To the Graduate Council:

I am submitting herewith a dissertation written by Clayton M. Hair entitled "Solventless Suzuki-Coupling Reactions on Palladium Doped Potassium Fluoride Alumina". I have examined the final copy of this dissertation for form and content and recommend that it be accepted in partial fulfillment of the requirements for the Doctor of Philosophy, with a major in Chemistry.

George W. Kabalka, Major Professor

We have read this dissertation
and recommend its acceptance:

Accepted for the Council:

Associate Vice Chancellor and
Dean of The Graduate School

Solventless Suzuki-Coupling Reactions on Palladium Doped Potassium Fluoride Alumina

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A Dissertation

Presented for the

Doctor of Philosophy

Degree

The University of Tennessee, Knoxville

Clayton Maxwell Hair

December 1999

DEDICATION

In special recognition of their love and support, I dedicate this dissertation to my family, my mother, Bobbie S. Chafin, my father, Frank L. Hair, my grandmother, Juanita P. Hair, and my brother, Le Hair. There are no words that can possibly express my love and appreciation for so many years of patience and understanding. Thank you for having faith in me when sometimes I didn't.

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ABSTRACT

Reactions of boronic acids with organic halides in the presence of palladium catalysts, the Suzuki Reaction, play an important role in modern organic chemistry. Numerous organic syntheses performed in the presence of alumina, Al_2O_3, exist in the literature. It has been found that the Suzuki-Coupling reaction can be carried out on commercially available alumina doped with potassium fluoride, 40% by weight, in the complete absence of organic solvents. This new solid phase synthesis is convenient, efficient, and environmentally friendly. The effects of substrate, temperature, reactant ratio, base, catalyst concentration, and the unique character of the KF/Al_2O_3 solid are presented. The development of a completely recyclable catalytic medium and the use of microwave irradiation with this methodology is also demonstrated.

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LIST OF ABBREVIATIONS

β	beta
9-BBN	9-borabicyclo[3.3.1]nonane
°C	degrees celsius
χ	chi
CCP	cubic close packed
dba	dibenzylideneacetone
Δ	heat
δ	delta
DMF	dimethylformamide
dppf	1,1´-bis(diphenylphosphino)ferrocene
dppp	1,3-bis(diphenylphosphino)propane
E	Entgegagan "opposite" trans
e.g.	exempli gratia, "for example"
equiv.	equivalent, equivalents
ή	eta
et al.	et alii, "and others"
Et_2O	diethyl ether
EtOH	ethanol
γ	gamma
GC	gas chromatograph; gas chromatography

g	gram, grams
hr, hrs	hour, hours
HCP	hexagonal close packed
i.e.	id est, "that is"
κ	kappa
MHz	megahertz
MeOH	methanol
MeCN	acetonitrile
mL	milliliter, milliliters
mmol	millimole, millimoles
min	minute, minutes
N/A	not applicable
Pd°	palladium metal; palladium black submicron powder
p-	para
π	pi
R	general hydrocarbon moiety
rt, RT	room temperature; ambient temperature
RBF	round bottomed flask
rxn	reaction
tech.	technical grade
Temp	temperature
THF	tetrahydrofuran

θ	theta
TLC	thin layer chromatography
X	general halide species (I, Br, Cl, F)
Z	Zusammen "together" cis

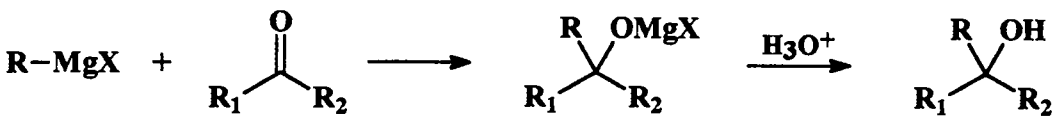
Chapter I. Introduction:

The focus of this dissertation is the development of a novel, solventless Suzuki coupling methodology involving the use of a ligandless, zero valent palladium-doped potassium fluoride γ-alumina, KF/Al_2O_3, surface. A brief overview of carbon-carbon bond forming reactions, heterogeneous catalysis, and the nature of the alumina surface including KF/ Al_2O_3 is presented in this chapter.

A. Background:

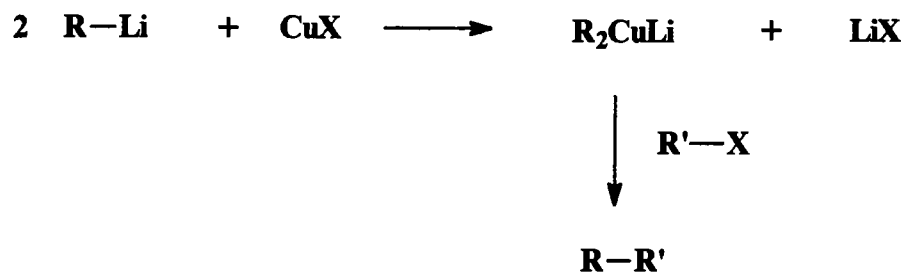
The foundation of synthetic organic chemistry rests on the ability to manipulate carbon-carbon bonds. Without such expertise, organic chemistry would be reduced to natural product isolation, petrochemical fractionation, and purifications much like that available to scientists in the premodern era.

One of the preeminent examples of carbon-carbon bond forming reactions is the Grignard reaction, which involves the use of an organomagnesium agent and a suitable electrophilic carbon, e.g. carbonyl compound, Scheme 1-1.



Scheme 1-1

Numerous other organometallic compounds using common metals, as well as more exotic examples, have also been widely utilized in carbon-carbon bond forming reactions. These include organocopper[3] (Scheme 1-2), organozinc,[4] and organomercury reagents,[5] as well as the more unconventional organocesium,[6] antimony,[7] and tellurium compounds.[8]



Scheme 1-2

In 1972, Kumada and Tamao[9] and Corriu[10] independently reported that Ni(II) complexes greatly enhanced the rates of reactions of Grignard reagents with aryl and alkenyl halides. Within a few years, similar results were realized by Murahasi[11] using

palladium complexes. This innovation made it possible to utilize organoborane reagents in metal-catalyzed carbon-carbon bond forming reactions

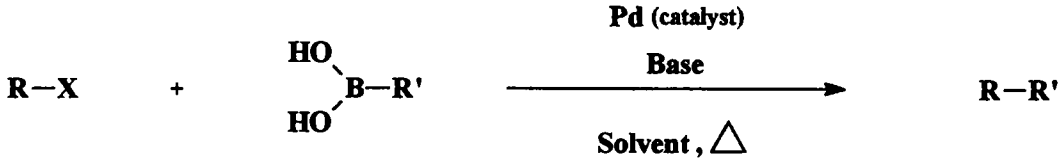
Boron hydrides have been used extensively for various reductive strategies,[12] but the nature of the boron atom itself left little hope for "Grignard-like" reactions. While organoboron compounds are strongly electrophilic, organic groups attached to boron are only weakly nucleophilic due to boron being a six-electron center. The ionic nature of other organometallic reagents is simply not present in organoboranes.[13]

Transmetallations of boron compounds, including boronic acids and esters, have been known for some time.[14] The coordination of a suitable base to the central atom markedly increases the nucleophilic nature of the attached groups allowing for transfer to adjacent electropositive centers.[15] Negishi[16] first reported an alkynyl transfer to iodobenzene using an 1-alkynyl(trialkyl)borate through a palladium-catalyzed addition-elimination sequence analogous to the Heck[17] reaction. While many other organometallic reagents undergo similar cross-coupling reactions, this organoborane methodology has undergone extensive development which can be attributed to the availability of a wide variety of synthetically useful boron compounds.

Organoboronic acids and esters are thermally stable, relatively inert to both air and water, and easily handled without special precautions, allowing for a wide range of selective carbon-carbon bond formations,[18] the most celebrated of which came to be known as the Suzuki coupling reaction.[19] Recent innovations have led to a number of analogous organoborane-based carbon-heteroatom bond forming reactions, including coupling to anionic amides,[20] thiolates,[21] and alkoxides.[22]

B. Suzuki-Coupling Reaction:

The fundamental Suzuki reaction is presented below, Reaction 1-1.



Reaction 1-1

A suitable halogenated moiety is mixed with an excess, ranging from 0.1 to 3 equivalents, of a boronic acid and the mixture is usually heated in the presence of a palladium catalyst, moderate to strong base, and an organic or mixed protic solvent.[23]

The catalysts utilized are diverse and numerous. The earliest methods employed tetrakis(triphenylphosphino)palladium, $Pd[P(Ph_3)]_4$, or Pd(II) salts containing two triphenylphosphine ligands almost exclusively.[24] These complexes were generally soluble and avoided the problems inherent to heterogeneous catalysis with transition metals.[25] Contemporary examples include a host of different palladium moieties that offer various advantages to their unique protocols. These include $PdCl_2(dppf)$, $PdCl_2[PPh_2(m\text{-}C_6H_4SO_3Na)]_2$,[26] $Pd(OAc)_2$/dppp, $Pd(PCy_3)_2Cl_2$,[27] $Pd_2(dba)_3{:}C_6H_6$, and $[(\acute{\eta}^3\text{-}C_3H_5)PdCl]_2$ [28] and even Pd(0)[29] among others.

The alkaline reagents and solvents currently used in Suzuki reactions also vary, but bases are limited primarily to those which are ionic in nature. Examples include NaOH, K_2CO_3, K_3PO_4, Na_2CO_3, $NaHCO_3$ [26,30-33] as well as the less familiar CsF, [27] $Ba(OH)_2$,[34] Ag_2O,[35] and Cs_2CO_3.[35,36] Novel examples also exist in which trialkylamines are used, but results are generally poor even with dramatically increased reaction times.[37] As noted previously, organic solvents such as benzene, DMF, THF, acetone, toluene, acetonitrile [28,38-39] are commonly used, but more recent protocols use mixed solvents in which water, methanol, or ethanol are combined.[40a-f] These mixtures offer enhanced solubility of both the ionic base and the palladium moiety.

Temperatures at which these reactions occur depend on the choice of solvent, since most Suzuki reactions are run at reflux. When mixed solvents are used, convenient reaction temperatures below 100 °C are employed, increasing only when higher boiling organic liquids are chosen, e.g. toluene, DMF, etc. However, recent applications using ionic accelerants are often run at ambient temperature with fair to good results.[30d,41] Reaction times vary from as little as 0.75 hour for highly reactive species, primarily aryl-aryl couplings, to upwards of 72 hours for highly hindered substrates and milder bases. Polymer based systems have also been exploited quite extensively as a Suzuki coupling vehicle.[42]

The mechanism of this reaction, Figure 1-1, is strikingly similar to that proposed for the Ni(0)[9] and Fe(1)[43] catalyzed couplings mentioned previously. No matter which palladium catalyst is used, it is first reduced to Pd(0) [**1**].[44] This species then undergoes oxidative insertion into the organic halide forming a *trans*-σ-palladium

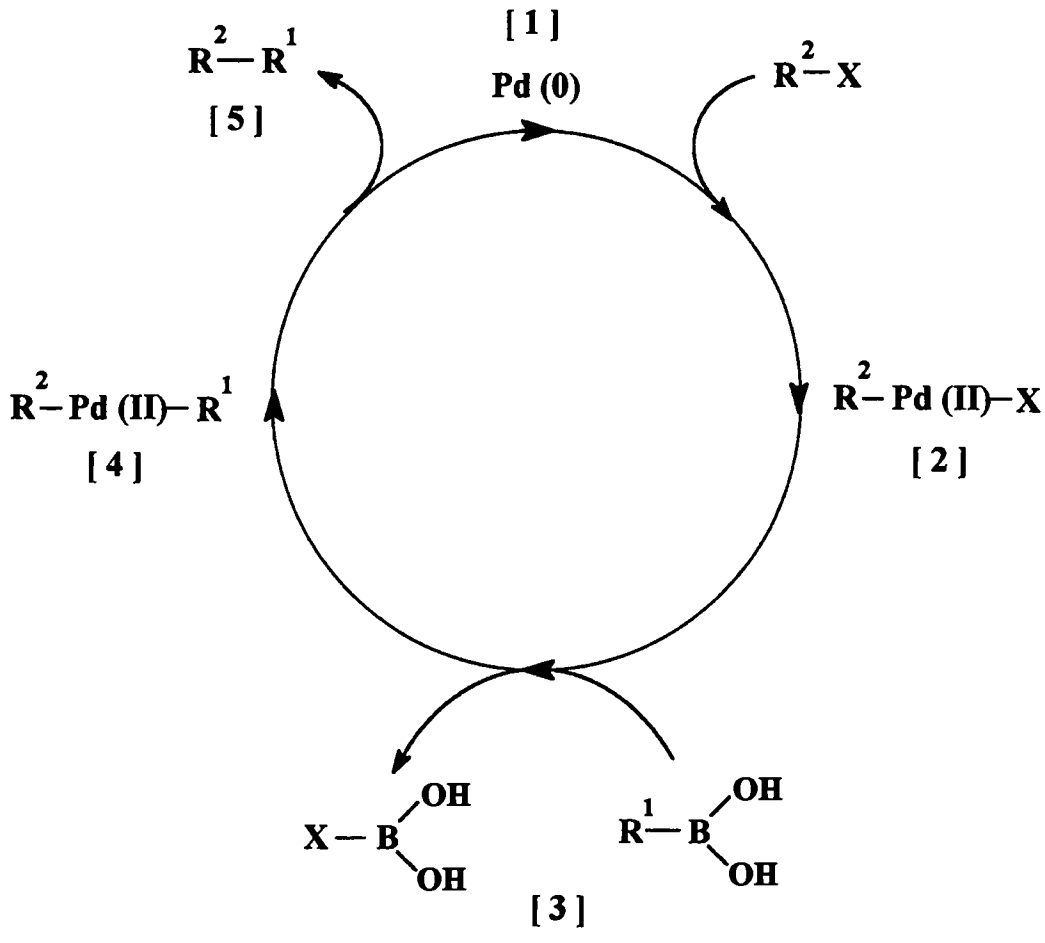


Figure 1-1 Mechanistic Cycle of Common Suzuki Reaction

(II) complex [**2**].[45] Alkyl halides possessing β-hydrogens rarely participate in the Suzuki reaction as this oxidative step is very slow and, once the adduct is formed, the palladium moiety can undergo β-hydride elimination.[44,46] Transmetallation with the boron reagent [**3**] then occurs followed by rapid reductive elimination of the organic ligands [**5**] from the Pd (II) complex [**4**] with ultimate regeneration of the zero valent palladium. Unlike Negishi's palladium cross-coupling reaction using organozincs[47] and Stille's using organostannates,[48] in which the transmetallation is the rate limiting step, the oxidative addition is slowest in this instance. While not explicitly detailed in Figure 1-1, the reacting boron species is the tetravalent borate, supporting the need for both ionic bases and hydroxylic solvents.[44] After transmetallation, the borate complex allows for the generation of a stable trivalent boron by-product, but not necessarily $(HO)_2BX$.

The order of halide reactivity, I > Br >> Cl, with F being unreactive, reflects the rate-determining nature of the oxidative insertion process and related carbon-halogen bond strength.[49] Reactivity of the organic halide species also decreases in the order aryl > alkynyl ≈ alkenyl > allyl >> alkyl. The proximity of the π-orbitals contributes to the formation of the palladium (II) complex,[50] which has led to alternate suggestions for the alkyl mechanistic cycle.[51] Bidentate palladium ligands are favorable for alkyl transfers as they suffer less from premature β-hydride reductive elimination.[52] Although exceptions do exist,[30a,31b,53] allylic reagents rarely undergo reaction since elimination from the complex is much faster on the reaction time scale. Suzuki reactions generally proceed with retention of configuration of both the

organohalide and boron compound where applicable,[51] however case-dependent exceptions do exist.[19]

Noteworthy modifications of the standard Suzuki reaction include the use of chromium salts and complexes to incorporate an element of asymmetry into the coupled products. Resultant yields are generally fair to excellent with superb, >95%, enantiomeric excesses.[54] Tetrasubstituted borate salts have also been explored in an effort to eliminate the use of ionic bases.[55]

C. Catalysis:

A catalyst is, by definition, a substance that reduces the transition state energy between a set of reactants and the desired product without itself being consumed in the reaction. Catalysis is, at present, one of the central endeavors of industrial scale organic chemistry. The petrochemical and bulk chemical trades could not function cost-effectively without it.[56] The Suzuki reaction detailed above does not occur without the use of the palladium catalyst.

Homogeneous catalysts are familiar to even novice chemists, Lewis acids such as H^+ used in esterification and $AlCl_3$ in Friedel-Crafts alkylations/acylations are common examples. Just as widely employed but not as universally known, at least to the bench-top chemist, are heterogeneous catalysts.[56] These include polymer based examples,[57] but they are typically ionic in nature. Aggregate aluminosilicate solids such as clays[58] and zeolites[59] have been used extensively in the petroleum industry.

Zeolites, the more highly ordered crystalline allotrope of the two, have also found extensive use in laboratory scale transformations. Their internal, three-dimensional pore sites can be tailored to individual reagent specifications. Clays, more amorphous solids, in contrast offer greater surface effects. Another class of silicates collectively know as silica also induce a variety of transformations, but are more commonly known for their chromatographic properties, e.g. silica gel.[60]

The reagents mentioned above, among others, comprise a large class of heterogeneous catalysts collectively known simply as oxides, of which alumina is a member. The collective advantages and disadvantages of ionic solids as catalysts in organic reactions are summarized in Table 1-1.[61]

D. Alumina:

Alumina is a generic term used to describe a variety of aluminum oxides, $Al_2O_3 \cdot nH_2O$, that differ only in their amount of "hydration". Hydration here refers not only to H_2O molecules within the crystal lattice, but to surface hydroxyls that can combine to liberate water and a free surface oxygen. Almost all aluminas are prepared from the naturally occurring aluminum ore, bauxite, via a technique known as the Bayer process.[62] They are commercially available for an assortment of uses. The only natural anhydrous species, corundum or α-alumina, is composed of oxygen atoms and aluminum atoms arranged in a hexagonal close-packed, HCP, lattice structure. This allows for an extremely compact matrix of high density with low porosity, good

Table 1-1: Advantages and Disadvantages of Solid Ionic Catalyst

Advantages
• They are generally non-volatile, odorless, solids which are easy to handle.
• Several surface modified reagents are commercially available and can be used with little or no further preparation.
• Superior reaction selectivity compared to solution analogues is routinely encountered.
• Product isolation is rudimentary.
• Catalytic solids are often recyclable and environmentally benign.
Disadvantages
• Commercial reagents can vary significantly from supplier to supplier.
• Associated apparati for preparing surfaces can be costly and complex.
• Physical and chemical characteristics are often obscure and difficult to quantify.
• Typical low 'loading' of reactants is a significant deterrent to large scale reactions.

thermal stability, and exceptional mechanical strength. While chemically inert and resistant even to most mineral acids, and thus useless as a catalyst, α-alumina has found widespread industrial uses as fillers, refractories, abrasives, and ceramics.[63, 64]

The remaining forms, γ, δ, θ, κ, χ, η, are classified as the transition aluminas and are prepared by the calcination and dehydration of their hydrated naturally occurring minerals. Continued heating of any transition alumina species eventually produces the inert α-alumina species described previously, Figures 1-2 and 1-3.[65] Of the transition aluminas, γ-alumina has been most extensively studied with regard to its catalytic nature. It possesses a strikingly irregular surface coupled with a large surface area, 200 m^2/g, compared to its α-alumina derivative. Its lattice structure differs as well, exhibiting a cubic close packing, CCP, orientation. This accounts for the discrepancy in its catalytic nature. The surface is amphoteric, containing both acidic and basic sites, which can be manipulated by heating the solid under vacuum at varying temperatures. Surface pH levels can be augmented by preparative methods involving suitable acid or base impregnation.

Kronberg developed a generalized model of HCP lattice structures using Al_2O_3 as an archetype in the late 1950's. It was a simple highly symmetrical mathematical construct based on what was then known of the surface.[66] In 1965, Peri further developed the model with extensive computer modeling based on an idealized (1 0 0) surface lattice.[67] His prototype suffers from this assumption, which was necessary due to the computational limitations of his day. His primary contribution to the understanding of the chemical nature of Al_2O_3 was the realization of multiple types

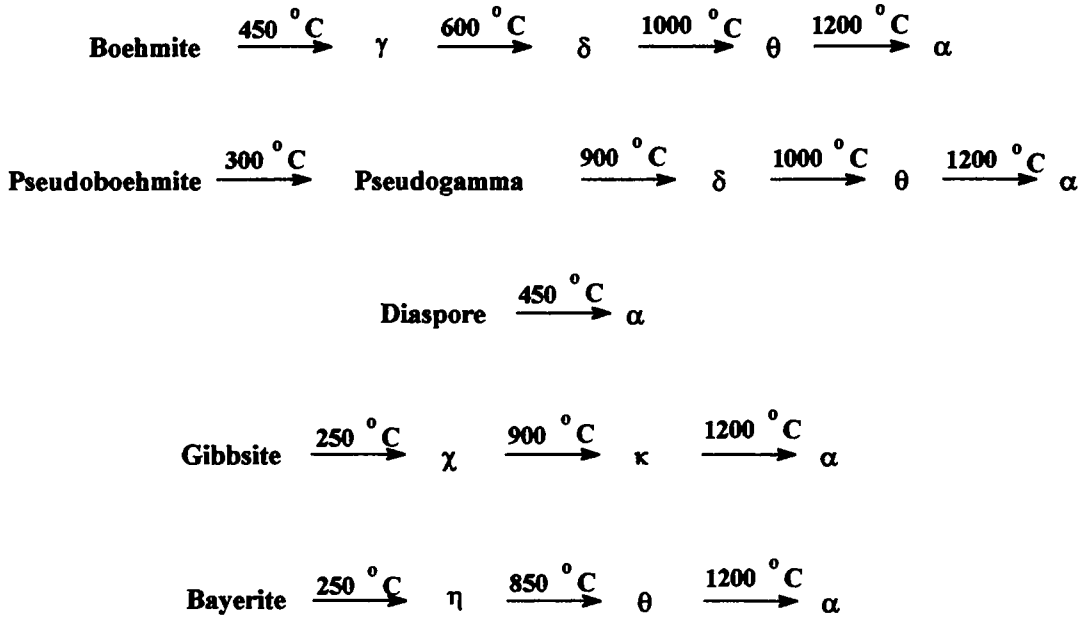


Figure 1-2 Formation Of Transition Aluminas

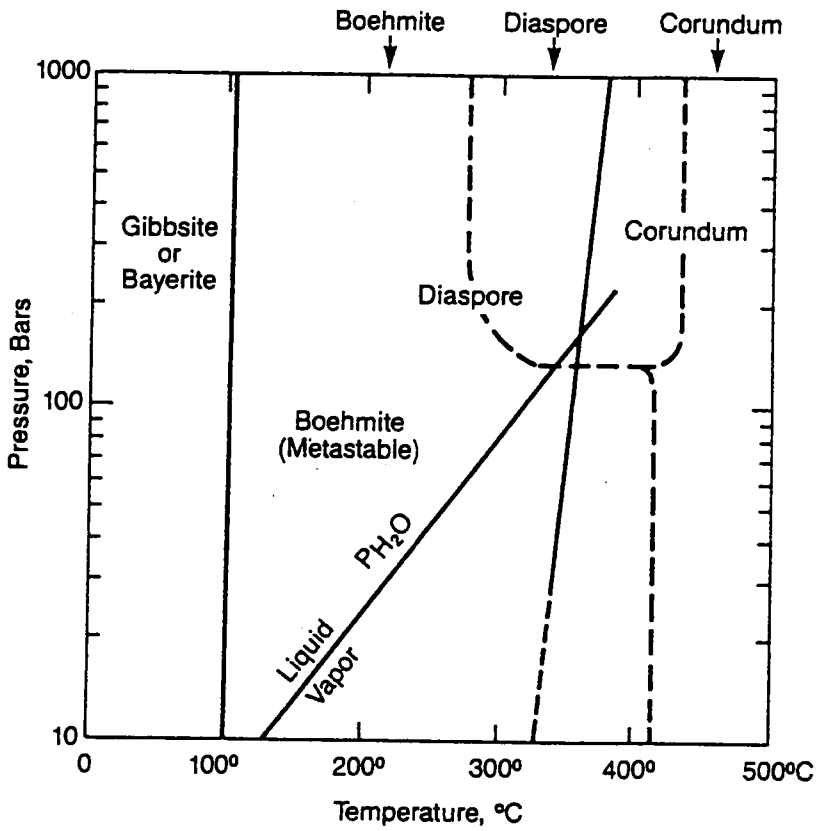


Figure 1-3 Pressure/Temperature Relationship of Various Transition Alumina Precursors

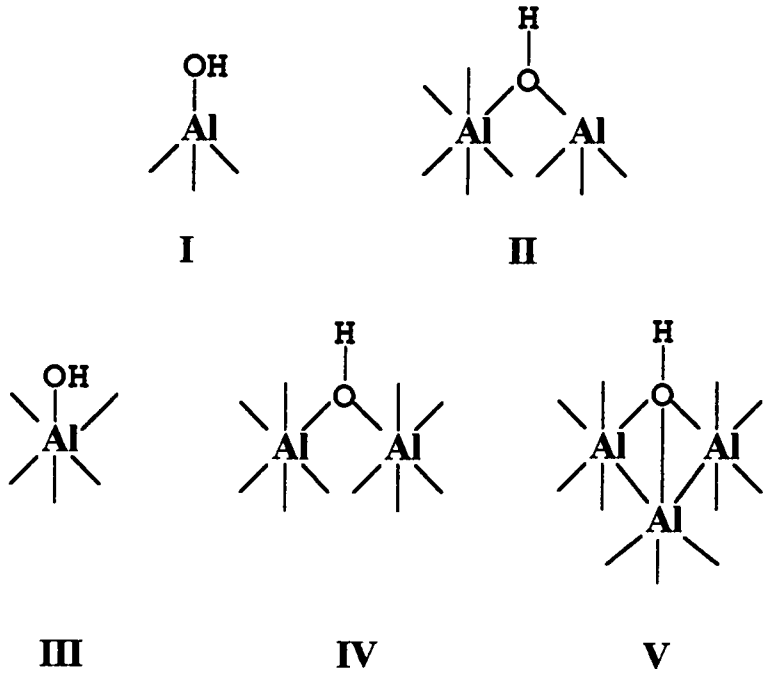


Figure 1-4 Hydroxyls of Peri's Alumina Model

of hydroxyl groups and cationic environs on the surface.[68] These five major types of hydroxyls, I-V, are represented in Figure 1-4.

The late 1970's saw another improvement in understanding alumina structures based on a spinel defect model applied by Knozinger and Ratnasamy which most closely mimics the physical γ-alumina surface and has become the prevailing interpretation.[69] While the aluminum cations exist in quasiregular positions, the oxygen anions exist in four uniformly distinct layers in descending order from the surface: A, B, C, and D (Figure 1-5).

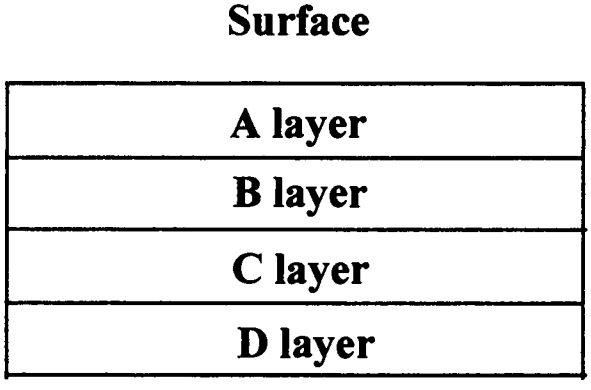


Figure 1-5 Layering of Alumina

Each of these discrete tiers is defined by the distribution of aluminum cations within their respective stratum (Figure 1-6). The lower layers are often exposed in clefts or craters within the A layer mantle and therefore contribute to the general catalytic nature of the surface.[69] The hallmark of this design is its ability to account for surface defects or "holes" associated with the dehydration process.

This dehydration is usually conducted by heating the solid under vacuum and is commonly referred to as activation. "Off-the-shelf " γ-alumina contains approximately 3 mmols of surface hydroxyls per gram of material, determined by gasimetry.[70] The extent of activation is related to the amount of surface hydroxyls removed, a direct correlation of the temperature and its duration, typically ranging from 4 hours to days (Figure 1-7). The surface can be easily rehydrated, sometimes in a matter of minutes, by exposure to air, especially in more humid climes. Activation generates a unique catalytic surface proliferated with both acidic and basic sites. The diversity of organic reactions catalyzed by both activated and native alumina is vast and too numerous to list here.[71] One must only note the number of commercially available catalysts which are sold as alumina mixtures.[72]

The initial studies of γ-alumina were carried out primarily by Posner[73] and coworkers and later propagated by Kropp[74] among others. Notable contributions by Kabalka and Pagni and coworkers, of whom the author is included, over the last few decades also merit attention. One of the more stunning examples of this utility is the finding by Kabalka and Gooch that organoboranes react with sodium iodide to produce alkyl iodides on mere contact with an Al_2O_3 TLC plate, Reaction 1-2.[75]

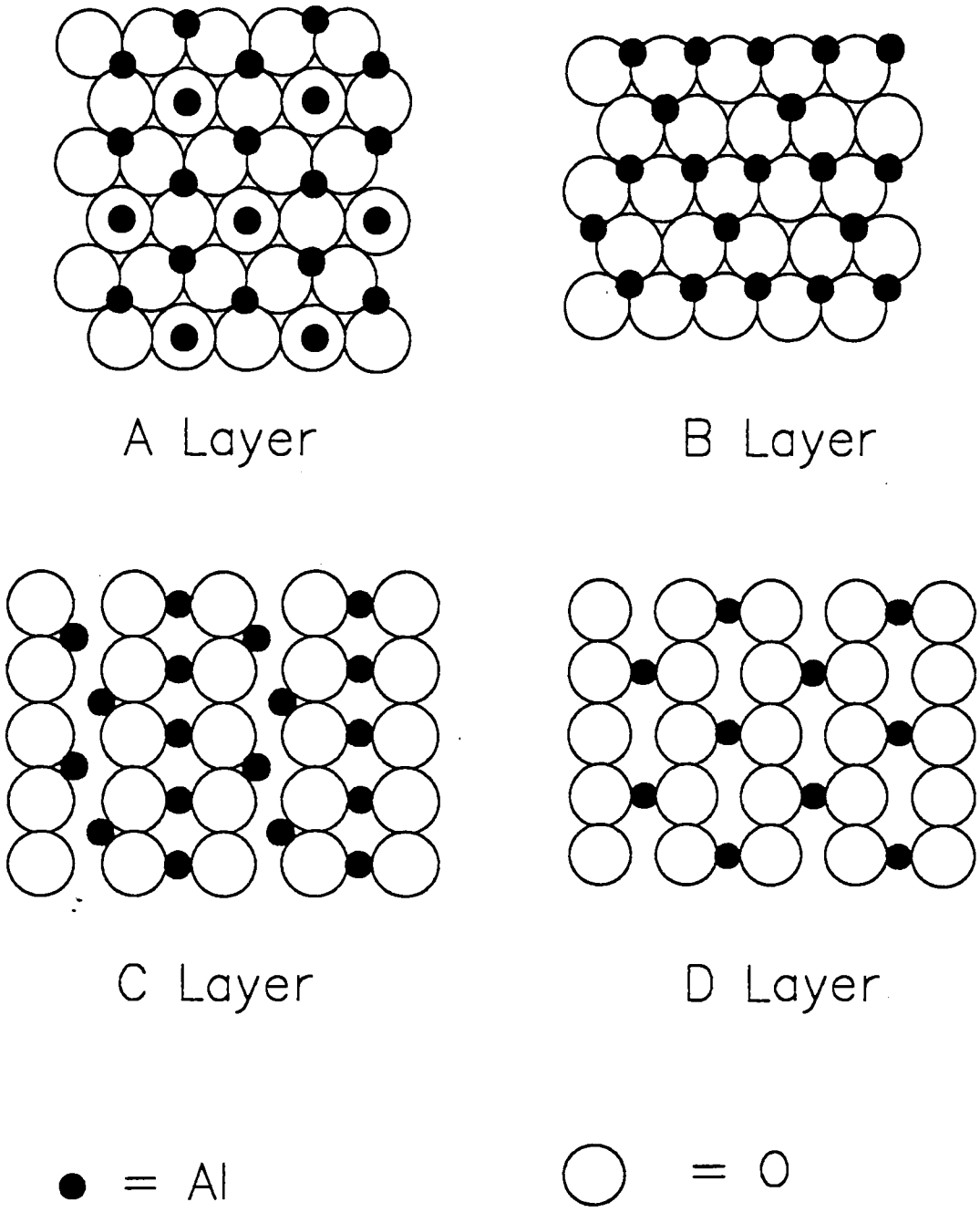


Figure 1-6 A-D Layers of γ-Alumina[69]

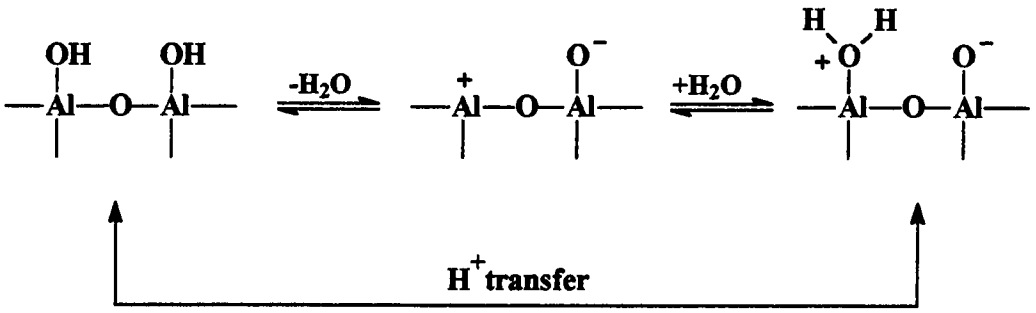
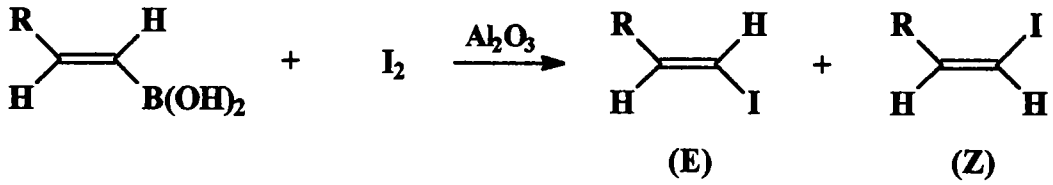


Figure 1-7 Dehydration of γ-Alumina

A later study found that molecular iodine reacts with alumina-bound vinyl boronic acids to produce mixtures of (E) and (Z) vinyl iodides, Reaction 1-3.[76]

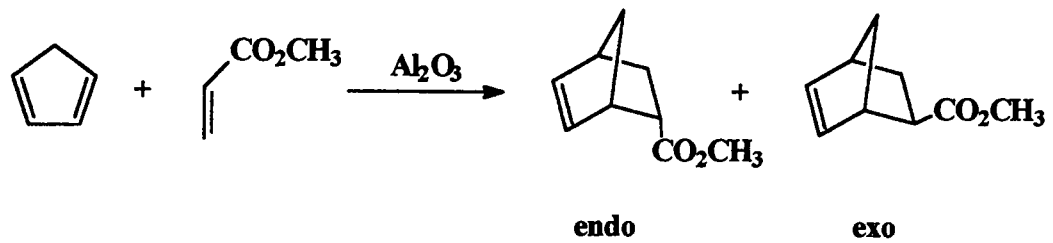
$$R_3B + NaI \xrightarrow{Al_2O_3} RI$$

Reaction 1-2



Reaction 1-3

The elegance of this transformation is that the E/Z ratio can be manipulated by varying the amount of surface hydration or activation.[76] The classic Diels-Alder reaction has also been catalyzed, in the complete absence of solvent, on 400 °C activated alumina in a better than 50:1 endo:exo ratio for the particular product detailed in Reaction 1-4.[77]



Reaction 1-4

E. Modified Aluminas: KF/Al_2O_3:

The catalytic activity of γ-alumina is not limited to natural and activated forms, a myriad of surface and internal lattice modifications are available.[78] New physical environs can be contrived in this manner, tailoring the surface to a specific chemical requirement. Our group has altered the alumina surface with BBr_3 to produce an enhanced medium for the Lewis acid catalyzed Diels-Alder, Reaction 1-4, mentioned previously, Figure 1-8.

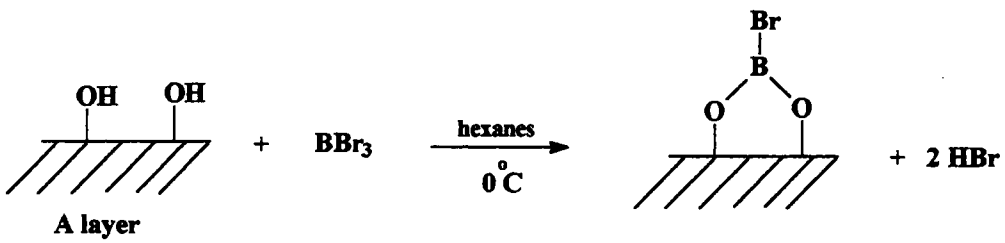


Figure 1-8 BBr_3 Modified Alumina

Another surface augmentation technique utilized quite extensively involves combining insoluble ionic salts with the γ-alumina matrix either by dry blending or aqueous mixing followed by evaporation. Numerous salts have been employed. Fluorides, especially cesium fluoride and potassium fluoride, have received particular

attention in organic chemistry for the unique properties they bring to the surface.

The utility of fluoride salts as potential non-nucleophilic bases in a variety of synthetic reactions has been recognized for some time.[79] However, associated low solubilities in standard organic solvents have hampered their widespread use. Affixing these salts to inorganic surfaces offers advantages not realized by their homogenous and biphasic analogs. Principally, in the absence of solvent, fluoride ions are strong bases. However, these supported reagents also generally offer some selectivity and ease of product isolation. This attribute has been exploited using many different types of supports including silica gel, Celite® (diatomaceous earth), and molecular sieves (clathrates). None, including pure KF, offer the enhanced basicity of KF/Al_2O_3.[80-83] This augmentation comes from an advantageous reaction between KF and the alumina surface during the aqueous mixing process associated with commercial production, Reaction 1-5.

$$12\ KF + Al_2O_3 + 3\ H_2O \longrightarrow 2\ K_3AlF_6 + 6\ KOH$$

Reaction 1-5

If the resulting KF/Al_2O_3 slurry is dried in air, K_2CO_3 also forms on the surface. The overall basicity of the surface can be attributed to the combination of these three components, unsolvated F^-, KOH, and K_2CO_3. Their presence has been confirmed by IR spectroscopy and X-ray diffraction patterns. It has been suggested that K_3AlF_6 and KOH are actually responsible for the augmented basicity of the surface and that unsolvated fluoride ions play, at best, a secondary role.[80] Others maintain that the "total basicity of all the reagents is extremely high, and notably higher than could be explained by simple [hydroxide] formation." [83] It should be noted that the basic characteristics depend greatly on KF loading ratios, drying procedures, and temperatures.[81]

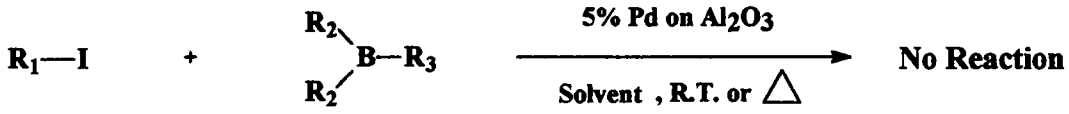
Regardless of the surface idiosyncrasies, KF/Al_2O_3 has been used for a diverse number of organic transformations including Michael additions[84], Knoevenagel condensations,[85] carbon, nitrogen, oxygen, and sulfur alkylation reactions,[86-92] Wittig reactions,[93] Darzens and aldol condensations,[93,94] and elimination reactions,[85b] among others.[95] We have developed a new application: a solventless Suzuki coupling reaction.

Chapter II. Results and Discussion:

The primary focus of this research was the development of a solventless solid state Suzuki coupling reaction using palladium doped γ-alumina as the catalytic matrix. This method would include the advantages associated with solids as viable reaction media, such as ease of handling, nonvolatility, environmentally safe, low health hazard, commercial availability at low cost, and ease of product isolation. Secondary objectives included the possibility of a recyclable catalytic surface as well as an ambient temperature reaction system. The focus of this investigation was the utility of the catalytic surface and not its underlying structure or properties, which were outside the scope of this probe but suggest an obvious direction for the future of this work.

A. Preliminary Work:

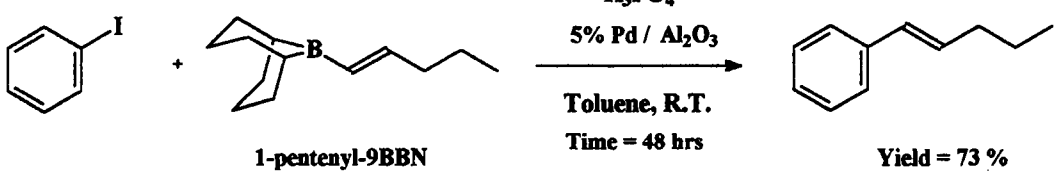
Initial investigations were conducted using unactivated γ-alumina, Brockmann I standard grade, doped with five percent by weight palladium metal, 99.9+% submicron powder. A variety of iodo-compounds (both aryl and alkyl) and boron compounds (primarily trialkyl and alkenyl 9-BBN derivatives) were investigated, Reaction 2-1. To facilitate homogeneous mixing, solvents were used in these initial studies. These preliminary experiments, conducted at both ambient, rt, and elevated temperatures less than 100 °C were unsuccessful. It was felt that the system was not sufficiently basic, based on literature precedents.[23] Basic alumina, Brockmann I standard



R_1 = aryl, alkyl R_2 = R_2 = alkyl, 9-BBN R_3 = butyl, 1-pentenyl

Reaction 2-1

grade, was then used with the same negative result. Finally ionic bases were added to the alumina (see chapter one page 5) and dramatic improvements in yield were observed, Reaction 2-2.

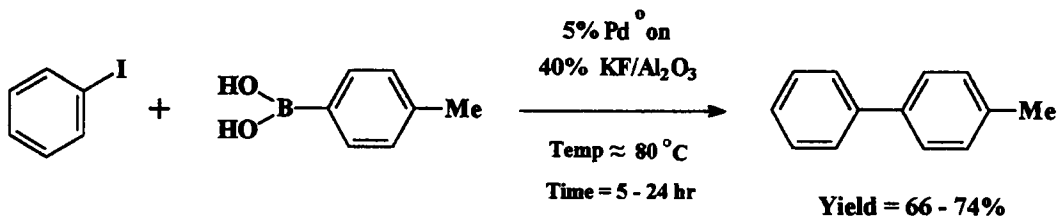


1-pentenyl-9BBN

Yield = 73 %

Reaction 2-2

While the efficiency of the reaction rivaled polymer experiments, the new methodology offered little advantage over solution phase reactions. A commercially available matrix of 40%, by weight, potassium fluoride on alumina was then examined. This homogeneous mixture has been used extensively as a strongly basic catalytic surface for numerous organic transformations (see Chapter I, page 20). After preliminary reactions in the presence of solvent led to successful coupling, a number of solvent free reactions were successfully carried out, Reaction 2-3.



Reaction 2-3: Initial Dry Reactions

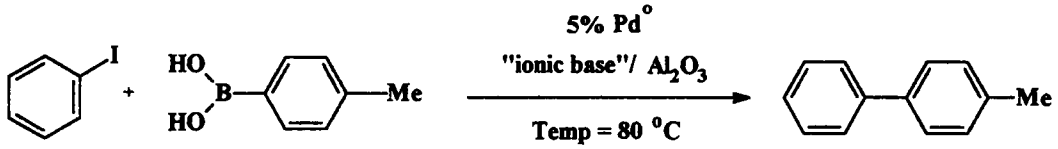
The reagents were chosen as representative examples of common Suzuki coupling species, and became the model reactants throughout the optimization phase of this investigation.

Initially, procedures closely paralleled those of established literature protocols for solution reactions. Reactant loading was kept low, approximately 1-3 mmol per gram total weight of solid, Pd° and KF/Al_2O_3. The amount of palladium used was 5% by weight, patterned directly after a commercially available reagent, 5% Pd on Al_2O_3, available from Aldrich. Temperature and reaction times were originally chosen after surveying solution phase precedents.

B. Alternate Base Study:

Having established the effectiveness of KF, other bases were added to γ-alumina in an effort to establish the generality of the Al_2O_3-based reactions. The results of this study are presented in Table 2-1. The bases listed are those most commonly employed in solution phase routines. The sodium fluoride, NaF, experiment suggests that this fluoride source is not as effective as KF. Recalling the distinctive reaction that takes place between KF and the alumina surface, Reaction 1-5, this might have been predicted.

Table 2-1: Alternate Base Study



"ionic base"[a]	Rxn Time	Yield (%)
NaOH	3 hr	23.4
K_2CO_3	3 hr	26.7
K_3PO_4	3 hr	70.6
KF	3 hr	85.6
NaF	4 hr	5.0
KF/silica gel[b]	4 hr	18.1
Al_2O_3 (basic)	5 days	0.0

[a] 40 % by weight
[b] Reactions run at 100 °C

C. KF/Al_2O_3 Preparation:

Having established the effectiveness of the KF/Al_2O_3 surface, the question arose as to the uniformity of the surface, i.e. do all 40% potassium fluoride doped aluminas show this type of reactivity or is it limited to a single commercial source? Table 2-2 contains a summary of the results of this probe. The sporadic nature of the results is evidence of the variable nature of the surface. The most significant factor appears to be the water content of the solid matrix. As noted previously, recent studies[44] suggest that water is an essential component of the mechanistic cycle of the Suzuki reaction, not merely an agent to improve solubility. In solution phase reactions, aqueous mixed solvents (or water dissolved in 'neat' organics) and base generate a borate salt, greatly increasing the nucleophilicity of the R group, Reaction 2-4.

$$R{-}B(OH)_2 + K_2CO_3 + H_2O \longrightarrow R{-}B(OH)_3^- K^+ + KHCO_3$$

Reaction 2-4

Table 2-2: Prepared vs. Commercially Available KF/Al_2O_3

Entry	KF / Al_2O_3	Conditioning / Prep.	Yield (%)
1	commercial-old[a] (1g)	none	91.4
2	commercial-new (1g)	none	43.6
3	prepared (1g)	physically stirred, R.T.	35.4
4	prepared (1g)	dissolved H_2O, evap.	37.0
5	prepared (2g)	dissolved H_2O, evap.	32.9
6	commercial-new (1g)	5% H_2O in THF, evap.	69.5
7	commercial-new (1g)	open to air (~1 week)	71.0
8	commercial-old (1g)	dried 110 °C (~1 week)	25.1

[a] Stored on shelf since 1978 (Aldrich Lot # 02313KR)

It is much more straightforward to envision palladium insertion into this borate complex than the electron-deficient trivalent precursor. Entries 1 and 8, Table 2-2, suggest that water content also plays a role in the 'dry' reactions. The same argument can be used to explain the discrepancies in the commercial-old versus the commercial-new entries. Both batches of KF/Al_2O_3 were obtained from Aldrich, albeit 20 years apart. Commercial preparation of KF/Al_2O_3 involves mixing aqueous dissolved potassium fluoride with γ-alumina followed by evaporation of the water at elevated temperature; the exact conditions being a trade secret. The reagent arrives in a sealed plastic bottle containing quarter-sized chunks of material which must be ground, with some effort, to a suitable powder before use. While exterior surface sites can be readily rehydrated by atmospheric moisture, this accounts for only a small portion of the total, considering the low surface area to volume ratio of these quarter-sized masses. The problem of reagent variability, and subsequent activity, has been spectroscopically documented by Clark *et al.* on a wide range of preparations for KF/Al_2O_3 and related systems.[81,82,96] It should be noted that, with regard to commercial-new entries in Table 2-2, yields eventually recovered to a reproducible 85-95% for the representative reaction after the ground reagent was exposed to air over a period of time.

D. Time of Reaction:

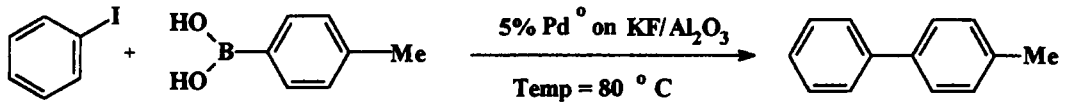
The effect of reaction time was determined employing two distinct techniques. The

first involved running parallel reactions for an allotted time period followed by quenching and workup. The results of this investigation are presented in Table 2-3.

Quenching in this methodology involved removing the reaction's energy source by simply lowering the hot oil bath. The solid was then stirred at room temperature in a suitable solvent, hexanes in this instance, followed by product isolation via filtration. It should be noted that vacuum filtration was preferable to simple gravity filtration, since the latter fails to remove product that is adsorbed onto the surface. Approximately 1-3 % of the product can be recovered by sodium hydroxide digestion of the alumina surface. Examination of the data contained in Table 2-3 reveals that the reaction is essentially complete in four hours.

In the second study, periodic sampling of a reaction mixture was carried out at 15 minute intervals for the first three hours and then at 30 minute increments for an additional two hours. This experiment is unusual because the reaction scale was tripled, approximately 3 mmol of the reactants were added to a three-gram solid sample, to allow for removal of small portions, in addition an internal GC standard, tetradecane, was used. The solid aliquots were washed with hexanes and *gravity* filtered, through a cotton filled pipet, due to sample size considerations. The filtrates were then analyzed by gas chromatography. The results of the study are displayed in Figure 2-1. The yield leveled off at approximately 2½ - 2¾ hours. The results are consistent with the earlier studies. With such large amounts of liquid reactants, iodobenzene and tetradecane, the solid clumped badly and would stir only intermittently, with great effort, during both mixing and reaction. Inhomogeneity may

Table 2-3: Reaction Time: Quench and Work-Up Method



Time (hr)	Average Yield (%)
1	46.2
2	79.0
3	85.6
4	89.3
5	88.2
6	85.5

have occurred which presumably led to the observed variability yields.

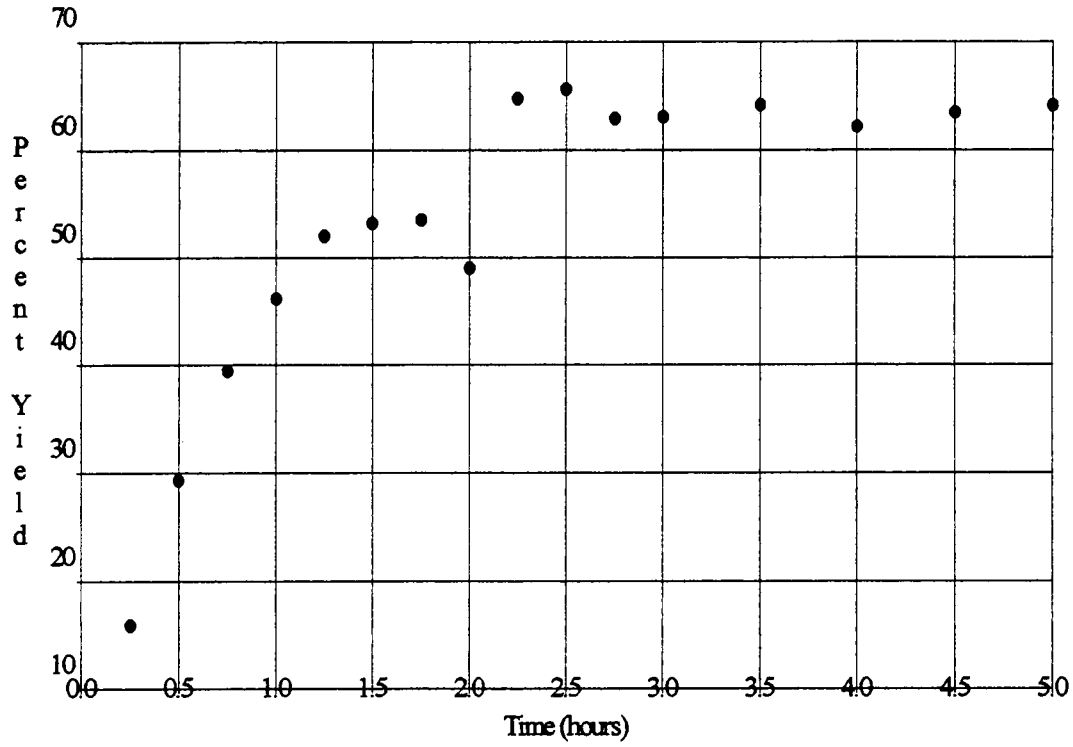


Figure 2-1 Time of Reaction: Sampling Method

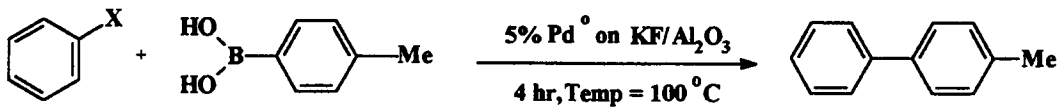
E. Reactant Trends:

The advantages of our solid-state methodology when compared to Suzuki reactions carried out in solution have been well documented. However, the overall scope of the reactions on the KF/Al_2O_3 surface remained to be determined.

1. Aryl Halide Study:

Suzuki reactions carried out in solution follow a general halide reactivity of iodo > bromo >> chloro, with fluoro unreactive. This same trend was also observed with the solid-state methodology, Table 2-4.

Table 2-4: Solventless Method: Aryl Halide Study

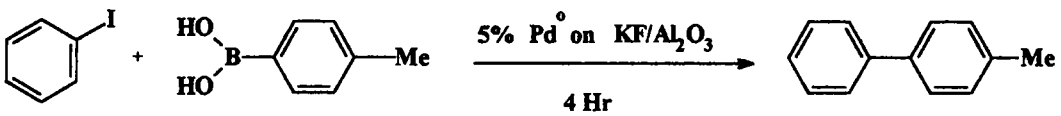


Halide (X)	Yield (%)	Recovered Halide (%)
I	99.3	< 1.0
Br	68.9	9.5
Cl	5.5	none
F	0.0	≈ 60

2. Temperature Study:

Before the advent of ionic accelerants, the yields of Suzuki-coupling reactions were directly proportional to temperature. Ambient temperature reactions were not utilized except for the most reactive systems, usually highly strained aryl-aryl reagents.[28] The results of our temperature study reveal that the classical trends appear to be followed, Table 2-5.

Table 2-5: Solventless Method: Temperature Study



Temperature (° C)	Avg. Yield (%)
R. T.[a] (hexanes, 24 hr)	3.60
45	45.9
80	82.4
100	91.3
120	86.3

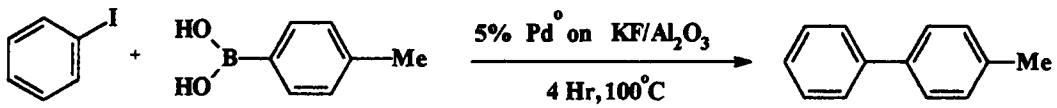
[a] Control Reaction, with solvent, shown for comparison

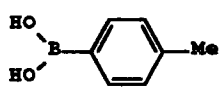
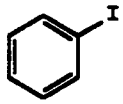
The entry for the reaction at 120 °C is notable. The result could be interpreted as a simple statistical digression. It is, however, reproducible. It can be readily explained based on the water content of the surface and the methodology of the reaction. In these experiments, the oil baths were preheated to the desired temperature prior to use. It was observed that during elevated temperature runs, a layer of condensation formed on the inside of the round-bottomed flask almost immediately after it was placed in the hot oil bath. A slight reflux was observed during each reaction. During the 120° trials, this condensation only rarely returned to the solid surface. As noted earlier, water is essential for efficient reaction, the dehydration at 120° C is therefore probably deleterious.

3. Reactant Ratio Study:

By convention, Suzuki reactions are usually conducted using an excess of the boron species, normally ranging from 1.1 to 3 equivalents based on the halide. It was determined that a slight excess of boronic acid also leads to improved yields. The results are summarized in Table 2-6. Yields suffer little as long as an approximate one to one ratio is maintained.

Table 2-6: Solventless Method: Reactant Ratio Study



 Equivalents	 Equivalents	Average Yield [a] (%)
1.0	1.5	66.2
1.0	1.1	89.3
1.0	1.0	92.6
1.1	1.0	96.3
1.3	1.0	96.0
1.5	1.0	92.6

[a] Based on the limiting reagent

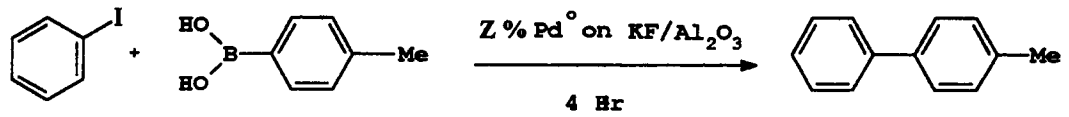
4. Percent Weight of Palladium:

The most costly reactant in the new methodology is the Pd^0 catalyst. A study was conducted to determine if the quantity of palladium could be reduced. The results of this study are presented in Table 2-7. It appears that the palladium content can be reduced by a full percentage point to 4% by weight. However, subsequent reactions were performed at the five percent level for consistency. It should be mentioned that if there is a drawback to the solid-state methodology described to this point, it is the slight excess of catalyst used compared to solution reactions. At five percent by weight, the amount of Pd^0 is approximately 50 mol percent, dropping to about 40 at 4%. This compares to the 5-10 mol percent palladium, based on the halide, utilized in traditional solution routines. However, if the secondary goal of surface recyclability can be realized, this point will be mute.

5. Reacting Boronic Species:

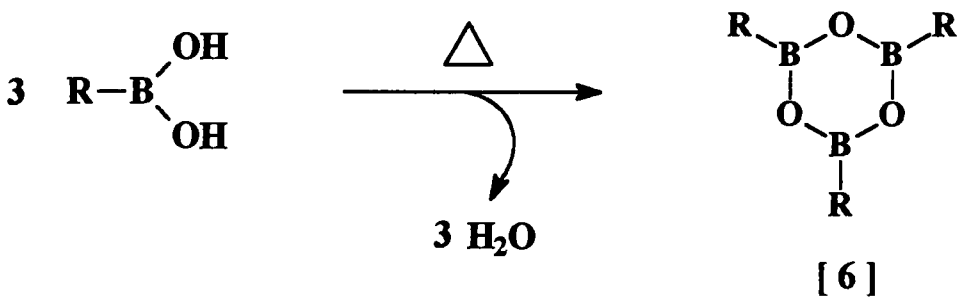
The amount of water generated during the Suzuki reaction appears to be greater than the amount simply adsorbed onto the solid surface and, at the reaction temperatures studied, could not be attributed to surface activation. The water can however be accounted for by a series of reactions of the boronic acid species with itself or with the surface.

Table 2-7: Percent weight of Palladium



Percent Palladium (Z) 1 gram total weight	Average Yield (%)
1	70.3
2	76.1
3	83.3
4	95.6
5	96.0

For example, the six-membered heterocycle, composed of boron and oxygen, known as a boronic anhydride or boroxine [**6**] is well known. They are readily prepared by

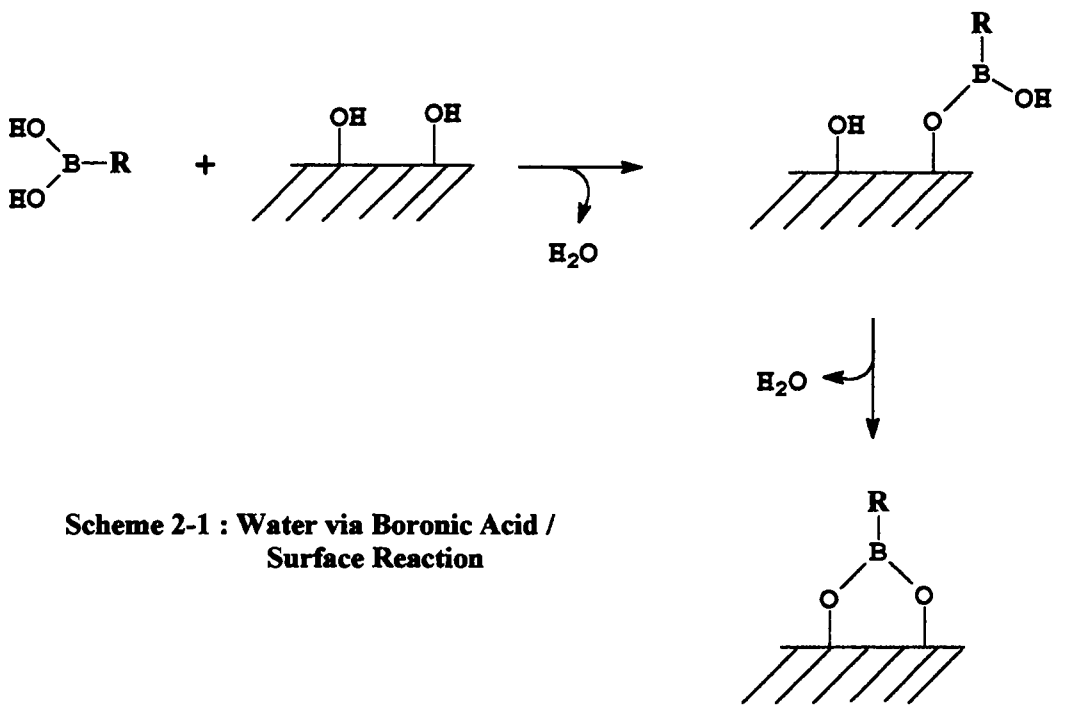


[**6**]

Reaction 2-5: Water via Boroxine Formation

dehydration, Reaction 2-5.[97,98] In fact, boroxines are routinely encountered in commercial boronic acid reagents because they are so readily formed during isolation.[99]

Water can also arise via a similar reaction between the boronic acid and the hydroxyls of the alumina surface, Scheme 2-1. Either method supplies a significant amount of water to the reaction system. Control experiments suggest that one or both of these reactions occurs during the solid-phase reaction. Note, however, that all boron-containing species are isoelectronic. This allows, in theory, any one of the species to react via the Suzuki pathway.

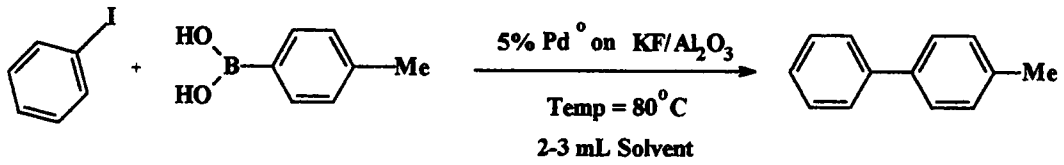


Scheme 2-1 : Water via Boronic Acid / Surface Reaction

F. Control Experiments: Solvents

The question arose as to whether running the Suzuki reaction in the presence of solvents could improve reaction yields by aiding in molecular transfer about the catalytic site. Control experiments were conducted in which small amounts, 2-3 mL, of various solvents were added to the reaction mixtures to create a loose slurry. The results of these experiments are presented in Table 2-8. Note that all neat solvents except methanol lead to lower yields than the optimized "**Dry**" reaction, listed here for comparison. This result can be explained based on the type of palladium catalyst utilized. Without the ligands usually associated with Suzuki catalysts, which are used for solubility purposes, the Pd° is intermixed with the KF/Al_2O_3 and the other solid reactant, *p*-methylphenylboronic acid, at the bottom of the reaction flask. However, the other reactant, iodobenzene, is freely soluble in the solvent(s) above; interaction, and eventual insertion into the palladium complex, can only occur at the solid/liquid interface. Since this is a catalytic cycle, it is conceivable that all of the aryl halide will come into contact with catalyst at this interface, these sites will eventually become depleted of the less mobile acid. Quantitative solubility studies of *p*-methylphenylboronic acid in various solvents follow the yield trend for the undiluted organic solvents from Table 2-8, i.e. hexanes < toluene < THF.

Table 2-8: Control Reactions: Solvent Slurries

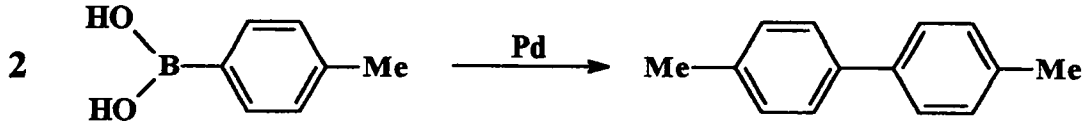


Solvent	Time (hr)	Yield	Recovery (R-X)
Dry	4	98.1	0.0
Hexanes	24	7.60	68.7
THF	17½	74.6	0.0
Toluene	20½	45.3	36.1
H_2O	4	71.3	1.4
Acetone/H_2O	4	93.8	0.3
MeOH/H_2O	4	96.7	0.0
MeOH	4	97.9	0.0

G. Organic Halide Survey:

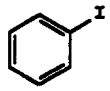
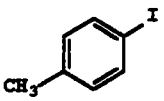
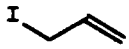
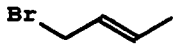
A survey of the reactions of various halides was conducted to evaluate the synthetic utility of the new solid-state procedure. Chloro derivatives were excluded due to their non-reactivity, see Table 2-4. None of the alkyl halides, 1-iodobutane, 1-iodohexane, 2-iodopropane, iodocyclohexane, and 1-bromobutane, participated in the coupling reaction, Table 2-9.2. Those reactions that were successful are listed in Table 2-9.1. The instances labeled with "(**MeOH**)" were carried out as slurries due to the low boiling points of those particular halides. The two allylic systems, allyl iodide and 1-bromo-2-butene, are of interest since only a handful of successful heterogeneous couplings of these agents have been reported.[30a,31b,53] It has been shown that these reagents suffer from premature elimination[100] from the palladium complex, similar to the alkyl examples discussed in chapter one (see page 6-7), leading to homogeneous dimeric coupling products.

The column labeled "By-product" in Table 2-9.1 and Table 2-9.2 refers to a



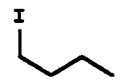
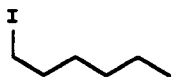
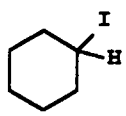
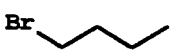
Reaction 2-6: Boronic Acid Self-Coupling "By-product"

Table 2-9.1: Organic Halide Survey

Halide[a]	Product (%)	Recovery R-X	By-product[b]
	98.3 (shown for comparison)	0.0	none
	68.5	0.0	N/A
	39.4	0.0	0.0
 (MeOH)	0.0	0.0	8.3
 (MeOH)	0.0	0.0	21.1
	65.8	0.0	trace

[a] Reaction with *p*-methylphenylboronic acid at 100 °C, 4 Hr.
[b] See Reaction 2-6

Table 2-9.2: Alkyl Halide Examples

Halide[a]	Product (%)	Recovery (R-X)	By-product[b]
 (MeOH)	0.0	0.0	84.5
 (MeOH)	0.0	56.7	7.5
 (MeOH)	0.0	0.0	86.5
	0.0	50.2	58.2
	0.0	0.0	29.4

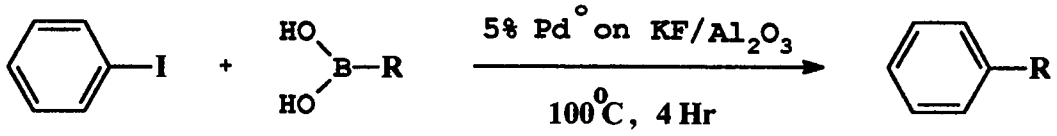
[a] Reaction with *p*-methylphenylboronic acid at 100 °C, 4 Hr.
[b] See Reaction 2-6

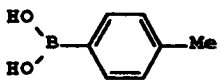
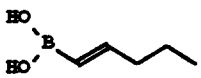
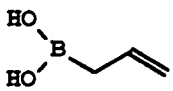
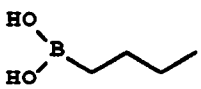
well-documented side-reaction of Suzuki coupling reactions, the self-coupling of the boronic acid, Reaction 2-6.[101] The tin equivalent in the Stille reaction is well known.[102] Dimerization of the organometallic precursors normally occurs when the desired cross-coupling reaction is very slow.[103] The instance of this by-product formation was especially pronounced in the alkyl halide experiments where no cross-coupling products were formed, Table 2-9.2. It should be noted that control reactions revealed that, in the absence of an organic halide, this "by-product" side reaction does not take place. If an inexpensive sacrificial organic halide could be found, this protocol could exploited to produce symmetrical biphenyls. Many of the yields listed in Table 2-9.2 surpass those previously reported in the literature and with dramatically lower reaction times.[101]

H. Boronic Acid Survey:

The reactivities of various boronic acids with iodobenzene were also investigated. The results are listed in Table 2-10. Allylic boronic acids also undergo the homo-coupling reaction described for aromatic derivatives. It occurs in both 'head to head' and 'head to tail' fashions which usually lead to dimerization products.[100] These products were not isolated in this study. The assistance of π-electron donation in the formation of the palladium complex is well known.[50] This could account for the notably lower yields in the butylboronic acid experiment.

Table 2-10: Boronic Acid Survey



Boronic acid	Product Yield (%)	Recovery (iodobenzene)
	98.3 (shown for comparison)	0.0
	78.8	0.0
	0.0	29.3
	26.3	trace[a]

[a] TLC evidence

I. Conclusion:

In conclusion, the primary goal of developing a synthetically useful solid-state Suzuki coupling methodology has been realized. The new methodology incorporates all the advantages associated with other surface routines including low health hazards, ease of handling, elementary product isolation, and convenient commercial availability. Reaction yields rival or exceed those reported in the literature. Novel attributes include the use of a ligandless and recoverable catalyst, zero valent palladium black, which obviates the need for air-sensitive procedures. The catalytic surface is also recycleable, which is a unique innovation. This aspect is discussed in more detail in chapter III.

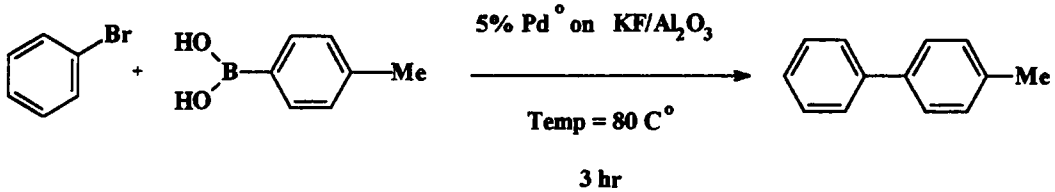
Chapter III. Surface Recyclability:

An important secondary objective of this study was the creation a recyclable Suzuki catalyst. The sensitive nature of the palladium catalysts customarily used in current solution-phase Suzuki reactions preclude their use in subsequent reactions without expensive and time-consuming regenerative manipulations. The stable, zero valent, ligandless palladium metal catalysts utilized in our new methodology, as well as its ease of recovery, suggests that they may be easily recycled.

A. Successive Trials I:

Initial experiments involved simply drying the reclaimed solid KF/Al_2O_3 under vacuum at ambient temperatures. The resultant mass was then agitated to generate a suitable powdery consistency prior to reuse. The results of these efforts are summarized in Table 3-1. Bromobenzene was used in the initial recycling studies, which accounts for the lower yields as compared to the previous aryl iodide studies. It should be noted that the product was isolated by *gravity* filtration rather than by the preferred vacuum filtration. As such, the yields are approximately 1-3% lower than would be expected. Celite®, often used as a filter aid during vacuum filtration, would have contaminated the recovered solid if employed here.

Table 3-1: Successive Trials on Reclaimed Solid



Trial	Yield
1	71.0 %
2	16.9 %
3	6.66 %

As can be seen, the yields plummeted after the first cycle suggesting a problem with the surface. The most logical explanation is that the KF is consumed during the reaction as the 'basic' reactants are depleted to regenerate the zero valent palladium catalyst, see Reaction 1-5. At 40% by weight, a 0.950 g KF/Al_2O_3 sample contains 6.5 mmol of KF. With a reactant loading of approximately one mmol, this quantity would appear to be sufficient for the three cycles listed above in Table 3.1. Without a 'mobile' phase, reactive sites exhaust the KF in their immediate vicinity and effectively lose their catalytic activity. This complication was overcome in the next phase of investigation.

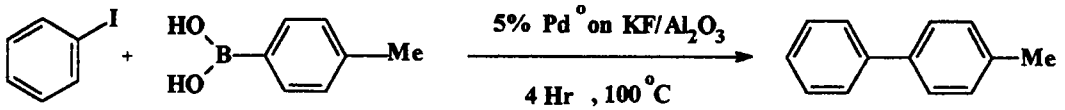
B. Successive Trials II: Dry Addition of KF

Assuming that loss of KF from the surface led to reduced activity, a series of experiments were conducted in which addition of 0.40 g (~6.5 mmol) of KF, with physical stirring at ambient temperature, occurred between each cycle. (See Table 3-2) The yields did improve slightly after the addition of the KF, but not to the levels achieved in Trial 1.

C. Successive Trials III: Addition of KF as a Methanol Slurry/Wash

A number of studies were conducted in which methanol was used to affect better coverage of KF on the alumina surface. Methanol was utilized because of the positive

Table 3-2: Successive Trials on Reclaimed Solid: Dry Addition of KF

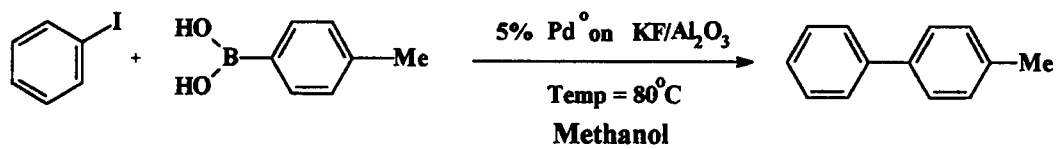


Trial	Product (%)	Recovered Starting Material (%)
1	91.1	< 1.0
2	39.7	28.8
3[a]	63.0	18.7

[a] 0.400g (~7 mmol) KF added with physical stirring

effects observed in early solvent studies, Table 2-8. The first goal was to evaluate methanol's effect on the reaction rate. Experiment were conducted exactly as they were in the dry reactions with the exception of the addition of a small quantity, 2-3 mL, of methanol to form a loose slurry. The results are presented in Table 3-3. Comparing these results to those presented in Table 2-3, improved yields were obtained even as quickly as 1-2 hr. Trial #6 was especially noteworthy. At reaction times comparable to those involving polymer methodologies,[104] ambient temperature yields were roughly the same as those of elevated trials at 80 °C and 100 °C.

Table 3-3: Time of Reaction: MeOH Slurry

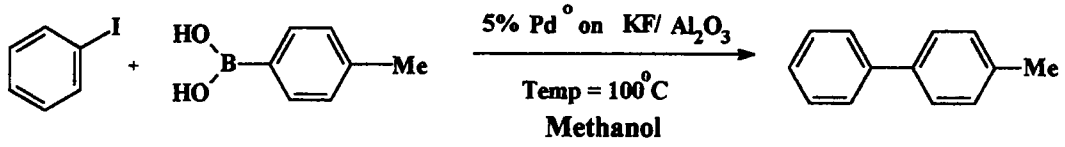


Trial	Time (hr)	Yield (%)
1	1	92.2
2	2	97.5
3	3	90.1
4	4[a]	98.0
5	24[b]	22.9
6	72[b]	90.8

[a] Temp = 100 °C
[b] Temp = Room Temperature

There were concerns that simply stirring KF with the depleted surface might not be sufficient to achieve the desired reaction (recall Reaction 1-5). It was felt that by combining this addition with the methanol slurry methodology, reproducible and higher yields could be realized. This, in fact, proved to be the case, Table 3-4.

Table 3-4: Successive Trials on Reclaimed Solid: Addition of KF (MeOH Slurry)

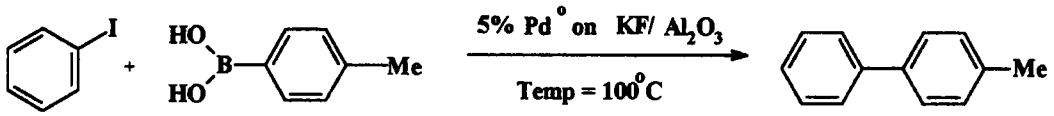


Trial	Product (%)	Recovery (R-X)
1	98.0	0.0
2	70.6	0.0
3[a]	98.9	0.0
4	95.4	0.0
5	84.1	trace[b]

[a] 0.400 g (~7 mmol) KF added
[b] TLC evidence

Dramatic improvements in yields were observed when compared to the 'dry' addition method. The solvent was believed to be acting simply as a vehicle to replenish depleted catalytic sites with essential reactants and could be removed prior to reaction. An experiment was conducted mimicking the dry KF addition trials (See Table 3-2). However, the KF was added along with ≈10 ml of methanol, stirred at ambient temperature, and the solvent eventually removed under vacuum. The remaining solid was then ground to a powdery consistency prior to reaction. The results of this study are presented in Table 3-5. Note the dramatic recovery in Trial 3.

Table 3-5: Successive Trials on Reclaimed Solid: Addition of KF (MeOH Wash and Removal)



Trial	Product (%)	Recovered Starting Material (%)
1	94.6	< 1.0
2	33.7	24.5
3[a]	96.5	0.0

[a] 0.400 g (~7 mmol) KF added with MeOH, Solvent removed before reaction

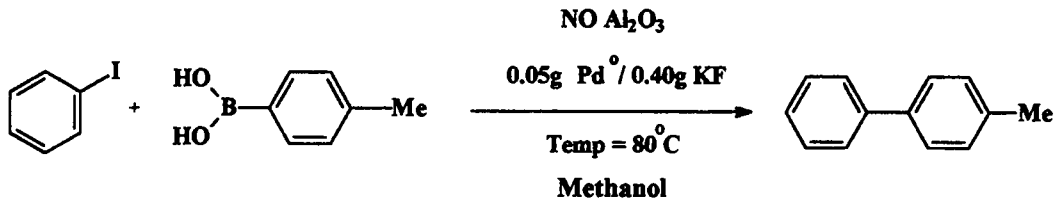
Another important consideration was whether the alumina surface was necessary in the methanol slurry reactions. Trials analogous to those above, Table 3-4, were conducted in the complete absence of Al_2O_3. The results of which are detailed in Table 3-6. It is clear that the methanol solvent alone is effective.

The KF/Al_2O_3 methodology represents one of only a handful of solution techniques incorporating a less costly ligandless palladium catalyst,[31c,36] and the *first*, to the author's knowledge, to involve complete recyclability. One attribute of the Al_2O_3 matrix is that it creates bulk which aids dramatically in the recovery of the catalyst. At pennies a gram, this represents a cost effective methodology when compared to the expense of traditional Suzuki reaction protocols.

D. Microwave Trials:

Solid supports lend themselves directly to synthetic methodologies incorporating the use of microwave irradiation as the external energy source. As such, this seemed a logical extension of the newly developed KF/Al_2O_3 methodology. Liquids used in microwave methods possess a property known as a high dielectric loss, which is the ability to absorb electromagnetic energy, e.g. microwaves, and then transmit or lose this energy as heat to the surrounding local environment. The ability of organic and inorganic solvents to absorb microwave energy, known as coupling, is optimal for low molecular weight molecules with large dipole moments. Examples of suitable solvents include H_2O, EtOH, MeOH as well as MeCN, DMF, and CH_2Cl_2.[105] Those exhibiting

Table 3-6: Successive Trails on Reclaimed Solid: MeOH Slurry with No Al_2O_3



Trial[a]	Product (%)	Recovery (R-I)
1	94.2	0.0
2	85.3	0.0
3[b]	98.7	0.0
4	95.1	0.0
5	78.6	3.4

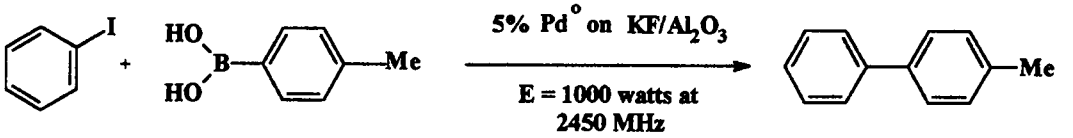
[a] Temp = 100 °C
[b] 0.400 g (~ 7 mmol) KF added

negligible dielectric losses, e.g. C_6H_6, petroleum ethers, CCl_4, can be utilized by adding small amounts of alcohols or water which dramatically improves their utility. Most organic solvents suffer from intrinsic problems in microwave schemes, notably, volatility and flammability. These shortcomings have been overcome in a variety of ways, both mechanical and chemical, in recent decades.[105,106] Substituting a solid support that doesn't couple easily with microwave frequencies, such as silica or alumina, overcomes this problem and allows the energy to be absorbed directly into the reacting molecules.[107]

The solid-phase chemistry we developed was modified slightly to accommodate microwave irradiation. All solids and reactants were mixed as previously described in a round-bottomed flask fitted with a punctured septum to allow pressurized gases to escape. The metallic, Teflon®-encased stir bar was then removed. The reaction flask, encased between two small cork rings, one upright one inverted, for stability, was then placed on the revolving plate of a standard microwave (Sharp, Model R-4A38, 1000 watts, 2450 MHz) and irradiated on "HIGH" (Power level = 100%) for the allotted time period. The results of this study are summarized in Table 3-7.

The results reveal that, after 1½ min, the yields level off in the 80-88 % range, for reasons which are unknown at this time. Qualitative arguments include support temperature and product/reactant mobility out of the catalytic site. During irradiation, the solid becomes extremely hot to the touch. While accurate temperature readings are impossible with this particular apparatus, a large amount of aqueous condensate

Table 3-7: Microwave Reactions



Time of Reaction (min.)	Yield (%)
1.0	69.9
1.5	84.4
2.0	80.9
2.5	88.4
3.0	80.3

was observed on the inside of the RBF *above* the solid support. Recalling the mechanistic necessity of H_2O, this suggests that the surface eventually becomes hot enough to boil off large quantities of adsorbed water and the reaction is curtailed. Secondly, the rapid rate of the microwave reactions, minutes versus hours for conventionally heated examples, might not allow sufficient time for products to move from the catalytic locale and permit fresh reactants to migrate to those sites. However, the applicability of microwave protocols to this new methodology is promising.

E. Future Work:

The work described in this dissertation characterizes the optimum parameters for the solid-phase Suzuki-coupling reaction. Future work should focus, in the author's opinion, on three primary outgrowths: 1) a survey of substituent effects, 2) optimization and elaboration of the microwave methodology, and 3) utilization of ionic accerlerants to reduce operating temperatures.

The optimization phase of this project concentrated only on unfuntionalized organic halides as reactants. Attention should now be turned to assessing the synthetic utility of the dry methodology using a variety of substituted aryl, alkenyl, and alkyl halides and boronic acids. The KF/Al_2O_3 media is moderately basic, however, other reaction conditions are rather innocuous. Any substituent that could tolerate the mildly basic conditions should be a candidate. Numerous synthetic examples employing KF/Al_2O_3 for a variety of purposes exist in the literature; nitro groups,[108]

carbonyl compounds,[109] ethers, thioethers, amines[110], etc. are known to be tolerated.

Development and utilization of the microwave routine should also be undertaken. The most conspicuous advantage of this method is the dramatically lower reaction times. It is important to note that the 'dehydration' of the solid medium, might be overcome by the use of intermittent irradiation. This would allow the solid matrix to cool between irradiation cycles and therefore avoid the loss of mechanistically-necessary water or a least allow for its reflux back onto the surface.

A recent solution-phase innovation has been the use of thallium hydroxide as the basic moiety under classical Suzuki conditions.[111] Yields are generally good to excellent. The primary advantage is that the reactions can be run at ambient temperatures but with longer reaction times, 12-16 hours. This change could easily be adapted to our surface method either in combination with the KF/Al_2O_3 or by replacing the KF altogether to create a novel $TlOH/Al_2O_3$ matrix.

A recent innovation has seen the incorporation of tricarbonyl chromium and alkyl aluminum complexes into solution-phase methodologies.[112] These complexes impart an axial bias on ortho-substituted aryl reactants. Their chemical reactivity would appear to preclude integration into our newly developed solid-state methodology.

IV. Experimental and Materials:

All ^{1}H and ^{13}C NMR spectra were recorded on a 250 MHz Bruker AC250 spectrometer. ^{11}B NMR spectra were recorded on a 90 MHz JEOL FX90Q spectrometer. Melting points were recorded on a MEL-TEMP melting point apparatus and are uncorrected.

Reagents and solvents were used unpurified straight from the bottle unless otherwise noted. Products were purified, if applicable, by flash chromatography on 230-400 mesh ASTM 60 Å silica gel, SiO_2.[113]

A. *p*-Methylphenylboronic acid:[114]

p-Methylphenylmagnesium bromide, prepared from *p*-methylphenyl bromide via established literature methods,[115] in Et_2O (approximately 30 mmol, i.e. in excess) was added dropwise to a well-stirred solution of freshly distilled trimethoxyborane(28.0 mL, 25.0 mmol) in Et_2O at -78 °C under inert atmosphere, Ar. After addition was complete, the mixture was stirred for an additional hour at this temperature. The reaction flask was then placed into an ice bath and 25 ml of 3M HCl (75 mmol) was added dropwise with stirring. After stirring at this temperature for 30 minutes, the layers were separated and the aqueous layer extracted (3 x 25 ml) with diethyl ether. The solvent was then removed at rt under reduced pressure. [^{11}B NMR δ 34.5 (boronic acid) δ 30.1(boroxine)]

B. *trans*-1-Phenyl-1-pentene:[116]

To a homogeneous mixture of Pd^{o}/Al_2O_3 (0.988 g, 5% by weight) was added K_3PO_4 (1.28 g, 6.04 mmol) with stirring. Toluene (2.50 mL) was then added to form a loose slurry. Iodobenzene (0.365 g, 1.79 mmol) was then added via syringe followed by 1-pentenyl-9-BBN (0.300 mL, 1.2 mmol, ~4.0 M in THF). The reaction mixture was allowed to stir at room temperature for 48 hrs. The slurry was vacuum filtered through a sintered glass funnel using celite as a filter aid. Et_2O was used to wash the filter cake. The filtrate was washed with water (3 x 10 ml), dried over $MgSO_4$, and the solvent remove under vacuum. The product was isolated via flash chromatography using silica gel and hexanes to give 0.114 g of product (73.9%). [^{1}H NMR ($CDCl_3$/TMS) δ 7.68 (*d*, 2H) δ 7.18 (*m*, 3H) δ 6.37 (*d*, 1H) δ 6.21 (*m*, 1H) δ 2.16 (*m*, 2H) δ 1.48 (*m*, 2H) δ 0.88 (*t*, 3H)]

C. General Procedures for Reaction of Iodobenzene with *p*-Methylphenylboronic acid:

C.1. 4-Methylbiphenyl:[117] **(KF/Al_2O_3)**

To a mixture of KF/Al_2O_3 (0.953 g , 40 % by weight) and Pd black (0.050 g, 99.9+ %, submicron powder) was added *p*-methylphenylboronic acid (0.150 g, 1.10 mmol) in a clean dry round-bottomed flask, RBF. These three solids were mechanically stirred in air at room temperature until homogeneous. Iodobenzene (0.209 g, 1.023 mmol) was then added with stirring via dropping pipet directly onto the solid. The mixture was stirred at room temperature for an additional 15-20

minutes to ensure complete mixing. The round-bottomed flask was then fitted with a condenser and placed in a preheated oil bath, Temp ≈ 100 °C. Stirring was continued during entire reaction period. After the four hours, the oil bath was lowered and the reaction allowed to cool to R.T. A small amount, approximately 5-8 mL, of hexanes was then added directly through the condenser and the slurry stirred at rt for an additional 20-30 minutes to ensure product liberation that might be adsorbed onto the surface. The slurry was then vacuum filtered through a sintered glass funnel using celite as a filter aid. Product isolated via flash chromatography using silica gel and hexanes , if necessary, gave 0.166 g of product (96.3 %). [m.p. 44-45.5 °C, ^{1}H NMR ($CDCl_3$/TMS) δ 7.40 (*m*, 9H) δ 2.37 (*s*, 3H)]

C.2.1. 4-Methylbiphenyl: (Alternate Base Study: NaOH)

40% by weight NaOH/Al_2O_3 was prepared by adding NaOH (2.01 g) to alumina, Brockmann I-neutral, (3.00 g). The mixture was then slurried in water, 10 mL, at rt overnight. The solvent was then removed under vacuum with heating and the solid physically agitated to a powdery/granular consistency.

Pd black (0.051 g) was added to the prepared NaOH/Al_2O_3 (0.952 g) in a clean dry round bottomed flask and stirred until homogeneous. *p*-Methylphenylboronic acid (0.272 g, 2.00 mmol) was added with stirring followed by iodobenzene (0.420 g, 2.06 mmol). The mixture was vigorously stirred at rt and then placed in a preheated oil bath, Temp = 80 °C, after being fitted with a condenser. After three hours, the oil bath was lowered and the reaction allowed to cool to rt. A small amount,

approximately 5-8 mL, of hexanes was then added directly through the condenser and the slurry stirred at rt for an additional 20-30 minutes to ensure product liberation. The slurry was vacuum filtered through a sintered glass funnel using Celite® as a filter aid. The product was isolated via flash chromatography using silica gel and hexanes to give 0.79 g of product (23%). [m.p. 44.2-46.0 °C]

C.2.2. 4-Methylbiphenyl: (Alternate Base Study: K_2CO_3)

4-Methylbiphenyl was prepared, as described previously (**C 2.1**), using K_2CO_3 as the basic species. *p*-Methylphenylboronic acid (0.268 g, 1.97 mmol) was added with stirring followed by iodobenzene (0.381 g, 1.87 mmol). The product was isolated via flash chromatography using silica gel and hexanes to give 0.84 g of product (27%). [melting point consistent with established literature value]

C.2.3. 4-Methylbiphenyl: (Alternate Base Study: K_3PO_4)

4-Methylbiphenyl was prepared, as described previously (**C 2.1**), using K_3PO_4 as the basic species. *p*-Methylphenylboronic acid (0.269 g, 1.98 mmol) was added with stirring followed by iodobenzene (0.391 g, 1.92 mmol). The product was isolated via flash chromatography using silica gel and hexanes to give 0.118 g of product (56.5%). [melting point consistent with established literature value]

C.2.4. 4-Methylbiphenyl: (Alternate Base Study: NaF)

4-Methylbiphenyl was prepared, as described previously (**C 2.1**), using NaF as the

basic species and a reaction time of 4 hours. *p*-Methylphenylboronic acid (0.162 g, 1.19 mmol) was added with stirring followed by iodobenzene (0.208 g, 1.02 mmol). The product was isolated via flash chromatography using silica gel and hexanes to give 0.009 g of product (5.0%). [^{1}H NMR ($CDCl_3$/TMS) δ 7.38 (*m*, 9H) δ 2.42 (*s*, 3H)]

C.2.5 4-Methylbiphenyl: (Alternate Base Study: KF/silica gel)

40% by weight KF/silica gel was prepared by adding (0.402 g) KF to silica gel (0.605 g). The mixture was slurried in water at rt overnight. The solvent was removed under vacuum with heating, dried invacuo, and the solid physically agitated to a powdery consistency.

Palladium black (0.051 g) was added to the prepared KF/silica gel (0.955 g) in a clean dry round bottomed flask and mechanically stirred until homogeneous. *p*-Methylphenylboronic acid (0.152 g, 1.12 mmol) was added with stirring followed by iodobenzene (0.208 g, 1.02 mmol). The mixture was vigorously stirred at rt and then placed in a preheated oil bath, Temp = 100 °C, after being fitted with a condenser. After four hours the oil bath was lowered and the reaction mixture allowed to cool to rt. A small amount of hexanes was then added directly through the condenser and the slurry stirred at rt for an additional 20 minutes to ensure product liberation. The slurry was vacuum filtered through a sintered glass funnel using Celite® as a filter aid. The product was isolated via flash chromatography using silica gel and hexanes to give 0.031 g of product (18.1%). [melting point consistent with

established literature value]

C.3.1. 4-Methylbiphenyl: (Prepared KF/Al_2O_3-physical stirring)

KF (0.402 g) was added to Al_2O_3, Brockmann I-neutral, (0.612 g) in a clean dry round bottomed flask and stirred overnight at rt in air. Palladium black (0.052g)was then added with stirring followed by *p*-methylphenylboronic acid (0.102 g, 0.751 mmol). These combined solids were mechanically stirred until homogeneous. Iodobenzene (0.147 g, 0.718 mmol) was then added. The round-bottomed flask was then placed in a preheated oil bath, Temp = 80 °C, for four hours. A small amount of hexanes was then added directly through the condenser and the slurry stirred at rt before being vacuum filtered through a sintered glass funnel using Celite®. The product was isolated via flash chromatography using silica gel and hexanes to give 0.043 g of product (35.4%). [melting point consistent with established literature value]

C.3.2. 4-Methylbiphenyl: (Prepared KF/Al_2O_3-H_2O slurry with evaporation under vacuum)

4-Methylbiphenyl was prepared, as described previously (**C 3.1**), with the exception of the KF and alumina being slurried in water overnight at rt followed by solvent evaporation under vacuum before reaction. The product was isolated via flash chromatography using silica gel and hexanes to give 0.077 g of product (37.0%). [melting point consistent with established literature value]

C.3.3. 4-Methylbiphenyl: (Prepared KF/Al_2O_3- 5% H_2O in THF slurry with evaporation under vacuum)

4-Methylbiphenyl was prepared, as described previously (**C 3.1**), with the exception of the KF and alumina being slurried in 5% H_2O in THF overnight at rt followed by solvent evaporation under vacuum before reaction. The product was isolated via flash chromatography using silica gel and hexanes to give 0.123 g of product (69.5%). [melting point consistent with established literature value]

C.3.4. 4-Methylbiphenyl: (Commercial KF/Al_2O_3-dried)

Commercial KF/Al_2O_3, Aldrich, was dried at 110 °C under air for a period of seven days. To a sample of dried KF/Al_2O_3 (0.953 g) was added palladium black (0.055g), followed by *p*-methylphenylboronic acid (0.155 g, 1.14 mmol). The mixture was then mechanically stirred until homogeneous. Iodobenzene (0.209 g, 1.03 mmol) was added with stirring and the reaction flask place in a preheated oil bath, Temp = 80 °C. A small amount of hexanes was then added through the condenser and the slurry stirred at rt before being vacuum filtered through a sintered glass funnel using celite. The product was isolated via flash chromatography using silica gel and hexanes to give 0.035 g of product (25.1%). [melting point consistent with established literature value]

C.4.1.1 4-Methylbiphenyl: (Reaction Time: 2 Hours)

To a mixture of KF/Al_2O_3 (0.949 g, 40 % by weight) and Pd black (0.052 g), *p*-

methylphenylboronic acid (0.394 g, 2.90 mmol) was added in a clean dry round bottomed flask. These three solids were mechanically stirred in air at room temperature for approximately 15 minutes. Iodobenzene (0.420 g, 2.06 mmol) was added with stirring via dropping pipet directly onto the solid. The mixture was then stirred at room temperature for an additional 15-20 minutes to ensure complete mixing. The round-bottomed flask was then fitted with a condenser and placed in a preheated oil bath, Temp ≈ 80 °C. After two hours the oil bath was lowered and the reaction mixture allowed to cool to rt. A small amount of hexanes was then added through the condenser and the slurry stirred at rt for an additional 20-30 minutes to ensure product liberation. The slurry was then vacuum filtered through a sintered glass funnel using Celite® as a filter aid. The product was isolated via flash chromatography using silica gel and hexanes to give 0.274 g of product (79.0%). [melting point consistent with established literature value]

C.4.1.2. 4-Methylbiphenyl: (Reaction Time: 3 Hours)

4-Methylbiphenyl was prepared, as described previously (**C 4.1.1**), with a three hour reaction time. The product was isolated via flash chromatography using silica gel and hexanes to give 0.285 g of product (85.6%). [melting point consistent with established literature value]

C.4.1.3. 4-Methylbiphenyl: (Reaction Time: 4 Hours)

See **C.1**

C.4.1.4. 4-Methylbiphenyl: (Reaction Time: 5 Hours)

4-Methylbiphenyl was prepared, as described previously (**C 4.1.1**), with a five hour reaction time. The product was isolated via flash chromatography using silica gel and hexanes to give 0.290 g of product (80.5%). [melting point consistent with established literature value]

C.4.1.5. 4-Methylbiphenyl: (Reaction Time: 6 Hours)

4-Methylbiphenyl was prepared, as described previously (**C 4.1.1**), with a six hour reaction time. The product was isolated via flash chromatography using silica gel and hexanes to give 0.335 g of product (85.5%). [melting point consistent with established literature value]

C.4.2. 4-Methylbiphenyl: (Reaction Time: Sampling Method)

To a mixture of KF/Al_2O_3 (2.85 g, 40 % by weight) and palladuim black (0.153 g, 5.1% by weight), *p*-methylphenylboronic acid (0.895g, 6.58 mmol) was added in a clean dry three-neck round-bottomed flask. Tetradecane (0.716 g, 3.61 mmol) was then added followed by iodobenzene (1.21 g, 5.94 mmol). The mixture was mechanically stirred, with some difficulty, in air at room temperature for approximately 45 minutes. The round-bottomed flask was fitted with a condenser and placed in a preheated oil bath, Temp = 80 °C. At appropriate intervals, from 15 min to 5 hours, solid samples were removed from the reaction flask. Samples were weighed in premassed pipets before being washed through a small amount of silica gel and cotton using hexanes. Filtrates were analyzed by standard gas chromatography using tetradecane as the

internal standard. Results presented in Figure 2-1, pg 33.

C.5.1. 4-Methylbiphenyl: (Aryl Halide Study: Iodobenzene)

To a mixture of KF/Al_2O_3 (0.951 g, 40 % by weight) and Pd black (0.050 g) was added *p*-methylphenylboronic acid (0.303 g, 2.23 mmol) in a clean dry round bottomed flask. These three solids were mechanically stirred in air at room temperature for approximately 15 minutes. Iodobenzene (0.366 g, 1.79 mmol) was added with stirring via dropping pipet directly onto the solid. The mixture was stirred at room temperature for an additional 10-15 minutes to ensure complete mixing. The round-bottomed flask was then fitted with a condenser and placed in a preheated oil bath, Temp ≈ 100 °C. After four hours the oil bath was lowered and the reaction mixture allowed to cool to rt. A small amount of hexanes was then added through the condenser and the slurry stirred at rt for an additional 20-30 minutes to ensure product liberation. The slurry was then vacuum filtered through a sintered glass funnel using Celite® as a filter aid. The product was isolated via flash chromatography using silica gel and hexanes to give 0.299 g of product (99.3%). [melting point consistent with established literature value]

C.5.2. 4-Methylbiphenyl: (Aryl Halide Study: Bromobenzene)

4-Methylbiphenyl was prepared, as described previously (**C 5.1**), using bromobenzene (0.154 g, 0.978 mmol) as the aryl halide species. The product was isolated via flash chromatography using silica gel and hexanes to give 0.113 g of

product (68.9%). [m.p. 43.5-45.6 °C]

C.5.3. 4-Methylbiphenyl: (Aryl Halide Study: Chlorobenzene)

4-Methylbiphenyl was prepared, as described previously (**C 5.1**), using chlorobenzene (0.126 g, 1.12 mmol) as the aryl halide species. The product was isolated via flash chromatography using silica gel and hexanes to give 0.010 g of product (5.5%). [^{1}H NMR ($CDCl_3$/TMS) δ 7.35 (*m*, 9H) δ 2.38 (*s*, 3H)]

C.5.4. 4-Methylbiphenyl: (Aryl Halide Study: Fluorobenzene)

The synthesis of 4-Methylbiphenyl was attempted, as described previously (**C 5.1**), using fluorobenzene (0.118 g, 1.23 mmol) as the aryl halide species. No product was isolated.

C.6.1 4-Methylbiphenyl:(Temperature Study: 45 °C)

To a mixture of KF/Al_2O_3 (0.948 g, 40 % by weight) and palladium black (0.049 g, 99.9+ %, submicron powder) was added *p*-methylphenylboronic acid (0.430 g, 3.16 mmol) in a clean dry round-bottomed flask. These three solids were mechanically stirred in air at room temperature until homogeneous. Iodobenzene (0.649 g, 3.18 mmol) was then added with stirring via dropping pipet. The round-bottomed flask was then fitted with a condenser and placed in a preheated oil bath, Temp ≈ 45 °C. After four hours the oil bath was lowered and the reaction allowed to cool to rt. A small amount of hexanes was then added through the condenser and the slurry stirred at rt

for an additional 10 minutes. The slurry was then vacuum filtered through a sintered glass funnel using Celite® as a filter aid. The product was isolated via flash chromatography using silica gel and hexanes to give 0.246 g of product (45.9%). [melting point consistent with established literature value]

C.6.2 4-Methylbiphenyl:(Temperature Study: 80 °C)

4-Methylbiphenyl was prepared, as described previously (**C 6.1**), with the exception of an 80 °C preheated oil bath. The product was isolated via flash chromatography using silica gel and hexanes to give 0.140 g of product (82.4%). [melting point consistent with established literature value]

C.6.3 4-Methylbiphenyl:(Temperature Study: 100 °C)

4-Methylbiphenyl was prepared, as described previously (**C 6.1**), with the exception of an 100 °C preheated oil bath. The product was isolated via flash chromatography using silica gel and hexanes to give 0.153 g of product (91.3%). [melting point consistent with established literature value]

C.6.4 4-Methylbiphenyl:(Temperature Study: 120 °C)

4-Methylbiphenyl was prepared, as described previously (**C 6.1**), with the exception of an 120 °C preheated oil bath. The product was isolated via flash chromatography using silica gel and hexanes to give 0.147 g of product (86.3%). [melting point consistent with established literature value]

C.7.1. 4-Methylbiphenyl: (Reactant Ratio Study: 1.0 / 1.5)

To a mixture of KF/Al_2O_3 (1.23 g, 40 % by weight) and Pd black (0.065 g) was added *p*-methylphenylboronic acid (0.165 g, 1.21 mmol) in a clean dry round-bottomed flask. These three solids were mechanically stirred in air at room temperature. Iodobenzene (0.411 g, 2.01 mmol) was added with stirring via dropping pipet directly onto the solid. The round-bottomed flask was then fitted with a condenser and placed in a preheated oil bath, Temp ≈ 100 °C. After four hours the oil bath was lowered and the reaction mixture allowed to cool to rt. A small amount of hexanes was then added through the condenser and the slurry stirred at rt for an additional 20-30 minutes. The slurry was then vacuum filtered through a sintered glass funnel using Celite® as a filter aid. The product was isolated via flash chromatography using silica gel and hexanes to give 0.135 g of product (66.2%, based on *p*-methylphenylboronic acid). [melting point consistent with established literature value]

C.7.2. 4-Methylbiphenyl: (Reactant Ratio Study: 1.0 / 1.1)

4-Methylbiphenyl was prepared, as described previously (**C 6.1**), with *p*-methylphenylboronic acid (0.244 g, 1.79 mmol) and iodobenzene (0.410 g, 2.01 mmol). The product was isolated via flash chromatography using silica gel and hexanes to give 0.269 g of product (89.3%, based on *p*-methylphenylboronic acid). [melting point consistent with established literature value]

C.7.3. 4-Methylbiphenyl: (Reactant Ratio Study: 1.0 / 1.0)

4-Methylbiphenyl was prepared, as described previously (**C 6.1**), with *p*-methylphenylboronic acid (0.244 g, 1.79 mmol) and iodobenzene (0.383 g, 1.88 mmol). The product was isolated via flash chromatography using silica gel and hexanes to give 0.279 g of product (92.6%, based on *p*-methylphenylboronic acid). [melting point consistent with established literature value]

C.7.4. 4-Methylbiphenyl: (Reactant Ratio Study: 1.1 / 1.0)

4-Methylbiphenyl was prepared, as described previously (**C 6.1**), with *p*-methylphenylboronic acid (0.344 g, 2.82 mmol) and iodobenzene (0.512 g, 2.51 mmol). The product was isolated via flash chromatography using silica gel and hexanes to give 0.407 g of product (96.3%, based on iodobenzene). [m.p.44.1-45.8 °C]

C.7.5. 4-Methylbiphenyl: (Reactant Ratio Study: 1.3 / 1.0)

4-Methylbiphenyl was prepared, as described previously (**C 6.1**), with *p*-methylphenylboronic acid (0.178 g, 1.31 mmol) and iodobenzene (0.205 g, 1.00 mmol). The product was isolated via flash chromatography using silica gel and hexanes to give 0.162 g of product (96.0%, based on iodobenzene). [melting point consistent with established literature value]

C.7.6. 4-Methylbiphenyl: (Reactant Ratio Study: 1.5 / 1.0)

4-Methylbiphenyl was prepared, as described previously (**C 6.1**), with *p*-

methylphenylboronic acid (0.274 g, 2.01 mmol) and iodobenzene (0.278 g, 1.34 mmol). The product was isolated via flash chromatography using silica gel and hexanes to give 0.198 g of product (87.7%, based on iodobenzene). [melting point consistent with established literature value]

C.8.1. 4-Methylbiphenyl: (Palladium Study: 1% by weight)

To a mixture of KF/Al_2O_3 (0.991 g, 40 % by weight) and palladium black (0.011 g) was added *p*-methylphenylboronic acid (0.182 g, 1.34 mmol) in a clean dry round-bottomed flask. The solids were mechanically stirred in air at room temperature. Iodobenzene (0.233 g, 1.14 mmol) was added with stirring via dropping pipet directly onto the solid. The round-bottomed flask was then fitted with a condenser and placed in a preheated oil bath, Temp ≈ 100 °C. After four hours the oil bath was lowered and the reaction mixture allowed to cool to rt. A small amount of hexanes was then added through the condenser and the slurry stirred at rt. The slurry was then vacuum filtered through a sintered glass funnel using Celite® as a filter aid. The product was isolated via flash chromatography using silica gel and hexanes to give 0.136 g of product (70.5%). [melting point consistent with established literature value]

C.8.2. 4-Methylbiphenyl: (Palladium Study: 2% by weight)

4-Methylbiphenyl was prepared, as described previously (**C 8.1**), with *p*-methylphenylboronic acid (0.170 g, 1.26 mmol) and iodobenzene (0.228 g, 1.12 mmol)

on a prepared homogeneous mixture of KF/Al_2O_3 (0.983 g, 40 % by weight) and palladium black (0.021 g). The product was isolated via flash chromatography using silica gel and hexanes to give 0.143 g of product (76.1%). [melting point consistent with established literature value]

C.8.3. 4-Methylbiphenyl: (Palladium Study: 3% by weight)

4-Methylbiphenyl was prepared, as described previously (**C 8.1**), with *p*-methylphenylboronic acid (0.153 g, 1.13 mmol) and iodobenzene (0.209 g, 1.02 mmol) on a prepared homogeneous mixture of KF/Al_2O_3 (0.972 g, 40 % by weight) and palladium black (0.031 g). The product was isolated via flash chromatography using silica gel and hexanes to give 0.131 g of product (76.0%). [melting point consistent with established literature value]

C.8.4. 4-Methylbiphenyl: (Palladium Study: 4% by weight)

4-Methylbiphenyl was prepared, as described previously (**C 8.1**), with *p*-methylphenylboronic acid (0.154 g, 1.13 mmol) and iodobenzene (0.210 g, 1.03 mmol) on a prepared homogeneous mixture of KF/Al_2O_3 (0.962 g, 40 % by weight) and palladium black (0.041 g). The product was isolated via flash chromatography using silica gel and hexanes to give 0.167 g of product (94.2%). [melting point consistent with established literature value]

C.8.5. 4-Methylbiphenyl: (Palladium Study: 5% by weight)

4-Methylbiphenyl was prepared, as described previously (**C 8.1**), with *p*-methylphenylboronic acid (0.239 g, 1.76 mmol) and iodobenzene (0.223 g, 1.09 mmol) on a prepared homogeneous mixture of KF/Al_2O_3 (1.42 g, 40 % by weight) and palladium black (0.076 g). The product was isolated via flash chromatography using silica gel and hexanes to give 0.170 g of product (92.6%). [melting point consistent with established literature value]

C.9.1. 4-Methylbiphenyl: (Solvent Study: Hexanes)

To a mixture of KF/Al_2O_3 (0.951 g, 40 % by weight) and palladium black (0.049 g), *p*-methylphenylboronic acid (0.372 g, 2.74 mmol) was added in a clean dry round-bottomed flask. The solids were mechanically stirred in air at room temperature until homogeneous. Iodobenzene (0.351 g, 1.72 mmol) was then added with stirring via syringe followed by hexanes (≈6.5 mL). The loose slurry was stirred briefly at room temperature before being placed in a preheated oil bath, Temp = 80 °C. After 24 hrs, the oil bath was lowered and the reaction mixture allowed to cool to rt. The slurry was the vacuum filtered through a sintered glass funnel using Celite® as a filter aid. The product was isolated via flash chromatography using silica gel and hexanes to give 0.022 g of product (7.6%). [^{1}H NMR ($CDCl_3$/TMS) δ 7.42 (*m*, 9H) δ 2.38 (*s*, 3H)]

C.9.2. 4-Methylbiphenyl: (Solvent Study: THF)

4-Methylbiphenyl was prepared, as described previously (**C 9.1**), with THF used

as the solvent for a 17½-hour reaction time. The product was isolated via flash chromatography using silica gel and hexanes to give 0.247 g of product (74.6%). [melting point consistent with established literature value]

C.9.3. 4-Methylbiphenyl: (Solvent Study: Toluene)

4-Methylbiphenyl was prepared, as described previously (**C 9.1**), with toluene used as the solvent for a 20½-hour reaction time. The product was isolated via flash chromatography using silica gel and hexanes to give 0.150 g of product (45.3%). [melting point consistent with established literature value]

C.9.4. 4-Methylbiphenyl: (Solvent Study: H_2O)

4-Methylbiphenyl was prepared, as described previously (**C 9.1**), with water used as the solvent for a 4-hour reaction time. The product was isolated via flash chromatography using silica gel and hexanes to give 0.243 g of product (68.3%). [melting point consistent with established literature value]

C.9.5. 4-Methylbiphenyl: (Solvent Study: Acetone/H_2O)

4-Methylbiphenyl was prepared, as described previously (**C 9.1**), with acetone/water (1/1 v/v) as the solvent for a 4-hour reaction time. The product was isolated to give 0.156 g of product (93.8%). [melting point consistent with established literature value]

C.9.6. 4-Methylbiphenyl: (Solvent Study: MeOH/H_2O)

4-Methylbiphenyl was prepared, as described previously (**C 9.1**), with methanol/water (1/1 v/v) as the solvent for a 4-hour reaction time. The product was isolated to give 0.185 g of product (96.7%). [melting point consistent with established literature value]

C.9.7. 4-Methylbiphenyl: (Solvent Study: MeOH)

4-Methylbiphenyl was prepared, as described previously (**C 9.1**), with methanol used as the solvent for a 4-hour reaction time. The product was isolated to give 0.158 g of product (95.9%). [melting point consistent with established literature value]

D. 4,4'-dimethylbiphenyl:[118]

To a mixture of KF/Al_2O_3 (0.950 g, 40 % by weight) and palladium black (0.052 g), *p*-methylphenylboronic acid (0.394 g, 2.90 mmol) was added in a clean dry round-bottomed flask. The solids were mechanically stirred in air at room temperature for approximately 30 minutes. 4-Iodotoluene (0.435 g, 2.00 mmol) was then added with stirring via dropping pipet. After stirring, the round-bottomed flask was placed in a preheated oil bath, Temp = 80 °C. After two hours, the oil bath was lowered and the reaction mixture allowed to cool to rt. A small amount of hexanes was then added through the condenser and the slurry stirred at rt before being vacuum filtered through a sintered glass funnel using Celite®. The product was isolated via flash chromatography using silica gel and hexanes to give 0.250 g of product (68.5%). [^{1}H

NMR ($CDCl_3$/TMS) δ 7.48 (*d*, 4H) δ 7.23 (*d*, 4H) δ 2.38 (*s*, 6H)]

E. 4-Allyltoluene:[119]

To a mixture of KF/Al_2O_3 (0.959 g, 40 % by weight) and palladium black (0.053 g), *p*-methylphenylboronic acid (0.203 g, 1.49 mmol) was added in a clean dry round-bottomed flask. The solids were mechanically stirred in air at room temperature until homogeneous. Allyl iodide (0.204 g, 1.22 mmol) was then added with stirring via dropping pipet. After stirring, the round-bottomed flask was placed in a preheated oil bath, Temp = 100 °C. After four hours, the oil bath was lowered and the reaction mixture allowed to cool to rt. A small amount of hexanes was then added through the condenser and the slurry stirred at rt before being vacuum filtered through a sintered glass funnel using Celite®. The product was isolated via flash chromatography using silica gel and hexanes to give 0.063 g of product (39.4%). [^{1}H NMR ($CDCl_3$/TMS) δ 7.23 (*d*, 2H) δ 7.07 (*d*, 4H) δ 5.96 (*m*, 1H) δ 5.06 (*dd*, 2H) δ 3.34 (*d*, 2H) δ 2.31 (*s*, 3H)]

F. 1-(*p*-Methylphenyl)-1-propene:[120]

To a mixture of KF/Al_2O_3 (0.960 g, 40 % by weight) and palladium black (0.050 g), *p*-methylphenylboronic acid (0.159 g, 1.17 mmol) was added in a clean dry round-bottomed flask. The solids were mechanically stirred in air at room temperature until homogeneous. 1-Bromo-1-propene (0.123 g, 1.06 mmol, mixture of isomers) was then added with stirring via dropping pipet followed by MeOH (≈2.0 mL). After stirring at

room temperature, the round-bottomed flask was placed in a preheated oil bath, Temp = 100 °C. After four hours, the oil bath was lowered and the reaction mixture allowed to cool to rt. A small amount of hexanes was then added through the condenser and the slurry stirred at rt before being vacuum filtered through a sintered glass funnel using Celite®. *No* product was isolated by flash chromatography.

G. **1-(4-Methylphenyl)-2-butene:**[121]

To a mixture of KF/Al_2O_3 (0.958 g, 40 % by weight) and palladium black (0.052 g, 99.9+ %, submicron powder) was added *p*-methylphenylboronic acid (0.196 g, 1.44 mmol) in a clean dry round-bottomed flask, RBF. The solids were mechanically stirred in air at room temperature until homogeneous. Crotyl bromide (0.143 g, 1.06 mmol, tech. 85%, 15% 3-bromo-1-butene) was then added with stirring via dropping pipet. The reaction mix was stirred at room temperature for an additional 15-20 minutes before being placed in a preheated oil bath, Temp ≈ 100 °C. After four hours the oil bath was lowered and the reaction mixture allowed to cool to rt. A small amount, approximately 5-8 mL, of hexanes was then added directly through the condenser and stirred at rt for an additional 20-30 minutes. The slurry was vacuum filtered through a sintered glass funnel using Celite® as a filter aid. The product was isolated via flash chromatography using silica gel and hexanes to give 0.131 g of product (84.6%). [^{1}H NMR (mixture of $C_{11}H_{14}$ isomers) δ 7.08 (*d*, 8H) δ 5.98 (*m*, 1H) δ 5.52 (*m*, 1H) δ 5.02 (*m*, 2H) δ 3.40 (*m*, 1H) δ 3.26 (*d*, 1H) δ 2.29 (*s*, 6H) δ 1.68 (*m*, 2H) δ 1.34 (*d*, 3H)]

H.1. Butylbenzene:[122] (From 1-Iodobutane)

To a mixture of KF/Al_2O_3 (0.949 g, 40 % by weight) and palladium black (0.051 g), *p*-methylphenylboronic acid (0.166 g, 1.22 mmol) was added in a clean dry round bottomed flask. The solids were mechanically stirred in air at room temperature until homogeneous. 1-Iodobutane (0.157 g, 0.855 mmol) was then added with stirring via dropping pipet followed by MeOH(≈2.0 mL). After stirring at room temperature, the round bottomed flask was placed in a preheated oil bath, Temp = 100 °C. After four hours, the oil bath was lowered and the reaction mixture allowed to cool to rt. A small amount of hexanes was added through the condenser and the slurry stirred at rt before being vacuum filtered through a sintered glass funnel using Celite®. *No* product was isolated by flash chromatography.

H.2. Butylbenzene: (From 1-Bromobutane)

Butylbenzene was prepared, as described previously (**H.1**), with 1-bromobutane (0.138 g, 1.01 mmol) as the organohalide. This reaction was done without solvent however. *No* product was isolated by flash chromatography.

I. Hexylbenzene:[123]

Hexylbenzene was prepared, as described previously (**H.1**), with 1-iodohexane (0.248 g, 1.17 mmol) as the organohalide. *No* product was isolated by flash chromatography.

J. **4-Isopropyltoluene:**[124]

To a mixture of KF/Al_2O_3 (0.963 g, 40 % by weight) and palladium black (0.050 g, 99.9+ %, submicron powder) was added *p*-methylphenylboronic acid (0.202 g, 1.49 mmol) in a clean dry round-bottomed flask, RBF. The solids were mechanically stirred in air at room temperature until homogeneous. 2-Iodopropane (0.200 g, 1.18 mmol) was then added with stirring via dropping pipet followed by MeOH(≈2.0 mL). The reaction mix was stirred at room temperature for an additional 5-10 minutes before being placed in a preheated oil bath, Temp ≈ 100 °C. After four hours, the oil bath was lowered and the reaction mixture allowed to cool to rt. A small amount of hexanes was then added directly through the condenser and stirred at rt for an additional 10-20 minutes. The slurry was vacuum filtered through a sintered glass funnel using Celite® as a filter aid. *No* product was isolated by flash chromatography.

K. **4-Cyclohexyltoluene:**[125]

4-Cyclohexyltoluene was prepared, as described previously (J), with iodocyclohexane (0.212 g, 1.01 mmol) as the organohalide. *No* product was isolated by flash chromatography.

L. ***trans*-1-Phenyl-1-pentene: (Boronic Acid Survey: *trans*-1-pentenylboronic acid)**

To a mixture of KF/Al_2O_3 (0.956 g, 40 % by weight) and palladium black (0.051 g) was added *trans*-1-pentenylboronic acid (0.177 g, 1.18 mmol) in a clean dry round-

bottomed flask, RBF. The solids were mechanically stirred in air at room temperature until homogeneous. Iodobenzene (0.216 g, 1.06 mmol) was then added with stirring via dropping pipet. The reaction mix was stirred at room temperature for an additional 10-20 minutes before being placed in a preheated oil bath, Temp ≈ 100 °C. After 4½ hours, the oil bath was lowered and the reaction allowed to cool to rt. A small amount of hexanes was then added directly through the condenser and stirred at rt for an additional 20-30 minutes. The slurry was vacuum filtered through a sintered glass funnel using Celite® as a filter aid. The product was isolated via chromatography using silica gel and hexanes to give 0.155 g of product (81.2%). [^{1}H NMR ($CDCl_3$/TMS) δ7.69 (*d*, 2H) δ 7.27 (*m*, 3H) δ 6.43 (*d*, 1H) δ 6.16 (*m*, 1H) δ 2.16 (*m*, 2H) δ 1.48 (*m*, 2H) 0.90 (*t*, 3H)]

M. 3-Phenyl-1-propene:[126] (Boronic Acid Survey: Allylboronic Acid)

3-Phenyl-1-propene was prepared, as described previously (**L**), with allylboronic acid (0.70 mL, ~1.5 mmol, ~2.1M in Et_2O, Solvent removed under vacuum) as the boronic species. *No* product was isolated by flash chromatography.

N. Butylbenzene: (Boronic Acid Survey: Butylboronic acid)

To a mixture of KF/Al_2O_3 (0.959 g, 40 % by weight) and palladium black (0.060 g) was added butylboronic acid (0.137 g, 1.22 mmol) in a clean dry round-bottomed flask, RBF. The solids were mechanically stirred in air at room temperature until homogeneous. Iodobenzene (0.210 g, 1.03 mmol) was then added with stirring

via dropping pipet. The reaction mix was stirred at room temperature for an additional 10-20 minutes before being placed in a preheated oil bath, Temp ≈ 100 °C. After four hours, the oil bath was lowered and the reaction mixture allowed to cool to rt. A small amount of hexanes was then added directly through the condenser and stirred at rt for an additional 20-30 minutes. The slurry was vacuum filtered through a sintered glass funnel using Celite® as a filter aid. The product was isolated via flash chromatography using silica gel and hexanes to give 0.050 g of product (35.9%). [^{1}H NMR ($CDCl_3$/TMS) δ 7.31 (*m*, 5H) δ 2.54 (*t*, 2H) δ 1.51 (*m*, 2H) δ 1.29 (*m*, 2H) δ 0.84 (*t*, 3H)]

O. General Procedures for All Successive Trials Reactions:

O.1.1. <u>4-Methylbiphenyl</u>: (From Bromobenzene, Trial #1)

To a mixture of KF/Al_2O_3 (0.953 g, 40 % by weight) and palladium black (0.050 g) was added *p*-methylphenylboronic acid (0.398 g, 3.26 mmol) in a clean dry round-bottomed flask. The solids were mechanically stirred in air at room temperature until homogeneous. Bromobenzene (0.464 g, 2.96 mmol) was then added with stirring via dropping pipet. The reaction mix was stirred at room temperature for an additional 30-45 minutes before being placed in a preheated oil bath, Temp ≈ 80 °C. After three hours, the oil bath was lowered and the reaction mixture allowed to cool to rt. A small amount of hexanes was then added directly through the condenser and stirred at rt for an additional 20-30 minutes. The solvent was decanted from the solid. The

product was isolated via chromatography using silica gel and hexanes to give 0.362 g of product (71.0%). [m.p. 44.1-45.8 °C]

O.1.2. 4-Methylbiphenyl: (From Bromobenzene, Trial #2)

The recovered solid from trial #1 (**O.1.1**) was dried overnight under vacuum. *p*-Methylphenylboronic acid (0.272 g, 2.00 mmol) was then added with stirring followed by bromobenzene (0.305 g, 1.94 mmol). After stirring the round-bottomed flask was placed in a preheated oil bath, Temp ≈ 80 °C. After three hours, the oil bath was lowered and the reaction mixture allowed to cool to rt. A small amount of hexanes (7 mL) was then added directly through the condenser and stirred at rt for an additional 20 minutes. The solvent was decanted from the solid. The product was isolated via chromatography using silica gel and hexanes to give 0.055 g of product (16.9%). [m.p. 44.0-45.3 °C]

O.1.3. 4-Methylbiphenyl: (From Bromobezene, Trial #3)

4-Methylbiphenyl was prepared, as described previously (**O.1.2**), with bromobenzene (0.317 g, 2.02 mmol) and *p*-methylphenylboronic acid (0.304 g, 2.24 mmol). However, the solvent slurry was vacuum filtered through a sintered glass funnel using Celite® as a filter aid. The product was isolated via flash chromatography using silica gel and hexanes to give 0.023 g of product (6.6%). [melting point consistent with established literature value]

O.2.1. 4-Methylbiphenyl: (Dry KF Addition, Trial #1)

To a mixture of KF/Al_2O_3 (0.950 g, 40 % by weight) and palladium black (0.055 g) was added *p*-methylphenylboronic acid (0.162 g, 1.19 mmol) in a clean dry round-bottomed flask. The solids were mechanically stirred in air at room temperature until homogeneous. Iodobenzene (0.215 g, 1.05 mmol) was then added with stirring via dropping pipet. The reaction mix was stirred at room temperature for an additional 5-15 minutes before being placed in a preheated oil bath, Temp ≈ 100 °C. After four hours, the oil bath was lowered and the reaction mixture allowed to cool to rt. A small amount of hexanes was then added directly through the condenser and stirred at rt for an additional 10-20 minutes. The solvent was decanted from the solid. The product was isolated via chromatography using silica gel and hexanes to give 0.161 g of product (91.1%). [melting point consistent with established literature value]

O.2.2. 4-Methylbiphenyl: (Dry KF Addition, Trial #2)

The recovered solid from trial #1 (**O.2.1**) was dried overnight under vacuum. *p*-Methylphenylboronic acid (0.158 g, 1.16 mmol) was then added with stirring followed by iodobenzene (0.212 g, 1.03 mmol). After stirring the round-bottomed flask was placed in a preheated oil bath, Temp ≈ 100 °C. After four hours, the oil bath was lowered and the reaction mixture allowed to cool to rt. A small amount of hexanes was then added directly through the condenser and stirred at rt for an additional 10-20 minutes. The solvent was decanted from the solid. The product was isolated via chromatography using silica gel and hexanes to give 0.069 g of product (39.7%).

[melting point consistent with established literature value]

O.2.3. 4-Methylbiphenyl: (Dry KF Addition, Trial #3)

4-Methylbiphenyl was prepared, as described previously (**O.2.2**), with iodobenzene (0.205 g, 1.01 mmol) and *p*-methylphenylboronic acid (0.168 g, 1.23 mmol). However, the solvent slurry was vacuum filtered through a sintered glass funnel using Celite® as a filter aid. The product was isolated via flash chromatography using silica gel and hexanes to give 0.107 g of product (63.0%). [melting point consistent with established literature value]

O.3.1. 4-Methylbiphenyl: (Reaction Time: MeOH Slurry, 1 Hour)

To a mixture of KF/Al_2O_3 (0.960 g, 40 % by weight) and palladium black (0.055 g) was added *p*-methylphenylboronic acid (0.158 g, 1.16 mmol) in a clean dry round-bottomed flask. The solids were mechanically stirred in air at room temperature until homogeneous. Iodobenzene (0.209 g, 1.03 mmol) was then added with stirring via dropping pipet followed by methanol (1.5 mL). The reaction flask was placed in a preheated oil bath, Temp ≈ 100 °C. After one hour, the oil bath was lowered and the reaction mixture allowed to cool to rt. A small amount of hexanes was then added directly through the condenser and stirred at rt for an additional 5-10 minutes. The slurry was vacuum filtered through a sintered glass funnel using Celite® as a filter aid. The product was isolated via chromatography using silica gel and hexanes to give 0.159 g of product (92.2%). [melting point consistent with established literature value]

O.3.2. 4-Methylbiphenyl: (Reaction Time: MeOH Slurry, 2 Hour)

4-Methylbiphenyl was prepared, as described previously (**O.3.1**), with iodobenzene (0.205 g, 1.00 mmol) and *p*-methylphenylboronic acid (0.157 g, 1.16 mmol) for a two-hour time period. The product was isolated via chromatography using silica gel and hexanes to give 0.164 g of product (97.5%). [melting point consistent with established literature value]

O.3.3. 4-Methylbiphenyl: (Reaction Time: MeOH Slurry, 3 Hour)

4-Methylbiphenyl was prepared, as described previously (**O.3.1**), with iodobenzene (0.204 g, 1.00 mmol) and *p*-methylphenylboronic acid (0.170 g, 1.25 mmol) for a three-hour time period. The product was isolated via chromatography using silica gel and hexanes to give 0.137 g of product (82.5%). [melting point consistent with established literature value]

O.3.4. 4-Methylbiphenyl: (Reaction Time: MeOH Slurry, 4 Hour)

See (**C.9.7**)

O.3.5. 4-Methylbiphenyl: (Reaction Time: MeOH Slurry, 24 Hour rt)

4-Methylbiphenyl was prepared, as described previously (**O.3.1**), with iodobenzene (0.202 g, 0.988 mmol) and *p*-methylphenylboronic acid (0.149 g, 1.10 mmol) for a 24-hour time period at room temperature. The product was isolated via chromatography using silica gel and hexanes to give 0.038 g of product (22.9%).

[melting point consistent with established literature value]

O.3.6. 4-Methylbiphenyl: (Reaction Time: MeOH Slurry, 72 Hour rt)

4-Methylbiphenyl was prepared, as described previously (**O.3.1**), with iodobenzene (0.204 g, 0.998 mmol) and *p*-methylphenylboronic acid (0.162 g, 1.19 mmol) for a 72-hour time period at room temperature. The product was isolated via chromatography using silica gel and hexanes to give 0.152 g of product (90.8%). [melting point consistent with established literature value]

O.4.1. 4-Methylbiphenyl: (KF Addition: MeOH Slurry, Trial #1)

To a mixture of KF/Al_2O_3 (0.956 g, 40 % by weight) and palladium black (0.053 g) was added *p*-methylphenylboronic acid (0.170 g, 1.25 mmol) in a clean dry round-bottomed flask. The solids were mechanically stirred in air at room temperature until homogeneous. Iodobenzene (0.208 g, 1.02 mmol) was then added with stirring via dropping pipet followed by methanol (≈1.5mL). The reaction flask was placed in a preheated oil bath, Temp ≈ 100 °C. After four hours, the oil bath was lowered and the reaction mixture allowed to cool to rt. A small amount of hexanes was then added directly through the condenser with stirring. The solvent was decanted. The product was isolated via chromatography using silica gel and hexanes to give 0.172 g of product (98.0%). [melting point consistent with established literature value]

O.4.2. 4-Methylbiphenyl: (KF Addition: MeOH Slurry, Trial #2)

The recovered solid from trial #1 (**O.4.1**) was dried for 3-4 hours under vacuum at rt. *p*-Methylphenylboronic acid (0.172 g, 1.27 mmol) was then added with stirring followed by iodobenzene (0.214 g, 1.05 mmol). After addition of MeOH (1.5 mL) the round-bottomed flask was placed in a preheated oil bath, Temp ≈ 100 °C. After four hours, the oil bath was lowered and the reaction mixture allowed to cool to rt. A small amount of hexanes was then added directly through the condenser with stirring. The solvent was decanted. The product was isolated via flash chromatography using silica gel and hexanes to give 0.125 g of product (70.6%). [melting point consistent with established literature value]

O.4.3. 4-Methylbiphenyl: (KF Addition: MeOH Slurry, Trial #3)

4-Methylbiphenyl was prepared, as described previously (**O.4.2**), with the addition of KF (0.400 g, 6.88 mmol) to the recovered solid with stirring. Iodobenzene (0.215 g, 1.05 mmol) and *p*-methylphenylboronic acid (0.170 g, 1.25 mmol) were then added with MeOH (1.5 mL). The product was isolated using silica gel and hexanes to give 0.175 g of product (98.9%). [melting point consistent with established literature value]

O.4.4. 4-Methylbiphenyl: (KF Addition: MeOH Slurry, Trial #4)

4-Methylbiphenyl was prepared, as described previously (**O.4.2**), with iodobenzene (0.217 g, 1.06 mmol) and *p*-methylphenylboronic acid (0.163 g, 1.20 mmol). The product was isolated via chromatography using silica gel and hexanes to

give 0.170 g of product (95.4%). [melting point consistent with established literature value]

O.4.5. 4-Methylbiphenyl: (KF Addition: MeOH Slurry, Trial #5)

4-Methylbiphenyl was prepared, as described previously (**O.4.2**), with iodobenzene (0.208 g, 1.02 mmol) and *p*-methylphenylboronic acid (0.169 g, 1.24 mmol). The product was isolated via chromatography using silica gel and hexanes to give 0.144 g of product (84.1%). [m.p. 43.8-44.9 °C]

O.5.1. 4-Methylbiphenyl: (KF Addition: MeOH Wash, Trial #1)

To a mixture of KF/Al_2O_3 (0.961 g, 40 % by weight) and palladium black (0.051 g) was added *p*-methylphenylboronic acid (0.154 g, 1.14 mmol) in a clean dry round-bottomed flask. The solids were mechanically stirred in air at room temperature until homogeneous. Iodobenzene (0.211 g, 1.04 mmol) was then added with stirring via dropping pipet. The reaction flask was placed in a preheated oil bath, Temp ≈ 100 °C. After four hours, the oil bath was lowered and the reaction mixture allowed to cool to rt. A small amount of hexanes was then added directly through the condenser with stirring. The solvent was decanted. The product was isolated using silica gel and hexanes to give 0.165 g of product (94.6%). [melting point consistent with established literature value]

O.5.2. 4-Methylbiphenyl: (KF Addition: MeOH Wash, Trial #2)

The recovered solid from trial #1 (**O.5.1**) was dried 1-2 hours under vacuum. *p*-Methylphenylboronic acid (0.157 g, 1.16 mmol) was then added with stirring followed by iodobenzene (0.209 g, 1.02 mmol). After stirring, the round-bottomed flask was placed in a preheated oil bath, Temp ≈ 100 °C. After four hours, the oil bath was lowered and the reaction mixture allowed to cool to rt. A small amount of hexanes was then added directly down the condenser and stirred at rt for an additional 10-20 minutes. The solvent was decanted. The product was isolated via flash chromatography using silica gel and hexanes to give 0.058 g of product (33.7%). [melting point consistent with established literature value]

O.5.3. 4-Methylbiphenyl: (KF Addition: MeOH Wash, Trial #3)

To the recovered, dried solid from trial #2 (**O.5.2**) was added KF (0.398 g, 6.85 mmol) in MeOH (≈10 mL). The mixture was stirred overnight. The solvent was removed under vacuum and the dried solid physically manipulated, with some difficulty, to a powdery consistency. *p*-Methylphenylboronic acid (0.156 g, 1.15 mmol) was then added with stirring followed by iodobenzene (0.212 g, 1.04 mmol). The reaction flask was placed in a preheated oil bath, Temp ≈ 100 °C. After four hours, the oil bath was lowered and the reaction mixture allowed to cool to rt. A small amount of hexanes was then added directly down the condenser with stirring. The slurry was vacuum filtered through a sintered glass funnel using Celite® as a filter aid. The product was isolated using silica gel and hexanes to give 0.169 g of product (96.5%). [melting point consistent with established literature value]

O.6.1. 4-Methylbiphenyl: (KF Addition: MeOH Slurry, No Al_2O_3 Trial #1)

To a mixture of KF (0.405 g) and palladium black (0.052 g) was added *p*-methylphenylboronic acid (0.154 g, 1.14 mmol) in a clean dry round-bottomed flask. The solids were mechanically stirred in air at room temperature until homogeneous. Iodobenzene (0.214 g, 1.05 mmol) was then added via dropping pipet followed by MeOH (1.5 mL) with stirring. The reaction flask was placed in a preheated oil bath, Temp ≈ 100 °C. After four hours, the oil bath was lowered and the reaction mixture allowed to cool to rt. A small amount of hexanes was then added directly through the condenser with stirring. The solvent was decanted. The product was isolated using silica gel and hexanes to give 0.166 g of product (94.2%). [melting point consistent with established literature value]

O.6.2. 4-Methylbiphenyl: (KF Addition: MeOH Slurry, No Al_2O_3 Trial #2)

The recovered solid from trial #1 (**O.6.1**) was dried overnight under vacuum at rt After physical agitation, *p*-Methylphenylboronic acid (0.184 g, 1.35 mmol) was added followed by iodobenzene (0.217 g, 1.06 mmol) and MeOH (≈1.5 mL). After stirring the round-bottomed flask was placed in a preheated oil bath, Temp ≈ 100 °C. After four hours, the oil bath was lowered and the reaction allowed to cool to rt. A small amount of hexanes was then added directly down the condenser and stirred for an additional 10-20 minutes. The solvent was decanted from the solid. The product was isolated via chromatography using silica gel and hexanes to give 0.153 g of product (85.8%). [melting point consistent with established literature value]

O.6.3. 4-Methylbiphenyl: (KF Addition: MeOH Slurry, No Al_2O_3 Trial #3)

To the recovered, dried solid from trial #2 (**O.6.2**) was added KF (0.402 g, 6.92 mmol) followed by *p*-methylphenylboronic acid (0.156 g, 1.14 mmol). The solids were mechanically stirred in air at room temperature until homogeneous. Iodobenzene (0.216 g, 1.06 mmol) was then added via dropping pipet followed by MeOH (1.5 mL). After stirring, the round-bottomed flask was placed in a preheated oil bath, Temp ≈ 100 °C. After four hours, the oil bath was lowered and the reaction mixture allowed to cool to rt. A small amount of hexanes was then added directly down the condenser and stirred at rt for an additional 10-20 minutes. The solvent was decanted. The product was isolated using silica gel and hexanes to give 0.176 g of product (98.7%). [melting point consistent with established literature value]

O.6.4. 4-Methylbiphenyl: (KF Addition: MeOH Slurry, No Al_2O_3 Trial #4)

4-Methylbiphenyl was prepared, as described previously (**O.6.2**), with iodobenzene (0.231 g, 1.13 mmol) and *p*-methylphenylboronic acid (0.169 g, 1.24 mmol). The product was isolated using silica gel and hexanes to give 0.182 g of product (95.1%). [melting point consistent with established literature value]

O.6.5. 4-Methylbiphenyl: (KF Addition: MeOH Slurry, No Al_2O_3 Trial #5)

4-Methylbiphenyl was prepared, as described previously (**O.6.2**), with iodobenzene (0.210 g, 1.03 mmol) and *p*-methylphenylboronic acid (0.168 g, 1.23 mmol). The product was isolated via flash chromatography using silica gel and

hexanes to give 0.136 g of product (78.6%). [melting point consistent with established literature value]

P. General Procedure for All Microwave Reactions:

P.1 4-Methylbiphenyl: (Microwave Reaction: 1.0 min)

To a mixture of KF/Al_2O_3 (0.956 g , 40 % by weight) and Pd black (0.054 g, 99.9+ %, submicron powder) was added *p*-methylphenylboronic acid (0.205 g, 1.51 mmol) in a clean dry round-bottomed flask, RBF. These three solids were mechanically stirred in air at room temperature until homogeneous. Iodobenzene (0.278 g, 1.36 mmol) was then added with stirring via dropping pipet directly onto the solid. The mixture was stirred at room temperature for an additional 15-20 minutes to ensure complete mixing. The metallic, Teflon®-encased stir bar was then removed. The round-bottomed flask was then fitted with a punctured septum, to allow pressurized gases to escape, encased between two small cork rings, one upright one inverted, for stability, and placed on the revolving plate of a standard microwave (Sharp, Model R-4A38, 1000 watts, 2450 Mhz). The reaction flask was irradiated on "HIGH" (Power level = 100%) for one minute. After cooling to rt, a clean Teflon® stir bar was added with a small amount, ≈6 ml, of hexanes. After stirring at room temperature for 1-2 hours, the slurry was vacuum filtered through a sintered glass funnel using Celite® as a filter aid. The product was isolated via flash chromatography using silica gel and hexanes to give 0.160 g of product (69.9%).

[m.p. 44.8-45.9 °C]

P.2 4-Methylbiphenyl: (Microwave Reaction: 1.5 min)

4-Methylbiphenyl was prepared, as described previously (**P.1**), with iodobenzene (0.210 g, 1.03 mmol) and *p*-methylphenylboronic acid (0.150 g, 1.10 mmol). The product was isolated via flash chromatography using silica gel and hexanes to give 0.146 g of product (84.4%). [melting point consistent with established literature value]

P.3 4-Methylbiphenyl: (Microwave Reaction: 2.0 min)

4-Methylbiphenyl was prepared, as described previously (**P.1**), with iodobenzene (0.214 g, 1.05 mmol) and *p*-methylphenylboronic acid (0.151 g, 1.11 mmol). The product was isolated via flash chromatography using silica gel and hexanes to give 0.142 g of product (80.9%). [melting point consistent with established literature value]

P.4 4-Methylbiphenyl: (Microwave Reaction: 2.5 min)

4-Methylbiphenyl was prepared, as described previously (**P.1**), with iodobenzene (0.211 g, 1.04 mmol) and *p*-methylphenylboronic acid (0.165 g, 1.21 mmol). The product was isolated via flash chromatography using silica gel and hexanes to give 0.154 g of product (88.4%). [melting point consistent with established literature value]

P.5 4-Methylbiphenyl: (Microwave Reaction: 3.0 min)

4-Methylbiphenyl was prepared, as described previously (**P.1**), with iodobenzene

(0.212 g, 1.04 mmol) and *p*-methylphenylboronic acid (0.160 g, 1.18 mmol). The product was isolated via chromatography using silica gel and hexanes to give 0.141 g of product (80.3%). [melting point consistent with established literature value]

Materials:

Gases

Argon (prepurified), MG Industries

Nitrogen (prepurified), MG Industries

NMR Solvent

Chloroform-d, Aldrich Chemical Company

Reagents

Allyl iodide, Aldrich Chemical Company

Alumina, Brockmann activity I-neutral, Fisher Scientific

Alumina, Brockmann activity I-basic, Fisher Scientific

Bromobenzene, Fisher Scientific

1-Bromobutane, Aldrich Chemical Company

trans-2-Bromo-2-butene, Aldrich Chemical Company

trans-1-Bromo-1-propene, Aldrich Chemical Company

4-Bromotoluene, Aldrich Chemical Company

Chlorobenzene, Fisher Scientific

Celite, Aldrich Chemical Company

Crotyl bromide, Aldrich Chemical Company

Cyclohexyl iodide, Aldrich Chemical Company

Fluorobenzene, Aldrich Chemical Company

Iodobenzene, Aldrich Chemical Company

1-Iodobutane, Aldrich Chemical Company

1-Iodohexane, Aldrich Chemical Company

2-Iodopropane, Aldrich Chemical Company

4-Iodotoluene, Aldrich Chemical Company

Palladium black (99.9+%, submicron powder), Aldrich Chemical Company

Potassium Carbonate, Fisher Scientific

Potassium Fluoride, Aldrich Chemical Company

Potassium Fluoride, 40% on Alumina, Aldrich Chemical Company

Potassium Phosphate tribasic, Fisher Scientific

Silica Gel (230-400 mesh, ASTM 60 Å), ICN Silitech

Sodium Fluoride, Fisher Scientific

Sodium Hydroxide, Fisher Scientific

Solvents

Acetone, Fisher Scientific

Diethyl Ether, Fisher Scientific

Hexanes, Fisher Scientific

Methanol (reagent grade), Fisher Scientific

Toluene, Aldrich Chemical Company

THF, Fisher Scientific

LIST OF REFERENCES

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