivity has been exploited in the Friedel-Crafts dimerization of 1,1-diphenylethylene, hydrodefluorination of fluoroalkanes, \(^{10,12,13}\) hydrosilylation of olefins, \(^{17}\) ketones, imines and nitriles, \(^{18}\) isomerization of 1-hexene, \(^{17}\) polymerization of isobutylene \(^{19}\) and THF, \(^{12}\) dehydrocoupling of alcohols and silanes, \(^{16}\) hydrodeoxygenation of ketones, \(^{20}\) as well as the direct hydrogenation of olefins. \(^{21}\) To provide sufficient background for this chapter, only those reactions which are mentioned in section 2.2.4.3 will be discussed below.

2.1.2.1 Friedel-Crafts Dimerization of 1,1-Diphenylethylene

The Friedel-Crafts type dimerization of 1,1-diphenylethylene has been probed with several EPC catalysts. \(^{22}\) While the reaction was initially shown to be catalyzed by the strong Lewis acid \(\text{B(C}_6\text{F}_5\text{)}_3\), \(^{23}\) it was later demonstrated that highly electrophilic phosphorous(V) salts are also active catalysts for this transformation. In all cases, using catalytic amounts of the desired Lewis acid resulted in the formation of the cyclodimerized 1-methyl-1,3,3-triphenyl-2,3-dihydro-1H-indene product.

2.1.2.2 Hydrodefluorination of Fluoroalkanes

The first C-F bond activation by a phosphorus(V) cationic species was demonstrated in 2013, when \([\text{B(C}_6\text{F}_5\text{)}_3\text{PF}][\text{B(C}_6\text{F}_5\text{)}_4]\) was shown to effect the hydrodefluorination of fluoroalkanes in the
presence of Et₃SiH. In this case, C(sp³)-F bonds were selectively reduced to C-H bonds through a proposed reaction pathway involving fluoride abstraction by the P(V) centre, followed by hydride delivery from the hydridosilane to the transient carbocation, affording the corresponding alkane and a transient silylium ion (Scheme 2-1). Subsequent abstraction of fluoride from difluorophosphorane intermediate by the transient silylium led to regeneration of the catalyst. This proposed mechanism is similar to that proposed by Ozerov for silylium-mediated C-F bond reduction, in that fluoride abstraction is followed by hydride delivery quenching the transient carbocation24, 25. In either case, the net transformation can be viewed as a Si-H/C-F σ-bond metathesis. The scope of phosphorus(V)-mediated C-F bond activation will be fully described in Chapter 4.

Scheme 2-1. Proposed hydrodefluorination mechanism by a Lewis acidic P(V) species.

[B(C₆F₅)₄]⁻ counterion has been omitted for clarity.

2.1.2.3 Hydrosilylation of Olefins and Carbonyls

Shortly thereafter, [(C₆F₅)₃PF][B(C₆F₅)₄] was shown to be an effective catalyst for the hydrosilylation of olefins and alkynes. A mechanistic study was conducted, and computational data supported the initial activation of the Si-H bond by the cationic P(V) centre, which generates a transient hypervalent silane species upon addition of olefin. Anti-1,2 addition of Si-H across the olefin then regenerates the active catalyst and releases the hydrosilylated product. A similar mechanism was proposed for the hydrosilylation of imines26 and carbonyl27 compounds with B(C₆F₅)₃ as the Lewis acid catalyst.

For the hydrosilylation of ketones, the reaction mechanism may be more complex. In a more recent report, Suesse et al. reported experimental findings that suggest the possibility for alternative
mechanistic pathways. In the first pathway, Si-H activation by the EPC catalyst generates a neutral hydridofluorophosphorane species as the transient hydride source, which delivers hydride to the silylcarboxonium ion to generate the silyl ether product (Scheme 2-2, Path A). Another possibility is that [(C₆F₅)₃PF][B(C₆F₅)₄] is an initiator for this reaction, wherein the neutral hydridofluorophosphorane degrades to give a siloxyphosphonium ion, which then may transfer the silyl group to the carbonyl. Addition of hydrosilane is then believed to deliver hydride to the silylcarboxonium ion, liberating the desired product (Scheme 2-2, Path B). Lastly, it is plausible that the silylcarboxonium generated through the initially proposed mechanism directly reacts with hydrosilanes to give the silyl ether and another donor (Do)-stabilized ion (Scheme 2-2, Path C).

Scheme 2-2. Proposed reaction pathways for the EPC-catalyzed hydrosilylation of ketones. [B(C₆F₅)₄]⁻ counterions have been omitted for clarity.

Based on the reported experimental data, the exact nature of the mechanism cannot be unambiguously determined at this point and competing pathways cannot be confidently excluded.
Moreover, it is important to note that while the mechanism for the EPC-catalyzed hydrosilylation of ketones may not be clearly defined, it is still believed that the first step in the reaction is Si-H bond activation by the EPC.

### 2.1.2.4 Dehydrocoupling of Hydrosilanes with Polar, Protic Substrates

The dehydrocoupling of silanes with anilines, phenols, thiophenols, and benzoic acids catalyzed by EPCs was initially demonstrated with \([(C_6F_5)_3PF][B(C_6F_5)_4]\).\(^{16}\) For this transformation, the mechanism is believed to be analogous to the olefin hydrosilylation reaction mechanism previously reported for EPCs.\(^{17}\) To this end, the initial step presumably involves activation of the Si-H bond by the Lewis acid catalyst, which then facilitates backside attack at the Si atom by the Lewis base \((E = N, O, S)\). Loss of \(H_2\) forms the Si-E dehydrocoupled product and regenerates the catalyst. Interestingly, when the analogous reaction was carried out in the presence of olefin, transfer hydrogenation was obtained.\(^{16}\)

### 2.1.2.5 Hydrodeoxygenation of Ketones

The ability of EPCs to activate silane and affect hydrosilylation reactions was further expanded to include the hydrodeoxygenation of ketones under mild reaction conditions.\(^{20}\) Interestingly, while \(B(C_6F_5)_3\) has previously been shown to effect the hydrosilylation of ketones,\(^{29}\) poor yields of the hydrodeoxygenated product were observed. Two possible mechanisms for this transformation were considered and supported computationally. In both pathways, the first step is proposed to be activation of the Si-H bond with the cationic P(V) centre, which forms a hypervalent silane species. While not supported directly with experimental evidence, a similar interaction has been proposed for the hydrosilylation of alkenes, alkynes, imines and nitriles\(^{17, 18}\) and for the \(B(C_6F_5)_3\)-mediated hydrosilylation of carbonyl compounds.\(^{27, 29-33}\) In one of the two proposed pathways, addition of \(Et_3SiH\) forms a transient hydridofluorophosphorane intermediate and subsequent introduction of the ketone generates a silylcarboxonium ion (Scheme 2-3). Addition of a second equivalent of \(Et_3SiH\) is then believed to facilitate Si-H addition across the silyl ether. Presumably, hydride delivery from the hydridofluorophosphorane intermediate then releases the deoxygenated product and the \((SiEt_3)_2O\) side product, subsequently regenerating the active catalyst. In the second proposed pathway, the hypervalent silane species reacts with silylated ketone to generate a bis-siloxy-carboxonium ion. Hydride delivery from the hydridofluorophosphorane intermediate would then eliminate \((Et_3Si)_2O\) and the deoxygenated product to regenerate the active catalyst.
Computations suggest that the latter pathway is energetically favorable; however, variations in the catalyst, substrate, and silane could reverse the energetic preference and thus alter the operative reaction mechanism.\textsuperscript{20, 34}

\textbf{Scheme 2-3.} Proposed hydrodeoxygenation mechanism for acetophenone with $[(C_6F_5)_3PF][B(C_6F_5)_4]$. [B(C\textsubscript{6}F\textsubscript{5})\textsubscript{4}] counterion has been omitted for clarity.

\section*{2.1.3 Pyridinium-based Phosphorus Scaffolds}

Recently, polycationic phosphorus compounds have been achieved with polyphosphate precursors\textsuperscript{13-15} or through the introduction of an imidazolium substituent with a delocalized cationic charge bound to a phosphonium centre.\textsuperscript{12} In both situations, Lewis acidity comparable or greater than that reported for $[(C_6F_5)_3PF][B(C_6F_5)_4]$ was observed, validating the effectiveness of these strategies for imparting Lewis acidic P(V) centres. However, challenges regarding stability and syntheses still limits further applications of these systems in catalysis and FLP chemistry.

Building on the previous work from our group and evidence supporting enhanced Lewis acidity upon increasing formal charge, we sought to create a family of phosphorus(V) salts with a versatile (i.e. multiple functionalities) and easily accessible pyridinium-based scaffold. In part, this project was also inspired by work done by Tinnermann \textit{et al}., wherein they demonstrated that N-alkyl pyridiniophosphines are weak $\sigma$-donors and strong $\pi$-acceptors.\textsuperscript{35} When bound to transition metals, these phosphines enhanced the Lewis acidity of the metal centre. Moreover, in addition to a $\pi$-
deficient pyridinium ring, the pyridine precursor would provide another unique framework for possible intramolecular FLP chemistry with a P/B Lewis acid/base pair.

In this regard, we envisioned a versatile framework wherein P(V) monocations afford intramolecular FLP reactivity and conversion to their corresponding dications leads to EPCs that are more robust and more reactive than previously reported fluorophosphonium mono- and dications.10,12

2.2 Results and Discussion

2.2.1 Synthesis of Pyridiniumphosphonium Monocations

Reaction of 2-pyridyldiphenylphosphine with CH₃I yielded only one product with a new resonance in the ³¹P{¹H} NMR spectrum at δ 17.4 ppm. The product was isolated in 96% yield and was identified as the P-methylated product [(o-C₆H₄N)Ph₂P(CH₃)]⁺I⁻ by NMR spectroscopy and elemental analysis (Scheme 2-4, left).36 The ¹H NMR spectrum (CD₂Cl₂) reveals a diagnostic doublet resonance at δ 2.98 ppm (d, ²JₚH = 14 Hz) corresponding to the P-bound methylene protons. As well, the carbon atom resonance for the P-bound methylene group can be seen in the ¹³C{¹H} NMR spectrum at δ 10.0 ppm (d, ¹JₚC = 58 Hz). The NMR spectra align with related monocationic salt [Ph₃PMe⁺][I⁻], with slight upfield shifts observed for 2-1.37 It is noteworthy that the reaction was carried out with 10 equiv. of CH₃I, yet no evidence of N-methylation was observed, suggesting that alkylation of the P centre occurs initially and subsequently decreases the nucleophilicity of the neighbouring N centre.

When an analogous reaction was conducted with a stoichiometric amount of MeOTf, two singlet resonances were observed in the ³¹P{¹H} NMR spectrum at δ 26.0 and δ –9.0 ppm (3:2 ratio). The resonance at δ –9.0 ppm was attributed to [(o-C₆H₄NCH₃)Ph₂P][OTf]²⁻, as reported by Tinnermann et al.35 The compound with a singlet at δ 26.0 ppm was determined to be [(o-C₆H₄NCH₃)Ph₂P(CH₃)][OTf]₂ 2-3, as reported in Chapter 3 (Scheme 2-4, right). Further attempts to synthesize one compound selectively were unsuccessful.
Oxidation of 2-pyridyldiphenylphosphine with XeF$_2$, resulted in the formation of the corresponding difluorophosphorane ($\alpha$-C$_6$H$_4$N)Ph$_2$F$_2$P 2-4 after stirring the solution (CH$_2$Cl$_2$) for 2 h at ambient temperature. 2-4 was subsequently isolated in high yield (94%) and fully characterized by NMR spectroscopy, mass spectrometry and elemental analysis. The $^{31}$P{$^1$H} NMR spectrum (CD$_2$Cl$_2$) contains a diagnostic triplet resonance at $\delta$ –52.7 ppm ($^1J_{PF} = 670$ Hz), indicative of a pentacoordinate difluorophosphorane.$^{11}$ The $^{19}$F{$^1$H} NMR spectrum shows the corresponding doublet resonance at $\delta$ –36.4 ppm. When mixed with 2-4, TMSOTf or [Et$_3$Si][B(C$_6$F$_5$)$_4$]•(C$_7$H$_8$) facilitated fluoride abstraction, generating the fluorophosphonium cation [(\(\alpha\)-C$_6$H$_4$N)Ph$_2$FP]$^+$ as the respective [OTf]$^-$(2-5) and [B(C$_6$F$_5$)$_4$]$^-$ (2-6) salts. These reactions were accompanied by the formation of Me$_3$SiF and Et$_3$SiF, respectively. The phosphonium salts 2-5 and 2-6 were isolated by filtration after precipitation with n-pentane in 92% and 97% yields, respectively (Scheme 2-5).

**Scheme 2-5.** Synthetic route to fluorophosphonium salts 2-5 and 2-6.

Although fluoride abstraction in the past has typically been favored with [Et$_3$Si][B(C$_6$F$_5$)$_4$]•(C$_7$H$_8$),$^{10,12}$ we also explored TMSOTf in an effort to provide a lower molecular weight compound and introduce a less expensive counterion into these EPCs. Compounds 2-5 and 2-6 were fully characterized by multi-nuclear NMR spectroscopy and elemental analysis. For 2-5, the $^{31}$P{$^1$H} NMR spectrum (CD$_2$Cl$_2$) exhibits a doublet resonance at $\delta$ 80.1 ppm ($^1J_{PF} = 1004$ Hz) with the corresponding doublet in the $^{19}$F{$^1$H} NMR spectrum (CD$_2$Cl$_2$) at $\delta$ –136.8 ppm. The $^{19}$F{$^1$H} resonance for the OTf counterion appears at $\delta$ –79.0 ppm (s), indicative of dissociated
Similarly, for 2-6, the $^{31}$P{$^1$H} NMR spectrum (C$_6$D$_5$Br) displays a doublet at $\delta$ 78.2 ppm ($J_{PF} = 1004$ Hz). In the $^{19}$F{$^1$H} NMR spectrum, the resonance attributed to the P-bound fluoride appears as a doublet at $\delta$ –137.3 ppm, and the resonances corresponding to the [B(C$_6$F$_5$)$_4$]$^-$ anion appear at $\delta$ –133.1, –163.5 and –167.4 ppm. Compared to [Ph$_3$PF][B(C$_6$F$_5$)$_4$], the $^{31}$P{$^1$H} NMR resonance of 2-6 is shifted upfield ($\Delta \delta = 16.6$ ppm) and the $^{19}$F{$^1$H} NMR P-F resonance is shifted downfield ($\Delta \delta = 9.1$ ppm). Attempts to characterize 2-5 or 2-6 by X-ray crystallography were unsuccessful; instead, the phosphine oxide [(o-C$_6$H$_4$NH)Ph$_2$P(O)]$^-$ was obtained, suggesting degradation upon interaction with atmospheric moisture.

With the presence of both a Lewis acidic P(V) centre and a pendant Lewis basic nitrogen atom, we wondered if compounds 2-5 and 2-6 could act as FLPs to activate small molecules. Inspired by work completed by Hounjet et al., we reacted compound 2-5 with CO$_2$; however, no reaction was observed. Moreover, analysis of the $^{13}$C{$^1$H} NMR spectrum (CD$_2$Cl$_2$) shows no evidence for CO$_2$ sequestration. As well, the desired FLP reactivity was not observed with compound 2-5 and 1,1-diphenylethylene, phenylacetylene nor N,N'‐diisopropylcarbodiimide. However, when equimolar amounts of 2-5 and Et$_3$SiH were mixed at room temperature, analysis of the $^{31}$P{$^1$H} NMR (CD$_2$Cl$_2$) spectrum after 24 h showed disappearance of the starting material and the formation of a new singlet at $\delta$ –5.3 ppm. The $^{19}$F{$^1$H} NMR of the crude mixture, shows a singlet resonance at $\delta$ –79.0 ppm corresponding to the [OTf]$^+$ anion and a multiplet at $\delta$ –175.9 ppm which corresponds to Et$_3$SiF. Independent synthesis confirmed the cation to be [(o-HNC$_3$H$_4$)PPh$_2$]$^+$ 2-8. In this regard, one possible route involves the activation of the Si-H bond in Et$_3$SiH by P(V), which prompts fluoride abstraction by the Si-moiety affording Et$_3$SiF and protonation of the N atom of the pyridyl substituent. Whether this proceeds via a transient hydridofluorophosphorane or a hypervalent silane species, has not been unambiguously determined (Scheme 2-6).

When equimolar amounts of 2-5 and benzaldehyde were mixed at ambient temperature for 20 min, the $^{31}$P{$^1$H} NMR spectrum (CD$_2$Cl$_2$) showed the complete disappearance of 2-5 and the formation of a new doublet resonance at $\delta$ –52.2 (d, $J_{PF} = 733$ Hz). The corresponding P-F doublet was observed in the $^{19}$F{$^1$H} NMR spectrum at $\delta$ –41.5 ppm, and the [OTf]$^+$ anion resonance appears at $\delta$ –77.7 ppm. Moreover, the $^{13}$C{$^1$H} NMR spectrum contains a singlet resonance at $\delta$ 191.1 ppm and the $^1$H NMR spectrum shows a singlet at $\delta$ 9.75 ppm.
Scheme 2-6. Summary of intramolecular FLP reactivity with 2-5. [OTf]– counterions have been omitted for clarity.

Collectively, these data demonstrate PhCHO (free PhCHO: $^{13}$C{H}: δ 194.0 ppm$^{43}$; $^1$H: δ 9.95 ppm$^{43}$) coordination to the cation of 2-5, affording the salt [(PhCH(O))(o-C$_6$H$_4$N)PPh$_2$]$^+$. 2-9. This result is similar to the DMF and Et$_3$PO coordination observed for [(C$_6$F$_5$)$_3$P]$^+$. 10 Unfortunately, attempts to isolate 2-9 have insofar been unsuccessful. Similarly, reaction of 2-5 with benzophenone resulted in the generation of a new $^{31}$P{H} chemical shift at δ –51.9 (d, $J_{PF}$ = 726 Hz); however, the equilibrium at room temperature lies heavily to the left, favoring 2-5. This result is unsurprising given the greater steric bulk of benzophenone would disfavor adduct formation.

While FLP small molecule activation (Lewis acid and base cooperation) was not observed with these select compounds, the interaction of 2-5 with PhCHO and benzaldehyde, as well as its reaction with Et$_3$SiH demonstrate the Lewis acidity of the P(V) centre. This stands in stark contrast to simple alkyl- or arylphosphonium species and highlights the electron-withdrawing capabilities of a fluorine substituent.

2.2.2 Synthesis of Pyridiniumphosphonium Dications

To access more Lewis acidic phosphorus cations, we targeted the synthesis of the corresponding phosphonium dications. Attempts to alkylate the N atom in the pyridine ring of 2-5 or 2-6 were unsuccessful, even with strong alkylating reagents such as MeOTf. Instead, we targeted the oxidation of difluorophosphorane 2-4. To this end, a mixture of 2-4 and MeOTf were combined
and stirred for 1.5 h at ambient temperature. After extracting the product with \( n \)-pentane to remove the excess MeOTf, \([(\alpha\text{-C}_6\text{H}_4\text{NCH}_3)\text{PPh}_2\text{F}_2][\text{OTf}]\) **2-11** was isolated in high yield (98%) and fully characterized by multinuclear NMR spectroscopy, elemental analysis and X-ray crystallography (Figure 2-2).

![](image)

**Scheme 2-7.** Syntheses of pyridinium-fluorophosphonium dication 2-12 and 2-13.

In the \(^1\text{H}\) NMR spectrum (CD\(_2\)Cl\(_2\)), a singlet resonance was observed at \( \delta \) 4.40 ppm, which corresponds to the N-bound CH\(_3\) protons.\(^{35}\) The \(^{31}\text{P}\{\text{^1}\text{H}\}\) NMR spectrum contains a triplet resonance at \( \delta \) –55.6 ppm (\(^1\text{J}_{\text{PF}} = 706\) Hz). Compared to the neutral difluorophosphorane **2-4**, the \(^1\text{J}_{\text{PF}}\) coupling constant for **2-11** has increased, consistent with a stronger P-F interaction which presumably arises from the presence of the electron-withdrawing pyridinium substituent. In the \(^{19}\text{F}\{\text{^1}\text{H}\}\) NMR spectrum, the doublet resonance corresponding to the P-bound fluoride atoms at \( \delta \) –40.9 ppm is shifted upfield relative to **2-4**. The resonance corresponding to the \([\text{OTf}]^-\) anion is observed at \( \delta \) –79.0 ppm (s).

The molecular structure of compound **2-11** was obtained by X-ray diffraction and possesses a distorted trigonal bipyramidal geometry around phosphorus (Figure 2-2). The fluoride substituents occupy the apical positions with a F-P-F angle of 171.8(4)\(^\circ\), which is comparable to the value reported for the related cationic difluorophosphorane \(((\text{SIMes})\text{PF}_2\text{Ph}_2)[\text{B}(\text{C}_6\text{F}_5)_4]\) (168.8(2)\(^\circ\)).\(^{12}\) It is noteworthy that, while cationic pyridiniumphosphines have been employed as ligands in transition metal chemistry by Alcarazo and coworkers,\(^{35}\) **2-11** is, to the best of our knowledge, the first example of a cationic pyridiniumphosphorane.
Fluoride abstraction to give the corresponding pyridinium-fluorophosphonium dications [(o-C₆H₄NCH₃)PPh₂F][X]₂ (X = OTf 2-12; B(C₆F₅)₄ 2-13) was achieved with either TMSOTf or [Et₃Si][B(C₆F₅)₄]•(C₇H₈) (Scheme 2-7). In the case of 2-12, equimolar amounts of cationic difluorophosphorane 2-11 and TMSOTf were stirred at ambient temperature for 24 h before removing the Me₃SiF side product in vacuo. The dication 2-12 was then isolated in 81% yield and characterized by NMR spectroscopy, elemental analysis and X-ray crystallography. The $^{31}$P{¹H} NMR spectrum (CD₃CN) of 2-12 contains a doublet resonance at $\delta$ 88.8 ppm ($^1J_{PF} = 1035$ Hz), which is shifted downfield relative to fluorophosphonium monocations 2-5 ($\Delta\delta = 8.7$ ppm) and 2-6 ($\Delta\delta = 10.6$). This shift highlights the influence of the additional positive charge on the phosphorus atom. The $^{31}$P{¹H} resonance of 2-12 is also shifted downfield relative to the related fluorophosphonium dication [(SIMes)PF₂Ph₂][B(C₆F₅)₄]₂.¹² The $^{19}$F{¹H} NMR spectrum contains the corresponding P-F doublet resonance at $\delta$ −123.9 ppm and the [OTf]⁻ signal is observed at $\delta$ −79.3 ppm, seemingly indicative of the free anion.³⁸,³⁹ Interestingly, the signal corresponding to the
N-bound CH$_3$ protons in the $^1$H NMR spectrum appear as a doublet at $\delta$ 4.40 ppm ($^4$J$_{PH}$ = 3 Hz), whereas no P-H coupling was observed in the $^1$H NMR spectrum for cationic difluorophosphorane 2-11.

The molecular structure of 2-12 was obtained by X-ray diffraction and shows a distorted tetrahedral geometry at the P(V) centre (Figure 2-3). Comparison of the metric parameters of the dicationic salt 2-12 to cationic difluorophosphorane 2-11 supports the notion of enhanced Lewis acidity resulting from the presence of the second positive charge, as the P-F bond distance has decreased from 1.676(8) Å (2-11) to 1.539(1) Å (2-12) and is comparable to the distance for the related fluorophosphonium dication [(SIMes)PFPh$_2$][B(C$_6$F$_5$)$_4$] (1.532(2) Å).$^{12}$ Relative to species 2-11, the P-C bond distances for 2-12 have slightly decreased, whereas the N-C bond lengths for the (N-CH$_3$) moiety are comparable (2-11: 1.485(2) Å; 2-12: 1.479(2) Å). The structure of the cation shows two sets of P, O inter-ion contacts, one of which is trans to the P-C$_{Ph}$ bond (3.364(2) Å) and the other trans to the P-F bond (3.876(2) Å). Interestingly, the former interaction is more closely related to the sum of the P, O van der Waals radii (3.32 Å) (Figure 2-3). Similar P-O inter-ion interactions with [OTf]$^-$ counterions were reported previously for P(III) phosphonium dicationic salts.$^{4d}$ Unfortunately, attempts to obtain spectroscopic evidence (with variable temperature NMR experiments) of a P-O inter-ion interaction in solution were unsuccessful.

To synthesize 2-13, 2-11 was reacted with 2 equiv. of [Et$_3$Si][B(C$_6$F$_5$)$_4$]•(C$_7$H$_8$) which facilitated fluoride abstraction and concurrent counterion exchange (Scheme 2-7). The TESOTf side product was removed with n-pentane washings and Et$_3$SiF was removed in vacuo, affording 2-13 in 72% yield. The $^{31}$P{$^1$H} NMR spectrum (CD$_2$Cl$_2$) contains a doublet resonance at $\delta$ 88.9 ppm ($^1$J$_{PF}$ = 1035 Hz). The corresponding doublet resonance in the $^{19}$F{$^1$H} NMR spectrum appears at $\delta$ –124.2 ppm, and resonances for the B(C$_6$F$_5$)$_4$ anion appear at $\delta$ –133.0, –162.0, –167.2 ppm. The $^1$H NMR spectrum displays a resonance at $\delta$ 4.50 ppm ($^4$J$_{PH}$ = 3 Hz) corresponding to the N-bound CH$_3$ protons. Interestingly, 2-13 readily dissolves in most polar organic solvents like CH$_2$Cl$_2$, whereas 2-12 was insoluble in most organic solvents except for CH$_3$CN.
**Figure 2-3.** Molecular structure of 2-12 (POV-ray depiction). P: orange, F: pink, C: black, H: white, N: blue, O: red, S: sulfur. Hydrogen atoms have been omitted for clarity. Selected bond distances (Å) and angles (°): P-F 1.539(1), P-C1 1.814(1), P-C7 1.759(1), P-C13 1.760(1), N-C6 1.479(2); F-P-C1 106.7(5), C7-P-C1 108.7(1), C13-P-C1 110.3(6).

### 2.2.3 Assessment of Pyridiniumphosphonium Salt Stability

With these new fluorophosphonium dications in hand, we next sought out to probe their stability. To this end, a solution of 2-13 was prepared in CH₂Cl₂ and exposed to air, resulting in degradation to a new product within minutes, as observed by multi-nuclear NMR spectroscopy. Analysis of the $^{31}$P{$^1$H} NMR spectrum (CH₂Cl₂) shows a singlet resonance at δ 28.7 ppm. Disappearance of the P-F resonance was observed in the $^{19}$F{$^1$H} NMR spectrum while the B(C₆F₅)₄ resonances were unchanged. Based on previous reports of fluorophosphonium salt degradation due to hydrolysis, the degradation product is likely the corresponding cationic phosphine oxide “[((o-C₆H₄NCH₂)Ph₂P(O)]⁺”, which aligns with the decomposition reported for monocation 2-6. One likely explanation involves reaction of 2-13 with atmospheric H₂O, which can lead to degradation and formation of the corresponding phosphine oxide. As LaFortune et al. noted in their report, it is possible the phosphine oxide formation proceeds through a hydroxyphosphonium species.
albeit we were unable to isolate or detect this species in situ. Similarly, when 2-11 was exposed to air, the same product was observed in the NMR spectra. Attempts to independently synthesize the degradation product through separate oxidation and subsequent methylation routes were unsuccessful, and in most cases a mixture of unidentifiable products was observed.

While the mechanism of degradation has not been thoroughly investigated, previous observations of fluoride-oxide exchange with EPCs in the presence of oxygen donors such as Et₃PO support the notion of an initial interaction between the P(V) centre and H₂O followed by loss of HF. Whether the hydroxyphosphonium or phosphine oxide is the major species has not been unambiguously determined; however, a rapid and dynamic acid-base equilibrium is likely present. These data align with the observed decomposition product of fluorophosphonium monocation 2-6 mentioned earlier in this chapter.

Inspired by the work of Hounjet et al., wherein deprotonation and fluoride abstraction with t-BuLi generated an amido fluorophosphorane compound which was capable of sequestering CO₂, we attempted a similar reaction with 2-11. We wondered if deprotonation of the N-bound methyl group with subsequent fluoride abstraction could facilitate the formation of a 4-membered C-N-C-P ring, providing us with a framework for further FLP-type activations. We began our investigation with n-BuLi, and in all cases, even upon varying the reaction conditions, complex product mixtures were obtained as evidenced by multi-nuclear NMR spectroscopy. Similarly, reactions of 2-11 with t-BuLi generated complex mixtures of unidentifiable products. Reactions with KHMDS were also unsuccessful. In another approach, we targeted deprotonation of pyridinium-fluorophosphonium 2-13 with a neutral Lewis base like PrBu₃. To this end, when equimolar amounts of 2-13 and PrBu₃ were mixed, a colour change was observed almost immediately and analysis of the ³¹P{¹H} NMR spectrum (CH₂Cl₂) after 24 h at ambient temperature shows the formation of a mixture of products. The identifiable species included: the cation of [tBu₃PH]⁺ at δ 60.7 ppm (dm, ¹JPF = 429 Hz), unreacted 2-13 at δ 90.2 ppm, and a new doublet at δ −54.0 ppm. Heating this reaction mixture to 45 °C for 12 h led to complete decomposition of 2-13 into the presumed cationic phosphine oxide “[(α-C₆H₄NCH₃)Ph₂P(O)]⁺”, observed at δ 27.7 ppm in the ³¹P{¹H} NMR spectrum. The other resonances were maintained, and the doublet resonance at δ −57.1 ppm displays strong P-F coupling (¹JPF = 764 Hz). This resonance is similar to the ³¹P{¹H} NMR chemical shift of 2-11 (³¹P(δ) = −55.6 ppm, t, ¹JPF = 705 Hz), suggesting that this compound may be a pentacoordinate phosphorane cationic species. In the ¹H
NMR spectrum (CD$_2$Cl$_2$), the P-H resonance for [tBu$_3$PH]$^+$ appears at $\delta$ 5.09 (d, $^1J_{PH} = 429$ Hz) and the tBu proton resonances appear as a doublet at $\delta$ 1.66 ppm (d, $^3J_{PH} = 16$ Hz). There is also a new resonance at $\delta$ 6.35 ppm (dd), which may be assigned to the protons in the N-CH$_2$-P fragment with P-H and F-H coupling constants of $J = 15$ Hz and $J = 6$ Hz, respectively. Unfortunately, attempts to accurately assign the resonances in the NMR spectra using 1-D and 2-D experiments were unsuccessful. As well, all attempts to remove [tBu$_3$PH]$^+$ from the reaction mixture and isolate the new product were unsuccessful. Therefore, based on the $^{31}$P{^1H} NMR spectra we can conclude that deprotonation occurred and a new doublet resonance in the phosphorane region with strong P-F coupling is observed. However, while this may align with our proposed reaction product, efforts to unambiguously identify the new product were unsuccessful. Further experiments are needed to obtain more information about this reaction.

2.2.4 Assessment of Pyridiniumphosphonium Salt Lewis Acidity

2.2.4.1 Gutmann-Beckett Tests

With a new family of Lewis acidic pyridinium-fluorophosphonium cations in hand, we probed their relative Lewis acid strengths. One common method often used in main group chemistry is referred to as the Gutmann-Beckett method$^{46, 47}$. This test utilizes Et$_3$PO as the donor molecule and its $^{31}$P NMR chemical shift to correlate the relative Lewis acidities of the compounds in question. While this method does provide an estimate of relative Lewis acidity, there are some limitations. For instance, binding of Et$_3$PO is more indicative of oxophilicity, and the strength of this interaction can be influenced by steric rather than solely Lewis acidity.

To begin our investigation, 2-5 was mixed with Et$_3$PO and analyzed by multi-nuclear NMR spectroscopy after 1 h at ambient temperature. Analysis of the $^{31}$P{^1H} NMR spectrum (CD$_2$Cl$_2$) shows some conversion to [Et$_3$PF][OTf] ($\delta$ 150.2 ppm, $^1J_{PF} = 955$ Hz), which has been previously characterized as the [B(C$_6$F$_5$)$_4$]$^-$ salt (Scheme 2-8)$^{12}$. As well, there are singlet resonances at $\delta$ 19.7 ppm (indicative of the formation of (o-C$_5$H$_4$N)Ph$_2$PO)$^{48}$, $\delta$ 64.1 ppm (Et$_3$PO) and $\delta$ 78.7 ppm (2-5). A similar result was obtained for the analogous reaction with 2-6.

For the reaction of 2-12 with Et$_3$PO, full consumption of the dication was observed after 1 h at ambient temperature. In this case, the $^{31}$P{^1H} NMR spectrum (CD$_2$Cl$_2$) also shows formation of [Et$_3$PF][OTf] ($\delta$ 150.3 ppm, $^1J_{PF} = 955$ Hz), as well as “[(o-C$_5$H$_4$NCH$_3$)Ph$_2$PO][OTf]” ($\delta$ 27.8
ppm) and 2-11 (δ = 55.7 ppm, t, $^{1}J_{PF} = 700$ Hz). For the analogous reaction with 2-13, full consumption of the dication was also observed after 1 h at ambient temperature. However, in this instance, only resonances for $[\text{Et}_3\text{PF}][\text{B(C}_6\text{F}_5)_4]$ (δ = 147.7 ppm, $^{1}J_{PF} = 981$ Hz) and “$[\text{o-C}_3\text{H}_4\text{NCH}_3\text{Ph}_2\text{PO}][\text{B(C}_6\text{F}_5)_4]$” (δ = 27.9 ppm) were observed in the $^{31}\text{P}\{^1\text{H}\}$ NMR spectrum. It is noteworthy that a similar fluoride-oxide exchange was observed with 2-13 and acetophenone. Collectively, these data provide preliminary support for an electrophilic P(V) centre, and the enhancement in oxophilicity resulting from increased formal charge and the use of a weakly coordinating anion.

For the cases where Et$_3$PO was not completely consumed in the reaction, the $^{31}\text{P}\{^1\text{H}\}$ chemical shift differences between bound Et$_3$PO and free Et$_3$PO ($^{31}\text{P}\{^1\text{H}\}$ δ = 50.7 ppm) were calculated. The values obtained for 2-5 (Δ = 13.4 ppm), 2-6 (Δ = 9.5 ppm) and 2-12 (Δ = 2.1 ppm) were then compared to known strong Lewis acids. When compared to B(C$_6$F$_5$)$_3$ (Δ = 26.6 ppm) and [(C$_6$F$_5$)$_3$PF][B(C$_6$F$_5$)$_4$] (Δ = 40.4 ppm), all pyridiniumphosphonium salts would be predicted to be less Lewis acidic. However, as previously noted, these results should be taken with a note of caution. Since the Gutmann-Beckett test is largely dependent upon the formation of an adduct between Et$_3$PO and the Lewis acid, steric factors can have a large impact in the strength of the adduct and thus, can perturb the results.

Another method for assessing relative Lewis acidity is analysis and comparison of the $^{31}\text{P}\{^1\text{H}\}$ NMR chemical shift of each phosphonium salt. Interestingly, while Caputo et al. noted $^{31}\text{P}\{^1\text{H}\}$ upfield NMR chemical shifts with increasingly electron-withdrawing substituents,$^{11}$ comparison of mono- and dicationic fluorophosphonium species 2-5, 2-6, 2-12 and 2-13 shows the opposite trend. In our case, downfield shifts were observed upon increasing electron-withdrawing character of the P-bound substituents (Figure 2-4). One possible explanation could be the increase in steric shielding from the N-bound methylene group which may affect shielding of the $^{31}\text{P}$ and/or $^{19}\text{F}$ nuclei. This observation has been reported previously for mesityl-substituted phosphonium salts.$^{11}$
2.2.4.2 Computational Investigation

To gain further insight into the electrophilicity of these phosphorus(V) cations, DFT computations were performed at the M11/def2-TZVP level of theory by fellow graduate student James LaFortune. For the cations of 2-5/2-6 and 2-12/2-13, both isomers were considered, wherein the N atom is oriented in the same direction (cis/“up”) or opposite (trans/“up”) to the P-F bond (Figure 2-5). In either case, there does not seem to be much difference in the lowest unoccupied molecular orbital (LUMO) between these two isomers. For the pyridinium fluorophosphonium monocations 2-5 and 2-6, the LUMO is delocalized across the whole molecule with a large contribution from the P-F σ* anti-bonding orbital, similar to the calculated LUMO of [(C₆F₅)₃PF][B(C₆F₅)₄],¹⁰ and the related species [(C₆F₅)₃P(OAr)][B(C₆F₅)₄].⁴⁰

It is noteworthy that when the N atom is oriented in the same direction as the fluoride, calculations show more contribution from the P-F σ* anti-bonding orbital (Figure 2-5, B) relative to the trans isomer. Depiction of the LUMO for the cations of 2-12 and 2-13 shows significant delocalization across the pyridinium ring with less contribution from P-F σ* anti-bonding orbital. The orbital composition for 2-5 and 2-6 suggests that the site of nucleophilic attack will occur at the P atom opposite the fluoride substituent. However, while the computations for 2-12 and 2-13 are not as definitive, the fluoride-oxide exchange (reported in section 2.2.3.1) with Et₃PO aligns with the expected nucleophilicity at phosphorus. Therefore, the computations reported herein should be

Figure 2-4. $^{31}$P{¹H} NMR stack plot of 2-5, 2-6, 2-12 and 2-13 (top to bottom).
interpreted with caution and all computation and theoretical data should be considered when assessing Lewis acidity.

Figure 2-5. Surface contour plots (isovalue 0.03) of the LUMO of the cations of 2-5/2-6 (A and B) and 2-12/2-13 (C and D).

Quantum chemical calculations of the Fluoride Ion Affinity (FIA)\textsuperscript{59} and Global Electrophilicity Index (GEI)\textsuperscript{50, 51} were also used to assess the relative Lewis acidities. FIA and GEI were calculated as previously described.\textsuperscript{52, 53} The FIA can be evaluated by combining the strength of a Lewis acid, with the energy that is released upon binding a fluoride ion,\textsuperscript{54} wherein the strength of the Lewis acid corresponds to the absolute value of the FIA. The reaction we modeled included the optimized phosphonium structures. In all cases, ΔH was calculated for the reaction of the Lewis acid with [CF_{3}O]^{-} to give the corresponding P-fluoride adduct and CF_{2}O. This enthalpy was then added to the experimental gas phase ΔH for the reaction of CF_{2}O with F^{-} (209 kJ mol^{-1}), affording the ΔH for the reaction of the Lewis acid with F^{-} to give the P-fluoride adduct (Equation 1). The FIA values for the cations of 2-5/2-6 and 2-12/2-13 were calculated using the MP2\textsuperscript{55} method and the Def2-TZVPP basis set at the BP86/Def2-TZVP optimized geometries and are reported in Table 2-1.
Equation 1. FIA calculations for optimized phosphonium structures.

For each cation, there exists a minimal energy (i.e. less than 2 kJ/mol) difference between two isomers in the gas-phase – *cis*/*up* and *trans*/*down* – suggesting a minimal energy barrier to rotation at room temperature. Therefore, for the purpose of these calculations, both isomers were used. Interestingly, for both the monocations and dications, the “up” isomer was predicted to have a larger FIA (reported as the upper limits in Table 2-1). One explanation may be the reduction in steric occlusion around the σ* P-F anti-bonding orbital in the “up” configuration. Comparison of the monocations to the dications shows a significant increase in FIA values upon addition of a second positive charge.

Table 2-1. FIA and ω values for the cations of 2-5, 2-6, 2-12 and 2-13.

<table>
<thead>
<tr>
<th>Phosphonium</th>
<th>$^{31}$P$^{[1H]}$ (δ/ppm)</th>
<th>$^{19}$F$^{[1H]}$ (δ/ppm)</th>
<th>FIA (kJ mol$^{-1}$)</th>
<th>ω (eV)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2-5</td>
<td>80.1 (d, $^1J_{PF} = 1004$ Hz)</td>
<td>−136.8 (d)</td>
<td>651.5 – 655.7</td>
<td>2.382 – 2.569</td>
</tr>
<tr>
<td>2-6</td>
<td>78.2 (d, $^1J_{PF} = 1004$ Hz)</td>
<td>−137.3 (d)</td>
<td>651.5 – 655.7</td>
<td>2.382 – 2.569</td>
</tr>
<tr>
<td>2-12</td>
<td>88.8 (d, $^1J_{PF} = 1035$ Hz)</td>
<td>−123.9 (d)</td>
<td>1010.7 – 1015.3</td>
<td>6.509 – 6.720</td>
</tr>
<tr>
<td>2-13</td>
<td>88.9 (d, $^1J_{PF} = 1035$ Hz)</td>
<td>−124.2 (d)</td>
<td>1010.7 – 1015.3</td>
<td>6.509 – 6.720</td>
</tr>
</tbody>
</table>

As well, when compared to [(C$_6$F$_5$)$_3$PF][B(C$_6$F$_5$)$_4$] (777 kJ mol$^{-1}$) and B(C$_6$F$_5$)$_3$ (440 kJ mol$^{-1}$), dications 2-12 and 2-13 are predicted to be significantly more fluorophilic.

While the FIA provides a relative measure of Lewis acidity, it is defined with respect to a specific base, and thus, does not measure general Lewis acidity, but rather the affinity for fluoride. A more modern approach to computing the general Lewis acidity is the GEI, which is a measure of the ability of a molecule to take up electrons (ω), wherein a molecule that is more electronegative and
softer will have a greater propensity to take up electrons. In addition to evaluating the capacity for a molecule to receive electrons, the GEI can be performed at a fraction of the computational costs needed for FIA calculations. For these calculations, the orbital energies were computed according to the specifications for FIA values reported above.\textsuperscript{40, 52}

Our group has recently reported this method for assessment of Lewis acidity for several main group systems and noted excellent correlation between FIA and GEI.\textsuperscript{50-52} Indeed, the GEI for the cations of 2-5/2-6 and 2-12/2-13 correlate to the FIAs, wherein dications 2-12 and 2-13 have larger \( \omega \) values compared to 2-5 and 2-6. Both isomers were also used in these calculations, and a similar trend was observed: “up” isomers have slightly larger \( \omega \) values compared to their “down” isomers. When compared to \([\text{[C}_6\text{F}_5)_3\text{PF}][\text{B(C}_6\text{F}_5)_4]\) (5.04 eV) and \(\text{B(C}_6\text{F}_5)_3\) (2.10 eV), 2-12 and 2-13 are predicted to have a greater capacity to accept electron density.

### 2.2.4.3 Lewis Acid Catalysis

As we strive to obtain a better understanding of Lewis acidity – its requirements and applications – we wanted to probe the reactivity of our pyridiniumphosphonium salts in useful organic transformations. Given the precedent for phosphonium-catalyzed organic reactions, this analysis would offer another experimental assessment of relative Lewis acidity. For this investigation, the reactions we chose included: Friedel-crafts dimerization of 1,1-diphenylethylene,\textsuperscript{13, 17} hydrodefluorination of 1-fluoropentane with \(\text{Et}_3\text{SiH}\),\textsuperscript{10, 12} hydrosilylation of \(\alpha\)-methylstyrene,\textsuperscript{17, 18} dehydrocoupling of phenol and \(\text{Et}_3\text{SiH}\),\textsuperscript{13, 16} and hydrodeoxygenation of benzophenone (Scheme 2-8).\textsuperscript{20}

For the Friedel-crafts dimerization of 1,1-diphenylethylene, 2 mol\% EPC was used. No dimerized product was observed for the monocations 2-5 and 2-6, or the [OTf]\textsuperscript{−} phosphonium dication 2-12, even after 10 h. On the other hand, the \([\text{B(C}_6\text{F}_5)_4]\)\textsuperscript{−} dication 2-13 rapidly catalyzed the reaction, giving 1-methyl-1,3,3-triphenyl-2,3-dihydro-1\(^1\)H-indene in \(>99\%\) conversion after 30 min (determined from the \(\text{^1H}\) NMR spectrum). When compared to \([\text{(SIMes)PF}_2\text{Ph}_2][\text{B(C}_6\text{F}_5)_4]\),\textsuperscript{12} 2-13 demonstrated similar reactivity for this reaction. The inactivity of the monocations highlights the influence of the increased formal charge on the Lewis acidity, subsequently supporting the need for electron-withdrawing groups to enhance the Lewis acidity of the monocationic species.

Since monocations 2-5 and 2-6 react with Et₃SiH, only the dications 2-12 and 2-13 were probed as catalysts for the reactions which involve Et₃SiH. For the hydrodefluorination of 1-fluoropentane, 5 mol% EPCs were used, and after 1 h at ambient temperature, 0% (2-12) and 92% (2-13) conversion was observed. It is noteworthy that - in addition to n-pentane - the formation of unidentifiable products has been previously reported for this reaction, due to the side reaction of the n-pentyl cation with [B(C₆F₅)₄]. Carbon skeleton rearrangements in the generated carbocation must also be considered and would lead to the formation of different constitutional isomers of n-pentane (denoted as quotations in Scheme 2-8, b). For the hydrosilylation of α-methylstyrene, in the presence of 2 mol% catalyst and Et₃SiH, heating the reaction mixture to 45 °C for 4 h gave 0% (2-12) and >99% (2-13) conversion to the corresponding hydrosilylated product. When 2 mol% of the catalysts were added to equimolar amounts of Et₃SiH and phenol, 0% (2-12) and >99% (2-13) conversions to Et₃SiOPh (with concurrent liberation of H₂) were
obtained after heating to 50 °C for 48 h. Finally, in the case of the hydrodeoxygenation of benzophenone with Et₃SiH, 1 mol% of catalyst affected 0% (2-12) and >99% (2-13) conversion to diphenylmethane after 2 h at ambient temperature. In all cases, 2-13 demonstrated comparable or greater reactivity to the related bis-fluorophosphonium dications, except for the hydrodeoxygenation of benzophenone, which is significantly faster at room temperature with 2-13 (previous reports required heating the reaction mixture to 50 °C for 36 h).

Overall, the pyridiniumphosphonium dication 2-12 was inactive for all the aforementioned transformations, whereas 2-13 demonstrated comparable, and in some cases superior, reactivity in comparison to other related phosphonium dications. This result supports the Lewis acid reactivity of the pyridinium-based salt 2-13, while also highlighting the need for a bulky non-coordinating counterion such as [B(C₆F₅)₄]⁻ to facilitate catalysis. The exact nature of the P-O interaction in 2-12 remains the subject of ongoing investigation in our laboratory.

2.3 Conclusions

Chapter 2 presents the synthesis and reactivity of pyridinium fluorophosphonium mono- and dications. Reaction of 2-pyridyl-diphenylphosphine with XeF₂ and either TMSOTf or [Et₃Si][B(C₆F₅)₄](C₇H₈) cleanly affords the corresponding fluorophosphonium salts 2-5 and 2-6. While attempts to achieve FLP reactivity with these compounds were unsuccessful, interaction of PhCHO and reactivity with Et₃SiH support a Lewis acidic P(V) centre. Methylation of 2-4 and subsequent fluoride abstraction gives pyridinium-fluorophosphonium salts 2-12 and 2-13.

The Lewis acidity of these EPCs was probed using computational and experimental methods. While the Gutmann-Beckett method proved insufficient due to fluoride-oxide exchange, FIA and GEI calculations predicted fluorophosphonium salts 2-12 and 2-13 to have superior fluoride affinity and Lewis acidity when compared to their monocationic counterparts and other known Lewis acids. This Lewis acidity was reflected in a series of organic transformations, wherein 2-13 was shown to be an active catalyst for the Friedel-Crafts type dimerization of 1,1-diphenylethylene, the hydrodefluorination of 1-fluoropentane, the hydrosilylation of α-methylstyrene, the dehydrocoupling of phenol with Et₃SiH and the hydrodeoxygenation of benzophenone. In some cases, 2-13 was shown to be more reactive than other related phosphonium dications previously reported in the literature. Interestingly, no conversion was observed using 2-
as the catalyst, supporting the need for a non-coordinating anion in catalysis for these systems. Collectively, these data support the notion of a Lewis acidic P(V) centre and highlight the tunability and reactivity of the pyridinium-based phosphorus scaffold.

2.4 Experimental Details

2.4.1 General Remarks

All manipulations were performed in a MB Unilab Glove box produced by MBraun or using standard Schlenk techniques under an inert atmosphere of anhydrous N₂. All glassware was oven-dried at temperatures above 180 °C prior to use. Dry, oxygen-free solvents (CH₂Cl₂, toluene, and n-pentane) were prepared using an Innovative Technologies solvent purification system or deoxygenated and distilled over sodium benzophenone. Fluorobenzene (C₆H₅F) was distilled from CaH₂ and stored over molecular sieves (4 Å) prior to use. Deuterated dichloromethane (CD₂Cl₂), acetonitrile (CD₃CN), and bromobenzene (C₆D₅Br) were purchased from Sigma-Aldrich and distilled from CaH₂ prior to use. Reagents such as 2-pyridyldiphenylphosphine, MeOTf, TMSOTf, HOTf, XeF₂, Et₃PO, Et₃SiH, 1-fluoropentane, benzophenone, phenol, 1,1-diphenylethylene and α-methylstyrene, were purchased either from Sigma-Aldrich, Strem Chemicals, TCI chemicals or Alfa Aesar and used as received. [Et₃Si][B(C₆F₅)₄]•(C₇H₈) was prepared according to a known literature procedure. NMR spectra were measured on a Bruker AVANCE 400 (¹H: 400 MHz, ¹¹B: 128 MHz, ¹³C: 101 MHz, ³¹P: 162 MHz, ¹⁹F: 377 MHz) or Agilent DD2 500 (¹H: 500 MHz, ¹³C: 125 MHz, ³¹P: 202 MHz, ¹⁹F: 471 MHz) at ambient temperature. ¹H, ¹³C, ³¹P, ¹⁹F, and ¹¹B NMR chemical shifts (δ/ppm) are referenced to Me₄Si, Me₄Si, H₃PO₄, CFCl₃, and BF₃•OEt₂, respectively. Chemical shifts (δ) are reported in ppm, multiplicity is reported as follows (s = singlet, d = doublet, t = triplet, m = multiplet) and coupling constants (J) are reported in Hz. Assignments of individual resonances were done using 2D techniques (HMBC, HSQC, HH-COSY) when necessary. High-resolution mass spectra (HRMS) were obtained on a micro mass an Agilent 6538 Q-TOF (ESI) or on a JOELAccuTOF-DART (DART) mass spectrometer. Elemental analyses (C, H, N) were performed at the University of Toronto employing a Perkin Elmer 2400 Series II CHNS Analyzer.
2.4.2 Synthesis of Compounds 2-1, 2-4, 2-5, 2-6, 2-8, 2-11, 2-12, and 2-13
[(o-C₅H₄N)PF₂Ph₂P(CH₃)]⁺[I]⁻ (2-1)

CH₃I (0.4 mL, 6.42, 10 equiv.) was added to a solution of 2-pyridylidiphenylphosphine (168 mg, 0.64 mmol, 1.0 equiv.) in CH₂Cl₂ (8 mL). The reaction mixture, transparent and bright yellow, was stirred for 2.5 h at ambient temperature. The solution was dried in vacuo to remove solvent/volatiles and washed with n-pentane (3 x 5 mL). The supernatant was removed and all volatiles were removed in vacuo to afford a pale-yellow microcrystalline powder (247 mg, 96% Yield).

¹H NMR (400 MHz, CD₂Cl₂, Me₄Si): δ 8.95 (m, 1H; m-py), 8.08 (m, 1H; p-py), 7.96 (m, 1H; o-py), 7.80 (m, 6H; m-py & Ph), 7.71 (m, 5H; Ph), 3.05 ppm (d, Jₚₗ₇ = 13 Hz, 3H; P-CH₃). ³¹P¹H NMR (162 MHz, CD₂Cl₂, H₃PO₄): δ 17.4 ppm (s). ¹³C¹H NMR (126 MHz, CD₃CN, Me₄Si): δ 152.7 (d, Jₚₗ₇ = 20 Hz, 1C; m-py), 145.0 (d, Jₚₗ₇ = 120 Hz, 1C; i-py), 138.6 (d, Jₚₗ₇ = 11 Hz, 1C; m-py), 135.8 (d, Jₚₗ₇ = 3 Hz, 2C; p-Ph), 133.9 (d, Jₚₗ₇ = 10 Hz, 4C; m-Ph), 131.5 (d, Jₚₗ₇ = 25 Hz, 1C; o-py), 130.8 (d, Jₚₗ₇ = 13 Hz, 4C; o-Ph), 128.8 (d, Jₚₗ₇ = 3 Hz, 1C; p-py), 118.6 (d, Jₚₗ₇ = 87 Hz, 2C; i-Ph), 10.0 ppm (d, Jₚₗ₇ = 58 Hz, 1C; P-CH₃), resonance for sulfur-bound carbon atom in [OTf⁻] anion was not observed. MS-ESI: Calculated mass for [M]⁺: 278.11. Obtained: 278.1104 amu. Anal Calcd. for C₁₈H₁₇INP: C, 53.3; H, 4.2; N, 3.5 %. Found: C, 53.5; H, 3.5; N, 3.7 %.

(o-C₅H₄N)PF₂Ph₂ (2-4)

A solution of 2-pyridylidiphenylphosphine (1.19 g, 4.53 mmol, 1.0 equiv.) in CH₂Cl₂ (8 mL) was added to a suspension of XeF₂ (768 mg, 4.54 mmol, 1.0 equiv.) in CH₂Cl₂ (5 mL). The reaction mixture, transparent and colourless, was stirred for 2 h at ambient temperature. The solution was
dried *in vacuo* to remove solvent/volatiles and washed with *n*-pentane (3 x 5 mL). The supernatant was removed and all volatiles were removed *in vacuo* to afford a white microcrystalline powder (1.28 g, 94% Yield).

\[ \text{[[(}\text{o-CsH}_4\text{N})\text{PFPPh}_2]\text{[OTf]}\text{ (2-5)}] \]

TMSOTf (0.2 mL, 1.11 mmol, 1.1 equiv.) was added dropwise to a solution of 2-4 (295 mg, 1.05 mmol, 1.0 equiv.) in CH\(_2\)Cl\(_2\) (5 mL). The reaction mixture was stirred for 15 min at ambient temperature. The solution was dried *in vacuo* to remove solvent/volatiles and washed with *n*-pentane (3 x 5 mL). The supernatant was removed, and all volatiles were removed *in vacuo* to afford a white microcrystalline powder. (390 mg, 92% Yield).

\[ \text{^1H NMR (400 MHz, CD}_2\text{Cl}_2, \text{Me}_4\text{Si):} \delta 9.00 \text{ (dm,} J_{PH} = 5 \text{ Hz, 1H; m-py), 8.20 (m, 2H; m- and o-py), 7.97 (m, 2H; p-Ph), 7.90 (dd,} J_{HH} = 15 \text{ Hz,} J_{HH} = 15 \text{ Hz, 4H; m-Ph), 7.82 (m, 1H; p-py), 7.80 \text{ ppm (m, 4H; o-Ph).}^{19}\text{F\{^1H\} NMR (377 MHz, CD}_2\text{Cl}_2, \text{CFCI}_3\):} \delta -79.0 \text{ (s, 3F; OTf), -136.8 ppm (d,} J_{PF} = 1004 \text{ Hz, 1F; PF).}^{31}\text{P\{^1H\} NMR (162 MHz, CD}_2\text{Cl}_2, \text{H}_3\text{PO}_4\):} \delta 80.1 \text{ ppm (d,} J_{PF} = 1004 \text{ Hz, 1P).} \]

\[ \text{^{13}\text{C\{^1H\} NMR (125 MHz, CD}_2\text{Cl}_2, \text{Me}_4\text{Si):} \delta 152.7 \text{ (dd,} J_{PC} = 24 \text{ Hz,} J_{FC} = 2 \text{ Hz, 1C; m-py), 141.7 \text{ (dd,} J_{PC} = 148 \text{ Hz,} J_{FC} = 18 \text{ Hz, 1C; i-py), 138.7 \text{ (d,} J_{PC} = 11 \text{ Hz, 1C; m-py).} ]\]

\[ \text{Anal. Calcd. for} \text{C}_17\text{H}_{14}\text{F}_2\text{NP: C, 67.8; H, 4.7; N, 4.7 \%. Found: C, 67.1; H, 4.7; N, 4.8 \%.} \]
py), 138.4 (dd, $^4\text{J}_{PC} = 3$ Hz, $^5\text{J}_{PC} = 2$ Hz, 2C; $p$-Ph), 134.2 (dd, $^2\text{J}_{PC} = 13$ Hz, $^3\text{J}_{PC} = 2$ Hz, 4C; $o$-Ph), 131.8 (d, $^2\text{J}_{PC} = 26$ Hz, 1C; $o$-py), 130.7 (d $^3\text{J}_{PC} = 14$ Hz, 4C; $m$-Ph), 130.4 (dd, $^4\text{J}_{PC} = 4$ Hz, $^5\text{J}_{PC} = 1$ Hz, 1C; $p$-py), 115.6 ppm (dd, $^1\text{J}_{PC} = 94$ Hz, $^2\text{J}_{PC} = 12$ Hz, 2C; $i$-Ph), resonance for sulfur-bound carbon atom in [OTf]$^-$ anion was not observed. **ESI-MS:** Calculated mass for [(o-C$_5$H$_3$N)PF$_2$O]$^+$: 280.1. Obtained: 280.0894 amu. **Anal. Calcd.** for C$_{18}$H$_{14}$F$_4$NO$_3$PS: C, 50.1; H, 3.3; N, 3.2 %. Found: C, 50.3; H, 3.7; N, 3.2 %.

[(o-C$_5$H$_3$N)PF$_2$O][B(C$_6$F$_5$)$_4$] (2-6)

A solution of freshly prepared [Et$_3$Si][B(C$_6$F$_5$)$_4$]·(C$_7$H$_8$) (87 mg, 0.089 mmol, 0.95 equiv.), in C$_6$D$_3$Br (0.6 mL) was added to 2-4 (28 mg, 0.093 mmol, 1.0 equiv.) The solution was agitated for 2 min at ambient temperature. 3 mL of n-pentane was added resulting in the formation of an orange oil. The supernatant was decanted, and the resulting oil was washed with n-pentane (3 x 3 mL). The supernatant was decanted again and the residue was dried in vacuo affording a white microcrystalline solid (88 mg, 97% Yield). Attempts to characterize 2-6 crystallographically resulted in decomposition.

$^1$H NMR (400 MHz, C$_6$D$_3$Br, Me$_3$Si): $\delta$ 8.30 (d, $^4\text{J}_{PH} = 5$ Hz, 1H; $m$-py), 7.38 (m, 1H; $p$-py), 7.27 (m, 6H; $o$-Ph & $p$-Ph), 7.09 (m, 5H; $m$-Ph & $o/m$-py), 6.98 ppm (m, 1H; $o/m$-py). $^{11}$B$^{'1}$H NMR (128 MHz, C$_6$D$_3$Br, BF$_3$·OEt$_2$): $\delta$ −16.2 ppm (s, 1B). $^{19}$F$^{'1}$H NMR (377 MHz, C$_6$D$_3$Br, CFCl$_3$): $\delta$ −131.7 (m(br), 8F; B($o$-C$_6$F$_5$)$_4$), −137.3 (d, $^1\text{J}_{PF} = 1004$ Hz, 1F; PF), −161.9 (t, $^3\text{J}_{PF} = 21$ Hz, 4F; B($p$-C$_6$F$_5$)$_4$), −165.8 ppm (m(br), 8F; B($m$-C$_6$F$_5$)$_4$). $^{31}$P$^{'1}$H NMR (162 MHz, C$_6$D$_3$Br, H$_3$PO$_4$): $\delta$ 78.2 (d, $^1\text{J}_{PF} = 1004$ Hz, 1P). $^{13}$C$^{'1}$H NMR (125 MHz, C$_6$D$_3$Br, Me$_3$Si): $\delta$ 152.3 (d, $^3\text{J}_{PC} = 22$ Hz, 1C; $m$-py), 148.6 (dd(br), $^1\text{J}_{FC} = 243$ Hz, 8C; B($o/m$-C$_6$F$_5$)$_4$), 141.3 (dd, $^1\text{J}_{PC} = 149$ Hz, $^2\text{J}_{FC} = 19$ Hz, 1C; $i$-py), 138.4 (dd(br), $^1\text{J}_{FC} = 245$ Hz, 4C; B($p$-C$_6$F$_5$)$_4$), 138.1 (d, $^4\text{J}_{PC} = 3$ Hz, 2C; $p$-Ph), 137.6 (d, $^3\text{J}_{PC} = 11$ Hz, 1C; $m$-py), 136.5 (dd(br), $^1\text{J}_{FC} = 240$ Hz, 8C; B($o/m$-C$_6$F$_5$)$_4$), 134.3 (d, $^2\text{J}_{PC} = 20$ Hz, 1C; $o$-py), 133.4 (dd, $^2\text{J}_{PC} = 13$ Hz, $^3\text{J}_{FC} = 2$ Hz, 4C; $o$-Ph), 130.3 (d, $^3\text{J}_{PC} = 14$ Hz, 4C; $m$-Ph), 130.0 (d, $^4\text{J}_{PC} = 25$ Hz, 1C; $p$-py), 115.9 ppm (dd, $^1\text{J}_{PC} = 105$ Hz, $^2\text{J}_{FC} = 13$ Hz, 2C; $i$-Ph), resonance for boron-bound carbon atoms in [B(C$_6$F$_5$)$_4$]$^-$ anion was not observed. **ESI-MS:**
Calculated mass for \([((o-C_5H_5N)PPh_2)O]^+\): 280.1. Obtained: 280.0895 amu. **Anal. Calcd.** for C_{41}H_{14}B_{21}NP: C, 51.2; H, 1.5; N, 1.5 %. Found: C, 50.9; H, 1.5; N, 1.7 %.

\([(o-C_5H_4NH)PPh_2][OTf] (2-8)\)

HOTf (20.4 µL, 0.23 mmol, 1.0 equiv.) was added to a solution of 2-pyridyldiphenylphosphine (60.7 mg, 0.23 mmol, 1.0 equiv.) in CD_2Cl_2 (0.6 mL). The reaction mixture was left at ambient temperature for 10 min resulting in a pale-yellow solution. The solution was dried *in vacuo*, affording a pale-yellow oil. (90.4 mg, 95% Yield).

**^1H NMR (400 MHz, CD_2Cl_2, Me_4Si):** δ 14.68 (s(br), 1H; NH), 8.90 (m, 1H; m-py), 8.34 (t, J_HH = 8 Hz, 1H; m-py), 7.89 (t, J_HH = 7 Hz, 1H; p-py), 7.48 ppm (m, 10H; Ph), resonance for the ortho-pyridyl substituted hydrogen atom was not observed. **^19F{^1H} NMR (377 MHz, CD_2Cl_2, CFCl_3):** δ −78.8 ppm (s, 3F; OTf). **^31P{^1H} NMR (162 MHz, CD_2Cl_2, H_3PO_4):** δ −5.2 ppm (s, 1P). **^13C{^1H} NMR (125 MHz, CD_2Cl_2, Me_4Si):** δ 161.0 (d, J_PC = 36 Hz, 1C; i-py), 146.0 (d, J_PC = 1 Hz, 1C; m-py), 144.3 (d, J_PC = 2 Hz, 1C; m-py), 135.1 (d, J_PC = 22 Hz, 4C; o-Ph), 131.9 (d, J_PC = 6 Hz, 1C; o-py), 131.8 (d, J_PC = 1 Hz, 2C; p-Ph), 130.6 (d, J_PC = 8 Hz, 2C; i-Ph), 130.2 (d, J_PC = 8 Hz, 4C; m-Ph), 126.7 (d, J_PC = 1 Hz, 1C; p-py), 120.7 ppm (q, J_FC = 320 Hz, 1C; OTf).

**MS-DART:** Calculated for [M]^+\: 264.1. Observed mass: 264.09378 amu.

\([(o-C_5H_4NCH_3)PF_2Ph_2][OTf] (2-11)\)

MeOTf (1 mL, 8.83 mmol, 2.5 equiv.) was added, dropwise, to a solution of 2-4 (1.05 g, 3.49 mmol, 1.0 equiv.) in CH_2Cl_2 (5 mL). The reaction mixture was stirred for 1.5 h at ambient temperature. The solution volume was reduced to ca. 1 mL and then 3 mL of *n*-pentane was added. After agitation for 2 min, a white solid settled out of solution. The supernatant was decanted and
the solid was washed with n-pentane (3 x 5 mL). All volatiles/solvents were removed in vacuo to afford a white microcrystalline solid. (1.58 g, 98% Yield). Single crystals of 2-11 suitable for X-ray diffraction were obtained from slow diffusion of n-pentane into a concentrated CH₂Cl₂ solution at −35 °C.

¹H NMR (400 MHz, CD₂Cl₂, Me₄Si): δ 9.10 (m, 1H; m-py), 8.50 (m, 1H; p-py), 8.20 (dd, ³JHH = 15 Hz, ³JHH = 15 Hz, 4H; m-Ph), 8.00 (m, 1H; o-py), 7.97 (m, 1H; m-py), 7.70 (m, 2H; p-Ph), 7.60 (m, 4H; o-Ph), 4.40 ppm (s(br), 3H; N-C₃H₃). ¹⁹F{¹H} NMR (377 MHz, CD₂Cl₂, CFCl₃): δ −40.9 (d, ¹JPF = 705 Hz, 2F; PF₂), −79.0 ppm (s, 3F; OTf). ³¹P{¹H} NMR (162 MHz, CD₂Cl₂, H₃PO₄): δ −55.6 ppm (t, ¹JPF = 705 Hz, 1P). ¹³C{¹H} NMR (125 MHz, CD₂Cl₂, Me₄Si): δ 156.9 (dt, ¹JPC = 210 Hz, ²JFC = 50 Hz, 1C; i-py), 149.0 (d, ³JPC = 7 Hz, 1C; m-py), 145.9 (d, ³JPC = 12 Hz, 1C; m-py), 136.6 (dt, ³JPC = 14 Hz, ⁴JFC = 11 Hz, 4C; m-Ph), 134.9 (dt, ⁴JFC = 4 Hz, ⁴JFC = 1 Hz, 1C; p-py), 130.9 (dt, ¹JPC = 177 Hz, ²JFC = 24 Hz, 2C; i-Ph), 130.4 (dt, ²JPC = 17 Hz, ³JFC = 2 Hz, 4C; o-Ph), 129.5, (d, ⁴JFC = 2 Hz, 2C; p-Ph), 121.4 (q, ¹JFC = 321 Hz, 1C, OTf), 50.3 ppm (m, 1C; N-CH₃), resonance for the ortho-bound pyridyl carbon atom was not observed. MS-ESI: Calculated for M⁺: 316.11. Observed mass: 316.1065 amu. Anal. Calcd. for C₁₉H₁₇F₅NO₃PS: C, 49.0; H, 3.7; N, 3.0 %. Found: C, 48.9; H, 3.7; N, 3.0 %.

[(o-C₅H₄NCH₃)PFPh₂][OTf]₂ (2-12)

TMSOTf (0.12 mL, 0.646 mmol, 1.0 equiv.) was added, dropwise, to a solution of 2-11 (301 mg, 0.646 mmol, 1.0 equiv.) in CH₂Cl₂ (5 mL). After stirring for 24 h at ambient temperature, a white solid settled out of the solution. The solvent volume was reduced to 1 mL in vacuo, 5 mL n-pentane was added, and the solution was cooled to −50 °C. The supernatant was decanted, and the solid was washed with n-pentane (3 x 5 mL). After drying in vacuo, a white powder was isolated (310 mg, 81% Yield).

¹H NMR (400 MHz, CD₃CN, Me₄Si): δ 9.32 (m, 1H; m-py), 8.81 (m, 1H; p-py), 8.63 (m, 1H; o-py), 8.37 (m, 1H; m-py), 8.27 (m, 2H; p-Ph), 8.12 (dd, ³JHH = 15 Hz, ³JHH = 15 Hz, 4H; m-Ph),
7.99 (m, 4H; o-Ph), 4.45 ppm (d, \( J_{PH} = 3 \) Hz, 3H; N-CH\(_3\)). \(^{19}\text{F}\{^{1}\text{H}\} \) NMR (377 MHz, CD\(_2\)CN, CFC\(_3\)): \( \delta \) –79.3 (s, 6F; OTf), –123.9 ppm (d, \( J_{PF} = 1035 \) Hz, 1F; [PF]\(^{2+}\)). \(^{31}\text{P}\{^{1}\text{H}\} \) NMR (162 MHz, CD\(_2\)CN, H\(_3\)PO\(_4\)): \( \delta \) 88.8 ppm (d, \( J_{PF} = 1035 \), 1P). \(^{13}\text{C}\{^{1}\text{H}\} \) NMR (125 MHz, CD\(_3\)CN, Me\(_4\)Si): \( \delta \) 155.5 (d, \( J_{PC} = 5 \) Hz, 1C; m-py), 147.8 (d, \( J_{PC} = 11 \) Hz, 1C; m-py), 141.5 (dd, \( J_{PC} = 18 \) Hz, \( J_{FC} = 2 \) Hz, 1C; o-py), 141.4 (dd, \( J_{PC} = 3 \) Hz, \( J_{FC} = 2 \) Hz, 1C; p-py), 136.6 (dd, \( J_{PC} = 14 \) Hz, \( J_{FC} = 1 \) Hz, 4C; m-Ph), 136.3 (d, \( J_{PC} = 2 \) Hz, 2C; p-Ph), 132.3 (d, \( J_{PC} = 16 \) Hz, 4C; o-Ph), 122.0 (d, \( J_{PC} = 320 \) Hz, 1C; i-py), 113.2 (dd, \( J_{PC} = 112 \) Hz, \( J_{FC} = 13 \) Hz, 2C; i-Ph), 51.2 ppm (dd, \( J_{PC} = 5 \) Hz, \( J_{FC} = 4 \) Hz, 1C; N-CH\(_3\)), resonance for sulfur-bound carbon atom in [OTf] – anion was not observed. MS-ESI: Calculated for [(o-C\(_5\)H\(_4\)N(CH\(_3\)))PPh\(_2\)]\(^{+}\): 294.10. Observed mass: 294.1042 amu. Anal. Calcd. for C\(_{20}\)H\(_{17}\)F\(_7\)NO\(_6\)PS\(_2\): C, 40.3; H, 2.9; N, 2.3 %. Found: C, 40.8; H, 2.7; N, 2.9 %.

\[ [\text{C}(\text{C}_{6}\text{F}_{5})]_{2} \text{P(BPh)}_{3} \text{F} \]

A solution of freshly prepared \([\text{Et}_{3}\text{Si}][\text{B(C}_{6}\text{F}_{5})_{4}]\text{•}(\text{C}_{7}\text{H}_{8})\) (1.0186 g, 1.04 mmol, 1.9 equiv.) in C\(_6\)D\(_8\)Br (3 mL) was added to a suspension of 2-11 (255 mg, 0.55 mmol, 1.0 equiv.) in toluene (5 mL). The reaction mixture was stirred at ambient temperature for 20 min, resulting in a bright yellow solution. The solvent volume was reduced to half volume and 5 mL of n-pentane was added to induce precipitation. The orange oil was re-dissolved in a minimal amount of CH\(_2\)Cl\(_2\), to which 3 mL of n-pentane was added. After sufficient agitation, the supernatant was decanted and the resulting solid was washed with n-pentane (3 x 3 mL) and dried in vacuo to afford a pale-yellow powder (650 mg, 72% Yield).

\(^{1}\text{H}\) NMR (400 MHz, CD\(_2\)Cl\(_2\), Me\(_4\)Si): \( \delta \) 9.10 (m, 1H; m-py), 8.90 (m, 1H; p-py), 8.70 (m, 1H; o-py), 8.33 (m, 2H; p-Ph), 8.27 (m, 1H; m-py), 8.00 (dd, \( J_{HH} = 15 \) Hz, \( J_{HH} = 5 \) Hz, 4H; o-Ph), 7.80 (dd, \( J_{HH} = 15 \) Hz, \( J_{HH} = 15 \) Hz, 4H; m-Ph), 4.50 ppm (d, \( J_{PH} = 3 \) Hz, 3H; N-CH\(_3\)). \(^{11}\text{B}\{^{1}\text{H}\} \) NMR (128 MHz, CD\(_2\)Cl\(_2\), BF\(_3\)OEt\(_2\)): \( \delta \) –16.7 ppm (s). \(^{19}\text{F}\{^{1}\text{H}\} \) NMR (377 MHz, CD\(_2\)Cl\(_2\), CFC\(_3\)): \( \delta \) –124.2 (d, \( J_{PF} = 1035 \) Hz, 1F; [PF]\(^{2+}\)), –133.0 (m(br), 16F; B(o-C\(_6\)F\(_5\))\(_4\)), –162.0 (t, \( J_{FF} = 20 \) Hz, 8F; B(p-C\(_6\)F\(_5\))\(_4\)), –167.2 ppm (m(br), 16F, B(m-C\(_6\)F\(_5\))\(_4\)). \(^{31}\text{P}\{^{1}\text{H}\} \) NMR (162 MHz, CD\(_2\)Cl\(_2\),
H$_3$PO$_4$): δ 88.9 ppm (d, $^1J_{PF} = 1035$ Hz, 1P). $^{13}$C($^1$H) NMR (125 MHz, CD$_2$Cl$_2$, Me$_4$Si): δ 154.0 (d, $^3J_{PC} = 5$ Hz, 1C; m-py), 148.8 (d, $^3J_{PC} = 10$ Hz, 1C; m-py), 148.5 (d(br), $^1J_{FC} = 240$ Hz, 16C; B(o/m-C$_6$F$_5$)$_4$), 143.0 (d, $^4J_{PC} = 2$ Hz, 2C; p-Ph), 140.4 (dd, $^2J_{PC} = 18$ Hz, $^3J_{FC} = 2$ Hz, 1C; o-py), 138.7 (d(br), $^1J_{FC} = 249$ Hz, 8C; B(p-C$_6$F$_5$)$_4$), 136.7 (d, $^4J_{PC} = 2$ Hz, 1C; p-py), 136.4 (d(br), $^1J_{FC} = 245$ Hz, 16C, B(o/m-C$_6$F$_5$)$_4$), 134.6 (dd, $^3J_{PC} = 14$ Hz, $^4J_{FC} = 1$ Hz, 4C; m-Ph), 133.3 (d, $^2J_{PC} = 16$ Hz, 4C; o-Ph), 109.9 (dd, $^1J_{PC} = 111$ Hz, $^2J_{FC} = 13$ Hz, 2C; i-Ph), 51.2 ppm (m, 1C; N-CH$_3$), resonances for boron-bound carbon atoms in [B(C$_6$F$_5$)$_4$]$^-$ anion and P-bound carbon of the pyridyl moiety were not observed. **MS-ESI:** Calculated for [(o-C$_5$H$_4$NCH$_3$)PPh$_2$O]$^+$: 294.10. Observed mass: 294.1062 amu. **Anal. Calcd.** for C$_{66}$H$_{17}$B$_4$F$_{41}$NP: C, 47.9; H, 1.0; N, 0.9 %. Found: C, 46.6; H, 0.8; N, 0.8 %.

### 2.4.3 FLP Reactivity of 2-5

#### 2.4.3.1 Reaction of 2-5 with Et$_3$SiH

Et$_3$SiH (5.5 µL, 0.03 mmol, 1.0 equiv.) was added to a solution of 2-5 (31.5 mg, 0.03 mmol, 1.0 equiv.) in CD$_2$Cl$_2$ (0.6 mL). The reaction mixture was left at ambient temperature for 3 h and then monitored with multi-nuclear NMR spectroscopy. The reaction mixture was transferred to a vial and the solvent/volatiles were removed in vacuo to remove the Et$_3$SiF side product.

**Figure 2-6.** $^{31}$P($^1$H) NMR spectrum (CD$_2$Cl$_2$) of the crude reaction mixture with 2-5 and Et$_3$SiH.
2.4.3.2 Reaction of 2-5 with Benzaldehyde

Benzaldehyde (PhCHO, 6 µL, 0.06 mmol, 1.0 equiv.) was added to a solution of 2-5 (25.3 mg, 0.06 mmol, 1.0 equiv.) in CD$_2$Cl$_2$ (0.6 mL). The reaction mixture was left at ambient temperature for 20 min and then monitored with multi-nuclear NMR spectroscopy.

Figure 2-7. $^{19}$F$\{^1$H$\}$ NMR spectrum (CD$_2$Cl$_2$) of the crude reaction mixture with 2-5 and Et$_3$SiH.

Figure 2-8. $^{31}$P$\{^1$H$\}$ NMR spectrum (CD$_2$Cl$_2$) of the crude reaction mixture with 2-5 and PhCHO.

Figure 2-9. $^{19}$F$\{^1$H$\}$ NMR spectrum (CD$_2$Cl$_2$) of the crude reaction mixture with 2-5 and PhCHO.
Figure 2-10. $^1$H NMR spectrum (CD$_2$Cl$_2$) of the crude reaction mixture with 2-5 and PhCHO.

Figure 2-11. $^{13}$C{$^1$H} NMR spectrum (CD$_2$Cl$_2$) of the crude reaction mixture with 2-5 and PhCHO.

2.4.3.3 Reaction of 2-5 with Benzophenone

Benzophenone (Ph$_2$CO, 9 mg, 0.05 mmol, 1.0 equiv.) was added to a solution of 2-5 (20 mg, 0.05 mmol, 1.0 equiv.) in CD$_2$Cl$_2$ (0.6 mL). The reaction mixture was left at ambient temperature for 7 d and then monitored with multi-nuclear NMR spectroscopy.

Figure 2-12. $^{31}$P{$^1$H} NMR spectrum (CD$_2$Cl$_2$) of the crude reaction mixture with 2-5 and Ph$_2$CO.
2.4.4 Air Stability Tests of Compounds 2-11 and 2-13

2.4.4.1 Decomposition of 2-11

A CH$_2$Cl$_2$ solution of 2-11 was exposed to air for 48 h. The resulting solution was then dried in vacuo and the off-white solid was washed with n-pentane (3 x 5 mL) to afford an off-white solid.

$^1$H NMR (400 MHz, CD$_2$Cl$_2$, Me$_4$Si): $\delta$ 9.21 (m, 1H; m-py), 8.48 (m, 1H; m-py), 8.23 (m, 1H; p-py), 7.73 (m, 6H; m/p-Ph), 7.61 (m, 5H; o-Ph & o-py), 4.52 ppm (s, 3H; NC$_3$H$_7$).

$^{19}$F$^1$H NMR (377 MHz, CD$_2$Cl$_2$, CFCl$_3$): $\delta$ –78.4 ppm (s, 3F; OTf).

$^{31}$P$^1$H NMR (162 MHz, CD$_2$Cl$_2$, H$_3$PO$_4$): $\delta$ 28.7 ppm (s).

$^{13}$C$^1$H NMR (125 MHz, CD$_2$Cl$_2$, Me$_4$Si): $\delta$ 151.8 (d, $^3$J$_{PC}$ = 4 Hz, 1C; m-py), 149.3 (d, $^1$J$_{PC}$ = 89 Hz, 1C; i-py), 145.6 (d, $^3$J$_{PC}$ = 8 Hz, 1C; m-py), 134.5 (d, $^4$J$_{PC}$ = 3 Hz, 2C; p-Ph), 133.9 (d, $^2$J$_{PC}$ = 13 Hz, 1C; o-py), 132.1 (d, $^3$J$_{PC}$ = 11 Hz, 4C; m-Ph), 131.3 (d, $^4$J$_{PC}$ = 2 Hz, 1C; p-Ph), 130.0 (d, $^2$J$_{PC}$ = 13 Hz, 4C; o-Ph), 126.9 (d, $^1$J$_{PC}$ = 111 Hz, 1C; i-Ph), 48.9 ppm (d, $^3$J$_{PC}$ = 3 Hz, 1C; NCH$_3$), resonance for the sulfur-bound carbon atom of [OTf]$^-$ anion was not observed. MS-ESI: Calculated mass for C$_{18}$H$_{17}$NOP: 294.1042. Observed: 294.1045 amu.

2.4.4.2 Decomposition of 2-13

A CH$_2$Cl$_2$ solution of 2-13 was exposed to air for 48h. The resulting solution was then dried in vacuo and the off-white solid was washed with n-pentane (3 x 5 mL) to afford an off-white solid. Partial characterization by NMR spectroscopy was obtained, which aligned with the data collected for the decomposition of 2-11, suggesting phosphine-oxide formation, as noted above.

$^{19}$F NMR (377 MHz, CD$_2$Cl$_2$, CFCl$_3$): $\delta$ –133.0 (s(br), 8F; B(o-C$_6$F$_5$)$_4$), –163.5 (t, $^3$J$_{FF}$ = 22 Hz, 4F; B(p-C$_6$F$_5$)$_4$), –167.3 ppm (m(br), 8F; B(m-C$_6$F$_5$)$_4$). $^{31}$P$^1$H NMR (162 MHz, CD$_2$Cl$_2$, H$_3$PO$_4$): $\delta$ 28.7 ppm (s).
2.4.5 Reaction of 2-13 with PrBu₃

PrBu₃ (6 mg, 0.03 mmol, 1 equiv.) was added to a solution of 2-13 (52 mg, 0.03 mmol, 1 equiv.) of CD₂Cl₂ (0.6 mL). The reaction mixture was agitated and then transferred to a NMR tube. The reaction progress was monitored by multi-nuclear NMR spectroscopy.

**Figure 2-13.** $^{31}$P{¹H} NMR spectrum (CD₂Cl₂) of 2-13 (top) and the reaction mixture of 2-13 and PrBu₃ after heating to 45 °C for 12 h (bottom).

**Figure 2-14.** ¹H NMR spectrum (CD₂Cl₂) of the reaction mixture after heating to 45 °C for 12 h.
2.4.6 Gutmann-Beckett Lewis Acidity Tests (Reaction with Et₃PO)\textsuperscript{46, 47}

A solution of the phosphonium cation (0.07 mmol) in CD₂Cl₂ (0.6 mL) was added to a separate vial containing Et₃PO (0.07 mmol). The reaction mixture was investigated by multi-nuclear NMR spectroscopy after 1 h at ambient temperature.

2-5. \textsuperscript{31}P\{\textsuperscript{1}H\} NMR (162 MHz, CD₂Cl₂, H₃PO₄): δ 150.2 (d, \textsuperscript{1}J_{PF} = 955 Hz, 1P; [Et₃PF]⁺), 78.7 (d, \textsuperscript{1}J_{PF} = 1000 Hz, 1P; [(o-C₅H₄N)PFPh₂]⁺), 64.1 (s(br), 1P; Et₃PO), 19.7 ppm (s, 1P; (o-C₅H₄N)Ph₂PO).

\textsuperscript{19}F\{\textsuperscript{1}H\} NMR (377 MHz, CD₂Cl₂, CFCl₃): δ −79.0 (s, 3F; OTf), −136.3 (d, \textsuperscript{1}J_{PF} = 1000 Hz, 1F; [(o-C₅H₄N)PFPh₂]⁺), −160.6 ppm (dm, \textsuperscript{1}J_{PF} = 955 Hz, \textsuperscript{3}J_{FH} = 15 Hz, 1F; [Et₃PF]⁺).

![Diagram of reaction](https://example.com/diagram)

**Figure 2-15.** \textsuperscript{31}P\{\textsuperscript{1}H\} NMR spectra (CH₂Cl₂) of Gutmann-Beckett Tests.

2-6. \textsuperscript{31}P\{\textsuperscript{1}H\} NMR (162 MHz, CD₂Cl₂, H₃PO₄): δ 148.1 (d, \textsuperscript{1}J_{PF} = 965 Hz, 1P; [Et₃PF]⁺), 76.8 (d, \textsuperscript{1}J_{PF} = 995 Hz, 1P; [(o-C₅H₄N)PFPh₂]⁺), 60.2 (s(br), 1P; Et₃PO), 20.0 ppm (s, 1P; (o-...
C₅H₄N)Ph₂PO. ¹⁹F{¹H} NMR (377 MHz, CD₂Cl₂, CFCl₃): δ –133.7 (m(br), 8F; B(o-B₆F₅)₄), –134.0 (d, 1F; [(o-C₅H₄N)PFPh₂]⁺), –159.0 (dm, 1JFF = 965 Hz, 3JFH = 15 Hz, [Et₃PF]⁺), –163.7 (t, 3JFF = 20 Hz, 4F; B(p-C₆F₅)₄), –167.5 ppm (m(br), 8F; B(m-B₆F₅)₄).

2-12. ³¹P{¹H} NMR (162 MHz, CD₂Cl₂, H₃PO₄): δ 150.3 (d, 1JPF = 955 Hz, 1P; [Et₃PF]⁺), 52.8 (s(br), 1P; Et₃PO), 27.8 (s, 1P; [(o-C₅H₄NCH₃)PPh₂O]⁺), –55.7 ppm (t, 1JPF = 700 Hz, 1P; 1).

¹⁹F{¹H} NMR (377 MHz, CD₂Cl₂, CFCl₃): δ –40.9 (d, 2F; 1), –79.0 (s, 6F; OTf), –160.8 ppm (dm, 3JFH = 15 Hz, [Et₃PF]⁺).

2-13. ³¹P{¹H} NMR (162 MHz, CD₂Cl₂, H₃PO₄): δ 147.7 (d, 1JPF = 981 Hz, 1P; [Et₃PF]⁺), 27.9 ppm (s, 1P; [(o-C₅H₄NCH₃)PF₃]⁺). ¹⁹F{¹H} NMR (377 MHz, CD₂Cl₂, CFCl₃): δ –133.7 (m(br), 16F; B(o-B₆F₅)₄), –159.0 (dm, 3JFH = 15 Hz, 1F; [Et₃PF]⁺), –163.7 (t, 3JFF = 20 Hz, 8F; B(p-C₆F₅)₄), –167.5 ppm (m(br), 16F; B(m-B₆F₅)₄).

2.4.7 Lewis Acid Catalysis

2.4.7.1 Friedel-Crafts Dimerization of 1,1-Diphenylethylene

In a 20 mL vial, a solution of the phosphonium catalyst (2 mol%) was prepared in 0.6 mL CD₂Cl₂. 1,1-diphenylethylene (0.2 mmol) was added at ambient temperature and the reaction mixture was transferred to a NMR tube. The sample was sealed, aggregated and allowed to react at ambient temperature for the desired time, giving 1-methyl-1,3,3-triphenyl-2,3-dihydro-1H-indene. For the reaction with 2-13, the reaction mixture was dried in vacuo and the solid was re-dissolved in 5 mL of n-pentane. The suspension was filtered through a Celite plug and dried in vacuo to afford a white microcrystalline solid (48.7 mg, 97% Yield).

¹H NMR (400 MHz, C₆D₆, Me₄Si): δ 7.23 (m, 19H; Ar-H), 3.47 (d, 3JHH = 13Hz, 1H; CH₂), 3.20 (d, 3JHH = 13 Hz, 1H; CH₂), 1.63 ppm (s, 3H; CH₃). ¹³C{¹H} NMR (125 MHz, C₆D₆, Me₄Si): δ 151.0 (s, 1C; Ph), 149.7 (s, 1C; Ph), 149.4 (s, 1C; Ph), 149.1 (s, 1C; Ph), 147.9 (s, 1C; Ph), 129.3 (s, 2C; Ph), 129.1 (s, 2C; Ph), 128.3 (s, 2C; Ph), 128.0 (s, 2C; Ph), 127.9 (s, 2C; Ph), 127.3 (s, 2C; Ph), 127.3 (s, 1C; Ph), 126.3 (s, 1C; Ph), 126.0 (s, 1C; Ph), 125.9 (s, 1C; Ph), 125.4 (s, 1C; Ph), 61.8 (s, 1C; CPh), 61.4 (s, 1C; CPh), 51.5 (s, 1C; CH₂), 29.1 ppm (s, 1C; CH₃).
2.4.7.2 Hydrodefluorination of 1-Fluoropentane With Et$_3$SiH$^{10, 12, 13}$

In a 20 mL vial, a solution of the phosphonium catalyst (5 mol%) was prepared in 0.7 mL CD$_2$Cl$_2$. Et$_3$SiH (0.04 mmol) was added at ambient temperature, the reaction was briefly stirred, and then 1-fluoropentane was added (0.04 mmol). Fluorobenzene (C$_6$H$_5$F, 0.03 mmol) was then added as an internal standard. The reaction mixture was transferred to a NMR tube and left at ambient temperature for 4 h, before being monitored by $^{19}$F{$^1$H} NMR spectroscopy. Conversions were determined from the proportion of Si-F bonds in Et$_3$SiF formed relative to C-F bonds in 1-fluoropentane consumed.$^{13}$

![Figure 2-16. $^{19}$F{$^1$H} NMR spectrum (CH$_2$Cl$_2$) for the hydrodefluorination of 1-fluoropentane with 2-13.](image)

2.4.7.3 Hydrosilylation of α-methylstyrene with Et$_3$SiH$^{12, 13, 17}$

In a 20 mL vial, a solution of the phosphonium catalyst (2 mol%) was prepared in 0.7 mL CD$_2$Cl$_2$. Et$_3$SiH (0.05 mmol) was added at ambient temperature, the reaction mixture was briefly stirred, and then α-methylstyrene (0.05 mmol) was added. The mixture was transferred to a NMR tube and heated at 45 °C for 4 h. For the reaction with 2-13, the solvent volume was reduced in vacuo to ca. 1 mL. 3 mL of $n$-pentane was added and the suspension was filtered through a Celite plug. The filtrate was dried in vacuo, giving a colourless oil. (50 mg, 85% Yield).

$^1$H NMR (400 MHz, C$_6$D$_5$Br, Me$_4$Si): $\delta$ 7.27 (m, 4H; o- & p-Ph), 7.18 (m, 1H; p-Ph), 2.37 (m, 1H; CH), 1.30 (d, $^3$J$_{HH}$ = 7 Hz, 3H; CH$_3$), 1.00 (m, 2H; CH$_2$), 0.91 (t, $^3$J$_{HH}$ = 8 Hz, 9H; SiCH$_2$CH$_3$), 0.46 ppm (m, 6H; SiCH$_2$CH$_3$). $^{13}$C{$^1$H} NMR (125 MHz, C$_6$D$_5$Br, Me$_4$Si): $\delta$ 149.8 (s, 1C; i-Ph),
128.4 (s, 2C; o/m-Ph), 126.7 (s, 2C; o/m-Ph), 125.9 (s, 1C; p-Ph), 36.2 (s, 1C; CH), 26.8 (s, 1C; CH₃), 21.6 (s, 1C; CH₂), 7.7 (s, 1C; SiCH₂CH₃), 3.9 ppm (s, 1C; SiCH₂CH₃).

2.4.7.4 Dehydrocoupling of Phenol and Et₃SiH\textsuperscript{13, 16}

In a 20 mL vial, a solution of the phosphonium catalyst (2 mol%) was prepared in 0.7 mL CD₂Cl₂. Et₃SiH (0.05 mmol) was added at ambient temperature, the reaction mixture was briefly stirred, and then added to a vial containing phenol (0.05 mmol). The mixture was transferred to a NMR tube and heated at 50 °C for 24 h. For the reaction with 2-13, the solvent volume was reduced in vacuo to ca. 1 mL. 3 mL of n-pentane was added and the suspension was filtered through a Celite plug. The filtrate was dried in vacuo, giving a colourless oil. (56 mg, 79% Yield).

\textsuperscript{1}H NMR (400 MHz, C₆D₅Br, Me₄Si): δ 7.00 (m, 2H; o/m-Ph), 6.72 (m, 3H; p-Ph & o/m-Ph), 0.80 (t, \textsuperscript{3}J_{HH} = 8 Hz, 9H; CH₃), 0.50 ppm (q, \textsuperscript{3}J_{HH} = 8 Hz, 6H; CH₂). \textsuperscript{13}C{\textsuperscript{1}H} NMR (125 MHz, C₆D₅Br, Me₄Si): δ 155.7 (s, 1C; i-Ph), 129.5 (s, 2C; o/m-Ph), 121.4 (s, 1C; p-Ph), 120.0 (s, 2C; o/m-Ph), 6.9 (s, 3C; CH₃), 5.2 ppm (s, 3C; CH₂).

2.4.7.5 Hydrodeoxygenation of Benzophenone with Et₃SiH\textsuperscript{20}

In a 20 mL vial, a solution of the phosphonium catalyst (1 mol%) was prepared in 0.7 mL CD₂Cl₂. Et₃SiH (0.04 mmol) was added at ambient temperature, the reaction was briefly stirred, and then the solution was added to a vial containing benzophenone (0.02 mmol). The reaction mixture was left to stir at ambient temperature for 2 h, before toluene (0.02 mmol) was added as an internal standard. The reaction mixture was transferred to a NMR tube and monitored by \textsuperscript{1}H NMR spectroscopy.

\textsuperscript{1}H NMR (400 MHz, CD₂Cl₂, Me₄Si): δ 7.29 (4H, m, Ph), 7.20 (6H, m, Ph), 3.98 ppm (2H, s, CH₂). \textsuperscript{13}C{\textsuperscript{1}H} NMR (125 MHz, CD₂Cl₂, Me₄Si): δ 141.4 (s, Ph), 128.8 (s, Ph), 128.4 (s, Ph), 126.0 (s, Ph), 41.9 ppm (s, CH₂).

2.4.8 Computational Details

All calculations were performed by fellow graduate student James La Fortune:

Electronic structure calculations, including geometry optimizations and frequency calculations, were performed using Gaussian 16\textsuperscript{58} using the BP86\textsuperscript{59, 60} functional and the Def2-TZVP\textsuperscript{61, 62} basis
set. Each geometry was confirmed to be a minimum on its potential energy surface by confirming the Hessian to be positive definite with a frequency calculation. Orbital and internal energies needed to calculate fluoride ion affinity (FIA)\textsuperscript{63} and the global electrophilicity index (GEI)\textsuperscript{50, 51} were obtained using the MP2\textsuperscript{64} method and the Def2-TZVPP basis set at the BP86/Def2-TZVP optimized geometries. FIA and GEI were calculated as previously described.\textsuperscript{65}

2.4.9 Crystallographic Analysis of 2-7, 2-11 and 2-12

Single crystals were coated with Paratone-N oil and mounted in a cryo-loop. Data were collected on a Bruker Kappa Apex II diffractometer using graphite monochromated MoKα radiation (\(\lambda = 0.71073\) Å). The temperature was maintained at 150 K using an Oxford Cryostream cooler for both, initial indexing and full data collection. Data were collected using Bruker APEX-2 program. All structures were solved by direct methods within the SHELXTL package\textsuperscript{66} and refined against \(F^2\) using first isotropic and anisotropic thermal parameters for all non-hydrogen atoms. Hydrogen atoms bonded to carbon atoms were generated with idealized geometries and isotropically refined using a riding model.
**Table 2-2.** Crystallographic details of the structure refinements of 2-7, 2-11 and 2-12.

<table>
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<th>2-7</th>
<th>2-11</th>
<th>2-12</th>
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2.5 References


47. V. Gutmann, *Coordination Chemistry Reviews*, 1976, **18**, 225-255.


3 Introduction

3.1 Air-stable Phosphonium Salts

Quaternary phosphonium salts derive considerable Lewis acidic character from their capacity to accept electron density into their $\sigma^*(P-X)$ orbitals. This innate Lewis acidity at phosphorus is significantly enhanced when the X-substituents are strongly electron-withdrawing, because the hypervalent bond formed by reaction between the phosphonium salt and the substrate is stabilized.\(^1\) Several Lewis acidic phosphonium cations have already demonstrated their efficiency as catalysts or initiators in different organic transformations. For example, Diels-Alder cycloadditions,\(^2\) and cyanosilylation of aldehydes and ketones\(^3,4\) reactions have been catalyzed by phosphorus(V) cations. The scope of phosphonium catalysts has also been expanded and now encompasses a library of enantiomerically pure chiral phosphonium salts (Figure 3-1).\(^5-10\) One notable feature in these compounds is the lack of a strong electron-withdrawing group (EWG) such as fluoride. While the overall reactivity of these robust catalysts may suffer, the enhancements in air and water-stability are desirable for benchtop, large-scale reactions and, in some cases, supersede the need for highly electron-withdrawing groups.

![Figure 3-1. Examples of chiral phosphonium salt catalysts.](Image)

The stability of tetraalkyl and tetraarylphosphonium salts in aqueous media has been exploited in ionic liquids, wherein phosphorus(V) cations have been widely used as phase transfer catalysts for a variety of different transformations.\(^6,7,11-14\) In these cases, the stability in water and solubility in both organic and aqueous media are necessary, and the catalysis is believed to be due to the ability
of the organic-soluble cations to repeatedly bring anions into the organic phase in a form suitable for reaction.\textsuperscript{15}

As was noted in Chapter 1, one of the most promising advances in the area of phosphorus(V) Lewis acid catalysis was work disclosed by Terada and Kouchi in 2006, wherein a phosphonium salt was shown to catalyze a Diels-Alder reaction.\textsuperscript{2} Specifically, these authors designed a family of electrophilic phosphonium cations (EPCs) with oxygenated functionalities as electron-withdrawing substituents and tested their reactivity with different donors.

Since this seminal report, the field of phosphorus Lewis acid chemistry has grown significantly; however, to date, most compounds require strict air- and moisture-free reaction conditions. Since the report in 2013 by Caputo \textit{et al.},\textsuperscript{16} there have been several attempts to develop more robust EPCs. In one report, substitution of the pentafluorophenyl groups in [(C\textsubscript{6}F\textsubscript{5})\textsubscript{3}PF]\textsuperscript{+} by less electron-withdrawing substituents (\textit{e.g.} C\textsubscript{6}Cl\textsubscript{5}, Ph) generates more stable compounds; however, the Lewis acidic reactivity decreases.\textsuperscript{17} Similarly, substitution of the reactive P-F bond for P-CF\textsubscript{3} increases stability but decreases reactivity.\textsuperscript{18}

\textbf{3.1.2 Mukaiyama-aldol Condensation Reactions}

One of the first phosphonium salt-catalyzed reactions was performed by Mukaiyama \textit{et al.} in 1989. In this classical reaction, catalytic amounts of various P(V) phosphonium salts were used to facilitate aldol reactions between different silyl enol ethers and aldehydes (Scheme 3-1).\textsuperscript{19} In this reaction, the phosphonium catalyst is believed to activate the carbonyl oxygen to increase the electrophilicity of the carbon atom, facilitating nucleophilic attack from the silyl enol ether to afford the desired aldol product. Different tetraalkylphosphonium salts were probed as catalysts for the reaction. Interestingly, changing the bromide anion to perchlorate resulted in increased catalytic activity, wherein the most active catalysts for this transformation were dicationic phosphonium species with a bridging oxygen atom.
The scope of this reaction was expanded to later include acetals and different silyl enolate nucleophiles. As well, the same dicationic phosphonium species was used to facilitate Michael additions between α,β-unsaturated aldehydes or acetals and silyl or alkyl enolates, and Imino-Mukaiyama-Aldol reactions, wherein imine substrates were used instead of carbonyl groups. Since the initial report of a Lewis acid-catalyzed Mukaiyama-aldol reaction in 1973 with TiCl₄, this reaction has become a valuable tool for the synthesis of stereochemically complex molecules from two carbonyl compounds, and in the development of natural products. Many other stoichiometric Lewis acidic additives have been developed, such as SnCl₄, AlCl₃, FeCl₃ and ZnCl₂ among others. As well, non-metal Lewis acids such as triphenylmethyl “trityl” salts and TMSOTf have been utilized as catalysts. However, in these cases, and most others, strict anhydrous conditions are required, which has spearheaded the development of water-stable Lewis acids. In 1991, Ln(OTf)₃ was shown to be an effective Lewis acid catalyst for the Mukaiyama-aldol reaction in aqueous media. Since this report, other rare-earth metal cations and transition metal compounds were strategically designed to enhance water stability; however, reports of robust Lewis acidic phosphorus species for this transformation remain scarce.

3.1.3 Lewis Acid Catalyzed Hydroarylation

Since the initial report in 1877 using an AlCl₃ catalyst, a variety of other Lewis acids have been shown to mediate Friedel-Crafts reactions. However, despite the widespread use of this transformation in organic chemistry, it wasn’t until 2015 that a report was published using a phosphorus(V) catalyst for Friedel-Crafts type hydroarylation and hydrothiolation reactions. In this report, [(C₆F₅)₃PF][B(C₆F₅)₄] was shown to be an efficient catalyst for the hydroarylation and hydrothiolation of olefins under mild conditions, facilitating formation of various substituted heterocycles and alkyl aryl thioethers, respectively. The reaction mechanism for both hydroarylation and hydrothiolation is believed to proceed through an initial activation of the olefin.
by the EPC catalyst. Then, generation of a transient carbocation facilitates interaction with the nucleophilic site (para-C or S atom), promoting C-C bond formation. Proton transfer then liberates the Friedel-Crafts product and regenerates the phosphonium catalyst (Scheme 3-2).

\[
\text{Scheme 3-2. Proposed mechanism for EPC-catalyzed hydrothiolation and hydroarylation reactions.} \quad [P] = [(C_6F_5)_3PF][B(C_6F_5)_4]; \text{the } [B(C_6F_5)_4] \text{ counterion has been omitted for clarity.}
\]

The scope of EPC-catalyzed Friedel-Crafts reactions was later expanded to encompass benzylation or alkylation of aryl and alkyl CF₃ groups and the C-C coupling of benzyl fluoride and various arenes. In these reactions, the initial generation of a carbocation is proposed to proceed through activation of a C-F bond. In the presence of Et₃SiH, nucleophilic attack at the transient carbocation facilitates the loss of H₂. In the case of the CF₃ substrates, rapid hydrodefluorination is believed to occur, generating the desired C-C coupled product.

3.2 Results and Discussion

3.2.1 Cyclopropenium and Pyridiniumphosphonium Dications as Lewis Acid Initiators for the Mukaiyama-Aldol Reaction

Given the previously reported instability of EPCs as a result of the polar P-F bond, we sought to modify the substituents around phosphorus to develop systems less susceptible to degradation. In addition to ease of handling, such stability would allow for more facile reaction monitoring and greater reaction efficiency, subsequently decreasing waste produced from the reaction and avoiding the use of energy-intensive systems (e.g. inert atmosphere chambers). In this regard, we
targeted systems with less polar P-C and P-O bonds, wherein the electrophilicity would be imparted by the addition of positive charges.

### 3.2.1.1 Synthesis of Cyclopropenium Phosphonium Salts

To begin our investigation, we targeted dications with cyclopropenium- and pyridiniumphosphonium scaffolds.\(^{31,32}\) While the quaternization of tertiary phosphines with aryl halides is not a common process, it can be carried out satisfactorily using electron-poor aryl halides.\(^{33}\) In a similar vein, we targeted 2,3-bis(diisopropylamino)-1-chlorocyclopropenium tetrafluoroborate 3-1 as the starting framework. Upon mixing 3-1 with PPh\(_3\) in the presence of [Na][BF\(_4\)], dication 3-2 was obtained in 95% isolated yield and characterized by NMR spectroscopy, mass spectrometry and X-ray crystallography (Scheme 3-3). The \(^{31}\)P{\(^1\)H} NMR spectrum (CD\(_3\)CN) displays a singlet resonance at \(\delta 9.3\) ppm, which is shifted downfield relative to PPh\(_3\) (\(\delta – 5.9\) ppm).\(^{34,35}\)

Similarly, the analogous phosphines Ph\(_2\)PR (R = Me, Bn, 2-pyridine) and P(4-(F)C\(_6\)H\(_4\))\(_3\) were reacted with 2,3-bis(diisopropylamino)-1-chlorocyclopropenium tetrafluoroborate to afford salts of the corresponding dications 3-2 to 3-6, respectively. All these salts were isolated as white solids in yields ranging from 85-96% (Scheme 3-3). The \(^{31}\)P{\(^1\)H} NMR spectra of these compounds all display the downfield resonance shift relative to PPh\(_3\), and the structure of several were confirmed by single crystal X-ray diffraction.\(^{34}\) It is noteworthy that similar to [OTf]\(^-\) salts synthesized in Chapter 2, these [BF\(_4\)]\(^-\) salts displayed limited solubility in a variety of organic solvents. Therefore, to increase the solubility of 3-2 to 3-6 in a common organic solvent like CH\(_2\)Cl\(_2\), we synthesized the corresponding [B(C\(_6\)F\(_5\))\(_4\)]\(^-\) salts. While 3-7 to 3-10 were all synthesized successfully by reaction with 2 equiv. [K][B(C\(_6\)F\(_5\))\(_4\)], the [B(C\(_6\)F\(_5\))\(_4\)]\(^-\) salt of 3-6 could not be isolated. The \(^{31}\)P{\(^1\)H} NMR spectra (CD\(_3\)CN) for the [B(C\(_6\)F\(_5\))\(_4\)]\(^-\) derivatives were almost identical to the resonances corresponding to the [BF\(_4\)]\(^-\) counterparts. Moreover, the [B(C\(_6\)F\(_5\))\(_4\)]\(^-\) salts were soluble in polar organic solvents such as CH\(_2\)Cl\(_2\) and Et\(_2\)O.
Scheme 3-3. Syntheses of cyclopropenium-substituted phosphonium salts.

In addition to the cyclopropenium-substituted phosphonium salts already described, the pyrrolidine-decorated cyclopropenium salt 3-12 was also prepared from precursor 3-11 using the same route and reaction conditions and isolated in 79% yield (Scheme 3-3). Counterion exchange with 2 equiv. of [K][B(C₆F₅)₄] yielded the corresponding [B(C₆F₅)₄]⁻ salt 3-13 in quantitative yield after 10 min at ambient temperature. Remarkably, all cyclopropenium-substituted salts herein described could be stored in air for extended periods of time without signs of decomposition.

3.2.1.2 Synthesis of Pyridinium Phosphonium Salts

Comparison of the donor properties of α-pyridinio- and α-cyclopropenio phosphine ligands reveals that the pyridinium group more efficiently depletes electron density from the phosphorus atom.32, 36-39 In this regard, we postulated that pyridinium-substituted phosphonium salts should exhibit higher Lewis acidity than their cyclopropenium analogues. Several different methods were used to synthesize these pyridiniumphosphonium salts. The first method – and the most commonly used – was a nucleophilic aromatic substitution reaction with tertiary phosphate nucleophiles and halopyridine electrophiles. In an initial reaction, 2-bromopyridine was heated at 140 °C for 3 h with an equimolar amount of PPh₃. After washing with EtOAc and Et₂O, the solid was treated with a saturated aqueous solution of [K][OTf] to generate triphenyl-2-pyridylphosphonium triflate 3-
14 in 87% yield. Analysis of the $^{31}$P{\textsuperscript{1}H} NMR spectrum (CD$_3$CN) reveals a singlet resonance $\delta$ 14.6 ppm, which aligns with the reported literature values,\textsuperscript{40,41} and is shifted downfield relative to (o-C$_6$H$_4$N)PPh$_2$ ($\delta$ –4.2 ppm).\textsuperscript{42} It is noteworthy that while Meciarova et al. followed a similar procedure with LiOTf, poor yields were obtained (40%).\textsuperscript{41} Afterwards, 3-14 was mixed with an excess amount of MeOTf and heated for 12 h at 60 °C, giving the dicatonic phosphonium salt 3-15 in 69% isolated yield (Scheme 3-4). The $^{31}$P{\textsuperscript{1}H} NMR spectrum (CD$_3$CN) of 3-15 contains a singlet resonance at $\delta$ 23.7 ppm, which is shifted slightly downfield relative to its monocationic counterpart 3-14. The methylene protons are observed in the $^1$H NMR spectrum as a singlet at $\delta$ 3.99 ppm, which is comparable to the cation [(o-C$_6$H$_4$NCH$_3$)PPh$_2$]⁺ ($\delta$ 4.30 ppm)\textsuperscript{38} and pyridinium-fluorophosphonium salt 2-12 ($\delta$ 4.50 ppm).

\begin{align*}
&\text{Scheme 3-4. Synthesis of pyridiniumphosphonium dications 3-15 to 3-19.}
\end{align*}

Reaction of 3-15 with 2 equiv. of [K][B(C$_6$F$_5$)$_4$] facilitated anion exchange upon removal of the [K][OTf] side product, giving the [B(C$_6$F$_5$)$_4$]⁻ salt 3-16 in quantitative yield. The multi-nuclear NMR spectra (CD$_3$CN) are comparable to those reported for the [OTf]⁻ salt 3-15. Following a similar protocol, 4-iodopyridine was converted to the corresponding phosphonium cation 3-17 by reaction with PPh$_3$. Then, alkylation with MeOTf, with concurrent anion exchange afforded the [OTf]⁻ phosphonium salt 3-18 in 63% isolated yield. The $^{31}$P{\textsuperscript{1}H} NMR spectrum (CD$_3$CN) contains a singlet resonance at $\delta$ 23.0 ppm, which is analogous to the ortho-substituted analogue 3-15. As well, Hilton et al. reported a related quaternary phosphonium salt (2-fluoropyridin-4-yl)triphenylphosphonium triflate with a $^{31}$P{\textsuperscript{1}H} resonance at $\delta$ 22.1 ppm.\textsuperscript{43} Similarly, the $^1$H NMR spectrum displays a singlet resonance at $\delta$ 4.47 corresponding to the N-bound methylene protons.
Anion exchange was then facilitated by reaction of 3-18 with 2 equiv. of [K][B(C₆F₅)₄], and removal of the [K][OTf] side product generated [B(C₆F₅)₄]⁻ salt 3-19 in quantitative yield.

In a similar vein, we targeted the synthesis of the meta-pyridylphosphonium analogue; however, the less reactive 3-position prevented the analogous nucleophilic aromatic substitution reaction. For this reason, a Pd-catalyzed coupling approach was pursued. In this reaction, 3-bromopyridine was reacted with 1 equiv. of PPh₃ in the presence of a catalytic amount of Pd₂(dba)₃ and heated for 12 h at 160 °C. After washing with EtOAc and Et₂O, the solid was treated with a saturated aqueous solution of [K][OTf], giving [(m-C₆H₄N)PPh₃][OTf] 3-20 in 89% isolated yield (Scheme 3-5). The NMR spectra are unexceptional; the ³¹P{¹H} NMR spectrum (CD₃CN) contains a singlet resonance at δ 20.7 ppm, which is closely related to the chemical shifts for 3-14 and 3-17. Subsequent methylation of 3-20 with MeOTf gives the desired dicaticionic salt 3-21 in 35% yield. Similar to the ortho- and para-substituted N-methylpyridinium phosphonium salts 3-15 and 3-18, the ³¹P{¹H} NMR spectrum (CD₃CN) of 3-12 contains a singlet resonance at δ 21.6 ppm, and the N-bound methylene protons appear at δ 4.38 ppm in the ¹H NMR spectrum. 3-21 was then transformed into its [B(C₆F₅)₄]⁻ salt 3-22 upon reaction with 2 equiv. of [K][B(C₆F₅)₄]. In this case, the ³¹P{¹H} and ¹H NMR spectra (CD₃CN) remain unchanged. Salts 3-15, 3-18 and 3-21 were also characterized by X-ray crystallography, however a detailed discussion has already been reported by Barrado et al.; thus, they have been excluded from this thesis report.

![Scheme 3-5. Synthesis of m-pyridiniumphosphonium salt 3-22.](image)

To further derivatize the phosphonium framework, we chose to substitute one of the phenyl substituents for a CH₃ group. To obtain the desired ortho-substitution, commercially available 2-pyridyldiphenyl phosphine was used, and methylation of both the N and P centres was achieved after stirring a solution of 2-pyridyldiphenylphosphine and 4 equiv. of MeOTf at ambient temperature for 3 d. Removal of excess MeOTf resulted in the isolation of salt 3-23 in 81% yield (Scheme 3-6). Analysis of the ³¹P{¹H} NMR spectrum (CD₃CN) reveals a singlet resonance at δ
26.0 ppm, which is shifted slightly downfield relative to 3-15. The $^1$H NMR spectrum contains resonances for the N-bound and P-bound methylene protons at $\delta$ 4.40 ppm (s) and $\delta$ 3.40 ppm (d, $^2J_{PH} = 13$ Hz), respectively. Counterion exchange could then be achieved at ambient temperature upon reaction with [K][B(C$_6$F$_5$)$_4$] and removal of the [K][OTf] side product, generating salt 3-24.


In addition, using a modified literature procedure, 45 3-pyridyldiphenylphosphine 3-25 was synthesized and subsequently subjected to double methylation with an excess amount of MeOTf, resulting in the formation of the corresponding salt 3-26 in 63% yield (Scheme 3-7). Then, counterion exchange with [K][B(C$_6$F$_5$)$_4$] furnished 3-27 in 69% isolated yield. The $^{31}$P{$^1$H} NMR spectra of 3-26 and 3-27 contain $^{31}$P{$^1$H} NMR singlet resonances at $\delta$ 22.6 and 22.7 ppm, respectively, which are slightly shifted upfield relative to the ortho-substituted analogues 3-23 and 3-24.

Scheme 3-7. Synthesis of $m$-pyridiniumphosphonium salt 3-27.

3.2.1.3 Mukaiyama-Aldol Condensation Reactions Initiated by Phosphorus(V) Dications

The P(V) dications prepared were employed as Lewis acid initiators for a typical Mukaiyama-Aldol reaction using 2-napthaldehyde and 1-methoxy-2-methyl-1-trimethylsiloxypropene (Table 3-1). 19, 20 Conversions for these reactions were determined by $^1$H NMR spectroscopy using toluene as an internal standard. In the absence of phosphonium salt, no conversion to product was observed after 48 h. A similar result (<5% conversion) was obtained when 10 mol% 3-2 was employed as
the initiator (Table 3-1, Entry 3). However, when the corresponding [B(C₆F₅)₄]⁻ salt 3-7 was employed in Et₂O, complete conversion to the desired product was observed after 1 h at ambient temperature (Table 3-1, Entry 4). This result suggests that the non-coordinating [B(C₆F₅)₄]⁻ anion is essential for reaction, which has been previously observed⁴⁶, ⁴⁷ and reported in Chapter 2. Moreover, reduction of the phosphonium salt loading to 3 mol% slowed the reaction, but quantitative conversion to product was nevertheless obtained after 3 h (Table 3-1, Entry 5).

![Mukaiyama-Aldol Condensation Reaction](image)

**Table 3-1.** Phosphonium-Initiated Mukaiyama-Aldol Condensation Reactions.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Phosphonium salt</th>
<th>Mol%</th>
<th>Time</th>
<th>Solvent</th>
<th>Conv.(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>none</td>
<td>-</td>
<td>24 h</td>
<td>Et₂O</td>
<td>0</td>
</tr>
<tr>
<td>2</td>
<td>3-2</td>
<td>2</td>
<td>24 h</td>
<td>CH₂Cl₂</td>
<td>0</td>
</tr>
<tr>
<td>3</td>
<td>3-2</td>
<td>10</td>
<td>24 h</td>
<td>CH₂Cl₂</td>
<td>&lt;5</td>
</tr>
<tr>
<td>4</td>
<td>3-7</td>
<td>10</td>
<td>1 h</td>
<td>Et₂O</td>
<td>&gt;99</td>
</tr>
<tr>
<td>5</td>
<td>3-7</td>
<td>3</td>
<td>3 h</td>
<td>Et₂O</td>
<td>&gt;99</td>
</tr>
<tr>
<td>6</td>
<td>3-8</td>
<td>3</td>
<td>3.5 h</td>
<td>Et₂O</td>
<td>&gt;99</td>
</tr>
<tr>
<td>7</td>
<td>3-9</td>
<td>3</td>
<td>2 h</td>
<td>Et₂O</td>
<td>&gt;99</td>
</tr>
<tr>
<td>8</td>
<td>3-10</td>
<td>3</td>
<td>9 h</td>
<td>Et₂O</td>
<td>80</td>
</tr>
<tr>
<td>9</td>
<td>[Ph₃PMe][B(C₆F₅)₄]</td>
<td>3</td>
<td>24 h</td>
<td>Et₂O</td>
<td>0</td>
</tr>
<tr>
<td>10</td>
<td>3-13</td>
<td>3</td>
<td>7 h</td>
<td>Et₂O</td>
<td>&gt;99</td>
</tr>
<tr>
<td>11</td>
<td>3-16</td>
<td>3</td>
<td>30 s</td>
<td>Et₂O</td>
<td>&gt;99</td>
</tr>
<tr>
<td>12</td>
<td>3-16</td>
<td>0.5</td>
<td>3.5 h</td>
<td>Et₂O</td>
<td>&gt;99</td>
</tr>
<tr>
<td>13</td>
<td>3-19</td>
<td>0.5</td>
<td>25 min</td>
<td>Et₂O</td>
<td>&gt;99</td>
</tr>
<tr>
<td>14</td>
<td>3-22</td>
<td>0.5</td>
<td>5 min</td>
<td>Et₂O</td>
<td>&gt;99</td>
</tr>
<tr>
<td>15</td>
<td>3-16</td>
<td>0.1</td>
<td>5 min</td>
<td>CH₂Cl₂</td>
<td>93</td>
</tr>
</tbody>
</table>
Compounds 3-8, 3-9 and 3-10 were also competent initiators for this reaction, although some inhibition was observed when using compound 3-10 (80% completion after 9 h) (Table 3-1, Entry 6-8). The reduced activity of 3-10 can be attributed to a decrease in Lewis acidity at the P centre as reflected in the calculated FIA s (see Section 3.2.1.4). When [Ph₃PMe][B(C₆F₅)₄] was used, no conversion was observed after 24 h at ambient temperature, consistent with the need for a highly Lewis acidic phosphonium centre to promote this reaction (Table 3-1, Entry 9). Finally, formal exchange of the i-Pr substituents by pyrrolidine groups on the cyclopropenium units did not have a significant effect on reactivity (Table 3-1, Entry 10). Pyridinium-substituted phosphonium salts 3-16, 3-19, 3-22, 3-24, and 3-27 were also tested in the reaction. When salt 3-16 was used (3 mol%), complete conversion was observed in Et₂O after 30 s (Table 3-1, Entry 11). Decreasing the phosphonium salt loading to 0.5 mol%, resulted in complete conversion after 3.5 h under identical conditions. Interestingly, dicaticonic salts 3-19 and 3-22 (0.5 mol%) proved to be even more efficient for this transformation, and these reactions led to complete conversion to the desired product after 25 min and 5 min, respectively (Table 3-1, Entry 13-14).

In an attempt to further optimize the reaction conditions and also to obtain a more quantitative indication of relative Lewis acidity of the phosphonium salts prepared, we further decreased the phosphonium salt loading and switched the solvent to CH₂Cl₂ because at these low concentrations the Lewis basicity of Et₂O partially inhibits activity. To start, we used 0.1 mol% of the phosphonium salt, and dried the solution in vacuo after 5 minutes to quench the reaction and then subsequently determined conversion via ¹H NMR spectroscopy. Under these reaction conditions, the use of triphenylphosphonium salts 3-16, 3-19, 3-22 resulted in 93%, 98%, and >99% conversion, respectively (Table 3-1, Entry 15-17). Salts 3-24 and 3-27 afforded conversions of 41% and 52% (Table 3-1, Entry 18-19).

Overall, pyridinium-substituted dications demonstrated superior Lewis acidity in this Mukaiyama-Aldol condensation reaction relative to the cyclopropenium-substituted phosphonium dications.
Within the family of pyridinium-substituted phosphonium salts, triphenyl derivatives 3-16, 3-19 and 3-22 outperformed both methylidiphenyl derivatives 3-24 and 3-27, which aligns with the electron-withdrawing8(410,367),(588,542)(256,554),(554,830) character of the substituents around phosphorus (i.e. Ph vs Me).

3.2.1.4 Mechanistic Insights into Mukaiyama-aldol condensation reaction

Addition of 2,6-di-t-butylpyridine as a proton-trap to the reaction mixture had no impact on the outcome, suggesting that the reaction is not a proton-catalyzed process.\textsuperscript{49} Similarly, the addition of 18-crown-6 had no influence on the reaction, indicating that residual alkali metal cations were also not promoting the reaction.\textsuperscript{50-53} Collectively, these data support the notion that the phosphonium cation is operative as a Lewis acid initiator. Moreover, independent control reactions of 3-24 with 2-napthaldehyde showed only a weak donor-acceptor interaction, whereas the reaction of 3-24 with 1-methoxy-2-methyl-1-trimethylsiloxypropene revealed adduct formation. While there is no evidence for the generation of a silylium cation by \textsuperscript{31}P or \textsuperscript{29}Si NMR spectroscopy, we propose that coordination of the phosphonium cation to 1-methoxy-2-methyl-1-trimethylsiloxypropene liberates [Me\textsubscript{3}Si]\textsuperscript{+} which catalyzes the addition product (Scheme 3-9).

![Scheme 3-8](image)

**Scheme 3-8.** Proposed reaction pathway for phosphonium-initiated Mukaiyama-Aldol reaction. [P] denotes the phosphonium salt. Counterions have been omitted for clarity.

To probe the experimental reactivity trend further, we calculated the calculated the FIA values and global electrophilicity indices (\(\omega\)) of the compounds (Table 3-2). As described in Chapter 2, FIA values...
were obtained with computed single point energies (MP2/def2-TZVPP) of the Lewis acid, the fluoride adduct of the Lewis acid, and a fluoride ion donor/acceptor pair (CF<sub>3</sub>O/CF<sub>2</sub>O), as well as the experimental FIA of CF<sub>2</sub>O. The FIA values for the cyclopropenium-substituted phosphonium cations ranged from 809 to 832 kJ mol<sup>-1</sup>, whereas those for the pyridinium-substituted phosphonium cations ranged from 829 to 920 kJ mol<sup>-1</sup>. The corresponding \( \omega \) ranges are 3.97-4.12 eV and 5.71-6.29 eV for the cyclopropenium- and pyridinium-substituted phosphonium cations, respectively. These \( \omega \) values were obtained using MP2/def2-TZVPP HOMO and LUMO energies, as described in section 3.4.4.1. The significant enhancement to Lewis acidity conferred by the cationic charges can be appreciated by comparing these values to those of B(C<sub>6</sub>F<sub>5</sub>)<sub>3</sub> (FIA: 452 kJ mol<sup>-1</sup>, \( \omega \): 1.41 eV) or [FP(C<sub>6</sub>F<sub>5</sub>)<sub>3</sub>]<sup>+</sup> (FIA: 777 kJ mol<sup>-1</sup>, \( \omega \): 5.04 eV).\textsuperscript{54}

**Table 3-2.** FIA and \( \omega \) values for cyclopropenium- and pyridinium-phosphonium salts.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Compound</th>
<th>FIA (kJ mol&lt;sup&gt;-1&lt;/sup&gt;)</th>
<th>( \omega ) (eV)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>3-7</td>
<td>809</td>
<td>3.97</td>
</tr>
<tr>
<td>2</td>
<td>3-8</td>
<td>831</td>
<td>4.07</td>
</tr>
<tr>
<td>3</td>
<td>3-9</td>
<td>825</td>
<td>4.02</td>
</tr>
<tr>
<td>4</td>
<td>3-10</td>
<td>810</td>
<td>3.98</td>
</tr>
<tr>
<td>5</td>
<td>3-13</td>
<td>814</td>
<td>4.13</td>
</tr>
<tr>
<td>6</td>
<td>3-16</td>
<td>834</td>
<td>5.99</td>
</tr>
<tr>
<td>7</td>
<td>3-19</td>
<td>837</td>
<td>6.15</td>
</tr>
<tr>
<td>8</td>
<td>3-22</td>
<td>829</td>
<td>5.71</td>
</tr>
<tr>
<td>9</td>
<td>3-24</td>
<td>889</td>
<td>6.29</td>
</tr>
<tr>
<td>10</td>
<td>3-27</td>
<td>859</td>
<td>5.93</td>
</tr>
<tr>
<td>12</td>
<td>[(C&lt;sub&gt;6&lt;/sub&gt;F&lt;sub&gt;5&lt;/sub&gt;)&lt;sub&gt;3&lt;/sub&gt;PF]&lt;sup&gt;+&lt;/sup&gt;\textsuperscript{54}</td>
<td>777</td>
<td>5.04</td>
</tr>
<tr>
<td>13</td>
<td>B(C&lt;sub&gt;6&lt;/sub&gt;F&lt;sub&gt;5&lt;/sub&gt;)&lt;sub&gt;3&lt;/sub&gt;</td>
<td>452</td>
<td>1.41</td>
</tr>
</tbody>
</table>

The experimental observation that the *meta*-substituted pyridinium-triphenylphosphonium salt 3-22 showed reactivity superior to its *ortho-* and *para-* analogues 3-16 and 3-19, respectively (Table 3-2, Entries 6-8) is unexpected. On the basis of either FIA or \( \omega \) values, slightly lower reactivity is
predicted for 3-22. We believe that the diminished reactivity of 3-16 when compared with that of 3-19 and 3-22 might reflect the higher steric congestion about the acidic P-centre. Note that during the activation of the silyl ketene acetal substrate, the central P-atom needs to adopt a pseudo-trigonal bipyramid conformation, which is surely hindered by ortho-substitution in any of the aromatic rings.

In this regard, we propose that the difference in observed chemical reactivity for this reaction may arise from differential steric occlusion of the acidic centre. To this end, compound 3-24 and 3-27 were investigated as an illustrative ortho/meta pair. In both compounds, the lowest energy conformer is one in which the pyridinium N–CMe vector is oriented in the same direction as the P–CMe vector (i.e. the conformer depicted in Figure 3-2). A relaxed surface scan about the P–NPy torsion angle reveals that for both compounds, rotation about the P–Cpy bond is facile and that the minima along this one-dimensional potential energy surfaces do not differ appreciably in energy (see Section 3.4.4.2). At room temperature, therefore, significant amounts of both conformers will be present and rapidly interconverting.

The routes of nucleophilic approach to 3-24 and 3-27 when the compounds are either in their most occluded or non-occluded conformations are depicted in Figure 3-2. The ortho-substitution pattern clearly blocks the route of approach to a greater extent than the meta-isomer. In the energetically accessible and thermally populated occluded conformations, a productive collision between the phosphonium and a putative substrate is inhibited, decreasing the rate of the reaction despite having no significant influence on the electrophilicity of the phosphorus centre or the stability of the final products, which are reflected in ω and FIA.
**Figure 3-2.** Structural diagrams depicting the dihedral angle scanned (shown in bold blue lines) to obtain the non-occluded and occluded conformers of 3-24 and 3-27 (a and b, shown with 3-24). Depictions along the P–CMe vector of the optimized (BP86/def2-TZVP) structures of 3-24 in the non-occluded (c) and occluded (d) conformations. The corresponding depictions for 3-27 (e and f). C: grey, N: blue, H: white, P: orange.

This argument does not explain, however, why 3-22 is more reactive than its *para*-analogue 3-19, especially given that the P-atom in 3-19 is calculated to be more electrophilic, and both methyl substituents cannot play any important steric role. This remains the subject of ongoing investigation in our laboratory.

In summary, we have probed the Lewis acidity of a family of air-stable cyclopropenium and pyridinium-substituted phosphonium dications, experimentally and computationally. As predicted by a computational investigation, pyridinium-substituted phosphonium salts outperformed the cyclopropenium derivatives. Within the family of pyridinium-substituted phosphonium salts, we observed that the *meta*-substituted pyridinium salt 3-22 outperformed both its *ortho*- and *para*-isomers. The same relative reactivity was observed for 3-27, relative to 3-24. Analysis of the occluded and non-occluded conformers of 3-24 and 3-27 shows that the *ortho*-substitution pattern clearly blocks the route of approach to a greater extent than the *meta*-isomer. Further mechanistic studies are needed to fully elucidate the atomistic underpinnings of the reactivity presented here,
but these results suggest that consideration of entropic effects should also be given prominence in the design of novel Lewis acid catalysts.

Overall, the experimental and theoretical results reported herein highlight the potential utility of highly electrophilic phosphorus cations as robust air-stable Lewis acid catalysts, and the importance of steric design parameters, in addition to electronic properties, in rationalizing and tuning catalytic activity, respectively.

3.2.2 Synthesis of a Phenoxyphosphonium Dication

Next, we sought to synthesize a phenoxyphosphonium dication in hopes of increasing the stability, while also enhancing the Lewis acidity at phosphorous of pyridiniumphosphonium salts. One synthetic strategy we targeted was inspired by the Pd-catalyzed coupling of 3-bromopyridine and PPh₃,⁴⁴,⁵⁵ wherein we envisioned the same C-P coupling reaction with (PhO)PPh₂ (as reported in Section 3.2.1.2) with subsequent methylation affording the meta-substituted phosphonium salt. To this end, 3-bromopyridine was mixed with (PhO)PPh₂ in the presence of a catalytic amount of Pd₂(dba)₃. After heating the reaction mixture to 160 °C for 12 h in mesitylene, the major product observed in the ³¹P{¹H} NMR spectrum was unreacted PhOPPh₂. Heating the reaction further resulted in a mixture of unidentifiable peaks, as observable by ³¹P NMR spectroscopy. However, when toluene was used as the solvent, the same reaction produced colorless crystals after heating at 110 °C for 5 h, which could be isolated by filtration. The product was characterized by multinuclear NMR spectroscopy, wherein the ³¹P{¹H} NMR (CDCl₃) spectrum shows a singlet resonance at δ 65.6 ppm. While we cannot unambiguously assign the product, based on the later reported synthesis of the analogous phenoxyphosphonium dicationic salt 3-29, the product of this reaction is likely [(m-C₅H₄N)P(OPh)Ph₂][Br] 3-28. Unfortunately, any attempt to further oxidize 3-28 with MeOTf was unsuccessful. Indeed, heating reaction mixtures of 3-28 and MeOTf for prolonged periods of time always contained at least 60% unreacted 3-28. Attempts to exchange the bromide counterion for the weakly coordinating [B(C₆F₅)₄]⁻ anion upon reaction with [K][B(C₆F₅)₄] yielded multiple unidentifiable products.

Targeting a different approach, we sought to exploit both the reactivity of the P-F bond and the strength of the Si-F bond to synthesize the desired ortho-phenoxyphosphonium dicationic salt. In this regard, we reacted equimolar amounts of fluorophosphonium salt 2-13 with commercially-
available phenoxy(trimethylsilane) (PhOTMS) in hopes of liberating Me₃SiF to form the desired product.

\[
\begin{align*}
\text{F} & \quad \text{Ph}\quad \text{Ph} \quad \text{P} \quad \text{P} \\
\text{Ph} & \quad \text{Ph} \quad \text{O} \quad \text{SiMe₃} \\
2\text{[B(C₆F₅)₄]} & \quad \text{CH₂Cl₂} \\
\text{2-13} & \quad \text{24 h, 45 °C} \\
\end{align*}
\]

\[
\begin{align*}
\text{Ph} & \quad \text{O} \quad \text{SiMe₃} \quad \text{P} \quad \text{P} \\
\text{Ph} & \quad \text{Ph} \quad \text{O} \quad \text{SiMe₃} \\
2\text{[B(C₆F₅)₄]} & \quad \text{Me₃SiF} \\
\text{3-29} & \quad \text{CH₂Cl₂} \\
\end{align*}
\]

**Scheme 3-9.** Synthesis of phenoxy pyridiniumphosphonium salt 3-29.

After heating the reaction mixture at 45 °C for 24 h, analysis of the ³¹P{¹H} NMR spectrum (CH₂Cl₂) shows the complete disappearance of the P-F doublet resonance and the formation of a new singlet resonance at δ 59.6 ppm. As well, the ¹⁹F{¹H} NMR spectrum contains a resonance at δ -159 ppm, indicative of Me₃SiF. Facile removal of Me₃SiF in vacuo afforded phenoxy pyridiniumphosphonium salt 3-29 in 96% yield (Scheme 3-8). 3-29 was fully characterized by NMR spectroscopy and elemental analysis. Unsurprisingly, the ³¹P{¹H} resonance for 3-29 is shifted upfield compared to pyridinium-fluorophosphonium salt 2-13 (δ = 88.9 ppm), but downfield shifted relative to the related [(C₆F₅)₃P(OPh)][B(C₆F₅)₄] (δ = 36.8 ppm). Remarkably, 3-29 could be stored in air for at least 7 days without any signs of decomposition.

Reaction of 3-29 with 1 equiv. of Et₃PO (Gutmann–Beckett Lewis acidity test) resulted in the formation of several unidentifiable products as evidenced by ³¹P{¹H} NMR spectroscopy, thereby suggesting this method is inadequate for assessing Lewis acidity of 3-29. Instead, the Lewis acidity of 3-29 was probed experimentally in a variety of previously reported benchmark reactions. Indeed, 3-29 was a viable catalyst for the hydrodefluorination of 1-fluoropentane, the hydrodeoxygenation of benzophenone, the hydrodihydrosilation of α-methylstyrene and the dehydrocoupling of phenol and Et₃SiH. It is noteworthy that analysis of the ³¹P{¹H} NMR spectrum for hydrodeoxygenation catalysis did not show any signs of catalyst decomposition, which stands in stark contrast to other electrophilic fluorophosphonium salts. Remarkably, this reaction could also be completed in air, after storing 3-29 on the benchtop for 24 h, without any decrease in reactivity.
In all reactions, 3-29 was shown to be a more effective catalyst compared to methylphosphonium derivative 3-24, but less reactive than fluorophosphonium salt 2-13. Interestingly, fewer differences were observed for the latter two reactions; however, shorter reaction times could provide more insight into the relative reactivity. Overall, these data support the notion that the polarity of the P-EWG bond impacts the reactivity of EPCs. As reported previously, increasing the electron-withdrawing nature of the substituent lowers the energy LUMO, resulting in a more energetically accessible orbital for interaction with an appropriate electron donor.

Scheme 3-10. Lewis acid-catalyzed reactions with pyridiniumphosphonium salts 2-13, 3-24 and 3-29 as catalysts.

These results are in accord with computational data indicating that the phosphorus atom is the locus of positive charge and that an energetically low-lying antibonding orbital is oriented opposite the P-O vector. This parallels results obtained for related fluoro phenoxyphosphonium salts. Computation of the fluoride ion affinity (FIA: 920 kJ mol⁻¹) and global electrophilicity index (GEI: 6.12 eV) indicate that 3-29 has a Lewis acidity greater than B(C₆F₅)₃ (FIA: 452 kJ mol⁻¹, GEI: 1.41 eV) and [(PhO)P(C₆F₅)₃]⁺ (FIA: 718 kJ mol⁻¹; GEI: 2.98 eV), albeit less than fluoro pyridiniumphosphonium salt 2-13 (FIA: 1011 kJ mol⁻¹; GEI: 6.51 eV), as expected.
3.2.3 Catalytic Double Hydroarylation of Alkynes and Arylamines with an Electrophilic Phenoxyphosphonium Dication

Given the unprecedented stability and Lewis acidity of 3-29, we investigated new synthetic applications of this highly electrophilic phosphorus(V) species. To this end, we discovered that 3-29 is an active hydroarylation catalyst. In a preliminary reaction, an equimolar mixture of (4-Tol)2NH and (4-Tol)CCH was combined with 5 mol% of 3-29 and left to stir at ambient temperature for 24 h. The 1H NMR spectrum (CDCl3) shows a resonance at δ 5.50 ppm and three methyl resonances at δ 1.86, δ 1.99 and δ 2.09 ppm, which is consistent with the formation of 2,7,9-trimethyl-9-(4-tolyl)-9,10-dihydroacridine. The product was subsequently characterized by mass spectrometry. Moreover, this reaction suggests that 3-29 can catalyze the double hydroarylation of the diarylamine at the ortho-positions, subsequently affecting reduction of the alkyne and cyclization to afford the dihydroacridine product. Interestingly, when compared to other known Lewis acids such as [Ph3PF][B(C6F5)4], [(PhO)P(C6F5)3][B(C6F5)4],54 FeCl3, AlCl3 and B(C6F5)3 among others, dicationic salt 3-29 demonstrated the highest conversion (62%). As well, no signs of decomposition were observed under these reaction conditions.

After reaction optimization with phosphonium salt 3-29, the ideal reaction conditions were used to expand the scope of this double hydroarylation reaction. Using 3-29 as the catalyst (5 mol%), (Tol)2NMe was reacted with a range of substituted alkynes, generating the corresponding 2,7,9,10-tetramethyl-9-(R)-9,10-dihydroacridine products (R = Ph; 4-biphenyl; 4-BrC6H4; 2,4-F2C8H3; 3-
thiophene-yl, 4-(MeO)C₆H₄) in good conversions (determined by \(^1\)H NMR spectroscopy), with isolated yields ranging from 26-76% (Table 3-3, Entries 3 – 8). For most cases, the electronic properties of the group at the para-position of the phenyl ring did not have a significant impact on the reaction outcome, as both electron-donating and electron-withdrawing substituents were incorporated into the product with high conversions. However, reaction of (Tol)₂NMe with (p-CF₃C₆H₄)CCH only resulted in 10% conversion to the desired product (Table 3-3, Entry 9). On the other hand, various 4-tolylacetylene compounds were successfully converted to the desired dihydroacridine products upon reaction with para-substituted diarylmethyl amines (X = OMe (97%); Br (23%); H (55%)) (Table 3-3, Entries 10-12). These results are unsurprising given the reduction in nucleophilicity of the arene ring upon halogen-substitution. Use of diaryl ether (4-Tol)₂O with 4-tolylacetylene only resulted in 21% conversion (Table 3-3, Entry 13). Interestingly, use of triarylamine (4-Tol)₃N with 4-tolylacetylene resulted in 65% conversion (Table 3-3, Entry 14), whereas reactions with (4-BrPh)₂NH, (4-Tol)₂NSiEt₃ or (4-Tol)NSPh were unsuccessful. As well, reactions with diphenylacetylene, ethynylcyclohexane and 1-octyne did not yield any of the desired product.

Table 3-3. Scope of phosphonium-catalyzed hydroarylation reactions.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Product</th>
<th>Conv. (%)</th>
<th>Entry</th>
<th>Product</th>
<th>Conv. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>![Product Image 1]</td>
<td>52</td>
<td>8</td>
<td>![Product Image 2]</td>
<td>65</td>
</tr>
</tbody>
</table>
Interestingly, when a more sterically-encumbered alkyne like (Mes)CCH was reacted with (Tol)₂NMe, only single hydroarylation was observed. The products obtained from the hydroarylation reactions have been characterized by NMR spectroscopy, mass spectrometry and
in some cases, X-ray crystallography. These data are excluded from this thesis report as they will be reported in fellow graduate student James LaFortune’s thesis report.

The mechanism of this hydroarylation reaction is believed to be related to the mechanism reported for the hydroarylation of olefins with \([(\text{C}_6\text{F}_5)_3\text{PF}][\text{B}(\text{C}_6\text{F}_5)_4]\).\(^{65}\) The first step in the reaction is proposed to be alkyne activation by 3-29. The transient carbocation is then prone to nucleophilic attack by the ortho-C atom of the aryl group, facilitating C-C bond formation. Subsequent proton transfer to the olefinic unit yields the Friedel-Crafts product and liberates 3-29 (Scheme 3-11). This observation is consistent with the ability of \([(\text{C}_6\text{F}_5)_3\text{PF}][\text{B}(\text{C}_6\text{F}_5)_4]\) to mediate terminal olefin isomerizations.\(^{66}\) In the presence of 3-29, the alkene species can then undergo a second electrophilic aromatic substitution reaction, which upon proton transfer, rearomatizes to give the 9,9-disubstituted 9,10-dihydroacridine product. While examples of main group alkyne activation are prevalent in the literature for B-based Lewis acids like B(\text{C}_6\text{F}_5)_3,\(^{67-69}\) reports with EPCs remain scarce.

Scheme 3-11. Proposed mechanism for the EPC-hydroarylation of terminal alkynes and diarylamines with 3-29.
In conclusion, these results highlight the importance of a robust and stable catalyst for organic transformations which involve Lewis bases. When compared to other known strong Lewis acids, 3-29 was superior for this reaction. As well, while similar reaction of alkynes with diarylamines lead to hydroamination products in the presence of B(C$_6$F$_5$)$_3$, the reactions reported herein effect the synthesis of a series of 9,9-disubstituted 9,10-dihydroacridines through a double hydroarylation mechanism. Collectively, these results illustrate the unique and versatile reactivity of EPCs and serve as a rare example of metal-free catalytic hydroarylation.

3.3 Conclusions

In the first part of the chapter we report the synthesis of a family of air-stable cyclopropenium- and pyridiniumphosphonium dication and their reactivity in the Mukaiyama-aldol reaction. As predicted by computations, pyridinium triphenyl-substituted phosphonium salts outperformed the cyclopropenium derivatives, wherein the meta-substituted pyridinium salts outperformed the ortho- and para-isomers. Similarly, the methyl analogue and meta-isomer 3-27 was shown to be more reactive than the corresponding ortho-isomer 3-24. This result opposes the FIA and ω values, which suggests other factors may be influencing the reactivity. One possible explanation is the entropic loss due to ortho-substitution, which has a more sterically congested occluded conformation compared to the meta-isomer. Further investigation into these reactivity differences is the subject of ongoing investigation in our laboratory.

In the latter part of the chapter we report the synthesis of an electrophilic phenoxyphosphonium dication with unprecedented air-stability. The Lewis acidity was first confirmed experimentally in a series of benchmark Lewis acid-catalyzed reactions and computationally with FIA and GEI calculations. The unique reactivity and stability was then exploited in the synthesis of a series of 9,9-disubstituted 9,10-dihydroacridine derivatives through a hydroarylation mechanism.

Collectively, these results represent major advances in the field of phosphorus Lewis acid chemistry, providing examples of Lewis acidic yet robust P(V) salts and their applications in a variety of organic transformations. As we continue to target the facile synthesis of P-based Lewis acid catalysts, these results provide valuable insight into the nature of stability and reactivity of cationic phosphorus compounds, ultimately moving us one step closer to commercially viable species.
3.4 Experimental Details

3.4.1 General Remarks

All manipulations were performed in a MB Unilab Glove box produced by MBraun or using standard Schlenk techniques\textsuperscript{72} under an inert atmosphere of anhydrous N\textsubscript{2}. All glassware was oven-dried at temperatures above 180°C prior to use. Dry, oxygen-free solvents (CH\textsubscript{2}Cl\textsubscript{2}, \textit{n}-pentane, and toluene) were prepared using an Innovative Technologies solvent purification system or deoxygenated and distilled over sodium benzophenone. Fluorobenzene (C\textsubscript{6}H\textsubscript{5}F) was distilled from CaH\textsubscript{2} and stored over molecular sieves (4 Å) prior to use. Deuterated dichloromethane (CD\textsubscript{2}Cl\textsubscript{2}), chloroform (CDCl\textsubscript{3}) and acetonitrile (CD\textsubscript{3}CN) were purchased from Sigma-Aldrich, distilled from CaH\textsubscript{2} and stored in an inert atmosphere at least two days prior to use. Reagents such as 2-pyridyldiphenylphosphine, MeOTf, Et\textsubscript{3}PO, Et\textsubscript{3}SiH, PhOTMS, 1-fluoropentane, benzophenone, phenol, \textit{α}-methylstyrene, Pd\textsubscript{2}(OAc)\textsubscript{3}, 3-bromopyridine, (phenoxy)diphenylphosphine, 2-naphthaldehyde, 1-methoxy-2-methyl-1-trimethylsiloxy-propene were purchased either from Sigma-Aldrich, Strem Chemicals, TCI chemicals or Alfa Aesar and used as received. 3-pyridyldiphenylphosphine\textsuperscript{45} and [Et\textsubscript{3}Si][B(C\textsubscript{6}F\textsubscript{5})\textsubscript{4}]•(C\textsubscript{7}H\textsubscript{8})\textsubscript{73} were prepared according to known literature procedures. NMR spectra were measured on a Bruker DPX 300 (\textit{1}H: 300 MHz, \textit{11}B: 96 MHz, \textit{13}C: 75 MHz, \textit{31}P: 121 MHz, \textit{19}F: 282 MHz), Bruker AVANCE 400 (\textit{1}H: 400 MHz, \textit{11}B: 128 MHz, \textit{13}C: 101 MHz, \textit{31}P: 162 MHz, \textit{19}F: 377 MHz) or Agilent DD2 500 (\textit{1}H: 500 MHz, \textit{13}C: 125 MHz, \textit{31}P: 202 MHz, \textit{19}F: 471 MHz) at ambient temperature. \textit{1}H, \textit{13}C, \textit{31}P, \textit{19}F, and \textit{11}B NMR chemical shifts (\(\delta/\text{ppm}\)) are referenced to Me\textsubscript{4}Si, Me\textsubscript{4}Si, H\textsubscript{3}PO\textsubscript{4}, CFCl\textsubscript{3}, and BF\textsubscript{3}•OEt\textsubscript{2}, respectively. Chemical shifts (\(\delta\)) are reported in ppm, multiplicity is reported as follows (s = singlet, d = doublet, t = triplet, m = multiplet) and coupling constants (\(J\)) are reported in Hz. Assignments of individual resonances were done using 2D techniques (HMBC, HSQC, HH-COSY) when necessary. High-resolution mass spectra (HRMS) were obtained on a micro mass 70S-250 spectrometer (EI), an Agilent 6538 Q-TOF (ESI), an ABI/Sciex QStar Mass Spectrometer (DART), or on a JOEL AccuTOF-DART (DART) mass spectrometer. Elemental analyses (C, H, N) were performed at the University of Toronto employing a Perkin Elmer 2400 Series II CHNS Analyzer.
3.4.2 Synthesis of Compounds 3-23, 3-24, 3-26, 3-27, 3-28 and 3-29

\[
[(o-C_5H_4NCH_3)P(CH_3)Ph_2][OTf]_2 (3-23)
\]

MeOTf (1.6 mL, 14.2 mmol, 3.9 equiv.) was added, dropwise, to a solution of 2-pyridyldiphenylphosphine (968 mg, 3.68 mmol, 1.0 equiv.) in CH_2Cl_2 (5 mL). The reaction mixture was stirred at ambient temperature for 3 d, after which time a white solid had settled out of solution. The supernatant was decanted, and a mixture of CH_2Cl_2 and n-pentane (1:4 ratio) was added. After agitation for 1 min, the supernatant was decanted, and the solid was washed with n-pentane (3 x 5 mL). The solid was dried in vacuo and isolated as a white powder (1.76 g, 81% Yield).

\(^1H\) NMR (400 MHz, CD_2Cl_2, MeSi): δ 9.10 (m, 1H; m-py), 8.60 (m, 1H; p-py), 8.60 (m, 1H; p-py), 8.40 (m, 1H; o-py), 8.05 (m, 2H; p-Ph), 8.00 (m, 1H; m-py), 7.90 (m, 8H; Ph), 4.40 (s, 3H; N-C_5H_4), 3.40 ppm (d, \(^3J_{PH} = 13\) Hz, 3H; P-C_H_3).

\(^19\)F NMR (377 MHz, CD_3CN, CFCl_3): δ –78.9 (s, 6F; OTf).

\(^{31}\)P\(^{1H}\) NMR (162 MHz, CD_3CN, H_3PO_4): δ 26.0 ppm (s).

\(^{13}\)C\(^{1H}\) NMR (126 MHz, CD_3CN, MeSi): δ 154.6 (d, \(^3J_{PC} = 4\) Hz, 1C; m-py), 147.8 (d, \(^3J_{PC} = 9\) Hz, 1C; m-py), 139.7 (d, \(^2J_{PC} = 14\) Hz, 1C; o-py), 138.0 (d, \(^3J_{PC} = 3\) Hz, 2C; p-Ph), 135.0 (d, \(^3J_{PC} = 12\) Hz, 4C; m-Ph), 134.2 (d, \(^4J_{PC} = 2\) Hz, 1C; p-py), 132.2 (d, \(^2J_{PC} = 14\) Hz, 4C; o-Ph), 122.0 (d, \(^1J_{PC} = 321\) Hz, 1C; i-py), 115.7 (d, \(^1J_{PC} = 90\) Hz, 2C; i-Ph), 51.0 (d, \(^3J_{PC} = 4\) Hz, 1C; N-CH_3), 9.6 ppm (d, \(^1J_{PC} = 55\) Hz, 1C; P-CH_3), resonance for sulfur-bound carbon atom in [OTf]⁻ anion was not observed.

**MS-ESI**: Calculated mass for [M]²⁺: 146.57. Obtained: 146.9739 amu. **Anal Calcd.** for C_{21}H_{20}F_6NO_6PS_2: C, 42.6; H, 3.4; N, 2.4 %. Found: C, 43.4; H, 3.3; N, 2.9 %.

\[
[(o-C_5H_4NCH_3)P(CH_3)Ph_2][B(C_6F_5)_{4}]_2 (3-24)
\]
A solution of freshly prepared [K][B(C₆F₅)₄] (146 mg, 0.205 mmol, 2.05 equiv.) in CH₂Cl₂ (0.5 mL) was added to a suspension of 3-23 (57 mg, 0.100 mmol, 1.0 equiv.) in toluene (2 mL). The reaction mixture was stirred at ambient temperature for 10 min, before being filtered through a Kimwipe plug. 5 mL of n-pentane was added to the filtrate to induce precipitation. The supernatant was decanted, and the solid was washed with n-pentane (3 x 3 mL) and dried in vacuo to afford a white powder (158 mg, 47% Yield).

¹H NMR (400 MHz, CD₂Cl₂, Me₄Si): δ 9.03 (m, 1H; m-py), 8.80 (m, 1H; p-py), 8.54 (m, 1H; o-py), 8.18 (m, 2H; Ph), 8.07 (m, 1H; m-py), 7.93 (dd, ³JHH = 15 Hz, ⁴JHH = 5 Hz, 4H; o-Ph), 7.66 (dd, ³JHH = 15 Hz, ³JHH = 15 Hz, 4H; m-Ph), 4.35 (s, 3H; N-CH₃), 3.13 ppm (d, ²JPH = 13 Hz, 3H; P-CH₃). ¹¹B{¹H} NMR (128 MHz, CD₂Cl₂, BF₃•OEt₂): δ −16.7 ppm (s). ¹⁹F NMR (377 MHz, CD₂Cl₂, CFCl₃): δ −133.0 (m(br), 16F; B(o-C₆F₅)₃). −167.2 ppm (m(br), 16F; B(m-C₆F₅)₃). ³¹P{¹H} NMR (162 MHz, CD₂Cl₂, H₂PO₄): δ 25.3 ppm (s). ¹³C{¹H} NMR (125 MHz, CD₂Cl₂, Me₄Si): δ 153.2 (d, ³JPC = 3 Hz, 1C; m-py), 148.8 (d, ³JPC = 8 Hz, 1C; m-py), 148.4 (d(br), ¹JFC = 244 Hz, 16C; B(o/m-C₆F₅)₃), 139.8 (d, ³JPC = 3 Hz, 2C; p-Ph), 138.9 (d, ²JPC = 13 Hz, 1C; o-py), 138.8 (d(br), ¹JFC = 246 Hz, 8C; B(p-C₆F₅)₃), 136.6 (d(br), ¹JFC = 246 Hz, 16C, B(o/m-C₆F₅)₃), 134.9 (d, ³JPC = 2 Hz, 1C; p-py), 133.2 (d, ²JPC = 14 Hz, 4C; o-Ph), 133.0 (d, ³JPC = 11 Hz, 4C; m-Ph), 111.2 (d, ¹JFC = 90 Hz, 2C; i-Ph), 50.6 (d, ³JPC = 4 Hz, 1C; N-CH₃), 9.8 ppm (d, ¹JFC = 56 Hz, 1C; P-CH₃), resonances for boron-bound carbon atoms in [B(C₆F₅)₄]⁻ anion and P-bound carbon of the pyridine moiety were not observed. Anal. Calcd. for C₆₇H₂₆B₂F₄₄NOP: C, 48.7; H, 1.2; N, 0.9 %. Found: C, 49.8; H, 1.1; N, 0.8 %.

[(m-C₅H₄NCH₃)P(CH₃)Ph₂][OTf]₂ (3-26)

MeOTf (0.2 mL, 1.6 mmol, 5.0 equiv) was added dropwise to a solution of 3-pyridyldiphenyl phosphine (84 mg, 0.32 mmol, 1.0 equiv.) in CH₂Cl₂. The solution was left to stir at ambient temperature for 3 d. The supernatant was decanted, the resulting solid was washed with CH₂Cl₂ (3 x 5 mL) and n-pentane (3 x 5 mL) and then dried in vacuo to afford an off-white microcrystalline powder (108 mg, 63% Yield).
**1H NMR (400 MHz, CD$_3$CN, Me$_4$Si):** δ 8.99 (m, 1H; p-py), 8.88 (m, 1H; o-py), 8.26 (m, 1H; m-py), 7.95 (m, 2H; p-Ph), 7.79 (m, 8H; o- & m-Ph), 4.38 (s, 3H; N-CH$_3$), 2.99 ppm (d, $^{1}J_{PH} = 14$ Hz, 3H; P-CH$_3$). **$^{19}$F{1H} NMR (377 MHz, CD$_3$CN, CFCl$_3$):** δ −79.4 ppm (s, 6F; OTf). **$^{31}$P{1H} NMR (162 MHz, CD$_3$CN, H$_3$PO$_4$):** δ 22.6 ppm. **$^{13}$C{1H} NMR (125 MHz, CD$_3$CN, Me$_4$Si):** δ 151.3 (br s, 1C; p-py), 150.5 (d, $^{2}$J$_{PC} = 8$ Hz, o-py), 150.2 (br s, 1C; 2-py), 137.3 (d, $^{4}$J$_{PC} = 3$ Hz, 2C; p-Ph), 134.9 (d, $^{2/3}$J$_{PC} = 11$ Hz, 4C; o-/m-Ph), 131.6 (d, $^{2/3}$J$_{PC} = 14$ Hz, 4C; o-/m-Ph), 130.3 (d, $^{3}$J$_{PC} = 11$ Hz, m-py), 124.6 (d, $^{1}$J$_{PC} = 91$ Hz, 1C; i-py), 117.0 (d, $^{1}$J$_{PC} = 90$ Hz, 2C; i-Ph), 50.3 (s, 1C; N-CH$_3$), 9.0 ppm (d, $^{2}$J$_{PC} = 57$ Hz, 1C; P-CH$_3$), resonance for sulfur-bound carbon atom in [OTf]$^-$ anion was not observed. **MS-DART:** Calculated for [C$_{19}$H$_{20}$NP]$^{2+}$: 146.57. Obtained: 146.5665 amu.

\[
[(o-C$_5$H$_4$NCH$_3$)P(CH$_3$)Ph$_2$][B(C$_6$F$_5$)$_4$]_2 \quad (3-27)
\]

A solution of freshly prepared [K][B(C$_6$F$_5$)$_4$] (162 g, 0.23 mmol, 2.05 equiv.) in CH$_2$Cl$_2$ (0.5 mL) was added to a suspension of 3-26 (64 mg, 0.11 mmol, 1.0 equiv.) in toluene (2 mL). The reaction mixture was stirred at ambient temperature for 10 min. The solution was filtered through a Kimwipe plug, dried in vacuo and then washed with n-pentane (3 x 3 mL) and Et$_2$O (3 x 4 mL). The supernatant was decanted and the oil was dried in vacuo to afford a white microcrystalline powder (125 mg, 69% Yield).

**1H NMR (400 MHz, CD$_2$Cl$_2$, Me$_4$Si):** δ 8.98 (m, 1H; p-py), 8.71 (m, 1H; o-py), 8.57 (d, J = 8 Hz, 1H; 2-py), 8.42 (m, 1H; m-py), 8.08 (m, 2H; p-Ph), 7.85 (m, 4H; m-Ph), 7.64 (m, 4H; o-Ph), 4.52 (s, 3H; N-CH$_3$), 2.92 ppm (d, $^{2}$J$_{PH} = 13$ Hz, 3H; P-CH$_3$). **$^{11}$B{1H} NMR (128 MHz, CD$_2$Cl$_2$, BF$_3$•OEt$_2$):** δ 16.7 ppm. **$^{19}$F{1H} NMR (377 MHz, CD$_2$Cl$_2$, CFCl$_3$):** δ −133.0 ppm (br m, 16F; B(o-C$_6$F$_5$)$_4$), −162.9 (t, $^{3}$J$_{FF} = 20$ Hz, 8F; B(p-C$_6$F$_5$)$_4$), −167.1 ppm (br m, 16F; B(m-C$_6$F$_5$)$_4$). **$^{31}$P{1H} NMR (162 MHz, CD$_2$Cl$_2$, H$_3$PO$_4$):** δ 22.7 ppm. **$^{13}$C{1H} NMR (126 MHz, CD$_2$Cl$_2$, Me$_4$Si):** δ 150.4 ppm (br s, 1C; p-py), 149.8 (d, $^{2}$J$_{PC} = 7$ Hz, 1C; o-py), 148.5 (br d, $^{1}$J$_{FC} = 240$ Hz, 16C; B(o/m-C$_6$F$_5$)$_4$), 147.5 (br s, 1C; 2-py), 138.9 (d, $^{4}$J$_{PC} = 3$ Hz, 2C; p-Ph), 138.5 (br d, $^{1}$J$_{FC} = 247$ Hz, 8C; B(p-C$_6$F$_5$)$_4$), 136.5 (br d, $^{1}$J$_{FC} = 247$ Hz, 16C; B(o/m-C$_6$F$_5$)$_4$), 133.4 (d, $^{3}$J$_{PC} = 11$ Hz,
1H; m-py), 132.6 (d, $^2J_{PC} = 14$ Hz, 4C; o-Ph), 131.6 (d, $^3J_{PC} = 10$ Hz, 4C; m-Ph), 127.4 (d, $^1J_{PC} = 85$ Hz, 1C; i-py), 113.0 (d, $^1J_{PC} = 90$ Hz, 2C; i-Ph), 51.4 (s, 1C; N-CH$_3$), 9.6 ppm (d, $^2J_{PC} = 57$ Hz, 1C; P-CH$_3$), resonance for boron-bound carbon atom in [B(C$_6$F$_5$)$_4$]$^-$ anion was not observed. **MS-DART:** Calculated mass for [C$_{19}$H$_{20}$NP]$^{2+}$: 146.57. Obtained: 146.5665 amu.

$$[(o-C_6H_4N)P(OPh)Ph_2][Br] \text{ (3-28)}$$

A solution of Pd$_2$(OAc)$_3$ (2 mg, 0.002 mmol, 1 equiv.) and 3-bromopyridine (11 μL, 0.11 mmol, 50 equiv.) was prepared in 3 mL toluene. The solution immediately turned bright red, and was then added to a separate vial containing (PhO)PPh$_2$ (30 mg, 0.11 mmol, 50 equiv.) before being transferred to a NMR tube. The reaction mixture was heated to 110 °C for 12 h, after which time colorless crystals settled out of solution. The supernatant was then decanted, the solid was washed with toluene (3 x 3 mL) and n-pentane (3 x 3 mL) before being filtered through a Kimwipe plug. After drying the solution in vacuo, a white microcrystalline solid was isolated (10 mg, 21% Yield).

$^1$H NMR (400 MHz, CDCl$_3$, Me$_4$Si): $\delta$ 7.97 (m, 2H; Ar-H), 7.84 (m, 9H; Ar-H), 7.73 (m, 1H; Ar-H), 7.54 (m, 1H; Ar-H), 7.28 (m, 4H; Ar-H), 6.96 ppm (2H; Ar-H). $^{31}$P-$^1$H NMR (162 MHz, CDCl$_3$, H$_3$PO$_4$): $\delta$ 65.6 ppm. $^{13}$C-$^1$H NMR (125 MHz, CDCl$_3$, Me$_4$Si): $\delta$ 137.2 (d, $J_{PC} = 3$ Hz), 134.2 (d, $J_{PC} = 12$ Hz), 134.1 (s(br)), 133.0 (d, $J_{PC} = 11$ Hz), 131.1 (d, $J_{PC} = 2$ Hz), 131.0 (d, $J_{PC} = 14$ Hz), 129.6 (s), 129.4 (d, $J_{PC} = 13$ Hz), 127.8 (s), 121.1 (d, $J_{PC} = 4$ Hz), 118.3 (d, $J_{PC} = 107$ Hz, 2C), 115.6 ppm (s). The resonance for ipso-pyridine carbon atom was not observed.

$$[(o-C_5H_4NCH_3)P(OPh)Ph_2][B(C_6F_5)_4] \text{ (3-29)}$$
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PhOTMS (31 mg, 0.19 mmol, 1.0 equiv.) was added to a solution of 2-I3 (310 mg, 0.19 mmol, 1.0 equiv.) in CH2Cl2 (0.6 mL). The reaction mixture was heated for 24 h at 45 °C, which yielded a bright yellow solution. The solvent volume was reduced to half and then 5 mL of n-pentane was added to induce precipitation. The pale-yellow oil was re-dissolved in a minimal amount of CH2Cl2, to which 3 mL of n-pentane was added. After sufficient agitation, the supernatant was decanted and the resulting solid was washed with n-pentane (3 x 3 mL) and dried in vacuo to afford a pale-yellow powder (312 mg, 96% yield).

1H NMR (400 MHz, CD2Cl2, Me4Si): δ 9.04 (m, 1H), 8.87 (m, 1H), 8.57 (m, 2H), 8.17 (m, 2H), 7.87 (m, 4H), 7.74 (m, 4H), 7.39 (m, 3H), 6.82 (m, 2H), 4.51 ppm (s, 3H).

11B{1H} NMR (128 MHz, CD2Cl2, BF3·OEt2): δ −16.7 ppm.

19F{1H} NMR (377 MHz, CD2Cl2, CFCl3): δ −133.0 (br, 16F; B(o-C6F5)4), −163.0 (t, 3JFF = 20 Hz, 8F; B(p-C6F5)4), −167.2 ppm (br m, 16F; B(m-C6F5)4).

31P{1H} NMR (162 MHz, CD2Cl2, H3PO4): δ 59.6 ppm.

13C{1H} NMR (125 MHz, CD2Cl2, Me4Si): δ 153.1 (d, JPC = 5 Hz), 149.0 (d, JPC = 10 Hz), 148.6 (d, JPC = 9 Hz), 148.5 (br d, JPC = 240 Hz, 16C), 141.4 (d, JPC = 3 Hz, 2C), 139.8 (d, 1JPC = 119 Hz), 138.5 (br d, JPC = 247 Hz, 8C), 138.3 (d, JPC = 14 Hz), 136.5 (br d, JPC = 247 Hz, 16C), 135.2 (d, JPC = 2 Hz), 134.6 (d, JPC = 13 Hz, 4C), 132.9 (d, JPC = 15 Hz), 132.3 (d, JPC = 2 Hz, 2C), 129.9 (d, JPC = 2 Hz), 119.9 (d, JPC = 4 Hz, 2C), 111.7 (d, JPC = 105 Hz, 2C), 50.9 ppm (d, JPC = 3 Hz). The resonance for boron-bound carbon atoms in [B(C6F5)4]− anion was not observed. MS-DART: Calculated for [(o-MeNC5H5)PPh2]+: 294.10. Obtained: 294.1056 amu. Anal. Calcd. for C72H22B2F40NOP: C, 50.00; H, 1.28; N, 0.81 %. Found: C, 50.05; H, 1.23; N, 0.70 %.

3.4.3 Lewis Acid Catalysis

3.4.3.1 General Method for Lewis Acid-initiated Mukaiyama-Aldol Condensation Reaction19,20

The corresponding phosphonium salt (0.1 mol%) and 2-naphthaldehyde (1.0 equiv.) were dissolved in CH2Cl2 and stirred for 5 min. Then, 1-methoxy-2-methyl-1-trimethylsiloxy-propene was added (1.2 equiv.). After 5 min at ambient temperature, the solution was dried in vacuo. The
remaining solid was dissolved in CDCl$_3$ and filtered through a Celite plug. Conversions were determined by $^1$H NMR spectroscopy with a toluene internal standard.

$^1$H NMR (400 MHz, CDCl$_3$, Me$_4$Si): $\delta$ 7.85 (m, 4H), 7.50 (m, 3H), 5.18 (s, 1H), 3.72 (s, 3H), 1.20 (s, 3H), 1.07 (s, 3H), 0.00 ppm (2, 9H). $^{13}$C($^1$H) NMR (101 MHz, CDCl$_3$, Me$_4$Si): $\delta$ 177.4, 138.6, 133.0, 132.8, 128.1, 127.7, 127.0, 126.7, 126.1, 125.9, 125.4, 79.4, 51.8, 49.4, 19.3, 0.1 ppm.

**HRMS:** Calculated mass for C$_{19}$H$_{26}$O$_3$Si$_1$: 353.1543 42. Obtained: 353.144270 amu.

### 3.4.3.2 Control Reactions with 3-24

#### 3.4.3.2.1 Reaction of 3-24 with 2-napthaldehyde

A solution of 2-napthaldehyde (100 mg, 0.64 mmol) in CH$_2$Cl$_2$ was added to 3-24 (11 mg, 0.007 mmol). The solution was stirred for 1 h at ambient temperature before being analyzed by multi-nuclear NMR spectroscopy.

#### 3.4.3.2.2 Reaction of 3-24 with 1-methoxy-2-methyl-1-trimethylsiloxy propene

A solution of 1-methoxy-2-methyl-1-trimethylsiloxypropene (150 mg, 0.86 mmol) in CH$_2$Cl$_2$ was added to 3-24 (28 mg, 0.017 mmol). The solution was stirred for 1 h at ambient temperature before being analyzed by multi-nuclear NMR spectroscopy.
3.4.3.3 Reactivity of 3-29

3.4.3.3.1 Gutmann-Beckett Test (reaction with Et₃PO)

A solution of the 3-29 (0.07 mmol) in CD₂Cl₂ (0.6 mL) was added to a separate vial containing Et₃PO (0.07 mmol). The reaction mixture was investigated by multi-nuclear NMR spectroscopy after 1 h at ambient temperature.
Figure 3-7. $^{31}\text{P}[^1\text{H}]$ (CD$_2$Cl$_2$) NMR spectrum of 3-29 with 1 equiv. of Et$_3$PO.

3.4.3.3.2 Hydrodefluorination of 1-fluoropentane with Et$_3$SiH$^{46, 75, 76}$

In a 20 mL vial, a solution of 3-29 (5 mol%) was prepared in 0.7 mL CD$_2$Cl$_2$. Et$_3$SiH (0.04 mmol) was added at ambient temperature, the reaction was briefly stirred, and then 1-fluoropentane was added (0.04 mmol). Fluorobenzene (C$_6$H$_5$F, 0.03 mmol) was then added as an internal standard. The reaction mixture was transferred to a NMR tube and left at ambient temperature for 1 h, before being monitored by $^{19}\text{F}[^1\text{H}]$ NMR spectroscopy. Conversions were determined from the proportion of Si-F bonds in Et$_3$SiF formed relative to C-F bonds in 1-fluoropentane consumed.$^{75}$ Refer to Chapter 2 for a full NMR analysis.

![Figure 3-8. $^{19}\text{F}[^1\text{H}]$ NMR spectrum for the hydrodefluorination of 1-fluoropentane with 3-29.](image-url)

3.4.3.3.3 Hydrosilylation of α-methylstyrene with Et$_3$SiH$^{46, 76}$

In a 20 mL vial, a solution of 3-29 (2 mol%) was prepared in 0.7 mL CD$_2$Cl$_2$. Et$_3$SiH (0.05 mmol) was added at ambient temperature, the reaction mixture was briefly stirred, and then α-methylstyrene (0.05 mmol) was added. The mixture was transferred to a NMR tube and heated at 45 °C for 4 h. The conversion was determined by the proportion of C-H bonds in the product.
formed relative to the CH₃ bonds in α-methylstyrene consumed. Refer to Chapter 2 for a full NMR analysis.

![Figure 3-9. ¹H NMR spectrum (CD₂Cl₂) of hydrosilylation catalysis with 3-29.](image)

3.4.3.3.4 **Dehydrocoupling of Phenol and Et₃SiH⁴⁶, ⁷⁵, ⁷⁷**

In a 20 mL vial, a solution of 3-29 (2 mol%) was prepared in 0.7 mL CD₂Cl₂. Et₃SiH (0.05 mmol) was added at ambient temperature, the reaction mixture was briefly stirred, and then added to a vial containing phenol (0.05 mmol). The mixture was transferred to a NMR tube and heated at 50 °C for 24 h.

![Figure 3-10. ¹H NMR spectrum (CD₂Cl₂) of dehydrocoupling catalysis with 3-29.](image)

3.4.3.3.5 **Hydrodeoxygenation of Benzophenone with Et₃SiH⁶¹**

In a 20 mL vial, a solution of 3-29 (1 mol%) was prepared in 0.7 mL CD₂Cl₂. Et₃SiH (0.04 mmol) was added at ambient temperature, the reaction was briefly stirred, and then the solution was added to a vial containing benzophenone (0.02 mmol). The reaction mixture was left to stir at ambient temperature for 48 h, before toluene (0.02 mmol) was added as an internal standard. The reaction
mixture was transferred to a NMR tube and conversions were determined by $^1$H NMR spectroscopy.

**Figure 3-11.** $^1$H NMR spectrum (CD$_2$Cl$_2$) of hydrodeoxygenation catalysis with 3-29.

**Figure 3-12.** $^{31}$P{$^1$H} NMR spectrum (CD$_2$Cl$_2$) of hydrodeoxygenation catalysis with 3-29.

3.4.3.3.6 Hydrodeoxygenation of Benzophenone after Exposure to Air

A 20 mL vial containing 3-29 (1 mol%) was exposed to air for 24 h before being transferred into the glovebox and adding 0.7 mL CD$_2$Cl$_2$. Et$_3$SiH (0.04 mmol) was then added at ambient temperature, the reaction was briefly stirred, and then the solution was added to a vial containing benzophenone (0.02 mmol). The reaction mixture was left to stir at ambient temperature for 48 h, before toluene (0.02 mmol) was added as an internal standard. The reaction mixture was transferred to a NMR tube and monitored by $^1$H NMR spectroscopy.
3.4.4 Computational Details

3.4.4.1 FIA and ω values for Cyclopropenium- and Pyridiniumphosphonium Salts (Table 3-2)

All calculations were performed by past post-doctoral fellow Dr. Timothy Johnstone:

The calculations were performed in the gas phase with Gaussian 09. When available, geometry optimizations were carried out using X-ray crystallographic coordinates as the input geometry, following normalization of hydrogen atom positions using Mercury 3.8. Otherwise, initial coordinates were obtained by building the molecule in GaussView 5.0. Geometry optimizations were performed at the BP86/def2-TZVP level of theory, followed by frequency calculations at this same level of theory to confirm that the optimized structures were minima on their respective potential energy surfaces. In no cases were imaginary frequencies obtained. The energies at these optimized structures were subsequently obtained at the MP2/def2-TZVPP level of theory. These MP2 energies were used to calculate FIAAs as previously described. The global electrophilicity index (ω) was calculated as reported previously using the MP2 HOMO and LUMO energies.

3.4.4.2 One-dimensional Potential Energy Surfaces of 3-24 and 3-27

The following computational investigation was conducted by past post-doctoral fellow Dr. Timothy Johnstone:
Figure 3-14. Relaxed potential energy surface scan (BP86/def2-TZVP) for torsional rotation about the P–C_{py} bond of the cation of 3-24 (ortho-isomer). The torsion angle is defined as depicted in Figure 3-2 with 0° as the conformation shown in Figure 3-2a and 180° as the conformation shown in Figure 3-2b.

Figure 3-15. Relaxed potential energy surface scan (BP86/def2-TZVP) for torsional rotation about the P–C_{py} bond of the cation of 3-27 (meta-isomer). The torsion angle is defined as depicted in Figure 3-2 with 0° as the conformation shown in Figure 3-2a and 180° as the conformation shown in Figure 3-2b.
3.5 References


47. M. Mehta, Doctor of Philosophy, University of Toronto, 2017.


Chapter 4

Applications of Air-stable Phosphorus(V) Trications in Reductive Amination and C-F Bond Activation Reactions

4 4.1 Introduction

4.1.1 Water-tolerant Lewis Acids

In the past decade, frustrated Lewis pair (FLP) chemistry has emerged as a metal-free alternative to transition metal-catalyzed reductions. In these systems, the unquenched reactivity of sterically encumbered Lewis acids (LA) and Lewis bases (LB) enable the activation of σ-bonds in small molecules like H₂ and R₃SiH, to generate useful reducing agents. However, most reactions require rigorous exclusion of H₂O because in most cases, water coordination to the Lewis acid results in irreversible O-H activation yielding the corresponding aqua species of the Lewis acid (e.g. [B(C₆F₅)₃•H₂O] has a pKa = 8.4 in CH₃CN, comparable to HCl). The deprotonation of bound LA-OH₂ is typically facilitated by a Lewis base in solution. However, in some cases, rigorous heating may favour intramolecular proton transfer from the bound H₂O to one of the aryl substituents of the borane Lewis acid. In either case, a catalytically inactive combination is formed, preventing further reactivity (Scheme 4-1, top).

![Scheme 4-1. Potential LA-deactivation pathways in the presence of H₂O.](image)

In a similar vein, the reactions of some highly electrophilic phosphorus(V) cations with water have been investigated. Exposure of [(C₆F₅)₃P(OAr)][B(C₆F₅)₄] (Ar = C₆H₅, 4-FC₆H₄, 2,4-F₂C₆H₃, C₆F₅) to H₂O resulted in a rapid establishment of dynamic acid/base equilibrium with
OP(C₆F₅)₃/HB(C₆F₅)₄ and [(C₆F₅)₃P(OH)][B(C₆F₅)₄] upon liberation of HOAr (Scheme 4-1, bottom).⁸ Similarly, exposure of [(C₆F₅)₃PF][B(C₆F₅)₄] to atmospheric moisture resulted in rapid degradation (1 min) to OP(C₆F₅)₃, observable by NMR spectroscopy.⁹

Efforts to increase the water-tolerance in FLP chemistry has witnessed significant advances.² For boranes, the intolerance to water-base combinations has been tackled by decreasing the Lewis acidity of the borane¹⁰ or by designing Lewis acids with increased steric bulk around the boron centre thus reducing the propensity for irreversible water-binding and subsequent activation.²

Another approach to overcome water intolerance in FLP and Lewis acid chemistry is the use of non-boron based Lewis acids. In this regard, carbenium¹¹⁻¹³ and tin(IV) cations,¹⁴,¹⁵ isoelectronic with boranes, are examples of Lewis acids that are more compatible with water-base combinations.¹⁶⁻²⁰

For selected phosphorus-based Lewis acids, trace water remains problematic as rapid P-F cleavage has been frequently observed in the case of fluorophosphonium species. Efforts have been made to increase the stability of these reactive EPCs by: 1) Decreasing the Lewis acidity and/or 2) Increasing the steric bulk of the substituents at the P centre (Figure 4-1).

![Figure 4-1. Examples of robust EPCs. Counterions have been omitted for clarity.](image)

In one approach, C₆F₅ substituents in [(C₆F₅)₃PF][B(C₆F₅)₄] were replaced with C₆Cl₅ rings to increase the steric bulk around the Lewis acidic P centre; however, the P-F bond remained prone to hydrolysis.²¹ Replacement of the fluoride with aryloxy groups increased the stability of the EPCs, but degradation upon exposure to atmospheric moisture was observed after 1.5 h.⁹ As detailed in Chapter 3, replacement of the fluoride substituent for an alkyl or aryl group increased the stability overall, but the reactivity was lessened and some decomposition was still observed in the present of oxygen donors.²² Bismethyl-pyridiniumphosphonium dication were also shown to be more stable, but less reactive than their P-F counterparts.²³ Encouragingly, the phosphorus(V)
cation [Ph₃PCF₃]⁺ was shown to be stable in the presence of water even at elevated temperatures. However, rapid decomposition was observed at room temperature in the presence of a combination of water and a moderate organic base, affording the corresponding phosphine oxide and HCF₃. In a different approach, the Radosevich group exploited the geometry of a tetraazamacrocycle to achieve water stability with pentacoordinate cationic phosphacorroles.

Overall, developing EPCs that are active for desirable bond activation reactions and stable in the presence of water/base combinations remains a challenge in main group Lewis acid chemistry, yet is critical for functional group tolerance and applications of these salts in FLP chemistry.

4.1.2 Reductive Amination Reactions

Reductive amination has become a well-known selective C-N bond-forming transformation for synthesizing amines, which are ubiquitous functionalities in natural products, pharmaceuticals and agrochemicals. For this reaction, judicious choice of the catalyst is required since the reaction proceeds through an imine and generates a stoichiometric amount of H₂O. As well, reactions require a reductant, such as a borohydride, H₂ or a hydrosilane. While borohydride derivatives are common, the use of milder and inexpensive silanes such as polymethylhydrosiloxane (PMHS) or tetramethyldisiloxane (TMDS) offer useful alternatives for large-scale reactions. In this regard, several metal-mediated reductive aminations employing hydrosilane reductants have been reported using iridium, indium, tin, molybdenum, zinc, iron, rhenium complexes, among others. While there are reports of stoichiometric trifluoroacetic acid and Et₃SiH effecting reductive amination reactions, examples of metal-free FLP-catalyzed transformations have limited precedence.

In one report, Fu et al. use catalytic B(C₆F₅)₃ for the reductive amination of primary and secondary amines using carboxylic acids; however, this process requires the use of 5 equiv. PMHS. In a later report, Fasano et al. improved the reaction conditions and catalytic amounts of B(C₆F₅)₃, with 1.2 equiv. of Me₂PhSiH were shown to affect the reductive amination of primary and secondary arylamines with aldehydes and ketones. Interestingly, N-arylimines did not deprotonate [B(C₆F₅)₃•H₂O], but irreversible deprotonation and subsequent inactivity was observed upon addition of the more basic alkyl amine tBuNH₂.
4.1.3 C-F Bond Activation

The strength of C-F bonds is particularly favourable for a variety of applications including plastics, refrigerants, coatings, surfactants and agro- and pharmaceutical chemicals\(^1\) because C-F bonds are thermally, chemically and metabolically-stable.\(^2\) At the same time, this stability generates a problem because some species containing C-F bonds are persistent in the biosphere and can either be toxic or cause deleterious effects. Most notably, global warming is attributed, in part, to the long lifetimes of chlorofluorocarbons (CFCs) and saturated perfluorocarbons (PFCs) in the stratosphere.\(^3\) Due to the robustness of these CFCs and PFCs (the lifetime of fluorocarbons in some cases can be up to 10,000 years),\(^4\) the development of methodologies capable of degrading these fluorocarbons is necessary in order to prevent further damage to our stratosphere.

The prospects of such new chemical pathways has prompted a variety of studies\(^5\) for C-F bond activation by Lewis acids, Brønsted superacids, and transition\(^6\)-\(^8\) and rare-earth metals. In this regard, the field of main group catalysts for C-F bond activation has garnered significant attention, due to the lower toxicity, cost and higher abundance relative to precious metals.\(^9\)\(^,\)\(^10\) After the first report by Olah in 1964 using BF\(_3\) to activate alkylfluorides and facilitate Friedel-Crafts reactions with benzene and benzene derivatives (Scheme 4-2, top),\(^11\) many other main group systems have been developed. Indeed, cationic and neutral silicon-, boron- and aluminum-based Lewis acids have all been examined in C(sp\(^3\))-F bond activation.\(^9\) More recently, Gabbaï et al. demonstrated that [Sb(C\(_6\)F\(_5\))\(_4\)][B(C\(_6\)F\(_5\))\(_4\)] is capable of abstracting fluoride from [SbF\(_6\)]\(^-\), and can catalyze the hydrodefluorination of fluoroalkanes in the presence of Et\(_3\)SiH.\(^12\) Similarly, Greb and coworkers have extended such reactivity to the neutral Si Lewis super acid, bis(perchlorocatecholato)silane.\(^13\) Other approaches to C-F activation chemistry that exclude the use of transition metals are much less common. In rare examples, mild bases such as K\(_2\)CO\(_3\) have been used to mediate C-F activation in a fluorohydrzone or effect 1,2 or 1,5 fluorine migrations in cyclopropyl-substituted fluoroexpoxides.\(^14\)\(^,\)\(^15\)
Several approaches to C-F bond activation exploiting phosphorus-based species have emerged in recent years. Phosphorus-based Lewis acids have been developed and used to achieve C-F catalytic hydrodefluorination and C-C bond formation reactions. Perhaps most notable was the report in 2013, wherein [(C₆F₅)₃PF][B(C₆F₅)₄] was shown to be an active catalyst for the hydrodefluorination of fluoroalkanes (Scheme 4-2, middle). In addition, the use of P(III)-based Lewis bases in FLP chemistry has also provided fruitful new avenues for C-F bond functionalizations. In particular, the monodefluorination of gem-difluoromethyl groups was achieved with the FLP combination of P(o-Tol)₃ and B(C₆F₅)₃ (Scheme 4-2, bottom).

4.2 Results and Discussion

4.2.1 Synthesis of P₃-trimethylated Triphosphonium(V) Trications

In Chapter 3, we highlighted the synthesis and reactivity of more robust phosphonium salts with P-aryloxy and P-alkyl substitutions instead of the reactive P-F fragment. While these compounds were shown to be more stable, there was a noticeable decrease in the reactivity relative to known phosphonium(V) dicaticionic species, including the fluoro-pyridiniumphosphonium dications mentioned in Chapter 2. Building on these previous results we wanted to combine the enhancement of Lewis acidity imparted from P-C bonds with the reactivity of polycationic species to develop more reactive, yet robust phosphorus(V) Lewis acid catalysts.

We began our investigation with the common “triphos” framework, prevalent in transition metal coordination chemistry. The diversity of this bis(diphenylphosphinoethyl)phenylphosphine...
flexible chelate was reported early on in 1971, wherein a family of coordination complexes were synthesized and characterized bearing the triphos ligand. In a similar vein, C₃v-symmetric 1,1,1-tris(diphenylphosphinomethyl)ethane is a well-known tripodal ligand in organometallic chemistry, and its ability to stabilize a wide variety of unprecedented bonding modes has been well documented. However, while the ability of the triphos isomers to act as Lewis bases is well-known, their reactivity umpolung as Lewis acids remains underexplored.

To start, we reacted commercially available triphosphate ligand PhP(CH₂CH₂PPh₂)₂ 4-I with CH₃I. When equimolar amounts were mixed and left to stir at ambient temperature for 20 h, a white precipitate settled out of solution. The solid was isolated and characterized by multi-nuclear NMR spectroscopy and mass spectrometry. Analysis of the ³¹P{¹H} NMR spectrum (CD₃CN) shows new doublets at δ 34.4 ppm (³JPP = 60 Hz) and δ 26.6 ppm (³JPP = 60 Hz). The ¹H NMR spectrum contains doublet resonances at δ 2.84 ppm (²JPH = 14 Hz) and δ 2.71 ppm (²JPH = 14 Hz) indicative of the P-bound methylene protons. It is noteworthy that 4-2 is insoluble in most polar organic solvents and only partially-soluble in CH₃CN. Moreover, a similar reaction was reported by Colton et al.; however, attempts to observe the tricationic species by mass spectrometry were unsuccessful.

On route to more soluble phosphorus tricationic species, we targeted the synthesis of [OTf] and [B(C₆F₅)₄] salts, since it was observed in Chapter 2 that the latter demonstrated improved solubility in polar organic solvents. In this regard, we were interested in investigating both triphosphate ligands 4-1 and MeC(CH₂PPh₂)₃ 4-4. To begin our investigation, both 4-1 and 4-4 were treated with an excess amount of MeOTf (6-10 equiv.) in CH₂Cl₂ at ambient temperature (Scheme 4-3). In both cases, after 10-15 minutes, a white solid precipitated from the solution. The reaction was left stirring at room temperature for 12 h to ensure complete conversion to the tricationic species, after which time solvent removal and washings with n-pentane gave the desired P₃-trimethylated phosphonium trications [PhPMe(CH₂CH₂PMePh₂)₂][OTf]₃ 4-3 and [MeC(CH₂PMePh₂)₃][OTf]₃ 4-5 in 88% and 96% yields, respectively. Both compounds were characterized by NMR spectroscopy, elemental analysis and X-ray crystallography.
Scheme 4-3. Syntheses of P₃-trimethylated phosphonium trications 4-2, 4-3 and 4-5.

For 4-3, the $^{31}$P{¹H} NMR spectrum (CD$_₂$Cl$_₂$) contains two doublet resonances at δ 33.4 ($^3J_{PP} = 58$ Hz) and δ 25.7 ppm, and the ¹H NMR spectrum displays the P-bound methylene resonances at δ 2.63 ppm (d, $^2J_{PH} = 14$ Hz) and δ 2.62 ppm (d, $^2J_{PH} = 14$ Hz). These data are in close agreement to those reported for 4-2. The NMR spectra for both 4-2 and 4-3 contain resonances which are shifted downfield relative to triphos starting material 4-1 ($^{31}$P{¹H}: δ –23.2, –54.1 ppm),$^{74}$ supporting the notion of deshielding upon methylation of the P-centres. A similar trend was observed for tricationic species 4-5. Single crystals of 4-3 and 4-5 were obtained and characterized by X-ray diffraction studies, further confirming their formation (Figure 4-2).

Interestingly, in the solid-state, the trication of 4-3 (which co-crystallized with one molecule of H₂O) has a trans orientation of the P-Me groups, wherein the middle phosphorus atom is pointed down towards two [OTf]$^-$ counterions. Each phosphorus centre adopts a pseudo-tetrahedral geometry and the bond lengths are unremarkable. However, there are several short inter-ion interactions of the O atom in the [OTf]$^-$ counterions with the C-H groups in 4-3. In this case, these approximate short O-H contacts (O1-H1: 2.656 Å; O1-H2: 2.199 Å; O2-H3: 2.290 Å; O2-H4: 2.169 Å; O3-H5: 2.565 Å) are within the sum of the O, H van der Waals radii (2.72 Å). This hydrogen bonding network is reminiscent of urea-based organocatalysts, where short anion-H contacts are also observed.$^{75}$ While O1 and O2 appear to occupy the electrophilic pocket of P2 and P3, all the P,O distances are longer than the sum of the P, O van der Waals radii (3.32 Å).
Figure 4-2. POV-ray depictions of 4-3. Non-interacting hydrogen atoms and H$_2$O molecule have been omitted for clarity. C: black, H: white, P: orange, O: red, S: yellow, F: purple.

Figure 4-3. POV-ray depictions of the trications of 4-5. Hydrogen atoms, non-interacting [OTf]$^-$ counterions, and co-crystallized solvent molecules have been omitted for clarity. C: black, H: white, P: orange, O: red, S: yellow, F: purple.
Notably, the trication of 4-5 shows an interesting arrangement in the solid-state, assuming pseudo-C₃ symmetry, with all the methyl groups oriented in the same direction. One of the three [OTf] counterions occupies the putative electrophilic pocket. However, the P-O_{(OTf)} contacts (O1-P1: 4.341(2) Å; O1-P2: 4.378(2) Å; O1-P3: 4.478(2) Å) are longer than the sum of the P, O van der Waals radii (3.32 Å). Interestingly, short contacts depicted in Figure 4-3 are seen between the [OTf] anion and the CH₂ protons of the cation (approximate inter-ion distances: O1-H1: 2.484 Å; O1-H2: 2.481 Å; O1-H3: 2.639 Å) which are within the sum of the O, H van der Waals radii (2.72 Å).

Both 4-3 and 4-5 can be converted to the corresponding [B(C₆F₅)₄] salts upon reaction with 3 equiv. of [Na][B(C₆F₅)₄]. After stirring at ambient temperature for 2 h and removing the [Na][OTf] side product, 4-6 and 4-7 were isolated in 75% and 81% yields, respectively (Scheme 4-4). Both trimethylated phosphonium salts were characterized by NMR spectroscopy and elemental analysis. For 4-6, the $^{31}$P{$^1$H} NMR spectrum (CD₂Cl₂) contains doublet resonances at δ 32.9 ppm ($^3J_{PP} = 55$ Hz) and δ 24.2 ppm. The resonances for the P-bound methylene protons appear in the $^1$H NMR spectrum (CD₂Cl₂) at δ 2.35 ppm (d, $^2J_{PH} = 13$ Hz) and δ 2.25 ppm (d, $^2J_{PH} = 13$ Hz). For 4-7, the $^{31}$P{$^1$H} NMR spectrum (CD₃CN) contains a singlet resonance at δ 18.1 ppm. The resonances for the P-bound methylene protons appear in the $^1$H NMR spectrum at δ 2.68 ppm (d, $^2J_{PH} = 14$ Hz). These data are in close agreement with those reported for the corresponding [OTf] salts 4-3 and 4-5; however, it is noteworthy that the [B(C₆F₅)₄] salts were soluble in polar organic solvents such as CH₂Cl₂, whereas the [OTf] salts were only partially soluble in CH₃CN.

Scheme 4-4. Syntheses of P₃-trimethylated phosphonium salts 4-6 and 4-7.
It is important to note that while polycationic phosphonium-based polymers and oligomers have found applications in material science and biology, as ionic liquids, metal scavengers, antibacterial agents, and dedrimers, their utility in FLP chemistry and Lewis acid catalysis remains unexplored.

4.2.2 Lewis Acidity Tests

With these new trimethylated tricationics in hand, we wanted to probe their relative Lewis acidity. The first method we chose was the Gutmann-Beckett test, which is outlined in detail in Chapter 2, section 2.2.3.1. In this case, when 4-3 was mixed with an equimolar amount of Et₃PO, a small downfield shift (Δ = 4.1 ppm, compared to free Et₃PO ³¹P(δ) = 51.0 ppm) of the Et₃PO signal was observed in the ³¹P{¹H} NMR spectrum (CH₂Cl₂). A slight broadening of the Et₃PO resonance was also observed, which suggests the formation a weak adduct. A similar observation was obtained for 4-5, suggesting a weak interaction with Et₃PO in both cases. Interestingly, these results are comparable to [(C₆F₅)₃P(OC₆F₅)][B(C₆F₅)₄] which contains strongly electron-withdrawing substituents at the phosphorus centre. Moreover, the Gutmann-Beckett test with [Ph₃PMe][OTf] 4-8 (in a 3:1 ratio of phosphonium to Et₃PO, to achieve equivalent [R₄P]⁺ content) showed a slightly smaller chemical shift change of Et₃PO by ³¹P{¹H} NMR spectroscopy (Δ = 3.8 ppm). Collectively, these initial results highlight the potential stability of these system relative to previously reported mono and dicationic phosphonium species, as no degradation was observed.

Another experimental measure of Lewis acidity involves probing reactivity in select reactions, wherein comparison to related Lewis acids can subsequently be completed. The reactions chosen were: Friedel-Crafts dimerization of 1,1-diphenylethylene, hydrodefluorination of 1-fluoroadamantane, hydrosilylation of α-methylstyrene, dehydrocoupling of phenol and Et₃SiH, and the hydrodeoxygenation of benzophenone, as previously reported in Chapter 2 and Chapter 3.

For the dimerization of 1,1-diphenylethylene, 2 mol% catalyst was used and after 2.5 h at ambient temperature, 10% and 25% conversion to 1-methyl-1,3,3-triphenyl-2,3-dihydro-¹H-indene was observed for 4-6 and 4-7, respectively (determined from the ¹H NMR spectra). For the hydrodefluorination of 1-fluoroadamantane, in both cases, 5 mol% catalyst yielded complete conversion to adamantane after stirring at ambient temperature for 1 h (determined from the consumption of C-F and formation of Si-F in the ¹⁹F{¹H} NMR spectra). For the hydrosilylation reaction, 2 mol% catalyst was used and after heating at 45 °C for 4 h, 82% and 85% conversion
(determined by \(^1\)H NMR) to the hydrosilylated product was obtained with \(\mathbf{4-6}\) and \(\mathbf{4-7}\), respectively. For the dehydrocoupling reaction, both catalysts yielded \(>99\%\) conversion to \(\text{Et}_3\text{SiOPh}\) (as determined by the \(^1\)H NMR spectra) after heating at \(50\ \degree\text{C}\) for \(48\) h. Lastly, the hydrodeoxygenation of benzophenone to diphenylmethane was completed with \(1\ \text{mol}\%\) catalyst and in both cases, \(>99\%\) conversion was observed after stirring at ambient temperature for \(2\) h.

It is noteworthy that in all cases, the [OTf] trications \(\mathbf{4-3}\) and \(\mathbf{4-5}\) were inactive for all catalytic reactions, even upon increasing reaction temperature and time, which is unsurprising given the same observation was reported in Chapter 2. Overall, the reactivity of \(\mathbf{4-6}\) and \(\mathbf{4-7}\) are similar, with \(\mathbf{4-7}\) being only slightly more active in some reactions. When the reactivity of \(\mathbf{4-6}\) and \(\mathbf{4-7}\) are compared to pyridinium fluorophosphonium dication \(\mathbf{2-13}\) and the phenoxy derivative \(\mathbf{3-29}\), both \(\mathbf{4-6}\) and \(\mathbf{4-7}\) underperform as catalysts for these reactions. However, when compared to pyridinium methylphosphonium dication \(\mathbf{3-24}\), both \(\mathbf{4-6}\) and \(\mathbf{4-7}\) are superior catalysts. Collectively, these results align with our proposed hypothesis of improved stability (no signs of decomposition during or after any of the catalysis) and reactivity upon increasing the formal charge of the molecule without the addition of any polar P-F/O bonds.

To gain some insight into the site of reactivity, we investigated the reactivity of \(\mathbf{4-6}\) and \(\mathbf{4-7}\) with different donor molecules (reactions with \(\mathbf{4-7}\) will be included in fellow graduate student Kevin Szkop’s thesis). Given the three cationic centres, there are a few different possibilities for the mode of activation: 1) All three \(\text{P}\) centres act synergistically to bind the substrate 2) Two \(\text{P}\) centres act synergistically, wherein one is simply an electron-withdrawing group, or 3) One \(\text{P}\) centre activates the substrate with two pendant cationic electron-withdrawing substituents. Inspired by recent work by Gabbaï \textit{et al.} wherein they demonstrated double electrophilic activation of a carbonyl with an air stable methylated distibonium dication, we first targeted oxygen donor species. However, reactions of \(\mathbf{4-6}\) with benzaldehyde, \(\text{N},\text{N}\)-dimethylformamide (DMF), \(\text{N},\text{N}\)-dimethylsulfoxide (DMSO) did not lead to any observable reaction or interaction, and all attempts to crystallize the adducts were unsuccessful. Similarly, reactions of \(\mathbf{4-6}\) with \(\text{Et}_3\text{SiH}\), PhSiH\(_3\) did not yield any spectroscopic changes, even upon cooling the solutions to \(-80\ \degree\text{C}\).

Efforts to form a FLP for further reactivity were met with some challenges. While no reaction or adduct formation was observed with \(\mathbf{4-6}\) and PPh\(_3\), addition of PtBu\(_3\) to a solution of \(\mathbf{4-6}\) resulted in the formation of a mixture of unidentifiable products as observable by \(^{31}\text{P}\{^1\text{H}\}\) NMR
spectroscopy. Reaction with \( N,N \)-dimethylaminopyridine (DMAP) afforded similar decomposition. Combinations of \( 4-6 \) and \( (p\text{-tol})_2\text{NSiEt}_3 \) or \( \text{t} \text{butylphenylimine} \) were used to attempt the activation of HD; however, no reaction was observed. Lastly, we attempted to capture fluoride and/or observe an interaction with a P(V) centre using \( p \)-bromotrifluorotoluene and \( \text{1-fluoroadamantane} \). However, even upon cooling reactions mixtures to \(-80^\circ \text{C}\), no spectroscopic evidence for an interaction of \( 4-6 \) with fluoride was obtained \( (i.e. \) no \( \text{P-F} \) coupling was observed). Similar observations were reported with \( 4-7 \).

To further understand the Lewis acidic properties of these tricationic species, DFT calculations were performed at the M11/def2-TZVP level of theory by post-doctoral fellow Dr. John De Backere. For the cations of \( 4-3/4-6 \) and \( 4-5/4-7 \), the isomers which reflect the solid-state structures were considered and their lowest unoccupied molecular orbitals (LUMOs) are depicted in Figure 4-4. The LUMO of \( 4-5/4-7 \) (Figure 4-4, left) is delocalized, with prominent contribution from the phosphorus atoms. Similarly, the LUMO+1 of \( 4-3/4-6 \) (Figure 4-4, right) is still quite low in energy \( (\Delta = 0.571 \text{ eV} \text{ vs LUMO}) \) and is delocalized across the molecule. The phosphorus-centered orbitals in the cation of \( 4-3/4-6 \) primarily constitute P-C(sp\(^3\)) (outer P atoms) and P-C(sp\(^3\)) (central P atom) antibonding interactions. These results are reminiscent of related tetragonal P(V) cationic phosphacorroles, wherein the LUMO+3 reveals basal P-N antibonding interactions.\(^{25} \) Collectively, these results are fundamentally different than most trigonal EPCs which have a \( \sigma \)-antibonding acceptor orbital \textit{trans} to the strongly electron-withdrawing apical substituent,\(^{56} \) and may contribute to the remarkable stability of the cations of \( 4-3/4-6 \) and \( 4-5/4-7 \).

\[ \text{Figure 4-4. Surface contour plots (isovalue 0.02) of the LUMO of the cation of 4-5/4-7 (left) and the LUMO+1 of the cation of 4-3/4-6 (right).} \]
Collectively, these data do not support nor discredit the mode of activation of trications 4-6 and 4-7. Given the precedent for phosphonium-catalyzed reactions, one would presume that the Lewis acidity and site of reactivity is derived from the P centres. However, based on the solid-state structures depicted in Figure 4-2 and 4-3, we cannot rule out the potential activation of substrate by the hydrogen bonding network.

4.2.3 Applications in Reductive Amination

4.2.3.1 Catalyst Optimization

While the field of EPC-catalyzed transformations has grown significantly in the last 5 years, transformations have been limited to reactions which do not employ strongly donating substrates or generate strongly donating products, including water. Moreover, reactions generally require strict air- and moisture-free conditions, limiting further applications of EPCs. In this regard, we first wanted to probe the robustness of the [OTf] and [B(C₆F₅)₄] salts in transformations which are incompatible for other EPCs. To our delight, all trimethylated phosphonium salts 4-3, 4-5, 4-6 and 4-7 can be stored as solids for months in air and dissolved in non-purified solvents such as CH₃CN and CH₂Cl₂ (obtained from the benchtop). It is also noteworthy that the phosphonium salts were stable in the presence of an excess (10 equiv.) amount of water and aniline, with no phosphine oxide formation or signs of other degradation observed upon heating solutions at 100 °C for 24 h.

Inspired by this observation, we sought to test the catalytic reactivity of these tricationic species in reductive amination reactions. For this transformation, the corresponding imine is formed and reduced in situ without purification, thus, reactivity in the presence of water and base is essential.

To begin our investigation, we chose the [OTf] salts 4-3 and 4-5 first as their synthesis can be completed on a gram scale, is more facile and has a lower molecular weight compared to the [B(C₆F₅)₄] salts. We targeted the reductive amination of carbonyl compounds with primary amines, which has recently been reported for boranes. To probe the reactivity of the trications as Lewis acid catalysts in reductive amination reactions, 5 mol% of 4-3 or 4-5 were dissolved in untreated and undried CH₃CN (taken from the benchtop) and then were mixed with benzoaldehyde (1 equiv.) aniline (1.2 equiv.) and PhMe₂SiH (1.2 equiv.). After stirring at ambient temperature for 18 h, a significant amount of imine was formed, as observable by ¹H NMR spectroscopy, without any evidence of the desired product. This result is similar to that previously reported for the borane-catalyzed reaction. However, heating the reaction mixtures to 100 °C in a sealed NMR tube for
5 h resulted in the formation of the desired N-benzyl-aniline using both 4-3 and 4-5. A control experiment without catalyst showed no conversion to the desired amine product under identical conditions (only aldehyde, aniline and imine were observed in the \(^1\)H NMR spectrum). As well, no degradation of catalyst was observed upon heating a solution of either 4-3 or 4-5 in “wet” CH\(_3\)CN to 100 °C for 24 h.

![Chemical reaction](image)

Table 4-1. Reductive amination reactions catalyzed the P(V) Lewis acids.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Catalyst</th>
<th>Time (h)</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>None</td>
<td>18</td>
<td>0</td>
</tr>
<tr>
<td>2</td>
<td>5 mol% 4-3</td>
<td>5</td>
<td>82</td>
</tr>
<tr>
<td>3</td>
<td>5 mol% 4-5</td>
<td>5</td>
<td>93</td>
</tr>
<tr>
<td>4</td>
<td>15 mol% 4-8</td>
<td>5</td>
<td>58</td>
</tr>
<tr>
<td>5</td>
<td>7.5 mol% 4-9</td>
<td>5</td>
<td>20</td>
</tr>
</tbody>
</table>

Notably, using [Ph\(_3\)PMe][OTf] 85 4-8 as the catalyst with 15 mol% (to provide comparable [R\(_4\)P]+ content) 58% conversion to the desired product was obtained after 5 h at 100 °C (Table 4-1, Entry 4). Longer reaction times were required for comparable conversion. Similarly, when 7.5 mol% of dicationic species [Ph\(_2\)PMe(CH\(_2\)_3MePPh\(_2\)][OTf]\(_2\) 4-9 was used as the catalyst (to provide comparable [R\(_4\)P]+ content), 20% conversion was observed after 5 h, and only 41% after 24 h. This decrease in reactivity compared to 4-8 may be a result of increased electron density around the P-centre from the alkyl linker.

4.2.3.2 Scope of Reductive Amination Reaction

Given the greater reactivity observed with 4-5 shown in Table 4-1, we opted to continue with 4-5 exclusively for further reductive amination reactions. To this end, all reactions were completed in air, with “wet” (i.e. unpurified and from the benchtop) and untreated reagent-grade CH\(_3\)CN as the
solvent. Reaction mixtures were heated in a tightly sealed NMR tube to 100 °C for 5 h unless otherwise stated. Several functional groups on both the aniline and aldehyde were compatible with our reaction conditions (Table 4-2). Anilines with electron-withdrawing groups were well tolerated. For example, when 2-bromoaniline and 2-fluoroaniline were used 99% and 93% conversion to the desired secondary amine was observed, respectively. 3-trifluoromethyl and 4-chloroaniline were also tolerated and yielded 99% and 93% conversions. The tolerance to the -CF₃ moiety is noteworthy as previously reported EPCs have been shown to activate the C-F bonds of trifluorotoluene and other trifluoromethyl arenes.⁵⁶, ⁵⁹ Electron-donating groups were also well tolerated, albeit the conversions were lower. When 2,6-diisopropylaniline was used, 49% conversion was obtained, and 4-hexylaniline yielded 61% of the desired product. When the aniline was replaced with the more basic t-butylamine, the reductive amination with benzaldehyde and PhMe₂SiH using 4-5 was unsuccessful likely due to catalyst decomposition. In this case, a complex ³¹P{¹H} NMR spectrum was observed, which was not studied further.

![Reductive amination reaction](image)

Table 4-2. Reductive amination reactions with aldehydes and anilines using 4-5.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Aldehyde</th>
<th>Aniline</th>
<th>Product</th>
<th>Conv. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>PhCHO</td>
<td><img src="image" alt="" /></td>
<td>![image]</td>
<td>99</td>
</tr>
<tr>
<td>2</td>
<td>PhCHO</td>
<td>![image]</td>
<td>![image]</td>
<td>93</td>
</tr>
<tr>
<td>3</td>
<td>PhCHO</td>
<td>![image]</td>
<td>![image]</td>
<td>49</td>
</tr>
<tr>
<td>No</td>
<td>Compound</td>
<td>Structure</td>
<td>Percentage</td>
<td></td>
</tr>
<tr>
<td>----</td>
<td>----------</td>
<td>-----------</td>
<td>------------</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>PhCHO</td>
<td><img src="image1" alt="PhCHO Structure" /></td>
<td>99</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>PhCHO</td>
<td><img src="image2" alt="PhCHO Structure" /></td>
<td>97</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>PhCHO</td>
<td><img src="image3" alt="PhCHO Structure" /></td>
<td>61</td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>Aniline</td>
<td><img src="image4" alt="Aniline Structure" /></td>
<td>84</td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>Aniline</td>
<td><img src="image5" alt="Aniline Structure" /></td>
<td>81</td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>Aniline</td>
<td><img src="image6" alt="Aniline Structure" /></td>
<td>83</td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>Aniline</td>
<td><img src="image7" alt="Aniline Structure" /></td>
<td>99</td>
<td></td>
</tr>
<tr>
<td>11</td>
<td>Aniline</td>
<td><img src="image8" alt="Aniline Structure" /></td>
<td>99</td>
<td></td>
</tr>
<tr>
<td>12</td>
<td>Aniline</td>
<td><img src="image9" alt="Aniline Structure" /></td>
<td>96</td>
<td></td>
</tr>
</tbody>
</table>
A variety of benzaldehyde compounds were also tolerated, with good conversion obtained by heating the reaction mixture to 100 °C for 5 to 24 h. Similarly, electron-withdrawing and donating groups were compatible with our conditions. After 5 h of heating, 2-chlorobenzaldehyde and 4-bromobenzaldehyde yielded the desired product in 84% and 81% conversion, respectively. For the reactions with 4-cyanobenzaldehyde (83%) and 4-carboxybenzaldehyde (99%), 24 h heating was required to obtain comparable reactivity. Electron-donating groups also required 24 h heating, and in these instances, reactions with 4-methoxybenzaldehyde and 2,4,6-trimethylbenzaldehyde yielded 99% and 96% conversions, respectively. Of particular interest are the reactions which include functional groups (e.g. CF₃, CN) previously shown to be incompatible with EPCs⁵⁹,⁸⁶,⁸⁷ as this highlights the robustness and potential further application of these tricationic species.

It is noteworthy that the hydrosilylation of the aldehyde was not a deterrent in these reactions, suggesting the reduction of the corresponding imine occurred faster than aldehyde reduction. Rapid imine reduction would therefore shift the equilibrium (according to Le Chatelier’s principle) away from the aniline and aldehyde starting materials to the formation of imine. Moreover, in the absence of a polar protic solvent like methanol or acetic acid, imine reduction is expected to proceed more rapidly than aldehyde reduction due to a stronger interaction between the more basic imine functionality and the Lewis acid catalyst.⁸⁸ As well, the use of a slight excess of amine starting material (1.2 equiv.) ensures the equilibrium lies towards the formation of imine. This observation is reminiscent of B(C₆F₅)₃-catalyzed reductive amination reactions with a hydridosilane,⁴⁰ wherein the imine is preferentially reduced over the aldehyde.

Given the robustness of 4-5, we wanted to probe the reusability of the catalyst, in hopes that the catalyst could be recycled without a significant decrease in activity. In this regard, we prepared a solution of benzaldehyde, aniline, PhMe₂SiH and 5 mol% of 4-5 and determined the yields based on the ¹H NMR spectra using mesitylene as an internal standard. The reaction was left for 24 h at 100 °C for each run, and each time a mixture of benzaldehyde, aniline, PhMe₂SiH and mesitylene was added to the reaction mixture. While a gradual diminishing in reactivity was observed (99% in the first run to 58% in the fourth and final run), it is nonetheless encouraging that after 4 runs (24 h each), 4-5 was still shown to be an active catalyst for this transformation. It is noteworthy that the catalyst remains intact throughout the reactions as evidenced by ³¹P{¹H} NMR spectroscopy.
4.2.3.3 Mechanistic Investigation

To probe the mechanism of these reductive amination reactions, we conducted a series of control experiments. While it is evident the phosphonium salt is required for catalysis (i.e. conversion of imine to amine), the operative mechanism is complex and may involve activation of silane or water, as was previously reported for B(C₆F₅)₃-catalyzed reductive amination reactions. In this regard, the three main pathways for amine formation involve: 1) Lewis acid activation of silane to facilitate silylation of the imine (Scheme 4-5, Path A, right); 2) Lewis acid activation of silane to facilitate protonation of the imine by [PhMe₂Si(OH₂)]⁺ via initial reaction with H₂O (Scheme 4-5, Path A, left); or 3) Lewis acid activation of water to facilitate protonation of the imine (Scheme 4-5, Path B). While Lewis acid-activation of water followed by reaction with silane is also a possibility, this reaction would presumably result in loss of H₂ and the formation of Me₂PhSiOH, thereby preventing reduction of the imine. As such, this pathway has been excluded from our discussion. We have also excluded the initial formation of imine from this discussion, since this reaction proceeds, to some extent (i.e. an equilibrium exists), in the absence of catalyst.

While silane activation by main group Lewis acids, namely B(C₆F₅)₃ has been well-documented, direct observation of silane activation by phosphorus(V) has yet to be reported. Nonetheless, there are reports which provide experimental and theoretical support for Si-H activation by P(V). To probe the feasibility of an initial Si-H activation and subsequent hydrosilylation with 4-5, we conducted an independent hydrosilylation reaction of N-benzylidene-aniline. For this reaction, 5 mol% 4-5 was mixed with N-benzylidene-aniline and PhMe₂SiH under anhydrous conditions and after 5 h at 100 °C, 20% of the desired product BnN(SiMe₂Ph)Ph was observed by ¹H and ²⁹Si NMR spectra and GC-MS analysis.
Scheme 4-5. Possible reaction pathways for P(V)-mediated reductive amination reactions.

As well, an independent H/D scrambling experiment with Et$_3$SiD/PhMe$_2$SiH was conducted,$^{12}$ however, no evidence of H/D scrambling was observed even upon heating to 100 °C for 24 h. The significant decrease in reactivity observed in anhydrous conditions and the absence of any observed H/D scrambling with silane suggests that H$_2$O may be the nucleophile attacking the Lewis acid activated silane [LA-H-SiPhMe$_2$]$^+$ species. Further conclusive evidence of silane activation (both experimentally and computationally) was not accessible.

When the reductive amination reaction of benzaldehyde and aniline was completed in the presence of a non-nucleophilic base like PMes$_3$ (Mes = 2,4,6-trimethylphenyl), only 17% of the desired amine formed after heating the reaction mixture to 100 °C for 5 h. Moreover, a similar decrease in reactivity was observed for the corresponding reaction with 2-pyridinecarboxaldehyde. Collectively, these results suggest that the presence of an exogenous base deprotonates a Lewis acid-water adduct and that protonation of the imine enables more rapid reduction. However, whether the adduct is [LA-OH$_2$] (Figure 4-5, Path B) or [Me$_2$PhSi-OH$_2$] (Figure 4-5, Path A, left) has not been unambiguously determined. As well, since the chemistry also proceeds in anhydrous solvents (albeit more slowly) reduction via an imine silylation process is likely also operative. It is noteworthy that previous reports have described mechanisms involving both Lewis acid and Brønsted acid activation of the reductant followed by silylation or protonation of the imine.$^{31,40,82,84,91-93}$
Overall, these results demonstrate the application of unprecedented water/base stability (for EPCs) of P₃-trimethylated tricationic species in one-pot reductive amination reactions of benzaldehydes and arylamines with a hydrosilane reductant. The facile synthesis, ease of handling and reactivity of these trications highlights the potential of 4-3 and 4-5 as versatile Lewis acid catalysts for other reactions which require conditions incompatible with previously reported EPCs. Studies to unambiguously define the mode of interaction between catalyst and substrate are part of an ongoing investigation in our laboratory.

4.2.4 C-F Bond Activation

Inspired by the stability and Lewis acid reactivity of these P₃-trimethylated tricationic phosphonium species, and given the precedent for C-F bond activation by EPCs, we explored the ability of 4-7 (due to improved solubility) to effect C-F bond activation and derivatization. In an initial reaction, we probed the catalytic C-C coupling of benzyl fluorides with allyl trimethylsilane, as was recently reported by our group for air-stable P(III) dicationic species. Under analogous reaction conditions, 5 mol% 4-7 was mixed with 1-fluoroadamantane and allyl trimethylsilane and full consumption of the C-F bond was observed after 1 h at ambient temperature, with concurrent formation of Me₃SiF as evidenced by ¹⁹F{¹H} NMR spectroscopy (Scheme 4-6a). Interestingly, when the analogous reaction was completed on the bench top with unpurified reagents and solvents, comparable reactivity required more harsh reaction conditions (98% conversion after 24 h at 55 °C). This observation aligns with the notion of an interaction between H₂O with 4-7, as was mentioned in section 4.2.3.3. When the same reaction was completed with 4-6 as the catalyst, only 62% conversion was obtained after 48 h at 55 °C.
For the C-C coupling reaction of allyl trimethylsilane and p-fluorobenzylfluoride, 4-7 affected 21% conversion to the desired product after 96 h at 55 °C (Scheme 4-6b). When compared to the previously reported P(III) dication,\textsuperscript{94} 4-7 underperforms as a catalyst for these C-C coupling reactions. Nonetheless, the ability of 4-7 to affect C-F bond activation and C-C coupling is remarkable. When the analogous reaction was attempted with p-cyanobenzyl fluoride, no conversion to the desired product was observed, possibly due to an interaction with the cyano group and P(V) centre(s).\textsuperscript{69, 86, 94}

While C-F bond activation and subsequent C-C coupling reactions have previously been reported with phosphorus(V) cations,\textsuperscript{59, 60} the derivatization of C-F bonds to C-E, wherein E is not hydrogen nor carbon, are much more limited. Inspired by the ability of 4-7 to affect C-F bond activation, we sought to exploit the strength of the Si-F bond in possible C-B bond forming reactions. In this regard, we chose commercially available PhMe\textsubscript{2}Si(Bpin) (Bpin = BO\textsubscript{2}C\textsubscript{2}(CH\textsubscript{3})\textsubscript{4}) as the coupling partner for a range of C(sp\textsuperscript{3})-F containing substrates.
While silylboranes have been used as versatile reagents for the synthesis of organo-boron and -silicon compounds, their reaction with C-F containing substrates is rare. Most examples in the literature exploit Suginome’s PhMe₂Si(Bpin)⁹⁵ as a source of nucleophilic silicon for several Si-C bond forming reactions. Perhaps most prevalent in the literature is the use of copper catalysts for reactions including protosilylation of alkynes,⁹⁶ and radical-mediated C-Si bond-forming reactions, among many others.⁹⁷ Au nanoparticles on TiO₂ have also been used as catalysts to mediate silylative reductive dimerization of aromatic aldehydes and acetophenones,⁹⁸ silaboration of terminal allenes,⁹⁹ oxetanes and unactivated epoxides,¹⁰⁰ and alkynes¹⁰¹ with PhMe₂Si(Bpin). While there have been several reports of alkoxy base-mediated boryl substitution reactions of organohalides (e.g. Br, I) with silylboranes such as PhMe₂Si(Bpin),¹⁰² examples including C-F containing substrates is limited. Nonetheless, a Cu-catalyzed defluorosilylation of polyfluoroalkenes¹⁰³ and a LiHMDS-mediated defluorosilylation of C-F bonds¹⁰⁴ were recently reported.

To begin our investigation, we mixed equimolar amounts of p-fluorobenzylfluoride and PhMe₂Si(Bpin) in the presence of a catalytic amount of 4-7 and monitored the reaction progress by multi-nuclear NMR spectroscopy. After heating the reaction mixture to 55 °C for 12 h, analysis of the ¹⁹F{¹H} NMR spectra (CH₂Cl₂) shows complete disappearance of the C(sp³)-F resonance of p-fluorobenzylfluoride and the formation of a new resonance at δ –176.5 ppm indicative of Si-F bond formation.¹⁰⁵ As well, the C(sp³)-F resonance of p-fluorobenzylfluoride is shifted slightly upfield (Δ = 5 ppm). The ¹¹B{¹H} NMR spectrum contains a new resonance δ 32.3 ppm, which is shifted slightly upfield from the starting material, and aligns with the reported literature value for 2-(4-fluorobenzyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (¹¹B(δ) = 33.1 ppm).¹⁰⁶ The absence of any FBpin resonances in either the ¹⁹F or ¹¹B NMR spectra¹⁰³,¹⁰⁷ also supports formation of the C-B coupled product (Scheme 4-6c). Interestingly, reaction of either p-cyano or p-nitrobenzylfluoride with PhMe₂Si(Bpin) did not lead to any product formation, presumably due to interaction with 4-7 as mentioned above.

When 1-fluoroadamantane was chosen as the substrate for reaction with PhMe₂Si(Bpin), full consumption of the C-F bond was observed in the ¹⁹F{¹H} NMR spectrum (CH₂Cl₂) after 1 h at ambient temperature, with concurrent formation of PhMe₂SiF. Analysis of the ¹¹B{¹H} NMR spectrum shows disappearance of PhMe₂Si(Bpin) and the formation of a new product at δ 32.3 ppm. Similar to the reaction with p-fluorobenzylfluoride, no FBpin is observed in either the ¹⁹F or
$^{11}$B NMR spectra, supporting the formation of the C-B coupled product. The NMR resonances are also in agreement with those reported for 2-((3r,5r,7r)-Adamantan-1-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane ($^{11}$B(δ) = 33.3 ppm)$^{108}$ shown in Scheme 4-6d.

While preliminary, these results support the ability of 4-7 to facilitate C-F bond activation and derivatization beyond the traditional C-C and C-H bond forming reactions. The mechanism of the C-B bond forming reactions is the subject of ongoing investigation in our laboratory.

### 4.3 Conclusions

The facile methylation of commercially available triphos ligands affords air and water-tolerant P$_3$-trimethylated phosphorus(V) cations upon oxidation with MeOTf. While counterion exchange with [Et$_3$Si][B(C$_6$F$_5$)$_4$]$^+$($C_7$H$_8$) affords the corresponding [B(C$_6$F$_5$)$_4$] salts, [OTf] salts 4-3 and 4-5 were shown to be active catalysts for one-pot reductive amination reactions using a hydrosilane reductant. In this regard, a variety of aldehydes and arylamines were successfully converted to their amine products, highlighting the unprecedented stability (for EPCs) in the presence of H$_2$O/base and appreciable functional group tolerance of these tricationic species. The mechanism of these reactions is complex and involves activation of the Si-H bond of silane and the O-H bond of H$_2$O.

While experimental evidence highlights the role of three proximal P(V)-centres in enhancing Lewis acidity (as was suggested by the solid-state structure of 4-5), conclusive evidence of silane activation (both experimentally and computationally) was not accessible in our hands. Therefore, the mode of activation for the cations of 4-3 and 4-5 has not unambiguously been determined and may be a combination of substrate activation by the P(V) centres and interaction with the C-H bonds in the alkyl linkers. The resistance to degradation by water and Et$_3$PO for the cations of 4-3 and 4-5 may arise from the unique acceptor orbitals which are fundamentally distinct from most fluorophosphonium cations. The exact nature of these interactions is the subject of ongoing investigation in our laboratory.

Tripodal tricationic species 4-7 has also been shown to effect C-F bond activation and derivatization. Remarkably, the preliminary results presented in the latter part of this chapter demonstrate C(sp$^3$)-F bond activation and subsequent C-C and C-B bond functionalizations facilitated by 4-7. While more data is required to determine the mechanism of these reactions,
these transformations nonetheless highlight the potential utility of these robust tricationic species as catalysts for this challenging, yet highly sought after, bond activation reaction.

4.4 Experimental Details

4.4.1 General Remarks

All manipulations were performed in a MB Unilab Glove box produced by MBraun or using standard Schlenk techniques under an inert atmosphere of anhydrous N₂.¹⁰⁹ Dry, oxygen-free solvents (CH₂Cl₂, n-pentane and toluene) were prepared using an Innovative Technologies solvent purification system. Fluorobenzene (C₆H₅F) and mesitylene (C₉H₁₂) were distilled from CaH₂ and stored over molecular sieves (4 Å) prior to use. Deuterated dichloromethane (CD₂Cl₂), acetonitrile (CD₃CN), benzene (C₆H₆) and bromobenzene (C₆D₅Br) were purchased from Sigma-Aldrich, distilled from CaH₂ and stored over molecular sieves (4 Å) (excluding CD₂Cl₂ and CD₃CN), for at least 2 d prior to use. (Bis(diphenylphosphinoethyl)phenylphosphine, 1,1,1-Tris(diphenylphosphinomethyl)ethane), MeOTf, CH₃I and all the reagents used for the catalysis screening were purchased from commercial sources and used as received unless otherwise stated. [Et₃Si][B(C₆F₅)₄]•(C₇H₈)¹¹⁰ and Et₃SiD was prepared according to the literature procedure.¹¹¹ All glassware was oven-dried at temperatures above 180°C prior to use. NMR spectra were measured on a Bruker AVANCE 400 (¹H: 400 MHz, ¹¹B: 128 MHz, ¹³C: 101 MHz, ³¹P: 162 MHz, ¹⁹F: 377 MHz) or Agilent DD2 500 (¹H: 500 MHz, ¹³C: 125 MHz, ³¹P: 202 MHz, ¹⁹F: 471 MHz) at ambient temperature. All ¹³C NMR spectra were exclusively recorded with composite pulse decoupling. Assignments of the carbon atoms in the ¹³C spectra were performed via indirect deduction from the cross-peaks in 2D correlation experiments (HMBC; HSQC). Chemical shifts were referenced to δ TMS = 0.00 ppm (¹H, ¹³C) and δ H₃PO₄(85%) = 0.00 ppm (³¹P, externally). Chemical shifts (δ) are reported in ppm, multiplicity is reported as follows (s = singlet, d = doublet, t = triplet, m = multiplet) and coupling constants (J) are reported in Hz. Assignments of individual resonances were done using 2D techniques (HMBC, HSQC, HH-COSY) when necessary. High-resolution mass spectra (HRMS) were obtained on a micro mass 70S-250 spectrometer (El), an ABI/Sciex QStar Mass Spectrometer (DART), or on a JOEL AccuTOF-DART (DART). Elemental analyses (C, H, N) were performed at the University of Toronto employing a Perkin Elmer 2400 Series II CHNS Analyzer.
4.4.2 Synthesis of Compounds 4-2, 4-3, 4-6, 4-9

[PhPMe(CH₂CH₂PMePh₂)₂][I]₃ 4-2

\[
\begin{array}{c}
\text{PhPMe(CH₂CH₂PMePh₂)₂} \\
\text{PhPMe(CH₂CH₂PMePh₂)₂}
\end{array}
\]

CH₃I (0.1 mL, 2.0 mmol, 10 equiv.) was added to a solution of Bis(diphenylphosphinoethyl)phenylphosphine (104 mg, 0.20 mmol, 1.0 equiv.) in CH₂Cl₂ (3 mL). The reaction mixture was left to stir at ambient temperature for 20 h, after which time a white precipitate settled out of solution. 3 mL of n-pentane was added to the solution, and after stirring for 2 h the supernatant was decanted and the remaining solid was washed with n-pentane (3 x 3 mL). The solid was dried in vacuo to afford a white microcrystalline solid. (177 mg, 95% Yield).

**1H NMR (400 MHz, CD₃CN, MeSi):** δ 8.04 (m, 2H; Ar-H), 7.93 (m, 8H; Ar-H), 7.83 (m, 5H; Ar-Ph), 7.68 (m, 10H; Ar-H), 3.67 (m, 2H; C(CH₂)₂), 3.37 (m, 6H; C(CH₂)₂), 2.84 (d, 2J_PH = 14 Hz, 6H; Ph₂P-CH₃), 2.71 ppm (d, 2J_PPH = 14 Hz, 3H; PhP-CH₃).

**31P{1H} NMR (162 MHz, CD₃CN, H₃PO₄):** δ 34.4 (d, 3J_PP = 60 Hz, 1P), 26.6 ppm (d, 3J_PP = 60 Hz, 2P).

**13C{1H} NMR (125 MHz, CD₃CN, MeSi):** δ 135.8 (m, 5C; p-Ph), 132.9 (dd, 2/3J_PC = 15 Hz, 2/3J_PC = 15 Hz, o/m-Ph), 132.6 (d, 2/3J_PC = 10 Hz, o/m-Ph), 130.9 (dd, 2/3J_PC = 13 Hz, 2/3J_PC = 12 Hz, o/m-Ph), 118.3 (d, 1J_PC = 87 Hz, 2C; i-Ph₂P), 117.1 (d, 1J_PC = 86 Hz, 2C; i-Ph₂P), 116.7 (d, 1J_PC = 84 Hz, 1C; i-PhP), 16.6 (m, 4C; CH₂), 8.2 (d, 1J_PC = 54 Hz, 2C; Ph₂P-CH₃), 5.9 ppm (d, 1J_PC = 50 Hz, 1C; PhP-CH₃).

**MS-ESI:** Calculated mass for [C₃H₄I₂P₃]⁺ : 833.06. Obtained: 833.0595 amu.

[PhPMe(CH₂CH₂PMePh₂)₂][OTf]₃ 4-3

\[
\begin{array}{c}
\text{PhPMe(CH₂CH₂PMePh₂)₂} \\
\text{PhPMe(CH₂CH₂PMePh₂)₂}
\end{array}
\]

MeOTf (0.4 mL, 3.66 mmol, 6.2 equiv.) was added to a solution of Bis(diphenylphosphinoethyl)phenylphosphine (314.7 mg, 0.59 mmol, 1.0 equiv.) in CH₂Cl₂ (3 mL). The reaction mixture was left to stir at ambient temperature for 20 h, after which time a white precipitate settled out of solution. 3 mL of n-pentane was added to the solution, and after stirring
for 2 h the supernatant was decanted and the remaining solid was washed with n-pentane (3 x 3 mL). The solid was dried in vacuo to afford a white microcrystalline solid. (531 mg, 88% Yield). Diffraction-quality single crystals of 4-3•H2O can be obtained by vapour diffusion of Et2O into saturated DMF solutions.

1H NMR (400 MHz, CD2Cl2, Me4Si): δ 7.76 (m, 15H; Ar-H), 7.65 (m, 8H; Ar-H), 7.55 (m, 2H; Ar-H), 3.42 (m, 2H; CH2), 3.04 (m, 6H; CH2), 2.63 (d, 2JPH = 14 Hz, 6H; Ph2P-CH3), 2.62 ppm (d, 2JPH = 14 Hz, 3H; PhP-CH3). 19F{1H} NMR (377 MHz, CD2Cl2, CFCl3): δ –78.8 ppm (s, 9F; OTf). 31P{1H} NMR (162 MHz, CD2Cl2, H3PO4): δ 33.4 (t, 3JPP = 58 Hz, 1P), 25.7 ppm (d, 3JPP = 58 Hz, 2P). 13C{1H} NMR (125 MHz, CD2Cl2, Me4Si): δ 135.8 (m, 5C; p-Ph), 132.9 (dd, 2/3 JPC = 15 Hz, 2JPC = 15 Hz, o/m-Ph), 132.6 (d, 2/3 JPC = 10 Hz, o/m-Ph), 130.9 (dd, 2/3 JPC = 13 Hz, 2/3 JPC = 12 Hz, 10C; o/m-Ph), 118.3 (d, 1JPC = 87 Hz, 2C; i-Ph2P), 117.1 (d, 1JPC = 86 Hz, 2C; i-Ph2P), 115.9 (d, 1JPC = 84 Hz, 1C; i-Ph), 16.6 (m, 4C; CH2), 6.5 (d, 1JPC = 55 Hz, 2C; Ph2P-CH3), 2.6 ppm (d, 1JPC = 52 Hz, 1C; PhP-CH3). MS-DART: Unable to observe [M]+ peak due to fragmentation. Anal. Calcd. for C40H42F9O3P3S3: C, 46.8; H, 4.1 %. Found: C, 46.0; H, 4.1 %.

[PhPMe(CH2CH2PMePh2)]3[B(C6F5)4] 4-6

Solid [Na][B(C6F5)4] (63 mg, 0.09 mmol, 3.0 equiv.) was added to a separate vial containing solid 4-3 (31 mg, 0.03 mmol, 1.0 equiv.). 5 mL CH2Cl2 was then added and the reaction mixture was left to stir at ambient temperature for 2 h. The solution was filtered through a Kimwipe plug and the filtrate was dried in vacuo. The solid was dissolved in 5 mL C2Cl2 and layered with 5 mL n-pentane and cooled to –35 ºC. After a few days, an oil settled out of solution. The top layer was then decanted, and the oil was washed with n-pentane (3 x 5 mL) and then dried in vacuo to afford a white microcrystalline solid (59 mg, 75% Yield).

1H NMR (400 MHz, CD2Cl2, Me4Si): δ 8.01 (m, 1H; p-PhP), 7.85 (m, 4H; p-Ph2P), 7.75 (m, 2H; m-PhP), 7.62 (m, 8H; m-Ph2P), 7.44 (m, 10H; o-Ph), 2.74 (m, 2H; CH2), 2.48 (m, 6H; CH2), 2.35 (d, 2JPH = 13 Hz, 6H; P-CH3), 2.25 ppm (d, 2JPH = 13 Hz, 3H; P-CH3). 11B NMR (128. MHz, CD2Cl2, BF3•OEt2): δ –16.6 ppm (s). 19F{1H} NMR (377 MHz, CD2Cl2, CFCl3): δ –166.9
(m(br), 8F; B(m-C₆F₅)₄), –162.7 (t, 2J_FF = 21 Hz, 4F; B(p-C₆F₅)₄), –132.7 ppm (m(br), 8F; B(o-C₆F₅)₄). ³¹P⁴¹H NMR (162 MHz, CD₂Cl₂, H₃PO₄): δ 32.9 (d, 3J_PP = 55 Hz, 1P), 24.4 ppm (d, 3J_PP = 55 Hz, 2P). ¹³C⁴¹H NMR (125 MHz, CD₂Cl₂, Me₅Si): δ 148.5 (d(br) ¹J_FC = 240 Hz, 24C; B(o/m-(C₆F₅)₄), 138.8 (d(br), ¹J_FC = 247 Hz, 12C; B(p-(C₆F₅)₄), 136.6 (d(br), ¹J_FC = 247 Hz, 24C; B(o/m-(C₆F₅)₄), 139.3 (d, 4J_PC = 3H, 1C; p-PhP), 137.8 (d, 4J_PC = 3 Hz, 2C; p-Ph₂P), 137.6 (d, 4J_PC = 3 Hz, 2C; p-Ph₂P), 133.0 (d, 3J_PC = 13 Hz, 1C; m-PhP), 131.9 (m, 18C; o/m-Ph₂P & o-PhP), 131.2 (d, 3J_PC = 10 Hz, 1C; m-PhP), 114.5 (d, ¹J_PC = 87 Hz, 2C; i-Ph₂P), 113.7 (d, ¹J_PC = 87 Hz, 2C; i-Ph₂P), 110.0 (d, ¹J_PC = 83 Hz, 1C; i-PhP), 17.8 (d, ¹J_PC = 52 Hz, 4C; CH₂), 7.0 (d, ¹J_PC = 56 Hz, 2C; Ph₂P-CH₃), 1.6 ppm (d, ¹J_PC = 54 Hz, 1C; PhP-CH₃). MS-DART: Unable to observe [M]⁺ peak due to fragmentation. **Anal. Calcd.** for C₁₁₀H₄₂B₃F₆₀P₃: C, 50.0; H, 1.6 %. Found: C, 49.4; H, 1.8 %.

[Ph₂PMe(CH₂)₃MePPh₂][OTf]₂ 4-9

MeOTf (0.08 mL, 0.73 mmol, 2 equiv.) was added to a solution of diphenylphosphinopropane (dppp, 157 mg, 0.38 mmol, 1 equiv.) in CH₂Cl₂ (3 mL). The reaction mixture was left to stir at ambient temperature for 24 h. The volume was reduced in vacuo to 1 mL, and 3 mL of n-pentane was added to induce precipitation. The supernatant was decanted and the solid was washed with n-pentane (3 x 5 mL). The solid was dried in vacuo to afford a white microcrystalline solid. (225 mg, 80% Yield).

¹H NMR (400 MHz, CD₃CN, Me₅Si): δ 7.72 (m, 20H; Ar-H) 3.65 (m, 4H; CH₂), 2.43 (d, 2J_PH = 14 Hz, 6H; P-CH₃), 1.70 ppm (m, 2H; CH₂). ¹⁹F⁻¹H NMR (377 MHz, CD₃CN, CFCl₃): δ –79.2 ppm (s, 6F; OTf). ³¹P⁻¹H NMR (162 MHz, CD₃CN, H₃PO₄): δ 22.3 ppm (s). ¹³C⁻¹H NMR (101 MHz, CD₃CN, Me₅Si): δ 136.0 (t, 4J_PH = 2 Hz, 4C; p-Ph), 133.3 (pent., 2J_PH = 4 Hz, 8C; o-Ph), 131.1 (m, 8C; m-Ph), 119.8 (d, 1J_PH = 87 Hz, 4C; i-Ph), 23.9 (d, 1J_PH = 54 Hz, 1C; CH₂), 23.7 (d, 1J_PH = 54 Hz, 1C; CH₂), 16.4 (s, 1C; CH₂), 6.8 ppm (d, 1J_PH = 56 Hz, 2C; P-CH₃). **MS-ESI:** Unable to observe [M]⁺ peak due to fragmentation. **Anal. Calcd.** for C₃₁H₁₉₂F₆₀O₆P₅S₂: C, 50.3; H, 4.4 %. Found: C, 49.7; H, 4.3 %.
4.4.3 Gutmann-Beckett Tests (Reaction with Et₃PO)\textsuperscript{112,113}

A solution of the phosphonium catalyst 4-3 (44 mg, 0.04 mmol) was dissolved in CD\textsubscript{3}CN and then added to a separate vial containing Et₃PO (6 mg, 0.04 mmol). The solution was then transferred to a NMR tube and monitored by $^{31}$P{$^1$H} NMR spectroscopy (free Et₃PO in CD\textsubscript{3}CN, $^{31}$P{$^1$H} (δ) = 51.05 ppm).

![Figure 4-5](image)

**Figure 4-5.** $^{31}$P{$^1$H} NMR spectrum (CD\textsubscript{3}CN) of the reaction with 4-3 and Et₃PO after 1 h at ambient temperature.

![Figure 4-6](image)

**Figure 4-6.** $^{31}$P{$^1$H} NMR spectrum (CD\textsubscript{3}CN) of the reaction with 4-5 and Et₃PO after 1 h at ambient temperature.
Figure 4-7. $^{31}$P{$^1$H} NMR spectrum (CD$_3$CN) of the reaction with **4-8** and Et$_3$PO (1:1) after 1 h at ambient temperature.

**4-8** (95 mg, 0.22 mmol) was dissolved in CD$_3$CN and then added to a separate vial containing Et$_3$PO (10 mg, 0.07 mmol). The solution was then transferred to a NMR tube and monitored by $^{31}$P{$^1$H} NMR spectroscopy.

Figure 4-8. $^{31}$P{$^1$H} NMR spectrum (CD$_3$CN) of the reaction with **4-8** and Et$_3$PO (3:1) after 1 h at ambient temperature.

### 4.4.4 Reductive Amination Reactions

A NMR tube was loaded with a solution of the catalyst in CH$_3$CN (0.5 mL), followed by the addition of benzaldehyde (25 µL, 0.241 mmol, 1 equiv.), aniline (26 µL, 0.289 mmol, 1.2 equiv.), PhMe$_2$SiH (45 µL, 0.289 mmol, 1.2 equiv.) and mesitylene as internal standard (25 µL, 0.179 mmol, 0.74 equiv.). The NMR tube was then sealed and heated at 100 °C for 18 h. The reaction progress was monitored by multi-nuclear NMR spectroscopy. The determination of the $^1$H NMR yields was based on the relative integral of the benzylic protons of BnNHP (δ 4.32 ppm) and the methyl signal of mesitylene (δ 2.26 ppm). The product distribution was then confirmed by GC-MS analysis (PhC(H)=NPh (R$_t$ = 14.46 min): m/z 181.1 [M$^+$], 77.0 [Ph$^+$]; BnNHP (R$_t$ = 14.99
min): m/z 183.1 [M]+, 91.0 [Bn]+; (PhMe₂Si)₂O (R₁ = 14.62 min): m/z 286.1 [M]+, 271.1 [M-CH₃]+. The data were in agreement with those reported in the literature.⁴⁰

### 4.4.4.1 Reductive Amination of Benzaldehyde and Aniline

4-3 (12.4 mg, 0.012 mmol, 0.05 equiv.). Upon heating the reaction mixture at 100 °C for 5 h, minimal degradation of the catalyst was observed and significant BnNHPh formation was detected (82%).

**Figure 4-9.** *In situ* ¹H, ³¹P{¹H} and ¹⁹F{¹H} NMR spectra of the standard reductive amination with 4-3 (5 mol%). Bottom (after 5 min), top (after 5 h at 100°C).

4-5 (13.4 mg, 0.012 mmol, 0.05 equiv.). Upon heating the reaction mixture at 100 °C for 5 h, no degradation of the catalyst was observed and significant BnNHPh formation was detected (93%)
4-8 (15.3 mg, 0.036 mmol, 0.15 equiv.). Upon heating the reaction mixture at 100 °C for 18 h, no degradation of the catalyst was observed and significant BnNHPh formation was detected (93%).

The disparity among the catalysts was further confirmed by repeating the standard reductive amination (general procedure) with 4-3 (5 mol%), 4-5 (5 mol%) or 4-8 (15 mol%) and monitoring BnN(H)Ph formation upon heating at 100°C.

![Graph](image_url)

**Figure 4-10.** *In situ* monitoring of the standard reductive amination with 4-3 (red), 4-5 (blue) or 4-8 (grey) after heating at 100 °C each hour.

### 4.4.4.2 Aniline substrate scope

A NMR tube was loaded with a solution of 4-5 in CH₃CN (0.5 mL), followed by the addition of PhCHO (25 μL, 0.241 mmol, 1.00 equiv.), aniline (0.289 mmol, 1.20 equiv.), PhMe₂SiH (45 μL, 0.289 mmol, 1.20 equiv.) and mesitylene as internal standard (25 μL, 0.179 mmol, 0.74 equiv.). The reaction mixture was heated to 100 °C for 5 h. The determination of the ¹H NMR yields was based on the relative integral of the benzylic protons of BnNHR’ and the methyl signal of mesitylene (δ 2.26 ppm).
Figure 4-11. $^1$H NMR (CD$_3$CN) spectrum of crude reaction mixture of $N$-benzyl-(2-bromophenyl)amine. Bottom (after 5 min), top (after 5 h at 100 °C). Data in agreement with those reported in the literature.$^{40}$

Figure 4-12. $^1$H NMR (CD$_3$CN) spectrum of crude reaction mixture of $N$-benzyl-(2-fluorophenyl)amine. Bottom (after 5 min), top (after 5 h at 100° C). Data in agreement with those reported in the literature.$^{40}$

Figure 4-13. $^1$H NMR (CD$_3$CN) spectrum of crude reaction mixture of $N$-benzyl-(2,6-diisopropylphenyl)amine. Bottom (after 5 min), top (after 5 h at 100° C). Data in agreement with those reported in the literature.$^{114}$
Figure 4-14. $^1$H NMR (CD$_3$CN) spectrum of crude reaction mixture of $N$-benzyl-(3-trifluoromethylphenyl)amine. Bottom (after 5 min), top (after 5 h at 100°C). Data in agreement with those reported in the literature.$^{115}$

Figure 4-15. $^1$H NMR (CD$_3$CN) spectrum of crude reaction mixture of $N$-benzyl-(4-chlorophenyl)amine. Bottom (after 5 min), top (after 5 h at 100°C). Data in agreement with those reported in the literature.$^{116}$
Figure 4-16. $^1$H NMR (CD$_3$CN) spectrum of crude reaction mixture of N-benzyl-(4-hexylphenyl)amine, $t = 24$ h. Bottom (after 5 min), top (after 5 h at 100°C). Data in agreement with those reported in the literature.$^{117}$

4.4.4.3 H/D Scrambling Experiment

A NMR tube was charged with Et$_3$SiD (32 L, 0.20 mmol, 1 equiv.) and 4-5 (11 mg, 0.01 mmol, 0.05 equiv.). Me$_2$PhSiH and “wet” CD$_3$CN were added to the NMR tube on the benchtop. The reaction was heated to 100 °C and monitored by multi-nuclear NMR spectroscopy. No evidence of any H/D scrambling was observed after 5 d at 100 °C.

4.4.5 C-F Bond Activation and Derivatization with 4-7

4.4.5.1 Reaction of 1-Fluoroadamantane and Allyl trimethylsilane with 4-7

Allyl trimethylsilane (3 μL, 0.024 mmol, 1.1 equiv.) was added to a CH$_2$Cl$_2$ (1 mL) solution of 1-fluoroadamantane (3 mg, 0.022 mmol, 1 equiv.) and 4-7 (3 mg, 0.001 mmol, 0.05 equiv.). The reaction mixture was transferred to a NMR tube and monitored by multi-nuclear spectroscopy. Conversions were determined from the proportion of Si-F bonds in Me$_3$SiF formed relative to C(sp$^3$)-F bonds in 1-fluoroadamantane consumed.$^{94}$
Figure 4-17. $^{19}$F-$^1$H NMR spectra (CH$_2$Cl$_2$) for the reaction of 1-fluoroadamantane and allyl trimethylsilane without (top) and with 4-7 (bottom). Reactions were completed under an inert atmosphere.

Figure 4-18. $^{19}$F-$^1$H NMR spectra (CH$_2$Cl$_2$) for the reaction of 1-fluoroadamantane and allyl trimethylsilane completed in air with 4-7. 14% (top), 55% (middle) and 98% conversions (bottom) were obtained.

4.4.5.2 Reaction of $p$-Fluorobenzylfluoride and Allyl trimethylsilane with 4-7

Allyl trimethylsilane (4 μL, 0.024 mmol, 1.1 equiv.) was added to a CH$_2$Cl$_2$ (1 mL) solution of $p$-fluorobenzylfluoride (3 μL, 0.022 mmol, 1 equiv.) and 4-7 (3 mg, 0.001 mmol, 0.05 equiv.). The reaction mixture was transferred to a NMR tube and monitored by multi-nuclear spectroscopy. Conversions were determined from the proportion of Si-F bonds in Me$_3$SiF formed relative to C(sp$^3$)-F bonds in $p$-fluorobenzyl fluoride consumed.$^{94}$
Figure 4-19. $^{19}$F-$^1$H NMR spectra (CH$_2$Cl$_2$) of reaction of $p$-fluorobenzylfluoride and allyl trimethylsilane with 4-7.

4.4.5.3 Reaction of $p$-Fluorobenzylfluoride and PhMe$_2$Si(Bpin) with 4-7

PhMe$_2$Si(Bpin) (8 μL, 0.024 mmol, 1.1 equiv.) was added to a CH$_2$Cl$_2$ (1 mL) solution of $p$-fluorobenzylfluoride (3 μL, 0.022 mmol, 1 equiv.) and 4-7 (3 mg, 0.001 mmol, 0.05 equiv.). The reaction mixture was transferred to a NMR tube and monitored by multi-nuclear spectroscopy. Conversions were determined from the proportion of Si-F bonds in PhMe$_2$SiF formed relative to C(sp$^3$)-F bonds in $p$-fluorobenzylfluoride consumed.$^{60}$

Figure 4-20. $^{19}$F-$^1$H NMR spectra (CH$_2$Cl$_2$) of reaction of $p$-fluorobenzylfluoride and PhMe$_2$Si(Bpin) with 4-7.
4.4.5.4 Reaction of 1-Fluoroadamantane and PhMe₂Si(Bpin) with 4-7

PhMe₂Si(Bpin) (37 μL, 0.13 mmol, 1 equiv.) was added to a CH₂Cl₂ (1 mL) solution of 1-fluoroadamantane (20 mg, 0.13 mmol, 1 equiv.) and 4-7 (18 mg, 0.007 mmol, 0.05 equiv.). The reaction mixture was transferred to a NMR tube and monitored by multi-nuclear spectroscopy after 1 h at ambient temperature. Conversions were determined from the proportion of Si-F bonds in PhMe₂SiF formed relative to C(sp³)-F bonds in 1-fluoroadamantane consumed.⁵⁶, ⁶⁹

Figure 4-21. ¹¹B{¹H} NMR spectra (CH₂Cl₂) of reaction of p-fluorobenzylfluoride and PhMe₂Si(Bpin) with 4-7.

Figure 4-22. ¹⁹F{¹H} NMR spectra (CH₂Cl₂) of reaction of 1-fluoroadamantane and PhMe₂Si(Bpin) without 4-7 (top) and with 4-7 (bottom).
Figure 4-23. $^{11}\text{B}\{^1\text{H}\}$ NMR spectra (CH$_2$Cl$_2$) of reaction of 1-fluoroadamantane and PhMe$_2$Si(Bpin) without 4-7 (top) and with 4-7 (bottom).

4.4.6 Computational Data

_all calculations in this chapter were performed by post-doctoral fellow Dr. John De Backere:_

Electronic structure calculations, including geometry optimizations and frequency calculations, were performed using Gaussian 16$^{118}$ using the BP86$^{119,120}$ functional and the Def2-TZVP$^{121,122}$ basis set. Each geometry was confirmed to be a minimum on its potential energy surface by confirming the Hessian to be positive definite with a frequency calculation.

4.4.7 Crystallographic Analysis of 4-3

Single crystals were coated with Paratone-N oil and mounted in a cryo-loop. Data were collected on a Bruker Kappa Apex II diffractometer using graphite monochromated MoK$_\alpha$ radiation ($\lambda = 0.71073$ Å). The temperature was maintained at 150 K using an Oxford Cryostream cooler for both, initial indexing and full data collection. Data were collected using Bruker APEX-2 program. All structures were solved by direct methods within the SHELXTL package$^{123}$ against $F^2$ using first isotropic and anisotropic thermal parameters for all non-hydrogen atoms. Hydrogen atoms bonded to carbon atoms were generated with idealized geometries and isotropically refined using a riding model.
Table 4-3. Crystallographic data and details of the structure refinement for 4-3.

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<th>4-3•H₂O</th>
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<td>Formula</td>
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4.5 References


Chapter 5
Diphosphonium Dications as Lewis Acids in Frustrated Lewis Pair Chemistry

5.1 Introduction

Since the seminal discovery of metal-free \( \text{H}_2 \) activation in 2006,\textsuperscript{1} the scope of Frustrated Lewis pairs (FLPs), namely the Lewis acids, has been expanded by multiple research groups. While initial reports used fluorinated organoboranes as the Lewis acid,\textsuperscript{2-8} the literature now contains a myriad of Lewis acids derived from groups 13-15 in combination with Lewis basic nucleophiles in both inter- and intramolecular FLP systems. In addition to boranes, alanes\textsuperscript{9,10} and tri-coordinated boron-\textsuperscript{11-13} carbon-\textsuperscript{14-17} or silicon-centered\textsuperscript{18-20} cations have been used as main group-based Lewis acids in FLP-type small molecule (in particular, \( \text{H}_2 \)) activation. It is noteworthy that strong Lewis acids based on heavier Group 15 elements (As,\textsuperscript{21} Sb,\textsuperscript{22-24} Bi\textsuperscript{25}) have been explored recently and in some cases, the activation of Si–H or Si–Cl bonds were observed. In terms of the Lewis base, a variety of sterically-hindered phosphines or amine compounds are most common, although examples of electron-deficient phosphines\textsuperscript{26} and ethers as Lewis bases also exist.\textsuperscript{4,27-29}

5.1.1 Phosphorus Lewis Acids in FLP Chemistry

Exploring electron-deficient Group 15 compounds, our group found that \([(C_6F_5)_3PF]^+\) is a highly electrophilic phosphonium cation (EPC) that exhibits remarkable Lewis acidity derived from strongly electron-withdrawing substituents and an energetically accessible \( \sigma^*(\text{P}–\text{F}) \) acceptor orbital.\textsuperscript{30} Since this report, the field of phosphorus Lewis acid chemistry has grown significantly\textsuperscript{31}; however, examples of P-based Lewis acids in FLP chemistry remains scarce. In one rare example, an electrophilic phosphorus centre in an amidofluorophosphorane framework was used to capture \( \text{CO}_2 \), in a manner analogous to that seen for FLPs.\textsuperscript{32} Later, a triphosphabenzene derivative was shown to react with \( \text{H}_2 \), and computational studies confirmed the role of the phosphorus as a Lewis acid in an FLP-type mechanism.\textsuperscript{33} Moreover, the use of \([(C_6F_5)_3PF][\text{B}(C_6F_5)_4]\) in conjunction with sterically encumbered aryl-substituted amines was shown to effect reversible \( \text{H}_2 \) activation and the hydrogenation of 1,1-diphenylethylene.\textsuperscript{34} In this regard, despite the growth of Lewis acidic phosphorus chemistry over the last six years, and the dominance of P-based Lewis bases in FLP chemistry, this field is still in its infancy.
5.1.2 Lewis Acidic Diphosphonium Dication Compounds

Given the diagonal relationship between carbon and phosphorus, several research groups have studied P-P homoatomic bonding as the inorganic analogue to the C-C homoatomic bond. In this regard, catena-phosphines, catena-phosphorus anions and catena-phosphinophosphonium cations have been studied, but there are still many frameworks observed in carbon chemistry not yet replicated with phosphorus.\[36,37\]

The electronic structure of 1,2-dications is interesting because despite the strong electronic repulsion between the two heteroatoms, these compounds can show remarkable stability.\[38\] To this end, it was initially believed that sterically bulky amines or polycyclic frameworks were needed to stabilize 1,2-diphosphonium dication species (Figure 5-1).\[39-45\]

![Figure 5-1. Examples of 1,2-diphosphonium dications.](image)

Interestingly, despite the facility of homolytic P-P dissociation, stable bis-triflate salts of hexaalkyldiphosphonium dications have been obtained.\[46\] The stability of these diphosphonium dications is attributed in large part to the lattice enthalpy expected from an MX$_2$ salt.\[47,48\] In this regard, weakly coordinating anions (e.g. OTf) dominate the literature of 1,2-dications, conveying the desired thermal stability.\[49\] The first synthesis of the hexamethyldiphosphonium dication was reported in 1980 from the reaction of red phosphorus with alkyl iodides in the presence of iodine.\[50,51\] [Me$_3$PPMe$_3$]$^+$ can also be generated from oxidation of trialkylphosphines with iodine.\[38\] Later, the development of more sophisticated methods dominated the literature. In one report, Weigand et al. access the hexamethyldiphosphinium triflate salt through methylation of tetramethyldiphosphine with MeOTf.\[46\] Methylation of a diphosphaacenaphthene with MeOTf or Me$_3$OBF$_4$ also proved to be a viable strategy for the syntheses of a P-P bonded 1,2-dicationic phosphorus species with a naphthalene-1,8-diyl framework.\[52\] While alkylation of tetrasubstituted diphosphines is most common when strong alkylating agents (e.g. MeOTf) are used, tBuCl and GaCl$_3$ have also been used as reagents to generate bulky 1,2-diphosphonium dications.\[53\]
Another strategy to synthesize the hexamethyldiphosphonium triflate salt relies on nucleophilic displacement, wherein PMe₃ displaces 4-dimethylaminopyridine from [Me₃P(DMAP)][OTf]₂. In another report, Chitnis et al. observe the formation of [Me₃PPMe₃][OTf]₂ upon reductive elimination from [Sb(PMe₃)₃][OTf]₃ or [Ph₃Sb(PMe₃)₂][OTf]₂. This type of reductive elimination is reminiscent of PMe₃ complexes with Cu(II) and Tl(III), wherein decomposition leads to the formation of [Me₃PPMe₃]+ and the corresponding reduced Cu(I) and Tl(I) species.

Electrochemical oxidation of P(NEt₂)₃ was also shown to be a viable strategy for the synthesis of [(NEt₂)₃PP(NEt₂)]⁺. While the synthesis and characterization of 1,2-diphosphonium dications has been reported, subsequent reactivity of these compounds is less explored. Experimental and theoretical investigations have shown that P-P bond cleavage is feasible due to the accumulation of electron density along this bond. In fact, when Nikitin et al. reacted in situ prepared 1,2-diphosphonium dications with a variety of nucleophiles, P-P bond cleavage was observed. Similar P-P bond cleavage was observed upon reaction of propellane diphosphonium dications with a range of nucleophiles (e.g. H⁺, OH⁻, H₂O). A 1,2-diphosphonium dication bearing a naphthalene framework was also shown to undergo nucleophilic attack opposite the P-P bond in the presence of fluoride.

While the reactivity has largely been studied to gain insight into the interesting P-P bonding mode of 1,2-diphosphonium dications, the use of these compounds as Lewis acids in either catalysis or FLP chemistry has, to the best of our knowledge, not been reported.

5.2 Results and Discussion

5.2.1 Synthesis of 1,2-Diphosphonium Dication 5-1

To synthesize the target diphosphonium dication, two equivalents of [Et₅Si][B(C₆F₅)₄](C₇H₈) were added to a C₆H₅F solution of difluorophosphorane (C₁₀H₆)(Ph₂PF₂)(Ph₂P), resulting in a double fluoride abstraction with concurrent loss of Et₅SiF (Scheme 5-1). Compound 5-1 as a [B(C₆F₅)₄]⁺ salt was isolated in high yields (95%) and fully characterized by NMR spectroscopy, mass spectrometry and elemental analysis. The ³¹P{¹H} NMR spectrum (CD₂Cl₂) contains a singlet resonance at δ 23.2 ppm, which is comparable to the related phosphonium centre of [Ph₃P-PPh₂]+ (³¹P δ = 15 ppm). The diphosphonium salt 5-1 is relatively stable and does not
decompose in coordinating solvents, like CH$_3$CN, and in the solid state, **5-1** can be exposed to air for 24 h without significant decomposition. Unfortunately, all attempts to obtain crystals suitable for X-ray diffraction were unsuccessful; thus, to gain insight into the structural characteristics of **5-1** we turned to the literature.

**Scheme 5-1.** Synthesis of diphosphonium dication **5-1**.

In this regard, while catena-phosphorus chemistry has been extensively studied by the Burford group, examples of cationic P-P bonded diphosphonium species with a rigid naphthalene framework are rare. In one unique example, Somisara and coworkers studied the related compound [(C$_{10}$H$_6$)(PhMeP)$_2$][OTf]$_2$, and report spectroscopic evidence for a P-P bond length (2.225(1) Å) that is within the range of an “ordinary” single P-P bond (2.22 ± 0.05 Å). Similarly, in the solid state [Me$_3$PMe$_3$][OTf]$_2$ contains a P-P bond length of 2.198(2) Å and computations support the existence of a typical, localized P-P single bond. As well, it is noteworthy that while two formal positive charges on directly bonded phosphorus atoms would be expected to have an elongated P-P bond due to coulombic repulsion, comparison to isoelectronic neutral Si-Si bonded molecules suggests this is not the case.

Collectively, these data suggest that the P-P bonds in diphosphonium dicationic species have significant covalent character. To this end, while we were unable to obtain crystals of **5-1** suitable for X-ray diffraction, the computed P-P distance (2.31 Å) and stability in air, support the existence of a robust P-P single bond in **5-1**, as reported by Somisara for closely related systems.

On route to a more facile and reliable synthesis, we took inspiration from Robertson *et al.* wherein they reported a two-electron reduction of Sb(V) with subsequent oxidation of a P(III) centre to form diphosphonium dications [R$_3$P-PR$_3$][OTf]$_2$ (R = Me, nPr). In this regard, we mixed commercially-available 1,8-diphenylphosphinonaphthalene (1,8-dppn) with 2 equiv. of *in situ* generated Ph$_3$Sb(OTf)$_2$ and after 18 h, the corresponding 1,2-diphosphonium [OTf] salt **5-3** was
isolated. The [OTf] salt could then be converted to the corresponding [B(C₆F₅)₄] salt through reaction with 2 equiv. of [Et₃Si][B(C₆F₅)₄](C₇H₈) (Scheme 5-2). In addition to fewer reaction steps, this protocol is higher yielding and utilizes less expensive reagents.

Scheme 5-2. Alternate route to 1,2-diphosphonium dication 5-1.

With 5-1 in hand, we probed the Lewis acidity using the Gutmann-Beckett method, as has been described in previous chapters.₆¹ In this regard, equimolar amounts of Et₃PO and 5-1 were mixed in CD₂Cl₂ and analyzed by ³¹P{¹H} NMR spectroscopy, which displays a broad singlet resonance for Et₃PO at δ 64.5 ppm, which is shifted upfield (Δ = 13.9 ppm) relative to free Et₃PO (δ 50.6 ppm). Compared to the bis(fluorophosphonium) dication ([C₁₀H₆](Ph₂PF)₂⁺ (δ)³¹PEt₃PO: 60.5 ppm), ⁵⁸ compound 5-1 demonstrates a greater interaction with Et₃PO. Notably, while mixtures of dicationic fluorophosphonium species reported in Chapter 2 and those in the literature ⁵⁸, ⁶² have been shown to react with Et₃PO via a fluoride-oxide exchange reaction, compound 5-1 exhibits increased stability, showing no degradation even in the presence of Et₃PO after 24 h at 50 °C.

To further probe the Lewis acidic nature of 5-1, DFT calculations were performed (by Dr. Roman Robrovetsky), and the geometry of the cation was optimized at the wB97XD/def2-TZV level of theory. ⁶³, ⁶⁴ The major component of the highest occupied molecular orbital (HOMO) of 5-1 is the naphthalene framework (Figure 5-2, left), while the lowest unoccupied molecular orbital (LUMO) is the anti-bonding σ* orbital of the P–P bond (Figure 5-2, right). These observations suggest that attack from a suitable nucleophile will likely occur on the outside where the LUMO is more exposed.
5.2.2 Frustrated Lewis Pair Reactivity with 5-1

Inspired by the stability of 5-1, we envisioned a robust FLP with a desirable Lewis base. Given the report by Gabbaï and coworkers wherein they reported the double electrophilic activation of carbonyl with a dicationic antimony compound, we wondered if 5-1 would bind carbonyl in a similar fashion. In this regard, we first reacted 5-1 with benzaldehyde; however, no reaction or carbonyl sequestration was observed. Similarly, no reaction was observed when 5-1 was mixed with CO₂. However, upon reaction with fluoride, 5-1 was transformed into the previously reported fluoro-phosphonium phosphorane \([\text{C}_{10}\text{H}_{6}(\text{Ph}_2\text{PF})(\text{PPH}_2)][\text{B}(\text{C}_6\text{F}_5)_4]\), which further supports the notion of a relatively strong P-P bond.

In search of a stable FLP pair with 5-1, we mixed 5-1 with equimolar amounts of PPh₃. Analysis of the \(^{31}\text{P}\{\text{H}\}\) NMR spectrum (CD₂Cl₂) displays only a weak interaction (slight broadening of the PPh₃ resonance was observed). On the other hand, reaction of 5-1 and PrBu₃ indicates no adduct formation.
5.2.2.1 Reactivity of 5-1 with E-H bonds

5.2.2.1.1 Reactivity of 5-1 with Si-H bonds

Examples of all-phosphorus-based FLPs are rare, and given the rich literature of Et₃SiH-activation by phosphorus(V), we were interested in probing FLP E-H activation with 5-1 and PPh₃ or PrBu₃. In this case, perhaps most notable would be the activation of H₂, which has only been reported once with a P(V) cationic species.

When equimolar amounts of 5-1 and PPh₃ were mixed with Et₃SiH, complete consumption of 5-1 was observed by multi-nuclear NMR spectroscopy after 24 h at ambient temperature. The ³¹P{¹H} NMR spectrum (C₆D₅Br) contains a sharp singlet resonance at δ 4.1 ppm and a broad singlet resonance at δ ~3.3 ppm. In the ³¹P NMR spectrum, the latter resonance appears as a doublet with strong P-H coupling (¹J₉H = 284 Hz). The former resonance can be assigned to the cation of [Ph₃PSiEt₃][B(C₆F₅)₄] 5-4 (Scheme 5-3), which was confirmed by independent synthesis via reaction of PPh₃ and [Et₃Si][B(C₆F₅)₄]·(C₇H₈). Moreover, the unidentified product was formulated to be [(C₁₀H₆)(Ph₂P)₂H][B(C₆F₅)₄]⁶⁶,⁶⁷ 5-5, which was further confirmed by independent synthesis of 1,8-bis(diphenylphosphine)(naphthalene) (1,8-dppn) and HN(SO₂CF₃)₂ (see section 5.2.2.1.2).

If the analogous reaction is carried out in the presence of a stronger Lewis base such as PrBu₃ (1 equiv.), formation of 5-5, 1,8-dppn, [tBu₃PH][B(C₆F₅)₄]⁶⁸ and a new product at δ 37.2 ppm are

Scheme 5-3. Si-H bond activation with 5-1 and PPh₃ or PrBu₃.
observed in the $^{31}$P{¹H} NMR spectrum (C₆D₅Br). The formation of 1,8-dppn and [tBu₃PH][B(C₆F₅)₄] support the notion of deprotonation of 5-5 when a strong base is present. This was corroborated when 5-1 was mixed with 2 equiv. of PrBu₃ and 1 equiv. of Et₃SiH, as there was no evidence of 5-5 in the $^{31}$P{¹H} NMR spectrum after 24 h at ambient temperature. Rather, complete conversion of 5-1 to 1,8-dppn was observed (Scheme 5-3, middle). The $^{31}$P{¹H} NMR spectrum (C₆D₅Br) also contains resonances for [tBu₃PH][B(C₆F₅)₄] 5-6 (δ = 60.9 ppm) and the same singlet as previously observed at δ 37.2 ppm. This latter species was determined to be [tBu₃PSiEt₃][B(C₆F₅)₄] 5-7 based on independent synthesis with PrBu₃ and [Et₃Si][B(C₆F₅)₄]+(C₇H₈). 5-7 was fully characterized by NMR spectroscopy, mass spectrometry and X-ray crystallography (Figure 5-3). The bond metrics are unexceptional; however, it is worth noting that the comparably large P-Si bond length (2.338(2) Å) is likely the result of steric congestion.¹⁸

![Figure 5-3. Molecular structure of 5-7 (POV-ray depiction). P: orange, Si: yellow, C: black. Hydrogen atoms and [B(C₆F₅)₄]+ counterion have been omitted for clarity.](image)

To probe the mechanism of these Si-H bond activation reactions, we wanted to investigate the reactivity of 5-1 with Et₃SiH. Interestingly, when 5-1 was mixed with Et₃SiH in the absence of an external Lewis base, complete consumption of 5-1 was observed, based on the $^{31}$P{¹H} NMR spectrum. When the reaction was conducted in CH₂Cl₂, only slow conversion to 5-5 was observed after 48 h (65%), and analysis of the $^{19}$F{¹H} NMR spectrum (CD₂Cl₂) showed decomposition of [Et₃Si]$^+$-. When the analogous reaction was completed in CD₃CN, complete conversion to 1,8-dppn was observed by $^{31}$P NMR spectroscopy (Scheme 5-3, bottom). In addition, the solvated [Et₃Si]$^+$ species 5-8 was detected via a $^{29}$Si{¹H} NMR experiment,⁶⁹-⁷¹ and the ¹H NMR spectrum (CD₃CN)
shows evidence of H₂ formation, presumably from the reaction of excess Et₃SiH and 5-5, suggesting the H atom in 5-5 is protic. To support this proposition, a control experiment was completed, wherein a mixture of 5-5, [Et₃Si][B(C₆F₅)₄]•(C₇H₈) and Et₃SiH in 1 : 1 : 10 stoichiometry in CD₃CN was monitored by NMR spectroscopy. Quantitative transformation of 5-5 to 1,8-dppn and H₂ was observed by means of ¹H and ³¹P NMR spectroscopy.

Collectively, these data demonstrate the ability of the FLP comprised of 5-1 and PPh₃ or PrBu₃ to affect Si-H bond activation and subsequent silylium sequestration. This transformation is believed to proceed through an initial hydride abstraction by 5-1. In the presence of a weak base like PPh₃, 5-5 and [Ph₃PSiEt₃]⁺ are generated, exclusively. On the other hand, when a strong base like PrBu₃ is used, 5-5 can be deprotonated generating 1,8-dppn and [tBu₃PH]⁺ in addition to [tBu₃PSiEt₃]⁺. Indeed, reaction of the [N(SO₂CF₃)₂]⁻ salt of 5-5 with PrBu₃ reveals quantitative formation of 1,8-dppn and [tBu₃PH][N(SO₂CF₃)₂]. Overall, these observations showcase the FLP reactivity of 5-1 and PPh₃/PrBu₃ and demonstrate the hydridophilicity of 5-1 as it competes with the strong Lewis acid [Et₃Si]⁺.

5.2.2.1.2 Structural Characteristics and Reactivity of 5-5

The observed hydridophilicity of 5-1, yet protic nature of 5-5 is intriguing. To probe the structure of these compounds and their respective modes of reactivity further, we independently synthesized the [N(SO₂CF₃)₂] salt of 5-5 from 1,8-dppn and HN(SO₂CF₃)₂ (Scheme 5-4). Analysis of the ³¹P and ³¹P{¹H} NMR spectra (C₆D₅Br) show resonances for two P-P containing species. In the ³¹P NMR spectrum (C₆D₅Br), resonances appear at δ 2.6 ppm (d, ¹JₚH = 576 Hz), δ –5.1 ppm (d, ¹JₚH = 284 Hz) and δ –20.6 ppm (broad, s), wherein the resonance at δ –5.1 ppm appears to be the major product (Figure 5-4, top). These data suggest an equilibrium likely exists at room temperature.

![Scheme 5-4](image.png)

Scheme 5-4. Synthesis of phosphonium salt 5-5[NTf] (NTf = N(SO₂CF₃)₂).
Figure 5-4. $^{31}$P (top) and $^{31}$P{${}^1$H} (bottom) NMR spectra (C$_6$D$_5$Br) of 5-5[NTf] at ambient temperature.

In fact, Karacar et al. have investigated this equilibrium and have reported a similar $^{31}$P NMR spectra. They report an equilibrium between monocations, wherein the proton is oriented closer to the P(V) centre in [5-5]$^+$ and closer to the P(III) centre in [5-5']$^+$. Their data, which align with ours, reveal that the P-P interaction in 5-5 is weak, and $^1$J$_{PP}$ coupling is only resolved at low temperatures. Collectively, these NMR data indicate a fast, intramolecular proton exchange between the P centres in 5-5 at ambient temperature.

The solid-state structure of 5-5[NTf] shows a monophosphonium salt, wherein the H atom is bonded to P2 which has a distorted tetrahedral geometry and P1 exhibits a slightly distorted trigonal pyramidal shape (Figure 5-5). The P1-P2 bond distance of 5-5[NTf] (3.107(1) Å) is comparable to the P-P distance (3.211 Å) of [(C$_{10}$H$_{16}$)(Ph$_2$P)$_2$H][OTf], and both are longer than the bis-phosphine 5-2 (3.052 Å) and much longer than a conventional P-P single bond (ca. 2.25 Å). It is noteworthy that one oxygen atom of the [NTf]$^-$ counterion is oriented between the two P centres, with P-O bond distances (P1-O1 3.580(2) Å; P2-O1 3.468(2) Å) close to the sum of the P,O van der Waals radii (3.32 Å). As well, the approximate O1-H1 distance (2.16(2) Å) is within the sum of the O, H van der Waals radii (2.72 Å).
Figure 5-5. Molecular structure of the cation of 5-5[NTf] (POV-ray depiction). P: orange, N: blue, H: white, Si: yellow, C: black, F: pink, O: red. Select hydrogen atoms and CH₂Cl₂ solvent molecule have been omitted for clarity.

With the spectroscopic and structural data obtained for 5-5[NTf], combined with the computational investigation for 5-1, it seems plausible that reaction of 5-1 with hydride is expected to yield [5-5']⁺. In this regard, the donation of electron density from the hydride into the LUMO of 5-1 cleaves the P–P bond, generating [5-5]⁺ which is in equilibrium with its isomer [5-5']⁺, wherein [5-5']⁺ is the major component at room temperature. This equilibrium was previously observed by NMR spectroscopy for other salts of the cation in [5-5]⁺.⁶⁶, ⁶⁷ The transformation of [5-5]⁺ to [5-5']⁺ was computed to be slightly exergonic (ΔG°₂⁹⁸ ≈ −1.2 kcal mol⁻¹).

Interestingly, while PrBu₃ was shown to deprotonate [5-5]⁺ generating 1,8-dppn and [tBu₃PH]⁺, reaction of [5-5]⁺ with [Ph₃C][B(C₆F₅)₄] generates 5-1 and Ph₃CH, suggesting that the H atom in [5-5]⁺ also displays hydridic character. Nonetheless, these results support the hydridophilicity of diphosphonium dication 5-1 wherein reaction with hydride generates [5-5]⁺ which is in equilibrium
with its isomer [5-5']+. These results suggest that further reactivity of [5-5+] can be modified by judicial choice of base or acid, which showcases the diverse nature of the diphosphonium dicatonic naphthalene framework.

5.2.2.1.3 Reactivity of 5-1 with B-H bonds

To further probe the hydridophilicity of 5-1, we chose [tBu3PH][HB(C6F5)3] 5-9 as a potential hydride donor. For this reaction, equimolar amounts of 5-1 and 5-9 were mixed and analyzed by multi-nuclear NMR spectroscopy. After 30 min at ambient temperature, the 31P{1H} NMR (CD2Cl2) contained resonances for [tBu3PH]+ (δ 60.5 ppm), 5-5 (δ –4.0 ppm) and unreacted 5-1 (δ 23.3 ppm) (Scheme 5-5, top). Analysis of the 1H NMR spectrum reveals a low field triplet resonance at δ 10.20 ppm corresponding to the P-H fragment of 5-5, and a broad singlet resonance at δ 3.60 ppm. The latter resonance can be attributed to the [H(B(C6F5)3)2]+ anion of 5-10, suggesting that hydride abstraction from 5-9 occurred liberating B(C6F5)3 which was subsequently captured by unreacted 5-9, thereby preventing complete consumption of 5-1 (Scheme 5-5, top). This was corroborated by a control reaction of 5-9 and B(C6F5)3 (1 : 1 equiv.), wherein analysis of the 1H NMR spectra (CD2Cl2) after 1 h at ambient temperature reveals the same broad singlet resonance at δ 3.60 ppm. Addition of a second equivalent of 5-9 led to complete consumption of 5-1 and the formation of 5-5, 5-10 and 5-6, as observed by multi-nuclear NMR spectroscopy.

Scheme 5-5. Reaction of 5-1 with [tBu3PH][HB(C6F5)3] 5-9 without (top) and with (bottom) PPh3.

To overcome B(C6F5)3 capture by 5-9, we conducted an analogous reaction with an external Lewis base. In this case, reaction of a 1 : 1 mixture of 5-1 and Ph3P was added to a solution of 5-9, and the reaction mixture was subsequently monitored by multi-nuclear NMR spectroscopy. After 30 min at ambient temperature, the reaction mixture changed colour and the 11B{1H} NMR spectrum
(CD$_2$Cl$_2$) of the reaction mixture revealed two resonances at δ –16.6 ppm and δ –0.3 ppm, which can be assigned to the [B(C$_6$F$_5$)$_4$]$^-$ anion and the phosphine borane adduct Ph$_3$P–B(C$_6$F$_5$)$_3$ 5-11, respectively. The $^{31}$P NMR spectrum reveals full conversion of diphosphonium dication 5-1 to 5-5 (δ –4.4 ppm) and contains a resonance at δ 60.3 ppm (dm, $^1$J$_{PH}$ = 429 Hz) assigned to [tBu$_3$PH][B(C$_6$F$_5$)$_4$]$^-$ 5-6. The resonance for 5-11 appears as a singlet in the $^{31}$P NMR spectrum at δ –4.1 ppm.

Overall, this reaction demonstrates that diphosphonium dication 5-1 abstracts hydride from 5-9 liberating B(C$_6$F$_5$)$_3$, which is subsequently trapped by PPh$_3$ and generates the adduct Ph$_3$P–B(C$_6$F$_5$)$_3$ (Scheme 5-5, bottom). This reaction can be viewed as an all phosphorus P/P FLP-type activation of the B–H bond in bond in [HB(C$_6$F$_5$)$_3$]$^-$ yielding 5-5 and 5-11. As well, this reactivity indicates that diphosphonium dication 5-1 possesses a higher hydridophilicity than the electrophilic Lewis acid B(C$_6$F$_5$)$_3$.

5.2.2.1.4 Reactivity of 5-1 with C–H bonds

The remarkable hydridophilicity of the diphosphonium dication 5-1, and the ability of 5-1 to promote FLP-type activations of Si–H and B–H bonds with tertiary phosphines, prompted our exploration into the stoichiometric activation of C–H bonds. In this regard, we began our investigation with 1,4-cyclohexadiene (CHD). When an equimolar amount of 5-1 and PPh$_3$ were mixed with CHD, no reaction was observed, even upon heating to 100 °C for several days in C$_6$D$_5$Br. However, when a more basic phosphine like PrBu$_3$ (2 equiv.) was used, complete consumption of 5-1 was observed after 24 h at 90 °C (Scheme 5-6, top). Analysis of the $^{31}$P($^1$H) NMR spectrum (C$_6$D$_5$Br) reveals resonances attributed to 1,8-dppn (δ –15.1 ppm), [tBu$_3$PH][B(C$_6$F$_5$)$_4$] (δ 60.0 ppm) and minor amounts of PrBu$_3$ (δ 61.7 ppm). Moreover, the $^1$H NMR spectrum contains a singlet resonance at δ 7.21 ppm, which indicates the formation of benzene.
When diphosphonium dication 5-1 is reacted with an equimolar amount of 1,3,5-cycloheptatriene (CHT) in the presence of 2 equiv. of PrBu₃, similar reactivity was observed (Scheme 5-6, bottom). After heating at 90 °C for 24 h, the $^{31}$P{¹H} NMR spectrum (C₆D₅Br) reveals two major singlet resonances which can be assigned to 1,8-dppn and 5-6, in addition to a new singlet resonance at δ 45.1 ppm. $^1$H NMR data suggest a cyclo-propanyl-motif based on the observation of a C-H resonance adjacent to the P atom (δ(¹H): 0.09 ppm). These data indicate the formulation as [C₇H₇PrBu₃][B(C₆F₅)₄] 5-12.⁷⁸

To support this view, the tropylium ion salt [C₇H₇][BF₄] was reacted with PrBu₃. After stirring at ambient temperature for 15 min, the cation of [C₇H₇PrBu₃][BF₄] 5-13 was isolated in 85% yield and fully characterized by NMR spectroscopy, mass spectrometry, elemental analysis and X-ray crystallography. The $^{31}$P{¹H} NMR spectrum (C₆D₅Br) contains a singlet resonance at δ 45.0 ppm, and analysis of the $^1$H NMR spectrum reveals a multiplet at δ 0.08 ppm which corresponds to the C-H adjacent to the P centre. The solid-state structure of 5-13 reveals the phosphonium substituent in the exo-position relative to the bicyclo[4.1.0]heptane framework (Figure 5-6). The remaining metric parameters are unexceptional.
These C-H bond activation reactions with diphosphonium dication 5-1 and CHD and CHT are thought to proceed via an initial hydride abstraction generating 5-5, as seen with the reaction of 5-1 with Si-H and B-H bonds. After this step, in the case of CHD, one equivalent of PrBu₃ sequesters the proton, affording benzene. For the reaction with CHT, hydride abstraction generates a transient tropylium cation which is in equilibrium with its isomeric bicyclic norcaradiene-derivative. This isomer is then sequestered by one equivalent of PrBu₃ yielding 5-12. In both cases, the generated cation 5-5 reacts with a second equivalent of phosphine to liberate 1,8-dppn and [tBu₃PH]⁺. It is noteworthy that the reaction still proceeds with 1 equiv. of PrBu₃, however, a mixture of 5-5 and 1,8-dppn is observed in the ³¹P NMR spectrum.

Although several C-H bond activation reactions by ambiphilic phosphonium cations have been reported previously, the present examples are to the best of our knowledge, the first examples of FLP-type C-H activations involving a phosphorus(V)-based Lewis acid.

5.2.2.1.5 Reactivity of 5-1 with H-H bonds

Finally, the FLP-type heterolytic splitting of H₂ utilizing the diphosphonium dication 5-1 as a Lewis acid was probed. In an initial reaction, 5-1 was mixed with 2 equiv. of PPh₃ and pressurized with ca. 4 atm of H₂. Even after heating the reaction mixture at 100 °C for 5 days, NMR spectroscopic investigation indicated no reaction had occurred. Contrarily, when 5-1 was mixed...
with 2 equiv. of PrBu3 in C6D5Br and was exposed to a pressure of 4 atm of H2 at 100 °C, within 48 h, complete conversion of 5-1 to 1,8-dppn and 2 equiv. of 5-6 was observed by NMR spectroscopy (Scheme 5-7). These data support the need for a strong Lewis base to facilitate the heterolytic splitting of H2. Like the reactions mentioned previously with CHD and CHT, it is believed that the first step in this reaction is the heterolytic cleavage of H2 generating 5-5 and 1 equiv. of [tBu3PH][B(C6F5)4]. Subsequent deprotonation of 5-5 by the second equivalent of PrBu3 then facilitates the reduction to 1,8-dppn.

Scheme 5-7. Reaction of 5-1 and PrBu3 with H2.

The analogous reaction was performed with 5-1 and PrBu3 (1 : 2 ratio) and D2 (4 atm). After heating the reaction mixture at 100 °C for 48 h, analysis of the 31P{1H} NMR spectrum (C6D5Br) reveals complete consumption of 5-1, and the formation of 1,8-dppn and a 1:1:1 triplet resonance at δ 58.9 ppm (1JPD = 65 Hz). This is consistent with the formation of [tBu3PD][B(C6F5)4] 5-13.18 In the presence of HD gas, a mixture of the salts [tBu3PH][B(C6F5)4] and [tBu3PD][B(C6F5)4] were obtained, without any evidence of HD scrambling (i.e. neither H2 nor D2 were observed by 1H/2D NMR spectroscopy). These data indicate that heterolytic cleavage of H2 is not reversible, which is directly analogous to the irreversible cleavage of H2 by the FLP PrBu3/B(C6F5)3.68 The present system is a rare example of an all-phosphorus based FLP capable of effecting stoichiometric H2 activation.33
5.2.2.2 Summary of FLP reactivity of 5-1 and PPh3/PtBu3

In section 5.2.2, we presented the facile and high-yielding synthesis of robust but highly Lewis acidic diphosphonium dication 5-1. While previously reported strong Lewis acids based on EPCs contain reactive P–F bonds, the present diphosphonium dication 5-1 achieves similar Lewis acidity as a result of the accumulation of positive charge on two adjacent P atoms. This phosphorus-based Lewis acid combined with tertiary phosphines generates the first examples of purely phosphorus-based FLP systems, which were used to activate E-H (E = Si, B, C, H, D) bonds. These unique examples of FLP reactivity (with an EPC) create new avenues for phosphorus-based Lewis acids in FLP chemistry and Lewis acid catalysis.

5.2.3 1-Diphenylphosphino-8-N,N-Dimethylamino Naphthalene as an Intramolecular FLP

5.2.3.1 Introduction

One of the main commonalities of intramolecular FLPs is the incorporation of a rigid aryl framework. In this regard, some of the most notable main group FLP systems with aryl scaffolds include boron-based Lewis acids and nitrogen-based Lewis bases. In one major advance, Fontaine and coworkers used the intramolecular FLP 1-TMP-2-BH2-C6H4 (TMP = 2,2,6,6-tetramethylpiperidine) for C-H bond activation and borylation. On the other hand, examples of P(V) Lewis acids used in intramolecular FLP chemistry are rare; in one example from our group, an amidofluorophosphorane was shown to capture CO2.

Similar to 1,2-disubstituted benzene rings, 1,8-disubstituted peri-naphthalenes have a rigid framework which is known to result in close interactions between the substituents on the 1- and 8-position (ca. 2.5 Å). In this regard, several research groups have synthesized 1-diphenylphosphino-8-N,N-dialkylamino phosphonium salts and studied their structural properties. However, while the rigid framework is believed to enforce the proximity of the atoms at the 1- and 8-positions, there has been debate among the exact nature of the N/P intramolecular interaction. Some research groups claim there is an N-P intramolecular interaction (Scheme 5-8, right), yet others offer conflicting evidence and do not support the claim of dative N-P interaction (Scheme 5-8, left).
5.2.3.2 Synthesis and Reactivity of 1-Diphenylphosphino-8-N,N-Dimethylamino Naphthalene

While 5-1 was a viable Lewis acid in FLP chemistry in conjunction with external Lewis bases like PPh$_3$ and PrBu$_3$, the robust P-P bond limits the scope of these reactions and may be preventing the use of 5-1 as an intramolecular FLP. To overcome this drawback, we targeted the synthesis of an analogous N-P naphthyl species, wherein the N-P interaction should be weaker relative to P-P if the hard-soft-acid-base (HSAB) theory is considered. In this regard, we envisioned this system as an intramolecular FLP with a N Lewis base and P(V) Lewis acid.

To begin our investigation, we synthesized 1-diphenylphosphino-8-N,N-dimethylamino naphthalene 5-14 according to a modified literature procedure from 8-dimethylamino-1-naphthalene (Scheme 5-9). While this framework has been studied previously for insight into the N/P donor/acceptor properties, reactivity studies are limited. With 5-14 in hand, we targeted oxidation of the phosphorus(III) centre with XeF$_2$. For this reaction, an equimolar amount of 5-14 and XeF$_2$ were stirred at ambient temperature for 3 h before being monitored by multi-nuclear NMR spectroscopy.

Analysis of the $^{31}$P{$^1$H} NMR spectrum (CH$_2$Cl$_2$) after this time shows complete consumption of 5-14 and the formation of a new triplet resonance at $\delta$ = -54.5 ppm ($^1J_{PF}$ = 758 Hz). The corresponding doublet can be found in the $^{19}$F{$^1$H} NMR spectrum at $\delta$ = -48.0 ppm. These data are closely related to the phosphine-phosphorane species (C$_{10}$H$_6$)(Ph$_2$PF$_2$)(PPh$_2$) ($^{31}$P{$^1$H} ($\delta$): -55.5 ppm).

Scheme 5-8. Equilibrium of 1-diphenylphosphino-8,N,N-dialkylamino phosphonium salts.

ppm, triplet, $^{1}J_{PF} = 742$ Hz; $^{19}F\{^{1}H\}$ ($\delta$): –42.0 ppm. Unfortunately, all attempts to further characterize or isolate the presumed difluorophosphorane 5-15 were unsuccessful. Instead, 5-15 was reacted in situ with 1 equiv. of [Et$_3$Si][B(C$_6$F$_5$)$_4$]•(C$_7$H$_8$) in hopes of abstracting fluoride and generating an amino-phosphonium species shown in Scheme 5-8. After 1 h at ambient temperature, analysis of the $^{31}P\{^{1}H\}$ NMR spectrum (C$_6$H$_5$F) shows complete consumption of the starting material and the formation of a new singlet resonance at $\delta$ 47.1 ppm and a doublet at $\delta$ 43.5 ppm ($^{1}J_{PF} = 804$ Hz). The resonances are observed in a 1 : 3.4 ratio, suggesting the latter is the major product (Figure 5-7, bottom). The increase in P-F coupling and downfield chemical shift in the $^{31}P$ NMR is consistent with the formulation of a fluorophosphonium moiety, supporting successful fluoride abstraction.\textsuperscript{30, 58, 62} However, it is interesting to note that most fluorophosphonium cations have P-F coupling constants around 1000 Hz,\textsuperscript{30, 58} which is much larger than the observed value (ca. $\Delta = 200$ Hz). A similar, unusually small, P-F coupling has been observed for [(2-PFPh$_2$)-(C$_6$H$_4$CO)Pd(PPh$_3$)$_2$Br][OTf] ($^{1}J_{PF} = 773$ Hz), wherein an O atom interacts with the fluorophosphonium to give a phosphorane-type geometry at phosphorus.\textsuperscript{91} Therefore, in this case, it is likely that the pendant N atom is donating electron density into the P-F antibonding orbital, giving the phosphorus centre more phosphorane-type character, and subsequently decreasing the P-F coupling relative to tetracoordinate fluorophosphonium cations.

\textbf{Figure 5-7.} $^{31}P\{^{1}H\}$ NMR spectra (C$_6$H$_5$F) of 5-14 (top) and the crude reaction mixture of 5-14 and 1 equiv. of [Et$_3$Si][B(C$_6$F$_5$)$_4$]•(C$_7$H$_8$) (bottom).

For this species, the corresponding P-F resonance is found in the $^{19}F\{^{1}H\}$ NMR spectrum at $\delta$ –72.0 ppm. The $^{19}F\{^{1}H\}$ NMR spectrum also contains resonances for the [B(C$_6$F$_5$)$_4$]$^-$ counterion
and a multiplet resonance at $\delta$ –175.3 ppm, indicative of Et$_3$SiF. Attempts to isolate the two products have insofar been unsuccessful.

It is noteworthy that reaction of 5-14 with Ph$_3$Sb(OTf)$_2$ (as reported in section 5.2.1) was attempted, but no reaction was observed after 3 days. Further reactivity and FLP chemistry with 5-14 remain part of an ongoing investigation in our laboratory; thus, these data are proof-of-principle preliminary results and will help guide reactions for future projects.

### 5.3 Conclusions

In this chapter we present the facile and high-yielding synthesis of a robust, but highly Lewis acidic 1,2-diphosphonium dicationic species 5-1, bearing a rigid naphthalene scaffold. Synthesis of 5-1 could be achieved through double fluoride abstraction with [Et$_3$Si][B(C$_6$F$_5$)$_4$]$^\bullet$(C$_7$H$_8$) or oxidation of 1,8-dppn with Ph$_3$Sb(OTf)$_2$ - the latter being a more viable and reliable route. While previously reported strong Lewis acids (from Chapter 2 and the relevant literature) based on P(V) species contain reactive P-F bonds, 5-1 achieves similar Lewis acidity as a result of the accumulation of positive charge on two adjacent P(V) atoms. Indeed, 5-1 can be stored in air for up to 24 h without significant decomposition.

The unprecedented stability of 5-1 was exploited in FLP chemistry, wherein most EPCs decompose in the presence of a strong Lewis base. In fact, combinations of PPh$_3$ or PrBu$_3$ with 5-1 yielded the first examples of purely phosphorus-based FLP systems. In this regard, combinations of PPh$_3$ or PrBu$_3$ and 5-1 were shown to activate Si-H, B-H, C-H and H-H bonds, supporting the notion that 5-1 is more hydridophilic than strong Lewis acids such as [Et$_3$Si]$^+$ and B(C$_6$F$_5$)$_3$. The mechanism of these E-H bond activation reactions is believed to be initiated by hydride abstraction with 5-1.

In the latter half of the chapter we report preliminary reactivity with 1-diphenylphosphino-8-N,N-dimethylamino naphthalene 5-14. NMR spectroscopic evidence suggests oxidation of the P(III) centre to P(V) with XeF$_2$ and subsequent fluoride abstraction with [Et$_3$Si][B(C$_6$F$_5$)$_4$]$^\bullet$(C$_7$H$_8$) are feasible transformations. Interestingly, for the latter transformation, the P-F coupling constant of the product is significantly less than those values reported for most tetracoordinate fluorophosphonium cations, suggesting electron donation from the pendant N atom may be present. While still in its infancy, this heteroatomic framework is believed to afford a weaker N/P
interaction relative to the P–P bond in 5-1, which renders 5-14 a good candidate for intramolecular FLP chemistry. The synthesis of related cations and their reactivity in FLP chemistry is the subject of ongoing investigation in our laboratory.

5.4 Experimental Details

5.4.1 General Remarks

All manipulations were performed in a MB Unilab Glove box produced by MBraun or using standard Schlenk techniques under an inert atmosphere of anhydrous N₂. Dry, oxygen-free solvents (CH₂Cl₂, Et₂O, n-pentane) were prepared using an Innovative Technologies solvent purification system. Fluorobenzene (C₆H₅F) was distilled from CaH₂ and stored over molecular sieves (4 Å) prior to use. Deuterated dichloromethane (CD₂Cl₂) and bromobenzene (C₆D₅Br) were purchased from Sigma-Aldrich, distilled from CaH₂ and stored over molecular sieves (4 Å) for at least two days prior to use. Reagents such as 1,8-bis(diphenylphosphino)naphthalene (1,8-dppn), n-BuLi, Ph₂PCl, XeF₂, Et₃PO, Et₅SiH, PrBu₃, B(C₆F₅)₃, hydrogen (H₂), deuterium hydride (HD), deuterium (D₂) [C₇H₇][BF₄]₂, CF₂Br₂ and HN(SO₂CF₃)₂ were purchased either from Sigma-Aldrich, Strem Chemicals or Alfa Aesar and, if applicable, distilled prior to use. Compounds [Et₃Si][B(C₆F₅)₄]·(C₇H₈), (C₁₀H₁₆)(Ph₂PF₂)(Ph₂P)²⁸ Ph₃SbCl₂,²⁴ and [tBu₃PH][HB(C₆F₅)₃]⁶⁸ were prepared according to literature known procedures. All glassware was oven-dried at temperatures above 180 °C prior to use. NMR spectra were measured on a Bruker AVANCE 400 (¹H: 400 MHz, ¹¹B: 128 MHz, ¹³C: 101 MHz, ³¹P: 162 MHz, ¹⁹F: 377 MHz) or Agilent DD2 500 (¹H: 500 MHz, ¹³C: 125 MHz, ³¹P: 202 MHz, ¹⁹F: 471 MHz) at ambient temperature. All ¹³C NMR spectra were exclusively recorded with composite pulse decoupling. Assignments of the carbon atoms in the ¹³C spectra were performed via indirect deduction from the cross-peaks in 2D correlation experiments (HMBC; HSQC). Chemical shifts were referenced to δTMS = 0.00 ppm (¹H, ¹³C) and δH₃PO₄(85%) = 0.00 ppm (³¹P, externally). Chemical shifts (δ) are reported in ppm, multiplicity is reported as follows (s = singlet, d = doublet, t = triplet, m = multiplet) and coupling constants (J) are reported in Hz. Assignments of individual resonances were done using 2D techniques (HMBC, HSQC, HH-COSY) when necessary. Yields of products in solution were determined by integration of all resonances observed in the respective NMR spectra if not stated otherwise. High-resolution mass spectra (HRMS) were obtained on a micro mass 70S-250 spectrometer (EI), an ABI/Sciex QStar Mass Spectrometer (DART), or on a JOEL AccuTOF-
DART (DART). Elemental analyses (C, H, N) were performed at the University of Toronto employing a Perkin Elmer 2400 Series II CHNS Analyzer.

5.4.2 Synthesis of Compounds 5-1, [5-5][NTf], 5-4, 5-7, and 5-12

\[(C_{10}H_6)(Ph_2P)_2][B(C_6F_5)_4]_2\] 5-1

[Et3Si][B(C6F5)4]•(C7H8) (1.275 g, 1.30 mmol, 2.0 equiv.) was added portion-wise to a solution of (C10H6)(Ph2PF2)(Ph2P) (348 mg, 0.65 mmol, 1.0 equiv.) in C6H5F (15 mL). This resulted in the instant formation of yellow oil and yellowish supernatant. The reaction mixture was stirred for 1 h at ambient temperature. n-Pentane (5 mL) was added and the supernatant was removed. Washing the oily residue with n-pentane (3 x 10 mL) resulted in the formation of a yellowish solid. All volatiles were removed in vacuo yielding 5-1 as yellowish powder (1.150 g, 95% Yield).

\(^1^H\) NMR (400 MHz, CD2Cl2, Me4Si): \(\delta \) 8.88 (m, 2H; p-naphthyl), 8.45 (m, 2H, o-naphthyl), 8.29 (m, 2H, m-naphthyl), 7.93 (m, 4H, p-Ph), 7.57 (m, 8H, m-Ph), 7.33 ppm (8H, o-Ph). \(^11^B\)\(^1^H\) NMR (128 MHz, CD2Cl2, BF3•OEt2): \(\delta \) −16.7 ppm (s). \(^19^F\)\(^1^H\) NMR (377 MHz, CD2Cl2, CFC1): \(\delta \) −133.0 (m, 16F; o-C6F5), −163.4 (t, \(^3J_{PF} = 20.4 \) Hz, 8F; m-C6F5), −167.3 ppm (m, 16F, m-C6F5). \(^31^P\)\(^1^H\) NMR (162 MHz, CD2Cl2, H3PO4): \(\delta \) 23.2 ppm (s, 2P). \(^13^C\)\(^1^H\) NMR (101 MHz, CD2Cl2, Me4Si): \(\delta \) 148.5 (d(br), \(^1J_{FC} = 241 \) Hz, 16C; C6F5), 140.8 (t, \(^2J_{FC} = 13 \) Hz 1C; C6), 139.5 (s, 2C; C4), 139.3 (s, 4C; p-Ph), 139.1 (dd, \(^2J_{FC} = 6 \) Hz, \(^3J_{FC} = 6 \) Hz, 2C; C2), 138.5 (d(br), \(^1J_{FC} = 241 \) Hz, 8C; p-C6F5), 136.6 (d(br), \(^1J_{FC} = 240 \) Hz, 16C; C6F5), 134.9 (d, \(^2J_{FC} = 13 \) Hz, 4C; o-Ph), 134.7 (t, \(^3J_{FC} = 9 \) Hz, 1C; C5), 131.6 (d, \(^3J_{FC} = 14 \) Hz, 2C; C3), 132.4 (dd, \(^3J_{FC} = 15 \) Hz, \(^4J_{FC} = 2 \) Hz, 8C; m-Ph), 124.2 (s(br), 8C; i-C6F5), 110.5 (d, \(^1J_{PC} = 82 \) Hz, \(^2J_{PC} = 19 \) Hz, 2C; C1), 108.7 ppm (dd, \(^1J_{PC} = 77 \) Hz, \(^2J_{PC} = 5 \) Hz 4C; i-Ph). MS-ESI: Calculated mass for M\(^{2+}\)OH\(^-\): 513.2. Obtained: 513.2 amu. Anal. Calcd. for C\(_{82}H_{26}B_2F_{40}P_2\): C 53.1, H 1.4 %. Found: C 53.1, H 2.1 %.

Alternate Synthesis of 5-1 with Ph3SbCl2\(^24\)
AgOTf (127 mg, 0.50 mmol, 2 equiv.) was added to a CH₂Cl₂ solution of Ph₃SbCl₂. The solution was left to stir at ambient temperature for 2 h before being filtered through a Kimwipe plug. The filtrate was then added to a solution of 1,8-dppn (123 mg, 0.25 mmol, 1 equiv.) The solution was left to stir at ambient temperature for 18 h. The formation of 5-3 was confirmed by multi-nuclear NMR spectroscopy. A solution of [Et₃Si][B(C₆F₅)₄]•(C₇H₈) (357 mg, 0.36 mmol, 2 equiv.) in C₆H₅Cl (3 mL) was added dropwise to a solution of 5-3 (145 mg, 0.18 mmol, 1 equiv.) in toluene (5 mL). The reaction mixture was stirred at ambient temperature for 2 h after which time an oil had settled out of solution. The supernatant was decanted and the residue was wased with n-pentane (3 x 5 mL) and dried in vacuo, affording 5-1 in 76% yield.

[(C₁₀H₆)(Ph₂P)₂H][N(SO₂CF₃)₂] [5-5][NTf]

HN(SO₂CF₃)₂ (70 mg, 0.25 mmol, 1.0 equiv.) was added to a solution of 1,8-bis(diphenylphosphino)naphthalene (126 mg, 0.25 mmol, 1.0 equiv.) in Et₂O/CH₂Cl₂ (1 : 1, 10 mL). The yellow solution turned colourless and the reaction mixture was stirred for 12 h at ambient temperature. n-Pentane (10 mL) was added resulting in the formation of a colourless, microcrystalline precipitate. The supernatant was removed and the residue was washed with n-pentane (3 x 3 mL). Removal of all volatiles in vacuo yielded 5-5[NTf]•(CH₂Cl₂) as a colourless, microcrystalline material (39 mg, 71% Yield). Single crystals of 5-5[NTf]•(CH₂Cl₂) suitable for X-ray diffraction, were obtained by storing the supernatant for 24 h at −35 °C.

¹H NMR (400 MHz, CD₂Cl₂, Me₄Si): δ 10.15 (d, ¹J₁PH = 284 Hz, 1H; PH), 8.36 (m, 2H; naphthyl), 7.71 (m, 4H; naphthyl), 7.55 (m, 4H; p-Ph), 7.42 (m, 8H; o-Ph), 7.21 (m, 8H; m-Ph), 5.33 ppm (s, CH₂Cl₂). ¹¹B{¹H} NMR (128 MHz, CD₂Cl₂, BF₃·OEt₂): δ −16.7 ppm (s). ¹⁹F{¹H} NMR (377 MHz, CD₂Cl₂, CFCl₃): δ −79.4 ppm (s). ³¹P NMR (162 MHz, CD₂Cl₂, H₂PO₄): δ −4.5 (d, ¹J₁PC = 284 Hz). ¹³C{¹H} NMR (101 MHz, CD₂Cl₂, Me₄Si): δ 142.6 (d, ¹J₁PC = 14 Hz, 2C; i-naphthyl), 141.8 (s(br), 2C; CH₃naphthyl), 138.5 (t, ²³J₁PC = 3 Hz 1C; Cnaphthyl), 136.5 (s(br), 2C; CH₂naphthyl), 136.0 (t, ²³J₁PC = 9 Hz 1C; Cnaphthyl), 133.5 (s(br), 8C; m-Ph), 132.6 (s(br), 4C; o-Ph), 130.2 (s(br), 8C; o-Ph), 127.2 (s(br), 2C; CH₂naphthyl), 122.0 (s(br), 4C; i-Ph), 120.3 ppm (quart.,
$^1$J$_{FC}$ = 322 Hz, 2C; CF$_3$). **MS-ESI:** Calculated mass for M$^+$: 497.1583. Obtained: 497.1576 amu. **Anal. Calcd.** for C$_{38}$H$_{27}$F$_6$NO$_4$P$_2$S$_2$: C 55.6, H 3.5, N 1.8 %. Found: C 55.3, H 3.3, N 1.8 %.

[Ph$_3$PSiEt$_3$][B(C$_6$F$_5$)$_4$] **5-4**

![Chemical structure of 5-4](image)

[Et$_3$Si][B(C$_6$F$_5$)$_4$]•C$_7$H$_8$ (96 mg, 0.10 mmol, 1.0 equiv.) was added portion-wise to a solution of Ph$_3$P (26 mg, 0.10 mmol, 1.0 equiv.) in toluene (3 mL) leading to the formation of a colourless oil. The reaction mixture was stirred for 24 h at ambient temperature. The supernatant was removed and the remaining oil was washed with n-pentane (3 x 5 mL). Removal of all volatiles in vacuo gave [Ph$_3$PSiEt$_3$][B(C$_6$F$_5$)$_4$] as a microcrystalline solid (94 mg, 89% Yield).

$^1$H NMR (400 MHz, CD$_2$Cl$_2$, Me$_4$Si): $\delta$ 7.67 (m, 15H; Ph), 1.23 (m, 6H; (C$_2$H$_2$)$_3$), 1.08 ppm (m, 9H; (CH$_3$)$_3$). $^{11}$B$^1$H NMR (128 MHz, CD$_2$Cl$_2$, BF$_3$•OEt$_2$): $\delta$ −16.6 ppm (s). $^{19}$F$^1$H NMR (377 MHz, CD$_2$Cl$_2$, CFCl$_3$): $\delta$ −133.0 (m, 8F; o-F), −163.7 (m, 4F; p-F), −167.5 ppm (m, 8F; m-F).

$^{31}$P$^1$H NMR (162 MHz, CD$_2$Cl$_2$, H$_3$PO$_4$): $\delta$ -2.9 ppm (s). $^{13}$C$^1$H NMR (101 MHz, CD$_2$Cl$_2$, Me$_4$Si): $\delta$ 135.1 (d, $^3$J$_{PC}$ = 3 Hz, 3C; Ph), 134.0 (d, $^3$J$_{PC}$ = 11 Hz, 6C; m-Ph), 131.3 (d, $^3$J$_{PC}$ = 12 Hz, 6C; o-Ph), 119.5 (d, $^1$J$_{FC}$ = 61 Hz, 3C; i-Ph), 7.7 (d, $^4$J$_{PC}$ = 4 Hz, 3C; CH$_2$CH$_3$), 5.1 ppm (d, $^3$J$_{PC}$ = 10 Hz, 3C; CH$_2$CH$_3$). **MS-ESI:** Calculated mass for [M−SiEt$_3$+H]$^+$: 263.1. Obtained: 263.1 amu. **Anal. Calcd.** for C$_{49}$H$_{34}$BF$_{20}$PSi: C, 54.6; H 2.9 %. Found: C, 53.9; H, 2.7 %.

[i$^t$Bu$_3$PSiEt$_3$][B(C$_6$F$_5$)$_4$] **5-7**

![Chemical structure of 5-7](image)

[Et$_3$Si][B(C$_6$F$_5$)$_4$]•(C$_7$H$_8$) (49 mg, 0.05 mmol, 1.0 equiv.) was added portion-wise to a solution of PrBu$_3$ (10 mg, 0.05 mmol, 1.0 equiv.) in toluene (3 mL) leading to the formation of a colourless oil. The reaction mixture was stirred for 3 h at ambient temperature. The supernatant was removed and the remaining oil was washed with n-pentane (3 x 3 mL). Removal of all volatiles gave **5-7** as
a microcrystalline solid (44 mg, 89% Yield). Single crystals of 5-7 suitable for X-ray diffraction, were obtained by vapour diffusion of n-pentane into a CH₂Cl₂ solution at −35 °C.

**¹H NMR (400 MHz, C₆D₅Br, Me₄Si)**: δ 1.05 (d, ³JₚH = 14 Hz, 27H; t-Bu), 0.84 ppm (s(br), 15H; Et). ¹¹B{¹H} NMR (128 MHz, C₆D₅Br, BF₃•OEt₂): δ −16.1 ppm (s). ¹⁹F{¹H} NMR (377 MHz, C₆D₅Br, CFCl₃): δ −131.5 (m, 8F; o-B(C₆F₅)₄), −162.0 (m, 4F; p-B(C₆F₅)₄), −165.8 ppm (m, 8F; m-B(C₆F₅)₄). ³¹P{¹H} NMR (162 MHz, C₆D₅Br, H₃PO₄): δ 36.5 ppm (s). ²⁹Si{¹H} NMR (C₆D₅Br, [ppm]): δ −21.8 (d, ¹JₚSi = 5 Hz). ¹³C{¹H} NMR (101 MHz, C₆D₅Br, Me₄Si): δ 148.6 (d, ¹JₚC = 243 Hz, 8C; C₆F₅), 138.5 (d, ¹JₚC = 245 Hz, 4C; C₆F₅), 136.5 (d, ¹JₚC = 246 Hz, 8C; C₆F₅), 40.3 (d, ¹JₚC = 14 Hz, 3C; CCH₃), 30.6 (s(br), 9C; CCH₃), 8.3 (d, ¹JₚC = 4 Hz, 3C; CH₂CH₃), 8.0 ppm (d, ¹JₚC = 7 Hz, 3C; CH₂CH₃). MS-ESI: Calculated mass for [M−SiEt₃+H]⁺: 203.2. Obtained: 203.2 amu; Calculated mass for [M−SiEt₃+OH]⁺: 219.2. Obtained: 219.2 amu. Anal. Calcd. for C₄₂H₄₂BF₂₀PSi: C, 50.6 %; H, 4.3. Found: C, 50.6; H, 4.4 %.

[tBu₃P(C₇H₇)][BF₄] 5-12

![Chemical Structure](image)

The tropylium salt [C₇H₇][BF₄] (79 mg, 0.44 mmol, 1.0 equiv.) was added portion-wise to a solution of PrBu₃ (98 mg, 0.44 mg, 1.0 equiv.) in CH₃CN (5 mL). After stirring for 15 min at ambient temperature, the brownish reaction mixture was filtered through a Kimwipe plug. Et₂O (15 mL) was added resulting in the formation of a white precipitate. The supernatant was removed and the residue was washed with Et₂O (3 x 3 mL) and dried in vacuo yielding 5-12 as a colourless, polycrystalline material (142 mg, 85% Yield).

**¹H NMR (400 MHz, C₆D₅Br, Me₄Si)**: δ 6.12 (m, 2H; CH), 6.02 (m, 2H; CH), 3.03 (m, 2H; CH), 1.16 (d, ³JₚH = 14 Hz, 27H; t-Bu), 0.09 ppm (m, 1H; CHP). ¹¹B{¹H} NMR (128 MHz, C₆D₅Br, BF₃•OEt₂): δ −0.6 ppm (s). ¹⁹F{¹H} NMR (377 MHz, C₆D₅Br, CFCl₃): δ −151.2 ppm (s). ³¹P{¹H} NMR (162 MHz, C₆D₅Br, H₃PO₄): δ 45.0 ppm (s). ¹³C{¹H} NMR (101 MHz, C₆D₅Br, Me₄Si): δ 125.7 (d, ³⁴JₚC = 4 Hz, 2C; CH), 125.2 (s, 2C; CH), 42.4 (s(br), 2C; CH), 40.8 (d, ¹JₚC = 29 Hz, 3C; CCH₃), 29.6 (s, 9C, CCH₃), 18.3 ppm (d, ¹JₚC = 56 Hz, 1C; CHP). MS-ESI:

5.4.3 Reactivity of 1,2-Diphosphonium Dication 5-1

5.4.3.1 Reaction of 5-1 with Et₃PO (Gutmann-Beckett test)

Et₃PO (4 mg, 0.03 mmol, 1.0 equiv.) was added to a solution of 5-1 (56 mg, 0.03 mmol, 1.0 equiv.) in CD₂Cl₂ (0.7 mL). The colourless solution was left at ambient temperature for 1 h and subsequently investigated by ³¹P{¹H} NMR spectroscopy. After 24 h at 50 °C the reaction mixture remained unchanged according to NMR spectroscopy.

\[ \text{5-1} \]
\[ \text{Et}_3\text{PO} \]
\[ \text{5-1 + Et}_3\text{PO} \]

**Figure 5-8.** ³¹P{¹H} NMR spectra (CD₂Cl₂) of Gutmann-Beckett test with 5-1.

5.4.3.2 Frustrated Lewis Pair Investigation

5.4.3.2.1 FLP Composed of 5-1 and PrBu₃

PrBu₃ (6 mg, 0.03 mmol, 1.0 equiv.) was added to a solution of 5-1 (56 mg, 0.03 mmol, 1.0 equiv.) in CD₂Cl₂ (0.7 mL). The colourless solution was left at ambient temperature for 1 h and subsequently investigated by multi-nuclear NMR spectroscopy which indicated no interaction between 5-1 and PrBu₃. After 24 h at 50 °C the reaction mixture remained unchanged according to NMR spectroscopy. Similar results were obtained using C₆D₅Br as a solvent and the reaction mixture remained unchanged after heating to 100 °C for 3 d.
5.4.3.2.2 FLP Composed of 5-1 and PPh₃

A solution of 5-1 (48 mg, 0.03 mmol, 1.0 equiv.) in CD₂Cl₂ (0.6 mL), was added to solid PPh₃ (7 mg, 0.03 mmol, 1.0 equiv.), resulting in a pale-yellow solution. The reaction mixture was left at ambient temperature for 1 h and subsequently investigated by multi-nuclear NMR spectroscopy which suggested a weak interaction between 5-1 and Ph₃P.

5.4.3.3 E-H Bond Activation Reactions with 5-1

5.4.3.3.1 Si-H Bond Activation Reactions with 5-1

Reaction of 5-1 and Ph₃P with Et₃SiH

A solution of Ph₃P (5.5 mg, 0.021 mmol, 1.0 equiv.) in C₆D₅Br (1 mL) was added to 5-1 (38 mg, 0.021 mmol, 1.0 equiv.) resulting in the formation of a colourless oil and supernatant. Et₃SiH (7 μL, 0.044 mmol, 2.1 equiv.) was added to the reaction mixture. After 24 h at ambient temperature the oil was completely consumed, and the reaction mixture turned yellow. The reaction mixture was investigated by means of multi-nuclear NMR spectroscopy.

Reaction of 5-1 and PtBu₃ with Et₃SiH

A solution of PtBu₃ (14 mg, 0.063 mmol, 2.1 equiv.) in C₆D₅Br (1 mL) was added to 5-1 (56 mg, 0.03 mmol, 1.0 equiv.) resulting in the formation of a colourless oil and supernatant. Et₃SiH (11 μL, 0.063 mmol, 2.1 equiv.) was added to the reaction mixture. After 24 h at ambient temperature the oil was completely consumed, and the reaction mixture turned yellow. The reaction mixture was investigated by means of multi-nuclear NMR spectroscopy.

Reaction of 5-1 with Et₃SiH in CD₂Cl₂

Et₃SiH (44 μL, 0.25 mmol, 10 equiv.) was added to a solution of 5-1 (46 mg, 0.025 mmol, 1.0 equiv.) in CD₂Cl₂. After 24 h at ambient temperature the oil was completely consumed and the reaction mixture turned yellow. The reaction mixture was investigated by multi-nuclear NMR spectroscopy after 48 h. [Et₃Si][B(C₆F₅)₄] is not stable in CD₂Cl₂ and its decomposition was followed by ¹⁹F NMR spectroscopy.
Reaction of 5-1 with Et₃SiH in CD₃CN

Et₃SiH (53 µL, 0.3 mmol, 10 equiv.) was added to a colourless solution of 5-1 (56 mg, 0.03 mmol, 1.0 equiv.) in CD₃CN. After 1 h at ambient temperature, the reaction mixture turned yellow. The reaction mixture was investigated by multi-nuclear NMR spectroscopy.

Mixture of [Et₃Si][B(C₆F₅)₄]•(C₇H₈) and Et₃SiH in CD₃CN

A solution of Et₃SiH (88 µL, 0.5 mmol, 10 equiv.) in CD₃CN was added to [Et₃Si][B(C₆F₅)₄]•(C₇H₈) (49 mg, 0.05 mmol, 1.0 equiv.). The reaction mixture was investigated by means of ²⁹Si{¹H} NMR spectroscopy.
Figure 5-11. $^{29}$Si($^1$H) NMR spectra (CD$_3$CN) of the reaction of 5-1 and Et$_3$SiH (top) and the reaction of [Et$_3$Si][B(C$_6$F$_5$)$_4$]*(C$_7$H$_8$) and Et$_3$SiH (bottom). Asterisks denote some amount of Et$_3$SiOSiEt$_3$ which was formed by Et$_3$SiH and residual H$_2$O in the CD$_3$CN.

5.4.3.3.2 B-H Bond Activation Reactions with 5-1

Reaction of 5-1 and PPh$_3$ with [tBu$_3$PH][HB(C$_6$F$_5$)$_3$] 5-9

A solution of 5-1 (48 mg, 0.03 mmol, 1.0 equiv.) in CD$_2$Cl$_2$ (0.6 mL) was added to solid PPh$_3$ (7 mg, 0.03 mmol, 1.0 equiv.), resulting in a pale-yellow solution. The reaction mixture was added to solid [tBu$_3$PH][HB(C$_6$F$_5$)$_3$] (19 mg, 0.03 mmol, 1.0 equiv.). After 30 min at ambient temperature, the colour of the reaction mixture had turned to bright yellow with a white precipitate. The reaction mixture was investigated by means of multi-nuclear NMR spectroscopy.

$^1$H NMR (400 MHz, CD$_2$Cl$_2$, Me$_4$Si): δ 10.02 (t, $^1$J$_{PH}$ = 278 Hz, 1H), 7.75 (m, Ar-H), 5.05 (d, $^1$J$_{PH}$ = 429 Hz, 1H; [(CH$_3$)$_3$C)$_3$PH]+), 1.64 ppm (d, $^3$J$_{PH}$ = 15 Hz, 27H; [(CH$_3$)$_3$C)$_3$PH]+).

$^{19}$B$^{[1]$H$]}$ NMR (128 MHz, CD$_2$Cl$_2$, BF$_3$•OEt$_2$): δ 0.3 (s(br), 1B; Ph$_3$P-B(C$_6$F$_5$)$_3$, $\Delta\nu_{1/2}$ = 100 Hz), −16.6 ppm (s, 2B; 2[B(C$_6$F$_5$)$_4$]).

$^{19}$F$^{[1]$H$]}$ NMR (377 MHz, CD$_2$Cl$_2$, CFCl$_3$): δ −133.0 (m(br), 8F; 2[B(o-B$_6$F$_5$)$_4$]), −135.8 (m(br), 6F; B(o-B$_6$F$_5$)$_3$), −162.0 (t, $^3$J$_{FF}$ = 20 Hz, 3F; B(p-B$_6$F$_5$)$_3$), −163.6 (t, $^3$J$_{FF}$ = 20 Hz, 8F; 2[B(p-B$_6$F$_5$)$_4$]), −166.6 (m(br), 6F; B(m-B$_6$F$_5$)$_3$), −167.4 (m(br), 16F; 2[B(m-B$_6$F$_5$)$_4$]).

$^{31}$P$^{[1]$H$]}$ NMR (162 MHz, CD$_2$Cl$_2$, H$_3$PO$_4$): δ 59.8 (s, 1P; [t-Bu$_3$PH]$^+$), −4.1 (s(br), 3P; 5-1, Ph$_3$P-B(C$_6$F$_5$)$_3$).

Reaction of 5-1 with [tBu$_3$PH][HB(C$_6$F$_5$)$_3$] 5-9 in 1:1 and 1:2 Stoichiometry
A solution of **5-9** (19 mg, 0.026 mmol, 1.0 equiv.) in CD$_2$Cl$_2$ (0.6 mL) was added to **5-1** (49 mg, 0.026 mmol, 1.0 equiv.) resulting in a pale-yellow, transparent solution. After 30 min at ambient temperature, the solution turned bright yellow. The reaction mixture was investigated by means of multi-nuclear NMR spectroscopy. After 24 h at 50 °C, the reaction mixture remained unchanged according to NMR spectroscopy, and the solution was added to solid **5-9** (19 mg, 0.026 mmol, 1.0 equiv.). After 30 min at ambient temperature, the reaction was investigated by means of multi-nuclear NMR spectroscopy.

**Figure 5-12.** $^{31}$P{$^1$H} NMR (CD$_2$Cl$_2$) spectra of the reactions of **5-1** with 1 equiv. **5-9** (top) and 2 equiv. of **5-9** (bottom).
Reaction of \([tBu_3PH][HB(C_6F_5)_3] 5-9\) with \(B(C_6F_5)_3\)

A solution of \(B(C_6F_5)_3\) (21 mg, 0.042 mmol, 1.0 equiv.) in \(CD_2Cl_2\) (0.3 mL) was added to a solution of 5-9 (30 mg, 0.042 mmol, 1.0 equiv.) in \(CD_2Cl_2\) (0.3 mL). After 1 h at ambient temperature, the reaction mixture was investigated by means of multi-nuclear NMR spectroscopy.

\[
[tBu_3PH][HB(C_6F_5)_3] + B(C_6F_5)_3 \leftrightarrow [tBu_3PH][H(B(C_6F_5)_3)_2]
\]

Figure 5-13. \(^{11}B\{^1H\} NMR spectrum (CD_2Cl_2) of 5-9 and B(C_6F_5)_3 after 1 h at ambient temperature.

Figure 5-14. \(^1H\) NMR spectrum (CD_2Cl_2) of 5-9 and B(C_6F_5)_3 after 1 h at ambient temperature.

Reaction of \([(C_{10}H_6)(Ph_2P)_2H][N(SO_2CF_3)_2]\) with PrBu3

A solution of PrBu3 (6 mg, 0.03 mmol, 1 equiv.) in C_6D_5Br (1 mL) was added to the \([N(SO_2CF_3)_2]^−\) salt of 5-5 (23 mg, 0.03 mmol, 1 equiv.) resulting in the formation of a yellow coloured reaction mixture. The reaction was investigated by multi-nuclear NMR spectroscopy, which indicated complete conversion to 1,8-dppn and \([tBu_3PH][N(SO_2CF_3)_2]\).
5.4.3.3.3 C-H Bond Activation Reactions with 5-1

Reaction of 5-1 and PtBu3 with 1,4-Cyclohexadiene (CHD)

A solution of PtBu3 (14 mg, 0.063 mmol, 2.1 equiv.) in C₆D₅Br (1 mL) was added to 5-1 (56 mg, 0.03 mmol, 1.0 equiv.) resulting in the formation of a colourless oil and supernatant. 1,4-Cyclohexadiene (9 μL, 0.1 mmol, 3.3 equiv.) was added to the reaction mixture. After 24 h at 90 °C the oil was completely consumed, and the reaction mixture turned yellow. The reaction mixture was investigated by multi-nuclear NMR spectroscopy.

![NMR spectra](image)

**Figure 5-15.** ¹H NMR spectra (C₆D₅Br) of (A) 5-6; (B) 1,8-dppn; (C) CHD; (D) Reaction of 5-1, PtBu3 and CHD (1 : 2 : 1)

Reaction of 5-1 and PtBu3 with 1,3,5-Cycloheptatriene (CHT)

A solution of PtBu3 (14 mg, 0.063 mmol, 2.1 equiv.) in C₆D₅Br (1 mL) was added to 5-1 (56 mg, 0.03 mmol, 1.0 equiv.) resulting in the formation of a colourless oil and supernatant. CHT (10 μL, 0.1 mmol, 3.3 equiv.) was added to the reaction mixture. After 24 h at 90 °C the oil was completely consumed and the reaction mixture turned yellow. The reaction mixture was investigated by multi-nuclear NMR spectroscopy.
An analogous reaction was performed using Ph₃P (17 mg, 0.063 mmol, 2.1 equiv.) as a base. However, even after 5 d at 100 °C the reaction mixture remained unchanged (based on NMR spectroscopy).

Figure 5-16. $^{31}$P-$^1$H (top) and $^{31}$P (bottom) NMR spectra (C₆D₅Br) of the crude reaction mixture of 5-1 and 2 equiv. of PrBu₃ and CHT.

Figure 5-17. $^1$H NMR spectra (C₆D₅Br) of (A) [tBu₃P(C₇H₇)][BF₄]; (B) CHT; (C) 5-6; (D) 1,8-dppn; (E) Crude reaction mixture of 5-1, PrBu₃ and CHT (1 : 2 : 1)
5.4.3.3.4  H-H/D Bond Activation Reactions with 5-1

Reaction of 5-1 with HD

C₆D₅Br (1 mL) was added to 5-1 (56 mg, 0.03 mmol, 1.0 equiv.) in a J-Young NMR tube resulting in the formation of colourless oil and supernatant. The NMR tube was pressurized with HD (1 atm). The reaction mixture was heated to 100 °C for 3 d and agitated in regular intervals. After this time, the oil was not consumed and monitoring the reaction by NMR spectroscopy did not show consumption of 5-1 nor formation of H₂ and D₂.

Reaction of 5-1 and PrBu₃ with H₂

A solution of PrBu₃ (14 mg, 0.063 mmol, 2.1 equiv.) in C₆D₅Br (1 mL) was added to 5-1 (56 mg, 0.03 mmol, 1.0 equiv.) in a J-Young NMR tube resulting in the formation of a colourless oil and supernatant. The NMR tube was pressurized with H₂ (4 atm). The reaction mixture was heated to 100 °C for 48 h and agitated in regular intervals. After 48 h, the oil was completely consumed and the reaction mixture turned yellow. The reaction mixture was investigated by multi-nuclear NMR spectroscopy. An analogous reaction was performed using Ph₃P (17 mg, 0.063 mmol, 2.1 equiv.) as a base. However, even after 5 d at 100 °C, the reaction mixture remained unchanged (based on NMR spectroscopy data).
**Figure 5.18.** $^{31}$P{$^1$H} NMR spectra (C$_6$D$_5$Br) of the reaction mixture of 5-1, PrBu$_3$ and H$_2$ at 100 °C at the denoted time points. Asterisks denote some contamination from 

$$[(\text{C}_{10}\text{H}_6)(\text{Ph}_2\text{P})(\text{Ph}_2\text{PF})][\text{B(C}_6\text{F}_5)_4].$$

Reaction of 5-1 and PrBu$_3$ with D$_2$

A solution of PrBu$_3$ (14 mg, 0.063 mmol, 2.1 equiv.) in C$_6$D$_5$Br (1 mL) was added to 5-1 (56 mg, 0.03 mmol, 1.0 equiv.) in a J-Young NMR tube resulting in the formation of a colourless oil and supernatant. The NMR tube was pressurized with D$_2$ (4 atm). The reaction mixture was heated to 100 °C for 48 h and agitated in regular intervals. After 48 h, the oil was completely consumed and the reaction mixture turned yellow. The reaction mixture was investigated by multi-nuclear NMR spectroscopy.
Figure 5-19. $^{31}$P{$^1$H} NMR spectra (C$_6$D$_5$Br) of the reaction of 5-1 and PrBu$_3$ with D$_2$ at 100 °C at the denoted time points.

*Note:* *1*: traces of [tBu$_3$PH]$^+$, probably due to hydrolysis; *2*: contamination from [(C$_{10}$H$_6$)(Ph$_2$P)(Ph$_2$PF)][B(C$_6$F$_5$)$_4$].

5.4.4 Reactivity of 1-Diphenylphosphino-8-$N$,$N$-dimethylamino Naphthalene (5-14)

5.4.4.1 Reaction of 5-14 with XeF$_2$

A solution of XeF$_2$ (7 mg, 0.04 mmol, 1 equiv.) in CH$_2$Cl$_2$ (1 mL) was added dropwise to 5-14 (15 mg, 0.04 mmol, 1 equiv.). The solution was left to stir at ambient temperature for 3 h before being monitored by multi-nuclear NMR spectroscopy.

Figure 5-20. $^{31}$P{$^1$H} NMR spectrum (CH$_2$Cl$_2$) of 5-14 and XeF$_2$ after 3 h at ambient temperature.
5.4.4.2 Reaction of 5-14 with [Et$_3$Si][B(C$_6$F$_5$)$_4$]•(C$_7$H$_8$)

A solution of [Et$_3$Si][B(C$_6$F$_5$)$_4$]•(C$_7$H$_8$) (79 mg, 0.03 mmol, 1 equiv.) in C$_6$H$_5$F (2 mL) was added to in situ generated “5-15” (0.03 mmol), prepared according to section 5.3.4.1. The solution immediately turned yellow. The reaction mixture was left to stir at ambient temperature for 1 h before being monitored by multi-nuclear NMR spectroscopy.

5.4.5 Computational Details

All calculations in this chapter were performed by Dr. Roman Dobrovetsky:

DFT calculations were performed using Gaussian 09.2. Geometry optimizations of all the molecules was carried out using the wB97X-D/def2-TZV basis sets implemented in the Gaussian 09 software. Thermal energy corrections were extracted from the results of frequency analysis.
performed at the same level of theory. Frequency analysis of all calculated molecules contained no imaginary frequency showing that these are energy minima.

5.4.6 Crystallographic Analysis of 5-5[NTf] and 5-7

Single crystals were coated with Paratone-N oil and mounted in a cryo-loop. Data were collected on a Bruker Kappa Apex II diffractometer using graphite monochromated MoKα radiation (λ = 0.71073 Å). The temperature was maintained at 150 K using an Oxford Cryostream cooler for both, initial indexing and full data collection. Data were collected using Bruker APEX-2 program. All structures were solved by direct methods within the SHELXTL package\textsuperscript{94} against $F^2$ using first isotropic and anisotropic thermal parameters for all non-hydrogen atoms. Hydrogen atoms bonded to carbon atoms were generated with idealized geometries and isotropically refined using a riding model.
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5.5 References


Chapter 6

Conclusions and Future Work

6.1 Thesis Summary

The work presented in this thesis explores the synthesis and reactivity of robust highly electrophilic phosphorus(V) cations (EPCs). The data presented herein progresses from reactive and unstable fluorophosphonium cations to air- and moisture-stable polycationic species, highlighting the diversity of phosphorus(V) Lewis acids and their potential applications in bench top chemistry.

Given the recent rapid development of EPCs, we sought to further expand the field of phosphorus(V) salts with a versatile and easily accessible pyridinium-based scaffold. To this end, fluoro pyridiniumphosphonium mono- and dications were synthesized and their Lewis acidity was probed using experimental and computational methods. While fluoro pyridiniophosphonium monocations were unable to capture small molecules (as an intramolecular FLP), interaction of these monocations with PhCHO and Et₃SiH was observed. For fluoro pyridiniumphosphonium dications, computational data (FIA and GEI) predicted greater fluoride and electron affinity when compared to their monocationic counterparts and other known Lewis acids. The Lewis acidity of these compounds was supported experimentally with the Gutmann-Beckett test and in several EPC-catalyzed organic transformations, wherein fluoro pyridiniumphosphonium dications outperformed their monocationic counterparts. It is noteworthy that a non-coordinating anion like [B(C₆F₅)₄]⁻ was required for catalysis.

While fluoro pyridiniumphosphonium salts demonstrated useful reactivity, the propensity to degradation was problematic. To develop systems less susceptible to decomposition, EPCs with less polar P-C and P-O bonds were targeted. In the first part of Chapter 2, cyclopropenium- and pyridiniumphosphonium dications bearing only P-C bonds were prepared and their Lewis acidity was probed in a Mukaiyama-aldol condensation reaction. Pyridinium triphenyl-substituted phosphonium salts outperformed the cyclopropenium derivatives, and the meta-substituted pyridinium salts were more active than the ortho- and para-isomers. The pyridinium diphenylmethyl analogue followed a similar trend wherein the meta-isomer was shown to be more reactive than the corresponding ortho-isomer. In the latter part of the chapter, an electrophilic phenoxyphosphonium dication was synthesized and its Lewis acidity was demonstrated in the
syntheses of a series of 9,9-disubstituted 9,10-dihydroacridine derivatives through a hydroarylation mechanism.

While the cyclopropenium- and pyridiniumphosphonium dications demonstrated appreciable stability relative to fluorophosphonium analogues, the stability of EPCs in the presence of water/base combinations remains a challenge in main group Lewis acid chemistry, yet is critical for several applications (e.g. FLP chemistry). To overcome this barrier, P₃-trimethylated phosphorus(V) trications were readily prepared from well-known triphos ligands and MeOTf. Both the [OTf] and [B(C₆F₅)₄] salts were accessible, and remarkably the [OTf] salts were shown to be active catalysts for one-pot reductive amination reactions using hydrosilanes as the reductant. As well, the tripodal tricationic species was shown to affect C-F bond activation and derivatization with Suginome’s PhMe₂Si(BPin). The rare resistance to degradation in the presence of water or Et₃PO may arise from the unique acceptor orbitals of these trications, which are fundamentally different from most fluorophosphonium cations. This observation is reminiscent of related P(V) phosphacorrole cations, wherein the acceptor orbitals primarily constitute P-N antibonding interactions. The mode of activation for these trications has not unambiguously been determined, and may be a combination of substrate activation by the P(V) centres and interaction with the C-H bonds in the alkyl linkers. The exact nature of these interactions is the subject of ongoing investigation in our laboratory.

Targeting robust phosphorus cations for applications in FLP chemistry, we report the synthesis of a robust 1,2-diphosphonium dication through double fluoride abstraction of the difluorophosphorane precursor with [Et₃Si][B(C₆F₅)₄]•(C₇H₈) or oxidation of 1,8-dppn with Ph₃Sb(OTf)₂. Combinations of this dicationic species with PPh₃ or PrBu₃, generate the first examples of all-phosphorus based FLPs, which were shown to facilitate stoichiometric Si-H, B-H, C-H and H-H bond activation reactions. The mechanism of these reaction is believed to be initiated by hydride abstraction with the 1,2-diphosphonium dication generating a P(III)/P(V) monocation. Reactions with PPh₃ generate the monocationic species, whereas reactions with PrBu₃ lead to deprotonation of the P(V) monocation, producing 1,8-dppn and [rBu₃PH]⁺. Preliminary reactivity with 1-diphenylphosphino-8-N,N-dimethylamino naphthalene is also presented, wherein oxidation with XeF₂ and subsequent fluoride abstraction with [Et₃Si][B(C₆F₅)₄]•(C₇H₈) is believed to generate a phosphorane-type species with electron donation from the pendant N atom to the P(V) centre.
6.2 Future Work

As we continue to target the facile synthesis of P-based Lewis acid catalysts, these results provide valuable insight into the stability and reactivity of cationic phosphorus compounds, ultimately moving us one step closer to commercially-viable species. Of particular interest is the reactivity of the P3-trimethylated trication with PhMe2Si(BPin) reported in Chapter 4, given that the activation of C-F bonds is a fundamental transformation in several chemical industries and subsequent formation of C-B bonds allows access to further cross coupling reactions. As well, the decrease in Lewis acidity and lack of reactivity with donor molecules demonstrated by these trications relative to most P-F containing EPCs, creates a new avenue for catalysis, wherein unprecedented (for EPCs) functional group tolerance can be accessed. Therefore, the substrate scope of this reaction and the operative mechanism should be pursued (Scheme 6-1, top). As well, given the stability of these trications, late-stage modification of pharmaceutical targets should also be investigated.

Scheme 6-1. Proposed C-B coupling reactions with a P3-trimethylated trication.

While preliminary reports in Chapter 5 report the defluorination of monofluorinated substrates, CF3-containing compounds should also be attempted for this reaction. While C-C coupling reactions have been reported with CF3-containing reagents in the presence of Et3SiH, rapid defluorination leads to the -CH2R product.5 The rate of defluorination with PhMe2Si(Bpin) is expected to be much slower, which may allow for isolation of the monodefluorinated product (Scheme 6-1, bottom).

The synthesis of novel diphosphonium dications is also of growing interest in our group; while their synthesis has been previously reported, their reactivity is comparatively underdeveloped. Building on the results presented in Chapter 5, future projects should target Pn-Pn (Pn = pnictogen)
bonds which are weaker than the 1,2-diphosphonium dication. In this regard, the chemistry with 1-diphenylphosphino-8-N,N-dimethylamino naphthalene should be further investigated. Given the donating abilities of the pendant amino group, double fluoride abstraction of the difluorophosphorane compounds should be possible (Figure 6-1). With this compound in hand, its reactivity with small molecules should be investigated (e.g. CO₂). While a 7-membered ring would be disfavoured upon reaction with CO₂, perhaps CO₂ reduction in the presence of the appropriate hydrosilane could be achieved.

Another strategy to weaken the PnPn bond is the inclusion of Sb atoms, wherein the greater atomic orbital size would presumably lead to less efficient Sb-Sb bonding orbital overlap (Figure 6-1). While the Gabbaï group has exploited the use of Sb(V) compounds for fluoride ion capture/sensing, a 1,2-distibonium dication has yet to be synthesized. The electropositivity and polarizability of Sb atomic orbitals relative to P are also intriguing and warrant further investigation with hydride sources and small molecules. These properties should also be exploited for CO₂ insertion and reduction with the corresponding Sb/Sb-H monocation (directly analogous to the phosphonium reported in Chapter 5), as was recently reported by the Kinjo group for NHP cations.

![Figure 6-1. Examples of Lewis acidic pnictogen-based cations. Counterions have been omitted for clarity.](image)

Targeting other diphosphonium dications for reactions with small molecules, notably fluoride and CO₂, a benzene scaffold should also be investigated. In one strategy, a reactive 4-membered ring may form, which would be highly reactive and could generate stable 6-membered rings upon reaction with the appropriate partner. On the other hand, a diphosphonium dication with a 6-membered ring backbone will likely be more robust (and easy-to-handle), which may lead to applications that require more harsh reaction conditions. As well, the stability of the 6-membered ring may act as a driving force in a catalytic reaction scheme.
6.3 References


