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PALLADIUM CATLYZED REDUCTIONS BY FLUORIDE
ACTIVATED POLYMETHYLHYROSILOXANE (PMHS)

presented by

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has been accepted towards fulfillment
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M.S. degree in Chemistry

Robert E Maleczka

Major Professor's Signature

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Date

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PALLADIUM CATALYZED REDUCTIONS BY FLUORIDE ACTIVATED POLYMETHYLHYDROSILOXANE (PMHS)

By

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ABSTRACT

PALLADIUM CATALYZED REDUCTIONS BY FLUORIDE ACTIVATED POLYMETHYLHYDROSILOXANE (PMHS)

By

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We initiated a synthetic venture aimed at developing methodology for the hydrodehalogenation of organic halides. A mild, selective, and efficient method for the reduction of aryl bromides and iodides catalyzed by $Cl_2Pd(PPh_3)_2$ and using hypercoordinate polymethylhydrosiloxane was developed. The limitation of this method to hydrodehalogenate aryl chlorides motivated the screening of phosphine free palladium catalyst. This screening led to the finding that a catalytic amount of palladium(II) acetate in combination with PMHS and aqueous KF will rapidly hydrodehalogenate aryl chlorides at room temperature.

To my father, sister, and nephews,
Dr. Ronald J. Rahaim, Jeanette Rahaim Sommer, Brian Sommer, and Dustin Sommer.

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LIST OF ABBREVIATIONS

Ac	acetyl
acac	acetylacetonate
AIBN	2,2'-azobisisobutyronitrile
aq.	aqueous
CCl_4	carbon tetrachloride
$Cl_2Pd(PPh_3)_2$	dichlorobis(triphenylphosphine)palladium(II)
dba	dibenzylideneacetone
DMF	N,N-dimethylformamide
DMSO	dimethyl sulfoxide
eq.	equivalent
g	gram
h	hour
KF	pottasium fluoride
LAH	lithium aluminum hydride
m	minutes
M	molar
mL	milliliter
mmol	millimole
P	product
$Pd(OAc)_2$	palladium(II) acetate
Ph	phenyl
PMHS	polymethylhydrosiloxane

r.b.	round bottom
r.t.	room temperature
R.T.	retention time
S.M.	starting material
THF	tetrahydrofuran

Chapter 1. Introduction and Prior Work

The formation of arenes from aryl halides represents an important chemical transformation in environmental clean up[1] and organic synthesis.[2] A plethora of reagents and systems have been developed for universal or reaction specific applications: elimination of PBB's (polybromobiphenyls) and/or PCB's (polychlorobiphenyls),[3] chemoselective deuterium labeling,[4] and reduction of halides that are used as directing or protective groups.[2] Organic halides follow the general order I > Br > Cl >> F for ease of dehalogenation. The dissociation energy of carbon-halogen bonds (C-I, 53 kcal/mol; C-Br, 67 kcal/mol; C-Cl, 81 kcal/mol; C-F, 109 kcal/mol) usually explains the order of dehalogenation. These differences in dissociation energy have made it possible to perform selective hydrodehalogenations of specific halides. There is also a trend in ease of dehalogenation based on structure of the substrate. Carbon-halogen bond cleavage is favored in the order benzylic > allylic > vinylic > aromatic > aliphatic. Dehalogenation via catalytic and transfer hydrogenation,[5,6] oxidative methods,[7] metal catalyzed hydride delivery,[5,8,9,10,11,12] and also under free radical conditions[5,13] are among the common ways to perform such hydrodehalogenations.

1.1. Catalytic and Transfer Hydrogenation

A variety of transition metals have been used as catalysts in hydrogenolysis reactions; nickel and palladium are the two most commonly employed catalysts.[2,5] Hydrogenolysis reactions can take place in either gas or liquid-phase, with the hydrogen source being molecular hydrogen (H_2) or a hydrogen donor (formate salts, hypophosphite salts, aliphatic alcohols, etc.). Typically these reactions are run in the presence of a base, ranging from alkali(ne) hydroxides to sodium acetate, amines, and ammonia for more

base-labile compounds. Halogenated acids are produced in the course of these reactions. Thus the role of the base additive is to buffer the reaction mixture and mop up the halide, thereby keeping the catalyst in its reduced state. Palladium catalysts are less susceptible to poisoning by the halide ion than other transition metal systems. The reaction conditions for catalytic and transfer hydrogenation vary widely, and the reaction mechanism may not follow a unified pathway.

1.2. Oxidative and Metal Catalyzed Hydride Delivery

Two methods are available for oxidative dehalogenation, via microorganisms[7] or transition metal catalyses.[7] The microorganism method uses enzymes to catalyze the dehalogenation reaction. Oxidative dehalogenation of chlorinated compounds is difficult with microorganisms due to the high redox potential of chlorine. To overcome this limitation a few transition metal catalysts have been developed for oxidative dehalogenation. The typical transition metals employed are Co, Fe, Mn, Rh, and Ru; which can be used as stoichiometric oxidizing agents or catalytically in the presence of a secondary oxidant (periodate, hypochlorite, Oxone®, etc.). Catalysts available for oxidative dehalogenation range from very simple complexes such as Fenton's reagent ($FeSO_4 + H_2O_2$), to metals incorporated in porphyrins.

Metal catalyzed hydride delivery[5,8-12] in dehalogenation reactions can be accomplished by a large number of catalysts developed from transition metals, in conjunction with a hydride source. Traditional hydride sources utilized are lithium aluminum hydride and sodium borohydride. Trialkyltin hydrides with a radical scavenger have been employed successfully in dehalogenation via metal catalyzed hydride delivery, along with a variety of silicon hydrides. This type of dehalogenation

generally proceeds by oxidative addition of the carbon halogen bond to the reduced form of the catalyst, followed by hydride transfer with the halogen on the metal. The halogen ion is countered by the metal of the hydride source to form a salt. The hydride on the metal center then under goes reductive elimination to afford the dehalogenated compound.

1.3. Free Radical

A hand full of reagents can be used for free radical dehalogenation, ranging from dissolving metal methods,[2,5] low-valent metal salts,[2,5] to main group hydrides (IIIA and IVA).[13] Alkali (Li, Na, K, Na-K alloy), alkaline earth (Mg, Ca, Ba), and transition metals (Zn, Fe) have been used in dissolving metal methods. These metals are typically dissolved in liquid ammonia or acetic acid, with the reaction being run in the presence of an alcohol additive. Dissolving metal reductions proceed by an electron transfer to the solvent then to the substrate, forming a radical anion. The alcohol donates a proton to the radical anion affording a radical intermediate, which is then reduced by the metal to a carbanion. The dehalogenated product is yielded by another proton abstraction of the alcohol by the carbanion. This method of dehalogenation usually results in side reactions yielding mixtures of products.

Of all of the low-valent metal salts that reduce halides, only chromium(II) salts involve a radical process.[5] Reductive dehalogenation reactions with chromium(II) salts are carried out in polar solvents (DMF or DMSO), usually with a chelating additive such as ethylenediamine or ethanolamine to enhance the reducing ability. As typical of a radical process, reductions with Cr^{II} salts is accompanied by side reactions, which can be suppressed with hydrogen donor additives, such as thiols.

The most common method for free radical dehalogenation[2,5,13] is with trialkyltin hydrides. Depending on the halogen being reduced, trialkytin hydride can be used in absence of solvent and without a radical initiator. However, most reactions of this type are generally run in the presence of a radical initiator. UV irradiation or thermal initiation are two methods used to initiate the radical reaction, but use of a chemical initiator such as, AIBN, is the most common means of free radical initiation. Unlike the previous methods discussed, R_3SnH dehalogenations are highly chemoselective, but side reactions can occur depending on the halogenated substrate, i.e. cyclizations, hydrogen atom abstraction, etc.

Drawbacks to using R_3SnH include the toxicity of tin and difficulty in purification. Partially motivated by these drawbacks, germanium, silicon, and indium hydride have been investigated as tin alternatives in free radical reactions. Germanium hydrides are not as toxic as tin hydrides, but the free radical dehalogenations are slower and the germanium reagents are more expensive. Most silicon hydrides are inexpensive and nontoxic, but the rate of dehalogenation is slower than in germanium hydride reactions, and much slower than in tin hydride reactions. The use of silicon hydrides also requires the use of large quantities of radical initiator and high reaction temperatures to produce high conversions. A major problem is that silicon hydrides in radical reactions are complicated by non-radical hydride chemistry. Dichloroindium hydride has recently been demonstrated to reduce some halides via a radical pathway; transmetalation between indium trichloride and a trialkyltin hydride generated the indium hydride.

1.4. Use of PMHS As a Hydride Source

Polymethylhydrosiloxane (PMHS)[14] has been available for over fifty years, with

the first synthesis reported in 1946 by Sauer.[15] Since its discovery PMHS has demonstrated itself as an air and moisture stable, non-toxic, and easily handled reducing reagent. The additional benefits of low cost, relative inertness toward organic functionality, and the ability to transfer its hydride to a variety of metal catalyst (including Sn, Ti, Zn, Cu, and Pd) that can then participate in a wide range of reductions, make PMHS an attractive alternative to more expensive or hazardous reducing agents. PMHS is used most frequently in trialkyltin hydride synthesis; first accomplished by Hayashi from the corresponding tin oxide species.[14a]

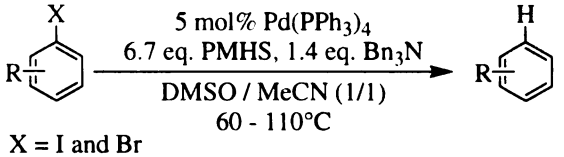
Preparation of tin hydrides, via reduction of the tin halides by PMHS alone, can not be accomplished. Our group theorized and proved that the fluorophilic nature of silicon could be taken advantage and that the action of KF can make PMHS hypercoordinate, thereby increasing the reducing properties of PMHS. Thus PMHS/KF efficiently converts organic tin halides to organic tin hydrides.[16] The in situ generation and reaction of trialkyltin hydride in subsequent chemical transformations was also studied. The combination of Bu_3SnCl, aqueous KF, and PMHS, performed well in free-radical dehalogenations, along with other "classical" tin hydride reactions. These reactions were also run with catalytic amounts of tin by recycling the tin halide byproduct. With these results in hand the PMHS, aqueous KF, catalytic Bu_3SnCl combination was successfully applied to a one-pot palladium catalyzed hydrostannlyation / Stille coupling.[17] While developing this protocol there was concern about side reactions, such as reduction of the halogen electrophile. Control reactions run to evaluate the degree of the side reactions, indicated that reduction of the halogen electophile could

be a problem. Fortunately for the Stille methodology the results of these studies showed hydrodehalogenations could be minimized. However, these experiments also suggested that an optimized combination PMHS, aqueous KF, and a palladium catalyst may be capable of efficiently performing hydrodehalogenation reactions.

Chapter 2. $Cl_2Pd(PPh_3)_2$ Mediated Reductions of Iodo and Bromoarenes

In 1986, Pri-Bar and Buchman[9b] reported that PMHS in the presence of a Pd(0) catalyst could effectively reduce aryl, styryl, and α-keto halides (Scheme 1). Milder than LAH, $NaBH_4$, etc., PMHS is air and moisture stable, soluble in a number of organic solvents, relatively non-toxic, and inexpensive.[14] Unfortunately, use of this attractive reductant in hydrodehalogenation also required the employment of excess tribenzylamine, relatively high boiling and polar solvents (DMSO/MeCN), elevated temperatures, and fairly high loads (5 mol%) of $Pd(PPh_3)_4$. As fluoride activation of PMHS is known,[14a,16,18] it was decided to investigate if a combination of PHMS and fluoride would facilitate aryl halide reductions and thereby minimize some of the disadvantages posed by the original protocol.

Scheme 1. Pri-Bar and Buchman's System

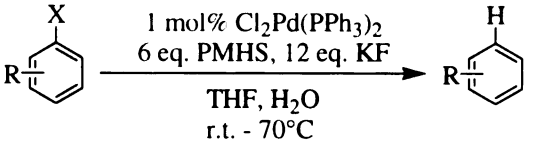


X = I and Br

R = aryl, Cl, styryl, α-keto, ketone, aldehyde, carboxylic acid, nitro

Screening various catalyst, solvent, stoichiometry, fluoride sources, and reaction temperature combinations revealed that like the original conditions ~6 equiv. of PMHS worked best (Scheme 2).[9a] Importantly though, adding 12 equiv. of KF (aq.) to the reaction obviated the need for tribenzylamine, allowed the Pd-loading to be reduced from 5 to 1 mol%, and facilitated the reactions so that they could now be performed in THF at 70°C or lower (Table 1). Fluoride clearly promoted these reductions. Control experiments run in the absence of KF saw yields diminish by ~80% for the aryl bromides to ~30% for the aryl iodides.[19]

Scheme 2. $Cl_2Pd(PPh_3)_2$ Reduction System



As compared to the hydrodehalogenations described by Pri-Bar and Buchman, reduction with PMHS/KF in THF tended to be higher yielding, though they often took longer to complete.[20] Despite this increased reaction time, by avoiding the amine and polar high boiling solvents, reaction monitoring (GC and NMR) as well as product isolation and purification were made much easier. Furthermore, it needs to be noted that reductions under Pri-Bar and Buchman's conditions at our temperatures and times were almost always incomplete. 2-Bromoacetophenone was an exception as its reduction was complete after 6 hours at room temperature.

Table 1 details the results of the $Cl_2Pd(PPh_3)_2$ catalyzed hydrodehalogenation experiments. Iodobenzene is efficiently reduced to benzene at room temperature (entry 1). In contrast, complete reduction of bromobenzene required heating to 70°C (entry 3). An iodide can be selectively reduced in the presence of a bromide and a bromide in the presence of a chloride (entries 4-5). However, with these dihalides Pd black tends to precipitate after reduction of the more facile halide. As illustrated in entries 6-10, dehalogenation of bromoarenes bearing nitro, aldehyde, ketone, or ester groups takes place smoothly in good to near quantitative yields. α-Bromo-carbonyl compounds (entries 11-12) can also be reduced, albeit with minor side product formation.[21]

Though the $Cl_2Pd(PPh_3)_2$ protocol holds certain advantages over Pri-Bar and Buchman's original procedure, it is not superior for all substrates. Fluoride activation

Table 1. $Cl_2Pd(PPh_3)_2$ Catalyzed Hydrodehalogenations with Fluoride Activated PMHS[a]

Entry	Starting Material	Temp. (°C)	Time (h)	Product	% Yield[b]
1	Iodobenzene	r.t.	24	Benzene	90[c]
2	Iodobenzene	70	11	Benzene	100[c]
3	Bromobenzene	70	36	Benzene	100[c]
4	1-Bromo-4-iodobenzene	r.t.	26	Bromobenzene	100
5	3-Bromochlorobenzene	70	48	Chlorobenzene	90
6	1-Bromo-4-nitrobenzene	70	3.5	Nitrobenzene	66[d]
7	1-Iodo-2,4-dinitrobenzene	70	0.25	1,3-Dinitrobenzene	80[d]
8	4-Bromobenzaldehyde	70	48	Benzaldehyde	79
9	4'-Bromoacetophenone	70	24	Acetophenone	99
10	Methyl 4-bromobenzoate	70	18	Methyl benzoate	92
11	2-Bromoacetophenone	r.t.	24	Acetophenone	90
12	2-Bromoacetophenone	70	15	Acetophenone	89
13	Chlorobenzene	110	24	Benzene	Trace
14	4'-Chloroacetophenone	110	72	Acetophenone	0
15	4-Bromobenzoic acid	70	24	Benzoic acid	0
16	α-Bromophenylacetic acid	70	48	Phenylacetic acid	0
17	4-Bromophenol	70	24	Phenol	17

[a] Conditions: A halide (1 eq) was reduced at room temperature using $Pd(OAc)_2$ (0.05 eq), KF (2.0 eq.) and PMHS (4.0 eq.) in THF and H_2O.

[b] Yields are the average of two runs determined by GC (calibration curve).

[c] Yields are the average of two runs determined by NMR (internal standard).

[d] Isolated yield

provides no advantage with aryl chlorides (entries 13-14), as they are nearly inert under both conditions. Moreover, while Pri-Bar and Buchman could successfully hydrodehalogenate *p*-bromobenzoic acid and α-bromophenylacetic acids, in the $Cl_2Pd(PPh_3)_2$ system the presence of carboxylic acids or phenols spelled failure (entries 15-17).

The reduction of β-bromostyrene represents another apparent departure from reductions with PMHS, Bn_3N, and Pd(0) in DMSO/MeCN. Pri-Bar and Buchman reported the reduction of β-bromostyrene to styrene in 37% yield (Table 2, entry 9). Under the $Cl_2Pd(PPh_3)_2$ conditions, β-bromostyrene was reduced over 24 hours at room temperature to PhEt (ethylbenzene) in 92% yield (entry 1). Low yield (24%) reduction of

styrene by Rh-mediated hydrogen transfer from PMHS has been described.[22] However, the efficiency of entry 1 led to probing this over reduction further. Subjecting styrene to the $Cl_2Pd(PPh_3)_2$ conditions afforded some PhEt after 24 h at room temperature, but in only 12% yield (entry 3). Heating the reaction at 70°C for 24 h proved more efficient affording PhEt in 72% yield (entry 4).

Table 2. Reduction of β-Bromostyrene, Styrene, and Control Experiments[a]

Entry	Starting Material	Temp (°C)	Time (h)	Product	% Yield[b]
1	β-bromostyrene	r.t.	24	PhEt	92[c]
2	β-bromostyrene	70	22	Styrene	42[c]
3	Styrene	r.t.	24	PhEt	12[c,d]
4	Styrene	70	24	PhEt	72[c,d]
5	50/50 Styrene + 2-bromoacetophenone	r.t.	24	PhEt	78[d]
6	50/50 Styrene + 2-bromoacetophenone	70	22	PhEt	43[d]
7	1eq. Styrene + 0.1 eq. 2-bromoacetophenone	r.t.	24	PhEt	27[d]
8	Styrene + KBr	r.t.	24	PhEt	12[c,d]
	Under Pri-Bar and Buchman's Conditions				
9	β-bromostyrene	60	3	Styrene[e]	37[e]
10	β-bromostyrene	60	3	PhEt[f]	25[d,f]
11	Styrene	60	3	No rxn[f]	-

[a] Conditions: A substrate (1 eq) was reduced at room temperature using $Pd(OAc)_2$ (0.05 eq), KF (2.0 eq.) and PMHS (4.0 eq.) in THF and H_2O.
[b] Yields are an average of two runs.
[c] As determined by GC (calibration curve).
[d] As determined by NMR (internal standard).
[e] Per Ref. 9b
[f] Our data

Returning to β-bromostyrene, its reduction at 70°C was examined. Surprisingly, after 22 h at this temperature a 42% yield of styrene was obtained along with 48% starting material and only a trace amount of PhEt (entry 2). Thus, it would appear that β-bromostyrene reduces first to styrene and then on to PhEt. However, if this were so then why would the reductions proceed further at room temperature than at 70°C, especially

since the reduction of pure styrene is much more facile at 70°C than at room temperature?

A potential answer to this question may lie in the observation of a Pd-black precipitate during the 70°C reduction of β-bromostyrene. Perhaps, some combination of halide and styrene contributes to an active but thermally unstable Pd-complex. Thus, reduction of β-bromostyrene is complete at room temperature, but stops considerably short of completion at elevated temperatures. This hypothesis is supported by several additional experiments. Room temperature reduction of a 50/50 mixture of styrene and 2-bromoacetophenone afforded a 78% yield of PhEt after 24 h (entry 5). In contrast, at 70°C, styrene reduction was retarded by the presence of 2-bromoacetophenone. After 22 h, the reaction afforded some PhEt (43%) along with 52% unreacted styrene and 51% of the normally easy to reduce 2-bromoacetophenone (entry 6).

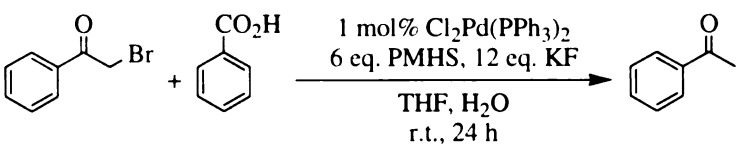
Substituting KBr for 2-bromoacetophenone failed to promote the reduction of styrene (entry 8); while adding 1 equiv. of *n*-Bu_4NBr turned the reaction into an intractable gel after 10 min. Decreasing the amount of added 2-bromoacetophenone met with a corresponding decrease in the yield of PhEt (entry 7). So while the results indicate that the bromide plays a role in these reductions, the specifics of this involvement as well as the mechanism by which the alkene is saturated remain unclear.[22b]

These results prompted repeating[23] the reduction of β-bromostyrene using Pri-Bar and Buchman's procedure. It was found that under their conditions, β-bromostyrene is also reduced to PhEt (25% yield + 38% β-bromostyrene), as judged by NMR analysis of the reaction mixture (entry 10).[24] No PhEt was observed when styrene was subjected to

these conditions (entry 11), suggesting again an involvement of the halide in the over reduction.

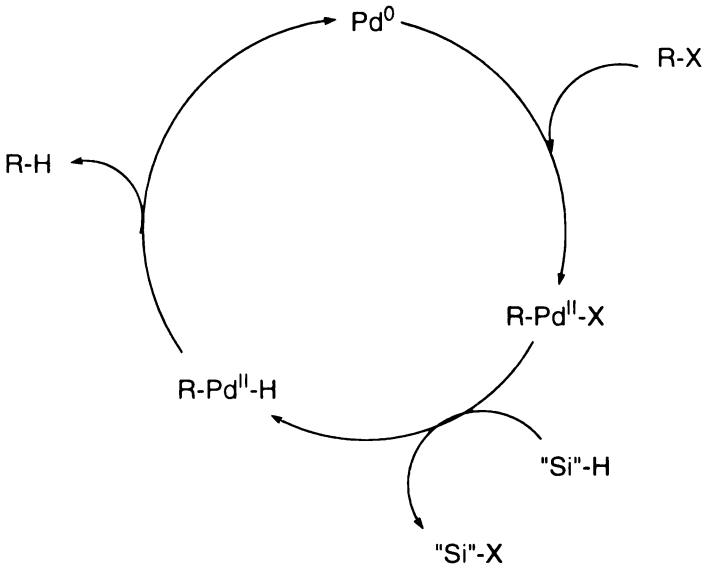
One additional experiment that sheds light onto the possible active Pd-complex, was one in which 2-bromoacetophenone was reduced in the presence of benzoic acid (Scheme 3). It was already found that *p*-bromobenzoic acid will not under go dehalogenation, and at the time we attributed this to the carboxylic group reacting with PMHS and shutting the reaction down . If this were the case, then the reduction of 2-bromoacetophenone in the presence of benzoic acid should not take place. In fact the reaction proceeds exceptionally well with a 99% conversion (GC analysis) to acetophenone after 24 h at room temperature. At this point and time it is not clear as what is causing this selectivity.

Scheme 3. Control Reaction with Benzoic Acid Additive



The mechanistic pathway of this system has not been determined yet, but is likely very similar to the mechanistic pathway in Pri-Bar and Buchman's system (Scheme 4.). In summary, the hydrodehalogenation of aryl- and α-keto-bromides are selectively reduced with KF (aq), PMHS, and catalytic $Cl_2Pd(PPh_3)_2$, in THF. This system tolerates nitro groups, aldehydes, ketones, and esters, however, carboxylic acids or phenols are incompatible. Under these conditions, β-bromostyrene reduces to ethylbenzene with the bromide playing an important but undefined role in the transformation.

Scheme 4. Catalytic Cycle via Pri-Bar and Buchman's System



Chapter 3. $Pd(OAc)_2$ Mediated Reductions

As demonstrated with the $Cl_2Pd(PPh_3)_2$ system, PMHS is capable of hydrodehalogenating aryl bromides and iodides under palladium catalysis.[9] However, literature searches indicate that all attempts to reduce chlorides under such conditions have failed.[25] This is unfortunate as the formation of arenes form aryl chlorides is an important chemical transformation.[2] As such, the reduction of chloroarenes has been studied under a variety of conditions including free radical,[13] catalytic and transfer hydrogenation,[6e-g] oxidative,[7] and metal catalyzed hydride delivery.[9-12] Several of these methods employ relatively expensive silanes[10c,10e,12b-c] or hazardous stannanes,[13] for which PMHS would be an attractive alternative.

3.1. Discovery and Development

Recently, phosphine free palladium catalysts have seen considerable success in reactions with aryl chlorides.[10a,11a,26] Thus, related systems were explored to see if the problem of reducing chloroarenes with PMHS could be solved.[27] This investigation revealed that catalytic palladium(II) acetate with PMHS in the presence of potassium fluoride reduced chlorobenzene to benzene (Scheme 4).[28] Impressively, this transformation could take place at room temperature in a matter of minutes.

Reaction optimization experiments carried out on 4-chlorotoluene indicated that fluoride was essential for efficient conversion as only trace quantities of toluene were produced upon reaction with 5 mol% $Pd(OAc)_2$ and 6 equiv. of PMHS (relative to chloroarene) at room temperature for 24 hours (Table 3, entry 1). While the presence of fluoride was beneficial, too much (> 50 mol% based on PMHS) decreased the efficiency of the reaction (entries 4-7). The use of 2 eq. KF with an excess of PMHS (6 eq.)

Table 3. Potassium Fluoride Optimization with 4-Chlorotoluene[a]

Entry	eq. KF	Time (h)	% Conversion[29]
1	0	24	Trace
2	2	2	95
3	4	2	59
4	6	2	40
5	8	2	34
6	10	2	43
7	12	2	41

[a] Conditions: 4-chlorotoluene (1.0 eq.) was reduced with $Pd(OAc)_2$ (0.05 eq.), PMHS (6 eq.), KF, THF, and H_2O.

produced the largest percent conversion (entry 2), so optimization of the PMHS concentration was performed using 2 eq. KF (Table 4). As for the amount of PMHS required, increasing the equivalency of PMHS increased the rate of dehalogenation. In all of the concentrations tested for PMHS, complete conversion could be accomplished with increased reaction times. The reaction of equal molar amounts of PMHS and 4-chlorotoluene was complete after 24 hours. Using a six-fold excess of PMHS allowed for near complete reduction after only 2 hours. Upon factoring in the low cost and mildness

Table 4. PMHS Optimization with 4-Chlorotoluene[a]

Entry	eq. PMHS	Time (h)	% Conversion[29]
1	1	2.5	43
2	2	2	75
3	3	2	73
4	4	2	85
5	5	2	90
6	6	2	95

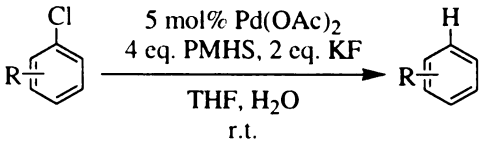
[a] Conditions: 4-chlorotoluene (1.0 eq.) was reduced with $Pd(OAc)_2$ (0.05 eq.), PMHS, KF (2.0 eq.), THF, and H_2O.

of PMHS[14] and the desire to maximize reaction efficiency as well as ease of purification and workup, the use of 4 equiv. PMHS and 2 equiv. of KF were settled on as the conditions of choice (Scheme 4).[30]

3.2. Substrate Screening

Variety of haloarenes were reacted with 4 equiv. of PMHS, 2 equiv. of an

Scheme 5. $Pd(OAc)_2$ Redution System



aqueous solution of KF, and 5 mol% $Pd(OAc)_2$[28] in THF (Table 5). Iodo-, bromo-, and chlorobenzene were efficiently reduced to benzene in 20 minutes (entry 1-3). Chloroarenes bearing electron neutral, donating or releasing groups were all reduced smoothly. Most reductions were complete in less than 4 hours. Even sterically hindered 2-chloro-*m*-xylene (entry 6) was quantitatively reduced at room temperature, albeit after a somewhat extended (8 h) reaction time. Substituted pyridines (entries 22-24) also perform well under the reaction conditions, even 2-chloropyridine, which has afforded poor yields in other systems.[11a] Dihalogenated arenes can also be reduced with 4 equiv. of PMHS per halogen[31] (entries 28, 31-33). These conditions are compatible with a variety of functional groups including ethers (entry 9), amines (entries 10-12), esters (entries14-15), amides (entries16-17), nitriles (entries 18-19), ketones (entry 25[32]), aryl fluorides (entry 20-21), and borate esters (entry 26[33]). Of the substrates studied only 4-chlorophenol (entry 8) and 4-chlorobenzoic acid (entry 13) did not reduce.

The presence of additional substituents can retard the reaction. For example, certain *para*-substituted aryl chlorides proved surprisingly sluggish. The reduction of 1-chloro-4-fluorobenzene (entry 27) was only 78% complete by GC after 12 hours and required 20 hours before the reaction was finished. Likewise, entry 25 required 18 hours for full consumption of 4-(4-chlorophenyl)butan-2-one. Most unusual was the hydrodehalogenation of 1-chloro-4-iodobenzene (entry 29). Even though chlorobenzene and iodobenzene are reduced in less than an hour, after 3 hours only chlorobenzene was

observed.[34] A similar result was encountered with 1-bromo-4-iodobenzene (entry 30) in which bromobenzene (96%) was the major product along with a small quantity of benzene (4%).

Table 5. Substrate Screening of $Pd(OAc)_2$ Mediated Dehalogenation[a]

Entry	Starting Material	Time (h)	Product	% Yield[b]
1	Iodobenzene	0.33	Benzene	96
2	Bromobenzene	0.33	Benzene	96
3	Chlorobenzene	0.33	Benzene	95
4	4-Chlorotoluene	3	Toluene	95
5	2-Chlorotoluene	3	Toluene	100
6	2-Chloro-*m*-xylene	8	Xylene	100
7	1-Chloronaphthalene	4	Naphthalene	96
8	4-Chlorophenol	17	Phenol	0
9	4-Chloroanisole	1.5	Anisole	100
10	4-Chloroaniline	0.5	Aniline	99
11	3-Chloroaniline	0.75	Aniline	94
12	2-Chloroaniline	0.75	Aniline	99
13	4-Chlorobenzoic acid	24	Benzoic acid	0
14	Methyl 4-Chlorobenzoate	3	Methyl benzoate	84
15	Methyl 2-Chlorobenzoate	1	Methyl benzoate	98
16	4-Chlorobenzamide	1.5	Benzamide	99
17	2-Chlorobenzamide	0.75	Benzamide	89
18	4-Chlorobenzonitrile	0.5	Benzonitrile	81
19	2-Chlorobenzonitrile	1	Benzonitrile	90
20	4-Chlorobenzotrifluoride	4	Trifluorotoluene	96
21	2-Chlorobenzotrifluoride	4	Trifluorotoluene	99
22	4-Chloropyridine•HCl	1.5	Pyridine	96
23	3-Chloropyridine	1	Pyridine	97
24	2-Chloropyridine	1.5	Pyridine	94
25	4-(4-Chlorophenyl)-butan-2-one	18	4-Phenyl-butan-2-one	95
26	3-Chloro-5-methylphenylpinacolborane	6	3-Methylphenyl-pinacolborane	85[c]
27	1-Chloro-4-fluorobenzene	20	Fluorobenzene	92
28	1-Bromo-4-chlorobenzene	24	Benzene	98
29	1-Chloro-4-iodobenzene	3	Chlorobenzene	93
30	1-Bromo-4-iodobenzene	3	Bromobenzene	90
31	1,4-Dichlorobenzene[d]	3	Benzene	98
32	1,3-Dichlorobenzene[d]	6	Benzene	98
33	1,2-Dichlorobenzene[d]	18	Benzene	98

[a] Conditions: a halide (1.0 eq) was reduced with $Pd(OAc)_2$ (0.05 eq.), PMHS (4.0 eq.), KF (2.0 eq.), THF and H_2O at room temperature.

[b] Yields were determined by NMR (internal standard) and are the average of two runs.

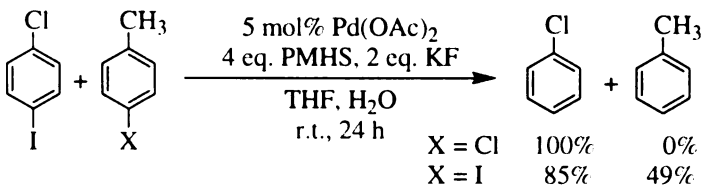
[c] Isolated yield.

[d] Run with 4.0 eq. of PMHS and 2.0 eq. of KF per halogen.

Intrigued by the result that only iodine is reduced in entries 29 and 30, and both halogens are reduced in 1-bromo-4-chlorobenzene, control reactions were conducted to

unveil the cause of this effect. Reaction of 1 equiv. 1-chloro-4-iodobenzene in the presence of 1 equiv. 4-chlorotoluene produced chlorobenzene with no observable reduction of the 4-chlorotoluene. Reducing 1 equiv. of 1-chloro-4-iodobenzene in the presence of 1 equiv. 4-iodotoluene produced chlorobenzene and toluene (Scheme 5). These results suggest that the halogenated arene is undergoing oxidative addition to the catalyst with the more facile halide. This process appears to change the activity of the catalyst so as to limit its reactivity towards chlorides.

Scheme 6. Competition Control Reaction



3.3. Catalyst Loading

Having proved the reduction of chloroarenes by hypercoordinate PMHS under Pd-catalysis to be mild, rapid, and general; examination of the palladium loading was conducted to see if the catalyst loading could be lowered below 5 mol % (Table 6). Though longer reaction times were required, the hydrodehalogenations of 4-chlorotoluene, 4-chloroaniline, and methyl 2-chlorobenzoate in the presence of only 1 mol % $Pd(OAc)_2$ were all high yielding (entries 2, 5, and 8 respectively). Decreasing the catalyst loading by another order of magnitude (0.1 mol %) still allowed for the efficient, though slow, dechlorination of 4-chloroaniline and methyl 2-chlorobenzoate (entries 6 and 9). However, for 4-chlorotoluene (entry 3) diminishing returns set in at this loading.

3.4. Product Isolation

Isolation of pure material was a surprisingly arduous task. Simple extraction of the reaction mixture followed by column chromatography[35] gave material contaminated

Table 6. Screening of Catalyst Loading[a]

Entry	mol % $Pd(OAc)_2$	Substrate	Time (h)	Product	% Yield[b]
1	5	4-Chlorotoluene	3	Toluene	95
2	1	4-Chlorotoluene	10	Toluene	96
3	0.1	4-Chlorotoluene	54	Toluene	24
4	5	4-Chloroaniline	0.5	Aniline	99
5	1	4-Chloroaniline	1	Aniline	98
6	0.1	4-Chloroaniline	29	Aniline	97
7	5	Methyl 2-chlorobenzoate	1	Methyl benzoate	98
8	1	Methyl 2-chlorobenzoate	9	Methyl benzoate	100
9	0.1	Methyl 2-chlorobenzoate	54	Methyl benzoate	100

[a] Conditions: a halide (1.0 eq.) was reduced with $Pd(OAc)_2$, PMHS (4.0 eq.), KF (2.0 eq.), THF and H_2O at room temperature.

[b] Yields were determined by NMR (internal standard) and are the average of two runs.

with silane byproducts. The first attempt to solve this problem involved stirring a base with the reaction mixture after complete reduction to hydrolyze unreacted PMHS and silane byproducts, followed by extraction and chromatography. A 3 M NaOH solution was utilized, and allowed for solid products to be collected via extraction and evaporation with no need for further purification. On the other hand liquid products still contained silane byproducts even after chromatography with various hexane/ethyl acetate solutions. It was finally found that liquid material could be obtained pure by running the column with an initial elution of CCl_4/hexanes (1/1). Distillation of the contaminated liquid material was also investigated as a possible route to obtain pure product. Distillation of aniline, obtained from 4-chloroaniline, afforded pure product in 76% yield (based on starting material).

3.5. Phosphine Free Palladium Catalyzed Reductions

The efficacy of other phosphine free[36] palladium sources was tested (Table 7). In these experiments $Pd(CN)_2$ and $Pd(NH_2)Cl_2$ failed to reduce 4-chlorotoluene (entries 1-2). While $Pd(acac)_2$, palladium black, $PdCl_2$, and $Pd_2(dba)_3$ dechlorinated 4-

chlorotoluene (entries 3, 4, 7, and 11), these catalysts proved considerably less efficient than $Pd(OAc)_2$ with other substrates (i.e. entries 6, 10, and 14). Thus, on balance, $Pd(OAc)_2$ appears to be the most universal catalyst for room temperature hydrodehalogenations with KF/PMHS.

Table 7. Phosphine Free Palladium Catalyzed Reductions[a]

Entry	Catalyst	Substrate	Time (h)	Product	%Yield[b]
1	$Pd(CN)_2$	4-Chlorotoluene	3	Toluene	0
2	$Pd(NH_2)Cl_2$	4-Chlorotoluene	3	Toluene	0
3	$Pd(acac)_2$	4-Chlorotoluene	3	Toluene	73
4	Pd black	4-Chlorotoluene	3	Toluene	94
5		4-Chloroaniline	0.5	Aniline	96
6		2-Chloropyridine	1.5	Pyridine	0
7	$PdCl_2$	4-Chlorotoluene	3	Toluene	78
8		4-Chloroaniline	0.5	Aniline	96
9		2-Chloropyridine	1.5	Pyridine	100
10		2-Chloro-*m*-xylene	14	Xylene	0
11	$Pd_2(dba)_3$	4-Chlorotoluene	3	Toluene	96
12		2-Chloroaniline	0.5	Aniline	74
13		2-Chloropyridine	1.5	Pyridine	75
14		2-Chloro-*m*-xylene	17	Xylene	50

[a] Conditions: the halide (1.0 eq.) was reduced with "Pd-catalyst" (0.05 eq.), PMHS (4.0 eq.), KF (2.0 eq.), THF, and H_2O at room temperature.

[b] Yields were determined by NMR (internal standard) and are the average of two runs.

3.6. Miscellaneous Control Reactions

The dehalogenation of 4-chlorobenzoic acid could not take place. To determine if the cause of this was from the carboxylic acid, 4-chloroaniline was reduced in the presence of benzoic acid. The benzoic acid additive did not affect the hydrodehalogenation of 4-chloroaniline, which proceeded with 100% conversion to aniline in 30 minutes. The carboxylic acid is not shutting the reaction down, so the inability of 4-chlorobenzoic acid to be dehalogenated could be the result of an unstable palladium intermediate after oxidative addition, or oxidative addition of 4-chlorobenzoic acid to palladium cannot take place. A more detailed investigation needs to be done.

When performing these hydrodehalogenations, the addition of PMHS to the reaction mixture results in the solution turning dark brown with excessive bubbling and gas evolution; followed by the reaction mixture turning clear and a highly insoluble solid (possibly the active catalyst?) precipitating out of solution within a few minutes. Intrigued by the volatile nature of PMHS with the reaction conditions, attempts were made to narrow down the specific reagents interacting. PMHS was mixed with aqueous KF, KF(aq) in THF, KF(aq) with chlorobenzene in THF, and $Pd(OAc)_2$ in THF. Addition of PMHS to $Pd(OAc)_2$ in THF was the only combination of reagents that resulted in a reaction. A mixture of PMHS, $Pd(OAc)_2$, and THF turned a dark brown with gas evolution affording a black solid. The black solid could be palladium black, but if PMHS reacts with $Pd(OAc)_2$ to form palladium black in the reaction mixture, then the results attained from screening palladium black as the catalyst (Table 7, entry 6) should not have been different. It is believed that PMHS is reacting with palladium(II) acetate to form the heterogeneous catalyst, via oxidative addition, transmetallation, or complexation. Determination of the solid material formed needs to be done.

Finally, a limited investigation suggests that the ratio of water to THF can influence the course of these reductions. Increasing the water/THF ratio from 2/5 to 3/5 decreased the required reaction time for the reduction of 4-chlorotoluene from 3 hours to 1. However, this proved a delicate balance as any further increase in the amount of water prohibited the reaction from going to completion. Additional studies on this water effect need to be conducted.

Chapter 4. Future Work

While screening substrates in the $Pd(OAc)_2$ catalyzed system a number of interesting reactions were encountered. In the case of 2-chloroacetophenone, 4'-chloroacetophenone, and 2-chlorobenzaldehyde, the chloride was efficiently reduced *along with deoxygenation of the carbonyl.* β-Chlorostyrene was screened and resulted in complete over reduction to ethylbenzene and 1-chloro-4-nitrobenzene under the developed conditions yielded aniline. It was also found that the chloride of 4-chlorobenzonitrile is smoothly and efficiently reduced to benzonitrile, but if the benzonitrile formed is allowed to stir in the reaction media reduction of the nitrile to the primary amine results. Further exploration into the optimum reaction conditions and substrate screening of each of these unique reactions needs to be conducted, to determine the efficacy of each of these reactions.

4.1. Deoxygenation: Discovery and Development

Having established that the hydrodehalogenation of 2-chloroacetophenone, 4'-chloroacetophenone, and 2-chlorobenzaldehyde also results in deoxygenation of the carbonyl, an exploration into the cause and utility of this intriguing reaction was initiated. The first step was to establish if acetophenone and benzaldehyde could be deoxygenated under the dehalogenation reaction conditions. Following these reactions for 24 hours by GC and NMR showed that only trace amounts of ethylbenzene and toluene were present in the reaction mixture. Indicating that a chloride, or even some simple halide source may be needed to facilitate the deoxygenation.

To answer the question as to what if any halide source is required for the deoxygenation, a number of acetophenone reductions were run in the presence of various

halide sources (Scheme 6, Table 8). What is interesting to note is that acetophenone is completely deoxygenated when using chlorobenzene as the halide source (entry 1), whereas bromo and iodobenzene yielded poor and no conversion to ethylbenzene respectively (entries 2-3). The question thus became can any added chloride facilitate deoxygenation, or is the effect specific to chlorobenzene? To help answer this question tetrabutylammonium chloride (entry 4) was tested, resulting in only trace amounts of ethylbenzene and polymerization of the reaction mixture; which is not a surprise for in previous work tetrabutylammonium bromide caused the reaction mixture to polymerize immediately.[37] At this point cesium and lithium chloride (entries 5-6) were tested, and again only produced trace amounts of the deoxygenated product.

Scheme 7. Control Reaction of Various Halide Sources for Deoxygenation

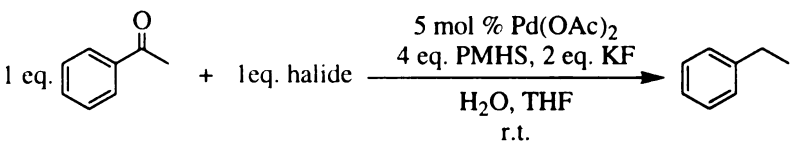


Table 8. Screening of Halide Sources for Deoxygenation

Entry	Halide Source	Time (h)	% Yield
1	Chlorobenzene	1	100
2	Bromobenzene	2	22
3	Iodobenzene	16	0
4	Bu_4NCl	3.5	Trace
5	CsCl	24	Trace
6	LiCl	24	Trace

These results can be explained by the hypothesis that the chloroarenes undergo oxidative addition to palladium and become ligands on the active catalyst. In the case of bromo and iodobenzene the same pathway is taking place, but they are not suitable ligands for a deoxygenation catalyst. If chlorobenzene is a ligand on the active catalyst, then only a catalytic amount should be needed to perform the deoxygenation. To

substantiate this hypothesis the concentration of chlorobenzene in the deoxygenation reaction was lowered (Scheme 7, Table 9). The results of which show that an equivalent amount of chlorobenzene to $Pd(OAc)_2$ (entry 7) can be used to effect deoxygenation, supporting the hypothesis that chlorobenzene is a ligand on the active catalyst.

Scheme 8. Deoxygenation via Chlorobenzene

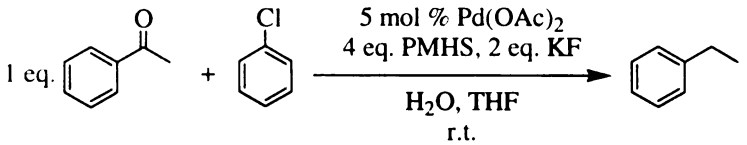


Table 9. Control Reaction of Chlorobenzene Concentration

Entry	eq. PhCl	Time (h)	% Yield
1	0	24	Trace
2	1	1	97
3	0.75	1	100
4	0.5	1	99
5	0.25	0.5	100
6	0.1	1	96
7	0.05	1	94

There is also the possibility that deoxygenation is facilitated by some byproduct in the dehalogenation of chlorobenzene. To evaluate this pathway chlorobenzene was reduced to benzene, at which point acetophenone was added to the reaction mixture. This resulted in no detectable deoxygenation, further substantiating the hypothesis that chlorobenzene is a ligand on the active catalyst.

4.1.1. Additional Work Needed

Establishing that a chloroarene is essential for deoxygenation, along with the minimum concentration needed, only the concentrations of PMHS, KF, THF, water, and $Pd(OAc)_2$ needed to be optimized. After such work, substrates can be screened to elucidate the utility and deficiencies of the reaction. It was also found that benzylic alcohols undergo deoxygenation with a chloroarene additive. This result dictates that a

number of alcohols need to be tested along with the carbonyl substrates. The benzylic alcohols can also be used to answer some questions. It is possible that the deoxygenation is taking place through a silyl ether intermediate, formed from PMHS. If this is the case, a benzylic alcohol can be substituted with a silyl group and subjected to the deoxygenation reaction conditions. If the silyl ether is reduced this does not prove or disprove the silyl ether intermediate pathway, but if the silyl ether is not reduced, it states at minimum that the silyl ether intermediate is unlikely. Along with performing this experiment, the deoxygenation reaction needs to be followed by React IR to try and obtain evidence of intermediates. Preliminary data indicates that alcohols $\geq \beta$, and carbonyls $\geq \alpha$ to an aromatic ring are not deoxygenated.[38]

4.2. Reduction of Alkenes, Alkynes, Nitriles, Nitro's, and Nonaflates

The over reduction of β-chlorostyrene to ethylbenzene was not a surprise, as similar results were encountered in the $Cl_2Pd(PPh_3)_2$ system. The question is, does the reduction require the presence of a halogenated arene, as in the case of the deoxygenation reactions, and the hydrogenation of styrene in the $Cl_2Pd(PPh_3)_2$ system? To answer this question the $Pd(OAc)_2$ reaction conditions were applied to styrene. This reaction afforded 100% ethylbenzene in 45 minutes; so in this case a halogenated arene additive is not needed. Following this finding phenylacetylene was tested to determine if alkynes can be reduced; full saturation of the triple bond was realized in less than an hour. These reaction conditions need to be optimized, followed by substrate screening to map out the limitations and benefits of the reaction.

The hydrodehalogenation of 4-chorobenzonitrile led to further examination of benzonitrile under prolonged reaction times, forming approximately 50% of the primary

amine. Adjustment of the reaction conditions needs to be done to increase the yield; if the yield cannot be increased then only a limited investigation of the nitrile hydrogenation is warranted. Previous findings initiated the idea to add chlorobenzene to the reaction, in an attempt to increase the yield of the primary amine. This was not the outcome; doping the reaction with chlorobenzene stopped the reduction of the nitrile.

The discovery that 4-chlorobenzonitrile is reduced to aniline, prompted subjecting nitrobenzene to the $Pd(OAc)_2$ reaction conditions. Aniline was afforded in 99% yield in less than one hour. A detailed investigation of this reduction is still required.

While running the control reactions for the deoxygenation, phenyl triflate was chosen to be one of the additives screened, but was not available. In lieu of preparing phenyl triflate, 4-acetylphenyl nonafluorobutanesulfonate was available, and answered two questions at once. Is the $Pd(OAc)_2$ system capable of reducing nonaflates, and can the nonaflate be used to facilitate deoxygenation? GC analysis of the reaction mixture containing 4-acetylphenyl nonafluorobutanesulfonate showed a 97% conversion to acetophenone with 2.5% ethylbenzene in one hour. Again more substrates should be tested to obtain a general trend for these nonaflate reductions.

4.3. Cross-Coupling Reactions: Stille, Suzuki, Tandem Heck-Hydrogenation

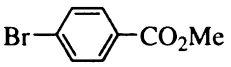
In the past few years there has been a surge in the development of catalyst for cross-coupling reactions with chlorinated substrates.[39,40] The ease in which the $Pd(OAc)_2$ system activates the carbon-chlorine bond makes its use in cross-coupling reactions interesting to consider. Attempts have been made to use the catalyst in Stille and Suzuki reactions, but at this point and time the endeavor has been unsuccessful. The Stille reaction has been run with increasing amounts of KF (2, 4, and 6eq.), various

fluoride sources (TBAF and CsF), and varying concentrations of PMHS (0.05 eq to 1.0 eq.) at room temperature and under reflux (70°C). It should be noted that even though the cross coupling did not take place, reduction of the chloroarene also did not occur. The experiments aimed at a Suzuki coupling have been done with various concentrations of PMHS (0.05 eq. to 1.0 eq.), all affording reduction of the chloroarene. Evaluation of the data collected also birthed the idea that a Heck coupling may be possible, followed by hydrogenation of the olefin in one pot. Unraveling the hydrogenation mechanism of alkenes with the $Pd(OAc)_2$ system shall tell if this route is possible. As these experiments continue, it is clear that elucidation of the active catalyst in the $Pd(OAc)_2$ system would be helpful, and remains a primary goal of our future studies.

Experimental Details

Materials and Methods

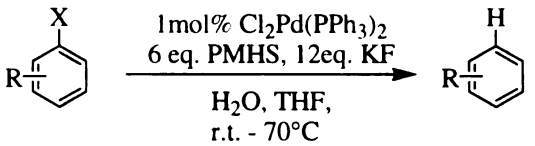
All air or moisture sensitive reactions were carried out in oven dried glassware under a nitrogen atmosphere unless otherwise noted. All commercial reagents were used without purification. All solvents were reagent grade. Diethyl ether and THF were freshly distilled from sodium/benzophenone under nitrogen. Benzene, and DMSO were freshly distilled from calcium hydride under nitrogen. Except as otherwise noted, all reactions were magnetically stirred and monitored by thin-layer chromatography with 0.25-mm precoated silica gel plates or capillary GC with a fused silica column. Flash chromatography was performed with silica gel 60 Å (particle size 230-400 mesh ASTM). Yields refer to chromatographically and/or spectroscopically pure compounds unless otherwise stated. Proton and carbon NMR spectra were recorded on a Varian Gemini-300 spectrometer. Chemical shifts for ^{1}H NMR are reported in parts per million (ppm) relative to $CDCl_3$ (δ = 7.24 ppm for ^{1}H NMR or δ = 77.0 ppm for ^{13}C NMR) unless otherwise stated. All products were compared to an authentic commercial sample unless otherwise stated.



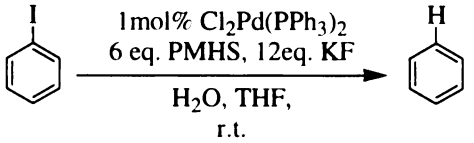
Preparation of methyl 4-bromobenzoate:[41] A 100 mL round bottom flask was charged with 1 equiv. 4-bromobenzoic acid (49.7 mmol, 10 g), 20 equiv. of anhydrous methanol (994 mmol, 40 mL), and a catalytic amount of con. HCl (0.2 mL). The r.b. was placed in an oil bath at 70°C and the reaction was refluxed for 12 hours. The reaction mixture was cooled to room temperature and diluted with 200 mL of water. The diluted reaction mixture was then extracted with Et_2O, followed by washing the organics with water and

saturated $NaHCO_3$. The organics were then dried over $MgSO_4$ and concentrated. The collected material was rinsed with water and air dried, yielding 8.47 g (90.6%) of methyl 4-bromobenzoate as a white crystalline powder; m.p. 79-81°. The crude material was of sufficient purity as to not require further purification. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.89 (d, J = 8.2 Hz, 2 H), 7.57 (d, J = 8.8 Hz, 2 H), 3.89 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.36, 131.68, 131.07, 128.98, 128.01, 52.26. Product data was identical to that from an authentic commercial sample.

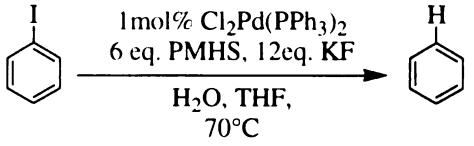
General Procedure A: $Cl_2Pd(PPh_3)_2$ mediated reductions



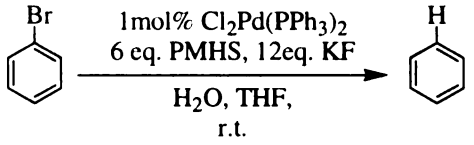
A 25 mL round bottom flask (oven dried) was charged with 1.0 equiv. aryl halide (1.0 mmol) in 5 mL THF (0.2 M solution, freshly distilled) and 0.01 equiv. of dichlorobis(triphenylphosphine)palladium(II) (0.01 mmol, 0.007 g). The flask was sealed with a septum and flushed with nitrogen. While flushing the reaction, 12 equiv. of KF (12.0 mmol, 0.697 g) in 2 mL of degassed water was injected into the reaction mixture. 6.0 equiv. PMHS (6.0 mmol, 0.36 mL) was then injected via syringe. If the reaction mixture was heated, a reflux condenser was attached to the round bottom and placed in a preheated oil bath. The reaction was stirred until complete as judged by disappearance of the starting material (GC analysis). Upon complete reduction, the reaction mixture was added to a 1 M solution of NaOH. After stirring overnight to hydrolyze unreacted PMHS, the mixture was extracted several times with Et_2O. The combined organics are dried over $MgSO_4$, concentrated, and purified by silica gel chromatography.



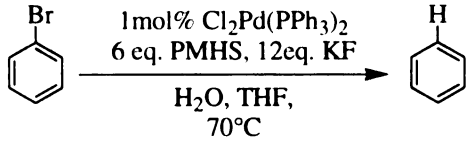
Iodobenzene was reduced following general procedure A using 1.0 equiv. (1.0 mmol, 0.112 mL) at room temperature for 24 hours, to yield 91.5% benzene. Yield was determined by NMR using an internal standard (CH_2Cl_2) in THF-d_8.



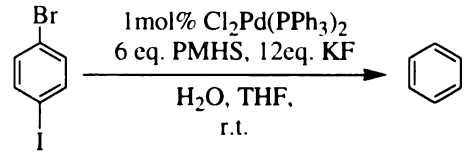
Iodobenzene was reduced following general procedure A using 1.0 equiv. (1.0 mmol, 0.112 mL) at 70°C for 11 hours, to yield 100% benzene. Yield was determined by NMR using an internal standard (CH_2Cl_2) in THF-d_8.



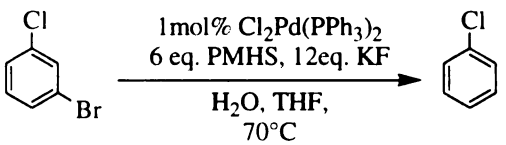
Bromobenzene was reduced following general procedure A using 1.0 equiv. (1.0 mmol, 0.105 mL) at room temperature for 24 hours, to yield 11.3% benzene. Yield was determined by NMR using an internal standard (CH_2Cl_2) in THF-d_8.



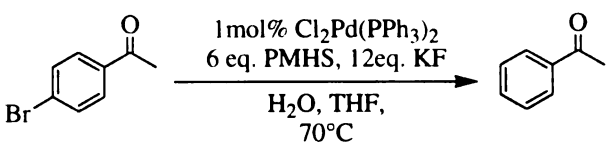
Bromobenzene was reduced following general procedure A using 1.0 equiv. (1.0 mmol, 0.105 mL) at 70°C for 36 hours, to yield 100% benzene. Yield was determined by NMR using an internal standard (CH_2Cl_2) in THF-d_8.



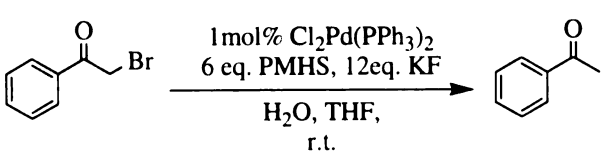
1-Bromo-4-iodobenzene was reduced following general procedure A using 1.0 equiv. (1.0 mmol, 0.283 g) at room temperature for 26 hours, yielding 100% bromobenzene. Yield was determined by GC using a calibration curve. GC conditions: starting temperature (30°C), ramp rate (10°C/m), final temperature (250°C), R.T. = 9.73 (S.M.), 4.03 (P).



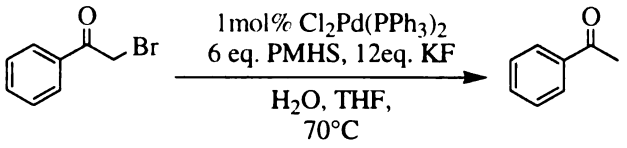
3-Bromochlorobenzene was reduced following general procedure A using 1.0 equiv. (1.0 mmol, 0.117 mL) at 70°C for 48 hours, to yield 90% chlorobenzene. Yield was determined by GC using a calibration curve. GC conditions: starting temperature (30°C), ramp rate (10°C/m), final temperature (250°C), R.T. = 6.5 (S.M.), 2.88 (P).



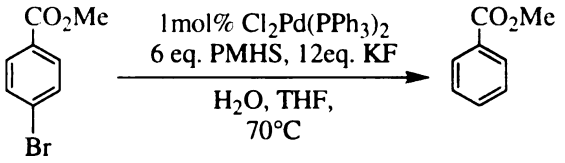
4'Bromoacetophenone was reduced following general procedure A using 1.0 equiv. (1.0 mmol, 0.199 g) at 70°C for 24 hours, to yield 99% acetophenone. Yield was determined by GC using a calibration curve. GC conditions: starting temperature (30°C), ramp rate (10°C/m), final temperature (250°C), R.T. = 10.06 (S.M.), 6.07 (P).



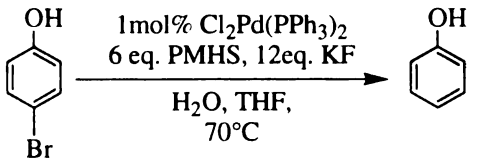
2-Bromoacetophenone was reduced following general procedure A using 1.0 equiv. (1.0 mmol, 0.199 g) at room temperature for 24 hours, to yield 90% acetophenone. Yield was determined by GC using a calibration curve. GC conditions: starting temperature (30°C), ramp rate (10°C/m), final temperature (250°C), R.T. = 10.49 (S.M.), 6.1 (P).



2-Bromoacetophenone was reduced following general procedure A using 1.0 equiv. (1.0 mmol, 0.199 g) at 70°C for 15 hours, to yield 89% acetophenone. Yield was determined by GC using a calibration curve. GC conditions: starting temperature (30°C), ramp rate (10°C/m), final temperature (250°C), R.T. = 10.49 (S.M.), 6.1 (P).

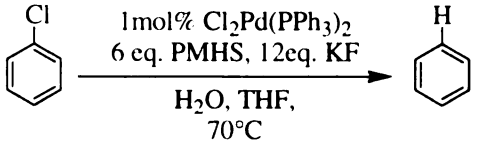


Methyl 4-bromobenzoate was reduced following general procedure A using 1.0 equiv. (1.0 mmol, 0.215 g) at 70°C for 18 hours, to yield 92% methyl benzoate. Yield was determined by GC using a calibration curve. GC conditions: starting temperature (30°C), ramp rate (10°C/m), final temperature (250°C), R.T. = 10.41 (S.M.), 6.56 (P).

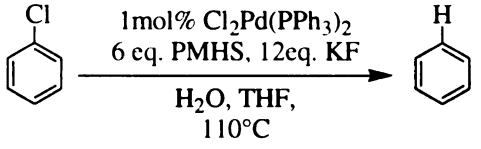


4-Bromophenol was reduced following general procedure A using 1.0 equiv. (1.0 mmol, 0.173 g) at 70°C for 24 hours, to yield 17% phenol. Yield was determined by GC

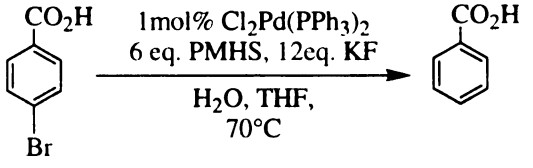
using a calibration curve. GC conditions: starting temperature (30°C), ramp rate (10°C/m), final temperature (250°C), R.T. = 9.64 (S.M.), 4.93 (P).



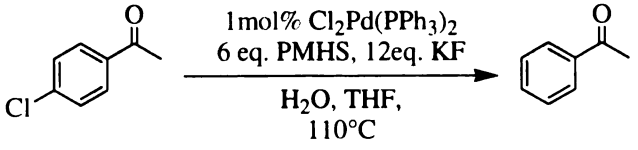
Chlorobenzene was reduced following general procedure A using1.0 equiv. (1.0 mmol, 0.102 mL) at 70°C for 48 hours, to yield 0% benzene. Yield was determined by NMR using an internal standard (CH_2Cl_2) in THF-d_8.



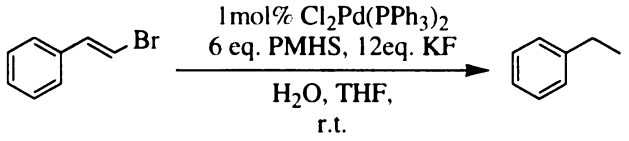
Chlorobenzene was reduced following general procedure A using 1.0 equiv. (1.0 mmol, 0.102 mL) at 110°C for 24 hours, to yield trace amounts of benzene. Yield was determined by NMR using an internal standard (CH_2Cl_2) in THF-d_8.



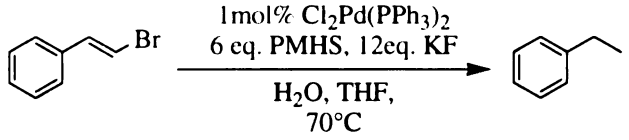
4-Bromobenzoic acid was reduced following general procedure A using 1.0 equiv. (1.0 mmol, 0.201 g) at 70°C for 24 hours, to yield 0% benzoic acid. Yield was determined by GC using a calibration curve. GC conditions: starting temperature (30°C), ramp rate (10°C/m), final temperature (250°C).



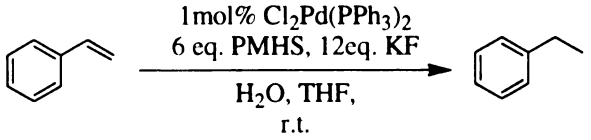
4'-Chloroacetophenone was reduced following general procedure A using 1.0 equiv. (1.0 mmol, 0.130 mL) at 110°C for 72 hours, to yield 0% acetophenone. Yield was determined by GC using a calibration curve. GC conditions: starting temperature (30°C), ramp rate (10°C/m), final temperature (250°C), R.T. = 8.8 (S.M.), 6.1 (P).



β-Bromostyrene was reduced following general procedure A using 1.0 equiv. (1.0 mmol, 0.128 mL) at room temperature for 24 hours, to yield 92% ethylbenzene. Yield was determined by GC using a calibration curve. GC conditions: starting temperature (30°C), ramp rate (10°C/m), final temperature (250°C), R.T. = 8.42 (S.M.), 3.07 (P).

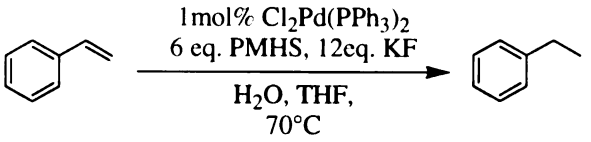


β-Bromostyrene was reduced following general procedure A using 1.0 equiv. (1.0 mmol, 0.128 mL) at 70°C for 22 hours, to yield 42% styrene. Yield was determined by GC using a calibration curve. GC conditions: starting temperature (30°C), ramp rate (10°C/m), final temperature (250°C), R.T. = 8.42 (S.M.), 3.47 (P).

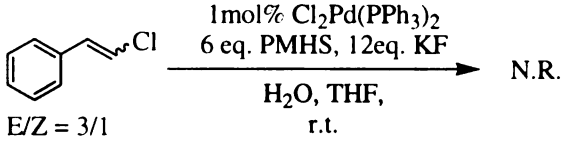


Styrene was reduced following general procedure A using 1.0 equiv. (1.0 mmol, 0.115 mL) at room temperature for 24 hours, to yield 12% ethylbenzene. Yield was determined by GC using a calibration curve and by NMR using an internal standard (CH_2Cl_2) in

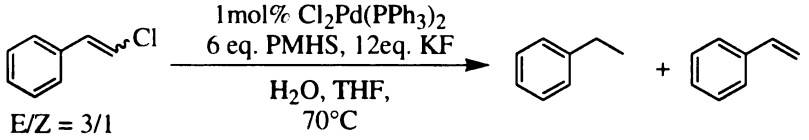
THF-d_8. GC conditions: starting temperature (30°C), ramp rate (10°C/m), final temperature (250°C), R.T. = 8.42 (S.M.), 3.05 (P).



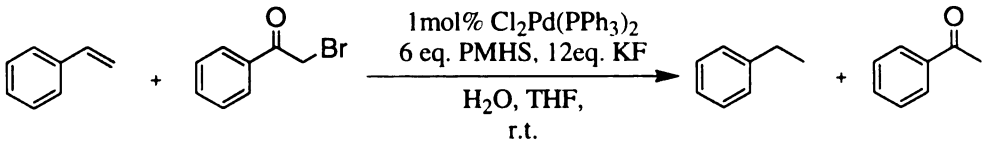
Styrene was reduced following general procedure A using 1.0 equiv. (1.0 mmol, 0.115 mL) at 70°C for 24 hours, to yield 72% ethylbenzene. Yield was determined by GC using a calibration curve and by NMR using an internal standard (CH_2Cl_2) in THF-d_8. GC conditions: starting temperature (30°C), ramp rate (10°C/m), final temperature (250°C), R.T. = 8.42 (S.M.), 3.06 (P).



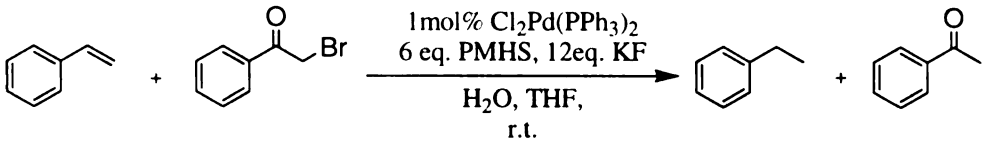
β-Chlorostyrene (E/Z:3/1) was reduced following general procedure A using 1.0 equiv. (1.0 mmol, 0.124 mL) at room temperature for 24 hours, yielding only starting material. Yield was determined by GC using a calibration curve. GC conditions: starting temperature (30°C), ramp rate (10°C/m), final temperature (250°C), R.T. = 7.1 (S.M.).



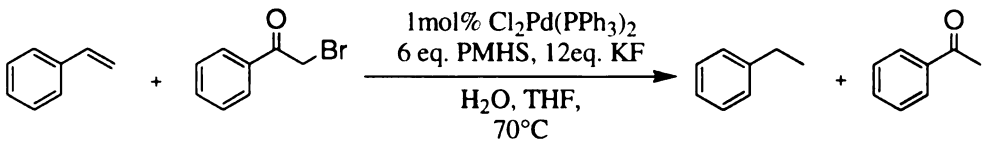
β-Chlorostyrene (E/Z:3/1) was reduced following general procedure A using 1.0 equiv. (1.0 mmol, 0.124 mL) at 70°C for 15 hours, to yield 7% styrene and 33% ethylbenzene. Yield was determined by NMR using an internal standard (CH_2Cl_2).



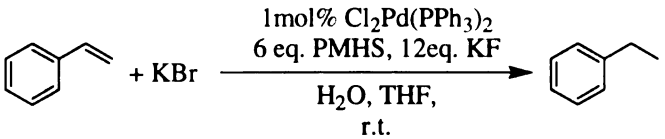
Styrene and 2-bromoacetophenone were reduced following general procedure A using 1.0 equiv. styrene (1.0 mmol, 0.115 mL) and 1.0 equiv. 2-bromoacetophenone (1.0 mmol, 0.199 g) at room temperature for 24 hours, to yield 78% ethylbenzene and 78% acetophenone. Yield was determined by NMR using an internal standard (CH_2Cl_2).



Styrene and 2-bromoacetophenone(cat.) were reduced following general procedure A using 1.0 equiv. styrene (1.0 mmol, 0.115 mL) and 0.1 equiv. 2-bromoacetophenone (0.1 mmol, 0.020 g) at room temperature for 24 hours, to yield 26% ethylbenzene. Yield was determined by NMR using an internal standard (CH_2Cl_2).

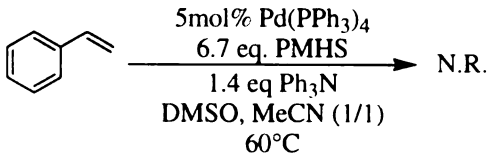


Styrene and 2-bromoacetophenone were reduced following general procedure A using 1.0 equiv. styrene (1.0 mmol, 0.115 mL) and 1.0 equiv. 2-bromoacetophenone (1.0 mmol, 0.199 g) at 70°C for 22 hours, to yield 43% ethylbenzene, 52% styrene, and 51% 2-bromoacetophenone. Yield was determined by NMR using an internal standard (CH_2Cl_2).

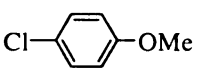


Styrene and potassium bromide were reduced following general procedure A using 1.0 equiv. styrene (1.0 mmol, 0.115 mL) and 1.0 equiv. KBr (1.0 mmol, 0.119 g) at room

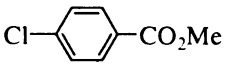
temperature for 24 hours, to yield 12% ethylbenzene. Yield was determined by NMR using an internal standard (CH_2Cl_2).



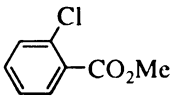
An oven dried schlenk tube was charged with 1.0 equiv. styrene (1.0 mmol, 0.115 mL) in 5 mL DMSO/CH_3CN (1/1), 1.4 equiv. triphenyl amine (1.4 mmol, 0.343 g), and 0.05 equiv. $Pd(PPh_3)_4$ (0.05 mmol, 0.055 g) in a glove bag under nitrogen. The schlenk tube was sealed followed by the addition of 6.6 equiv. PMHS down the side arm via syringe, under a positive flow of nitrogen. Upon PMHS addition the schlenk tube was closed and placed in an oil bath at 60°C and stirred for 3 hours. GC and NMR analysis indicated no reduction of styrene.



Preparation of 4-chloroanisole:[42] An oven dried 1 L round bottom flask was charged with 1 equiv. 4-chlorophenol (0.777 mol, 100 g), 1.2 equiv. MeI (0.933 mol, 132 g), 1.2 equiv. K_2CO_3 (0.99 mol, 129 g), in 300 mL of dry acetone. The reaction was refluxed in a 70°C oil bath for 20 hours, cooled to room temperature, and diluted with 300 mL water and 100 mL Et_2O. The layers were separated and the organic layer was washed with a 1 M H_2SO_4 solution and a 1 M NaOH solution. The crude liquid was dried over $MgSO_4$ and concentrated to yield 70.9 g (64%) of 4-chloroanisole as a clear yellow liquid. ^1H NMR (300 MHz, $CDCl_3$) δ 7.26 (d, J = 8.79 Hz, 2 H), 6.85 (d, J = 8.79 Hz, 2 H), 3.8 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 158.11, 129.19, 125.38, 115.06, 55.34. Product data was identical to that from an authentic commercial sample.

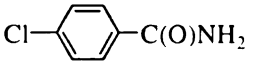


Preparation of methyl 4-chlorobenzoate:[41] A 500 mL round bottom flask was charged with 1 equiv. 4-chlorobenzoic acid (160 mmol, 25 g), 38.6 equiv. of anhydrous methanol (6.17 mol, 250 mL), and a catalytic amount of con. HCl (2.5 mL). The r.b. was placed in an oil bath at 60°C and the reaction refluxed for 12 hours under a positive flow of nitrogen. The reaction mixture was cooled to room temperature and concentrated. Water (300 mL) was added to the crude material and filtered. The collected material was rinsed with water and air dried, yielding 26.2 g (96.2%) of methyl 4-chlorobenzoate as a white solid; m.p. 42-44°. The crude material was of sufficient purity as to not require further purification. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.89 (d, J = 7.3 Hz, 2 H), 7.49 (d, J = 7.3 Hz, 2 H), 3.89 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.36, 138.40, 130.19, 127.93, 114.88, 51.53. Product data was identical to that from an authentic commercial sample.

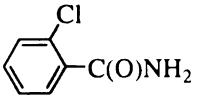


Preparation of methyl 2-chlorobenzoate:[42] An oven dried 250 mL round bottom flask was charged with 1 equiv. 2-chlorobenzoic acid (63.9 mmol, 10 g), 1.2 equiv. MeI (76.6 mmol, 4.77 mL), 1.2 equiv. K_2CO_3 (76.6 mmol, 10.6 g), in 100 mL of dry acetone. The reaction was heated to refluxed in an oil bath for 16 hours, cooled to room temperature, and filtered. The filtrate was diluted with ether and washed with a 1 M NaOH solution followed by an aqueous solution of $CaCl_2$, dried over $MgSO_4$ and concentrated to yield 7.2 g (66%) of methyl 2-chlorobenzoate as a clear yellow liquid. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.81 (d, J = 7.14 Hz, 1 H), 7.43 (m, 2 H), 7.29 (t, J = 7.69 Hz, 1 H), 3.93 (s,

3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.95, 133.49, 132.41, 131.23, 130.89, 129.85, 126.42, 52.23. Product data was identical to that from an authentic commercial sample.

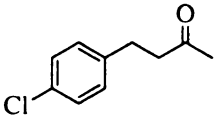


Preparation of 4-chlorobenzamide:[43] A 250 mL round bottom flask was charged with 1 equiv. 4-chlorobenzoic acid (159.7 mmol, 25 g) in 30 mL of DMF and 100 mL of CH_2Cl_2. The r.b. was placed in an oil bath at 65°C followed by the addition of 1.1 equiv thionyl chloride (175.6 mmol, 12.8 mL) via a syringe and refluxed for ~30 minutes. The cooled reaction mixture was poured into an addition funnel and attached to a r.b. with a side arm in an ice-salt bath with 12 equiv. of ammounium hydroxide (1.9 mol, 74.6 mL). The acid chloride reaction mixture was added slowly to the NH_4OH, so that gas evolution was not excessive. The reaction was stirred for 2 hours after addition of the acid chloride. The solvent was decanted from the reaction mixture and the solid was recrystallized in 100% EtOH, yielding 18.2 g (73.3%) of 4-chlorobenzamide as a white solid; m.p. 174 - 175°. ^{1}H NMR (300 MHz, d_6-DMSO) δ 7.3 (d, J = 8.79 Hz, 2 H), 6.79 (d, J = 8.79 Hz, 2 H), 6.47 (s, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.65, 136.74, 131.71, 128.57, 127.72. Product data was identical to that from an authentic commercial sample.



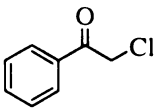
Preparation of 2-chlorobenzamide:[43] A 100 mL r.b. flask with a side arm was charged with 11 equiv. ammonium hydroxide (1.65 mol, 64.25 mL) and put in an ice-salt bath. An addition funnel with 1.0 equiv 2-chlorobenzoylchloride (0.150 mmol, 19 mL) was attached to the r.b. followed by the dropwise addition of the acid chloride to the NH_4OH

with vigorous stirring. The reaction mixture was stirred for 1 hour after the addition of acid chloride. The reaction mixture was filtered and washed with ice-cold water. The crude material was recrystallized from dry ethyl acetate and dried under high vacum, yielding 21.7 g (93%) of 2-chlorobenzamide as a white solid; m.p. 140-141°. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.33 (d, 1 H), 7.1 (m, 3 H), 6.88 (s, 1 H) 6.55 (s, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.39, 133.89, 131.79, 130.83, 130.57, 130.36, 127.13. Product data was identical to that from an authentic commercial sample.



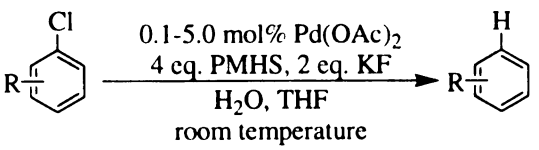
Preparation of 4-(4-chlorophenyl)-butan-2-one:[32] A 25mL round bottom flask was charged with 1.0 equiv. 1-chloro-4-iodobenzene (2.0 mmol, 0.477 g), 1.25 equiv. 3-buten-2-ol (2.5 mmol, 0.22 mL), 0.03 equiv. palladium acetate (0.06 mmol, 0.013 g), 1.25 equiv. triethyl amine (2.5 mmol, 0.35 mL) in 5 mL acetonitrile. The r.b. was connected to a reflux condenser. The reaction was placed under a nitrogen atmosphere and place in an oil bath at 90°C. The reaction was stirred at reflux for 16 hours then cooled to room temperature and diluted with 30 mL of ether. The diluted reaction mixture was washed with 3X10mL of water and the organic layer was dried over magnesium sulfate. The organic layer was filtered and concentrated. The crude material (700 mg) was collected and subjected to chromoatography with hexanes / ethyl acetate (1/1) yielding 333 mg (91.2%) of 4-(4-chlorophenyl)-butane-2-one as a dark yellow liquid. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.19 (d, J = 8.24 Hz, 2 H), 7.09 (d, J = 8.24 Hz, 2 H), 2.82 (t, J = 7.41 Hz, 2 H), 2.71 (t, J = 7.41 Hz, 2 H), 2.1 (s, 3 H); ^{13}C NMR (75 MHz,

$CDCl_3$) δ 207.34, 139.38, 131.621, 129.59, 128.92, 44.69, 29.92, 28.78. Product data is in agreement with reported literature.[44]



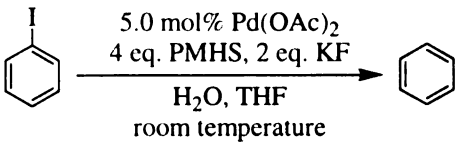
Preparation of 2-chloroacetophenone:[45] A 1 L round bottom flask was charged with 1.1 equiv. aluminum chloride (0.77 mol, 103 g), and 4.3 equiv. anhydrous benzene (3.0 mol, 265 mL). The r.b. was placed in an oil bath and heated to reflux. Chloroacetyl chloride, 1.0 equiv. (0.7 mol, 53 mL), was added slowly via syringe over an hour. The reaction was refluxed for 1 hour after the complete addition of chloroacetyl chloride, cooled to room temperature, quenched with water, and filtered. The filtrate was rinsed with Et_2O, and the resultant filtrates were flushed through a silica plug followed by an additional elution with 500 mL of hexanes/EtOAc (20/80). The collected fractions were concentrated and dried under high vacuum, affording 82.25 g (76%) of 2-chloroacetophenone as a bright orange crystalline solid; m.p. 56-57°. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.93 (d, J = 7.14 Hz, 2 H), 7.61 (t, J = 7.69 Hz, 1 H), 7.48 (t, J = 7.69 Hz, 2 H), 4.71 (s, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 191.01, 134.16, 133.97, 128.86, 128.45, 46.04. Product data was identical to that from an authentic commercial sample.

General Procedure B: $Pd(OAc)_2$ mediated reductions: halogens, olefins, alkynes, carbonyl, nitro, nitrile, nonaflate

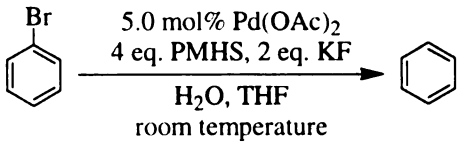


A round bottom flask (oven dried) was charged with 1.0 equiv. chloroarene (1.0 mmol) in 5.0 mL THF (0.2 M solution, based on halide) and 0.05 equiv. of $Pd(OAc)_2$ (0.05 mmol,

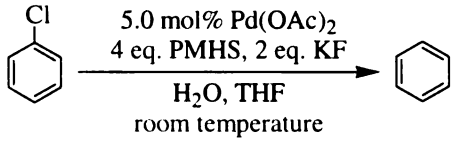
0.011 g). The flask was sealed with a septum and flushed with nitrogen. While flushing the reaction, 2.0 equiv. of KF (2.0 mmol, 0.116 g) in 2 mL of degassed water was introduced via syringe. 4.0 equiv of PMHS (4.0 mmol, 0.24 mL) was then injected dropwise into the reaction mixture. The reaction was stirred until complete as judged by disappearance of the starting material (GC analysis). Upon complete reduction, 2.0 mL of a 3 M NaOH solution was added to the reaction mixture. After stirring 5 hours to hydrolyze unreacted PMHS, the mixture was extracted several times with Et_2O. The combined organics were dried over $MgSO_4$ and concentrated. The crude material was then either distilled or purified by silica gel chromatography. When column chromatography was needed, initial elution with CCl_4/hexanes (1:1) was useful in removing silane byproducts.



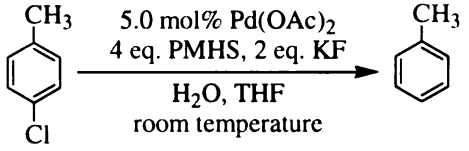
Iodobenzene was reduced following general procedure B using 1.0 equiv. (1.0 mmol, 0.112 mL) for 20 minutes, to yield 100% benzene. Yield was determined by NMR using an internal standard (CH_2Cl_2) in THF-d_8.



Bromobenzene was reduced following general procedure B using 1.0 equiv. (1.0 mmol, 0.105 mL) for 20 minutes, to yield 100% benzene. Yield was determined by NMR using an internal standard (CH_2Cl_2) in THF-d_8.



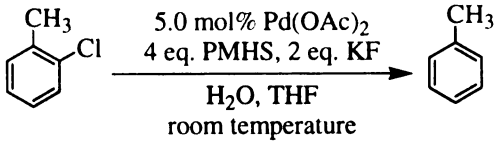
Chlorobenzene was reduced following general procedure B using 1.0 equiv. (1.0 mmol, 0.102 mL) for 20 minutes, to yield 95% benzene. Yield was determined by NMR using an internal standard (CH_2Cl_2) in THF-d_8.



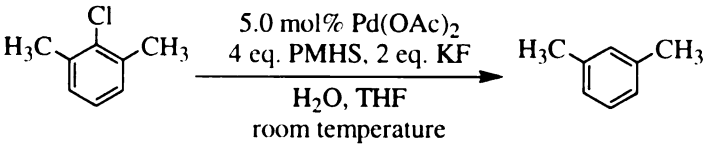
4-Chlorotoluene was reduced following general procedure B using 1.0 equiv. (1.0 mmol, 0.118 mL) for 3 hours, to yield 95% toluene. Yield was determined by NMR using an internal standard (CH_2Cl_2).

4-Chlorotoluene was reduced with 1 mol% $Pd(OAc)_2$ following general procedure B using 1.0 equiv. (1.0 mmol, 0.118 mL) 4-chlorotoluene and 0.01 equiv. (0.01 mmol, 0.002 g) $Pd(OAc)_2$ for 10 hours, to yield 96.2% toluene. Yield was determined by NMR using an internal standard (CH_2Cl_2).

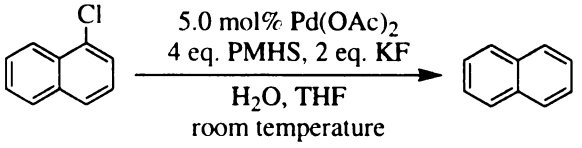
4-Chlorotoluene was reduced with 0.1 mol% $Pd(OAc)_2$ following general procedure B using 1.0 equiv. (1.0 mmol, 0.118 mL) 4-chlorotoluene and 0.001 equiv. (0.001 mmol, 0.0002 g) $Pd(OAc)_2$ for 54 hours, to yield 24% toluene. Yield was determined by NMR using an internal standard (CH_2Cl_2).



2-Chlorotoluene was reduced following general procedure B using 1.0 equiv. (1.0 mmol, 0.117 mL) for 3 hours, to yield 100% toluene. Yield was determined by NMR using an internal standard (CH_2Cl_2).



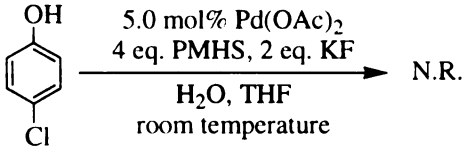
2-Chloro-*m*-xylene was reduced following general procedure B using 1.0 equiv. (1.0 mmol, 0.117 mL) for 8 hours, to yield 100% *m*-xylene. Yield was determined by NMR using an internal standard (CH_2Cl_2).



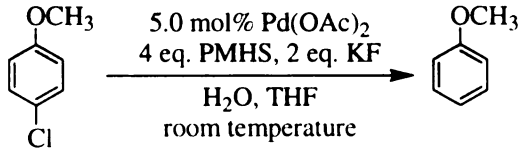
1-Chloronaphthalene was reduced following general procedure B using 1.0 equiv. (1.0 mmol, 0.136 mL) for 4 hours, to yield 96% naphthalene. Yield was determined by NMR using an internal standard (CH_2Cl_2).

Reduction of 1-chloronaphthalene: A round bottom flask (oven dried) was charged with 1.0 equiv. 1-chloronaphthalene (5.0 mmol, 0.68 mL) in 25.0 mL THF (0.2 M solution, based on halide) and 0.05 equiv. of $Pd(OAc)_2$ (0.25 mmol, 0.056 g). The flask was sealed with a septum and flushed with nitrogen. While flushing the reaction, 2.0 equiv. of KF (10.0 mmol, 0.581 g) in 10.0 mL of degassed water was introduced via syringe. 4.0 equiv of PMHS (20.0 mmol, 1.2 mL) was then injected dropwise into the reaction mixture. The reaction was stirred until complete as judged by disappearance of the starting material (GC analysis). Upon complete reduction, 10.0 mL of a 3 M NaOH solution was added to the reaction mixture. After stirring 5 hours to hydrolyze unreacted PMHS, the mixture was extracted several times with Et_2O. The combined organics were

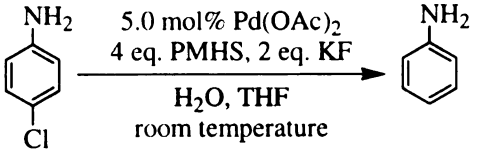
dried over $MgSO_4$ and concentrated. The crude material was then passed through a silica plug with hexanes, affording 0.527 g (82.2%) of a pure white solid; m.p. 80-82°. ^1H NMR (300 MHz, $CDCl_3$) δ 7.83 (q, J = 3.96 Hz, 4 H), 7.47 (q, J = 3.96 Hz, 4 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 133.41, 127.86, 125.81. Product data was identical to that from an authentic commercial sample.



4-Chlorophenol was reduced following general procedure B using 1.0 equiv. (1.0 mmol, 0.129 g) for 17 hours, to yield 0% phenol. Yield was determined by GC and NMR using an internal standard (CH_2Cl_2). Extraction of the reaction mixture with Et_2O afforded 0.118 g (91.5%) of starting material.



4-Chloroanisole was reduced following general procedure B using 1.0 equiv. (1.0 mmol, 0.123 mL) for 1.5 hours, to yield 100% anisole. Yield was determined by NMR using an internal standard (CH_2Cl_2).



4-Chloroaniline was reduced following general procedure B using 1.0 equiv. (1.0 mmol, 0.127 g) for 1 hour, to yield 99% aniline. Yield was determined by NMR using an internal standard (CH_2Cl_2).

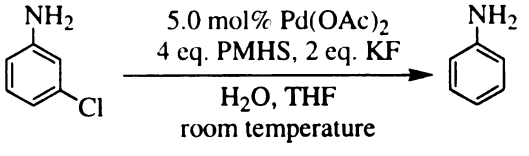
Reduction of 4-chloroaniline: A round bottom flask (oven dried) was charged with 1.0 equiv. 4-chloroaniline (5.0 mmol, 0.638 g) in 25.0 mL THF (0.2 M solution, based on halide) and 0.05 equiv. of $Pd(OAc)_2$ (0.25 mmol, 0.056 g). The flask was sealed with a septum and flushed with nitrogen. While flushing the reaction, 2.0 equiv. of KF (10.0 mmol, 0.581 g) in 10.0 mL of degassed water was introduced via syringe. 4.0 equiv of PMHS (20.0 mmol, 1.2 mL) was then injected dropwise into the reaction mixture. The reaction was stirred until complete as judged by disappearance of the starting material (GC analysis). Upon complete reduction, 10.0 mL of a 3 M NaOH solution was added to the reaction mixture. After stirring 5 hours to hydrolyze unreacted PMHS, the mixture was extracted several times with Et_2O. The combined organics were dried over $MgSO_4$ and concentrated. The crude material was taken up in CCl_4/hexanes (1/1) placed on a column, flushed with an initial elution of CCl_4/hexanes (100 mL) followed by 100 mL of EtOAc. The EtOAc fraction was concentrated affording 0.407 g (87.3%) of a pure clear liquid. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.21 (t, J = 7.8 Hz, 2 H), 6.82 (t, J = 7.4 Hz, 1 H), 6.64 (d, J = 7.9 Hz, 2 H), 3.65 (s, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 146.25, 129.0, 118.16, 114.86. Product data was identical to that from an authentic commercial sample.

Reduction of 4-chloroaniline: A round bottom flask (oven dried) was charged with 1.0 equiv. 4-chloroaniline (100 mmol, 12.7 g) in 500 mL THF (0.2 M solution, based on halide) and 0.01 equiv. of $Pd(OAc)_2$ (1.0 mmol, 0.225 g). The flask was sealed with a septum and flushed with nitrogen. While flushing the reaction, 2.0 equiv. of KF (200 mmol, 11.6 g) in 200 mL of degassed water was introduced via syringe. 4.0 equiv of PMHS (400 mmol, 24 mL) was then injected slowly into the reaction mixture. The reaction was stirred until complete as judged by disappearance of the starting material

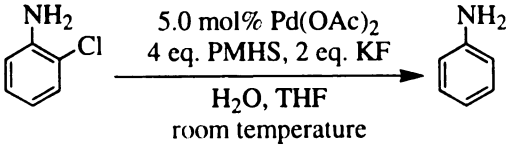
(GC analysis). Upon complete reduction, 200 mL of a 3 M NaOH solution was added to the reaction mixture. After stirring 5 hours to hydrolyze unreacted PMHS, the mixture was extracted several times with Et_2O. The combined organics were dried over $MgSO_4$ and concentrated. The crude material was distilled at 55°C under vacuum affording 7.1 g (76.2%) of a pure clear liquid. Product data was identical to that from an authentic commercial sample.

4-Chloroaniline was reduced with 1 mol% $Pd(OAc)_2$ following general procedure B using 1.0 equiv. (1.0 mmol, 0.127 g) 4-chloroaniline and 0.01 equiv. (0.01 mmol, 0.002 g) $Pd(OAc)_2$ for 1 hour, to yield 97.6% aniline. Yield was determined by NMR using an internal standard (CH_2Cl_2).

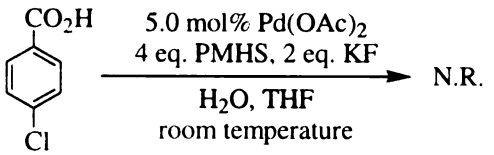
4-Chloroaniline was reduced with 0.1 mol% $Pd(OAc)_2$ following general procedure B; 1.0 equiv. (1.0 mmol, 0.127 g) 4-chloroaniline and 0.001 equiv. (0.001 mmol, 0.0002 g) $Pd(OAc)_2$ for 29 hours, to yield 97% aniline. Yield was determined by NMR using an internal standard (CH_2Cl_2).



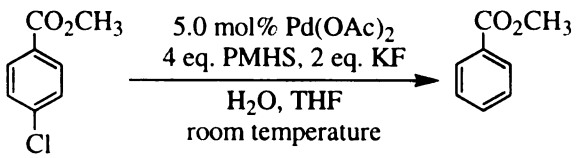
3-Chloroaniline was reduced following general procedure B using 1.0 equiv. (1.0 mmol, 0.127 g) for 45 minutes, to yield 94% aniline. Yield was determined by NMR using an internal standard (CH_2Cl_2).



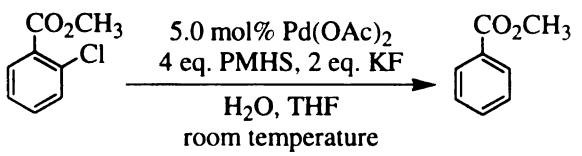
2-Chloroaniline was reduced following general procedure B using 1.0 equiv. (1.0 mmol, 0.127 g) for 45 minutes, to yield 99% aniline. Yield was determined by NMR using an internal standard (CH_2Cl_2).



4-Chlorobenzoic acid was reduced following general procedure B using 1.0 equiv. (1.0 mmol, 0.157 g) for 24 hours, to yield 0% benzoic acid. Yield was determined by GC and NMR using an internal standard (CH_2Cl_2). Extraction of the reaction mixture with Et_2O afforded 0.135 g (85.9%) of starting material.



Methyl 4-chlorobenzoate was reduced following general procedure B using 1.0 equiv. (1.0 mmol, 0.171 g) for 3 hours, to yield 84% methyl benzoate. Yield was determined by NMR using an internal standard (CH_2Cl_2).



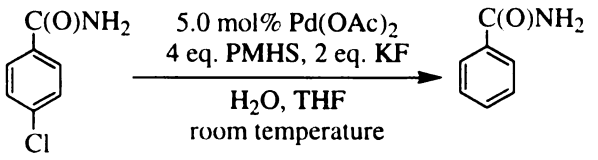
Methyl 2-chlorobenzoate was reduced following general procedure B using 1.0 equiv. (1.0 mmol, 0.171 g) for 1 hour, to yield 98% methyl benzoate. Yield was determined by NMR using an internal standard (CH_2Cl_2).

Reduction of methyl 2-chlorobenzoate: A round bottom flask (oven dried) was charged with 1.0 equiv. methyl 2-chlorobenzoate (5.0 mmol, 0.716 mL) in 25.0 mL THF (0.2 M solution, based on halide) and 0.05 equiv. of $Pd(OAc)_2$ (0.25 mmol, 0.056 g). The flask

was sealed with a septum and flushed with nitrogen. While flushing the reaction, 2.0 equiv. of KF (10.0 mmol, 0.581 g) in 10.0 mL of degassed water was introduced via syringe. 4.0 equiv of PMHS (20.0 mmol, 1.2 mL) was then injected dropwise into the reaction mixture. The reaction was stirred until complete as judged by disappearance of the starting material (GC analysis). Upon complete reduction, 10.0 mL of a 3 M NaOH solution was added to the reaction mixture. After stirring 5 hours to hydrolyze unreacted PMHS, the mixture was extracted several times with Et_2O. The combined organics were dried over $MgSO_4$ and concentrated. The crude material was taken up in CCl_4/hexanes (1/1) placed on a column, flushed with an initial elution of CCl_4/hexanes (500 mL) followed by 250 mL of EtOAc. The EtOAc fraction was concentrated affording 0.515 g (75.6%) of a pure clear liquid. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.03 (d, J = 8.24 Hz, 2 H), 7.52 (t, J = 6.86 Hz, 1 H), 7.4 (t, J = 7.69 Hz, 2 H), 3.88 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.88, 132.73, 129.97, 129.38, 128.18, 51.85. Product data was identical to that from an authentic commercial sample.

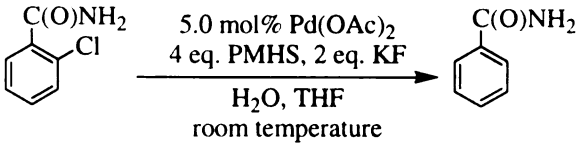
Methyl 2-chlorobenzoate was reduced with 1 mol% $Pd(OAc)_2$ following general procedure B using 1.0 equiv. (1.0 mmol, 0.143 mL) methyl 2-chlorobenzoate and 0.01 equiv. (0.01 mmol, 0.002 g) $Pd(OAc)_2$ for 9 hours, yielding 100% methyl benzoate. Yield was determined by NMR using an internal standard (CH_2Cl_2).

Methyl 2-chlorobenzoate was reduced with 0.1 mol% $Pd(OAc)_2$ following general procedure B using 1.0 equiv. (1.0 mmol, 0.118 mL) methyl 2-chlorobenzoate and 0.001 equiv. (0.001 mmol, 0.0002 g) $Pd(OAc)_2$ for 54 hours, to yield 100% methyl benzoate. Yield was determined by NMR using an internal standard (CH_2Cl_2).

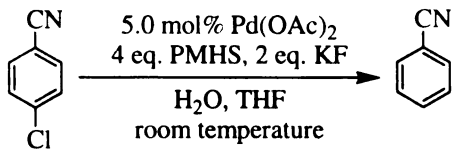


4-Chlorobenzamide was reduced following general procedure B using 1.0 equiv. (1.0 mmol, 0.156 g) for 1.5 hours, to yield 99% benzamide. Yield was determined by NMR using an internal standard (CH_2Cl_2).

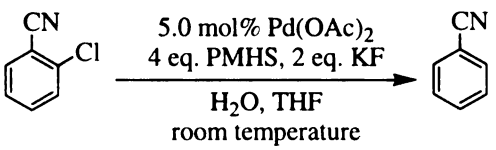
Reduction of 4-chlorobenzamide: A round bottom flask (oven dried) was charged with 1.0 equiv. 4-chlorobenzamide (5.0 mmol, 0.778 g) in 25.0 mL THF (0.2 M solution, based on halide) and 0.05 equiv. of $Pd(OAc)_2$ (0.25 mmol, 0.056 g). The flask was sealed with a septum and flushed with nitrogen. While flushing the reaction, 2.0 equiv. of KF (10.0 mmol, 0.581 g) in 10.0 mL of degassed water was introduced via syringe. 4.0 equiv of PMHS (20.0 mmol, 1.2 mL) was then injected dropwise into the reaction mixture. The reaction was stirred until complete as judged by disappearance of the starting material (GC analysis). Upon complete reduction, 10.0 mL of a 3 M NaOH solution was added to the reaction mixture. After stirring 5 hours to hydrolyze unreacted PMHS, the mixture was extracted several times with Et_2O. The combined organics were dried over $MgSO_4$ and concentrated. The crude material was then subjected to silica plug with hexanes, followed by EtOAc. The EtOAc fraction was concentrated affording 0.503 g (83%) of pure white solid; m.p. 127-128°. ^1H NMR (300 MHz, $CDCl_3$) δ 7.81 (d, J = 7.42 Hz, 2 H), 7.51 (t, J = 7.14 Hz, 1 H), 7.43 (t, J = 7.14 Hz, 2 H), 6.06 (s, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.7, 133.35, 131.94, 128.57, 127.29. Product data was identical to that from an authentic commercial sample.



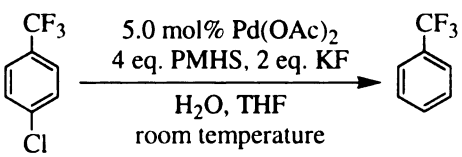
2-Chlorobenzamide was reduced following general procedure B using 1.0 equiv. (1.0 mmol, 0.156 g) for 45 minutes, to yield 89% benzamide. Yield was determined by NMR using an internal standard (CH_2Cl_2).



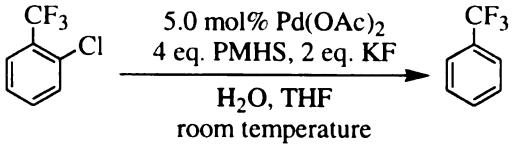
4-Chlorobenzonitrile was reduced following general procedure B using 1.0 equiv. (1.0 mmol, 0.138 g) for 30 minutes, to yield 81% benzonitrile. Yield was determined by NMR using an internal standard (CH_2Cl_2).



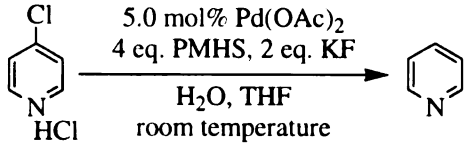
2-Chlorobenzonitrile was reduced following general procedure B using 1.0 equiv. (1.0 mmol, 0.138 g) for 1 hour, to yield 90% benzonitrile. Yield was determined by NMR using an internal standard (CH_2Cl_2).



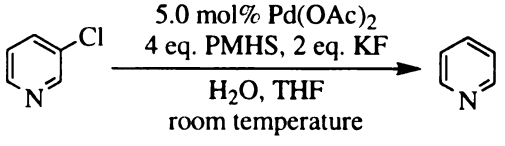
4-Chlorobenzotrifluoride was reduced following general procedure B using 1.0 equiv. (1.0 mmol, 0.133 mL) for 4 hours, to yield 96% trifluorotoluene. Yield was determined by NMR using an internal standard (CH_2Cl_2).



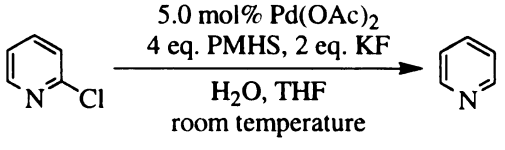
2-Chlorobenzotrifluoride was reduced following general procedure B using 1.0 equiv. (1.0 mmol, 0.131 mL) for 2 hours, to yield 99% trifluorotoluene. Yield was determined by NMR using an internal standard (CH_2Cl_2).



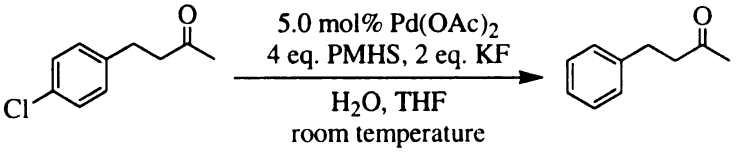
4-Chloropyridine hydrochloride was reduced following general procedure B using 1.0 equiv. (1.0 mmol, 0.150 g) for 1.5 hours, to yield 96% pyridine. Yield was determined by NMR using an internal standard (CH_2Cl_2).



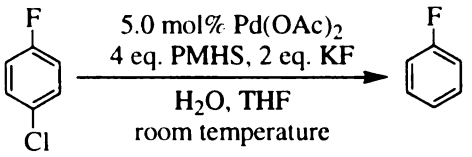
3-Chloropyridine was reduced following general procedure B using 1.0 equiv. (1.0 mmol, 0.095 mL) for 1 hour, to yield 97% pyridine. Yield was determined by NMR using an internal standard (CH_2Cl_2).



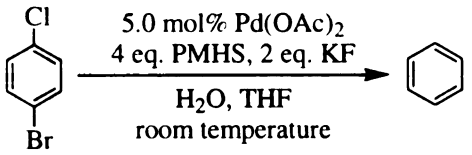
2-Chloropyridine was reduced following general procedure B using 1.0 equiv. (1.0 mmol, 0.095 mL) for 1.5 hours, to yield 94% pyridine. Yield was determined by NMR using an internal standard (CH_2Cl_2).



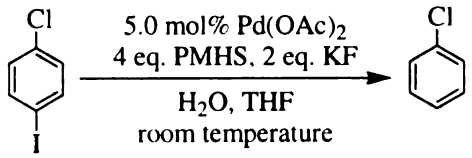
4-(4-chlorophenyl)-butan-2-one was dehalogenated following general procedure B using 1.0 equiv. (1.0 mmol, 0.129 g) for 18 hours, to yield 95% 4-phenyl-butane-2-one. Yield was determined by NMR using an internal standard (CH_2Cl_2), and also affording 0.126 g (85.4%) of a pure clear liquid. ^1H NMR (300 MHz, $CDCl_3$) δ 7.32 – 7.11 (m, 5 H), 2.89 (m, 2 H), 2.77 (m, 2 H), 2.15 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 207.72, 141.03, 128.5, 128.32, 126.11, 45.08, 29.93, 29.76. Product data was identical to that from an authentic commercial sample.



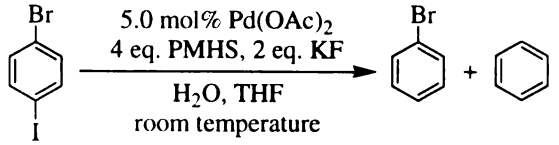
1-Chloro-4-fluorobenzene was reduced following general procedure B using 1.0 equiv. (1.0 mmol, 0.106 mL) for 20 hours, to yield 92% fluorobenzene. Yield was determined by NMR using an internal standard (CH_2Cl_2).



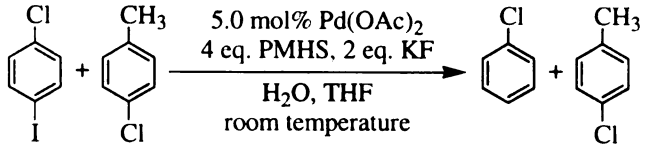
4-bromochlorobenzene was reduced following general procedure B using 1.0 equiv. (1.0 mmol, 0.191 g) for 24 hours, to yield 98% benzene. Yield was determined by NMR using an internal standard (CH_2Cl_2).



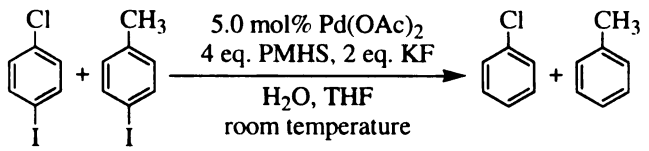
1-Chloro-4-iodobenzene was reduced following general procedure B using 1.0 equiv. (1.0 mmol, 0.238 g) for 24 hours, to yield 93% chlorobenzene. Yield was determined by NMR using an internal standard (CH_2Cl_2).



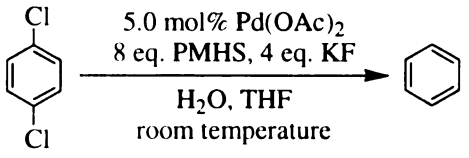
1-Bromo-4-iodobenzene was reduced following general procedure B using 1.0 equiv. (1.0 mmol, 0.283 g) for 24 hours, to yield 96% bromobenzene and 4% benzene. Yields were determined by NMR using an internal standard (CH_2Cl_2).



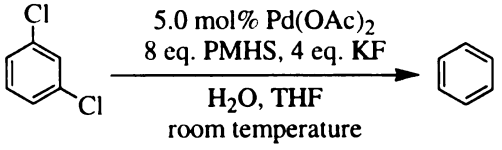
1-Chloro-4-iodobenzene and 4-chlorotoluene were reduced following general procedure B using 1.0 equiv. 1-chloro-4-iodobenzene (1.0 mmol, 0.238 g) and 1.0 equiv. 4-chlorotoluene (1.0 mmol, 0.118 mL) for 24 hours, with 100% conversion to chlorobenzene and 0% conversion to toluene as determined by GC analysis. GC conditions: starting temperature (30°C), ramp rate (10°C/m), final temperature (250°C), R.T. = 4.73, 8.6 (S.M.), 3.14 (P).



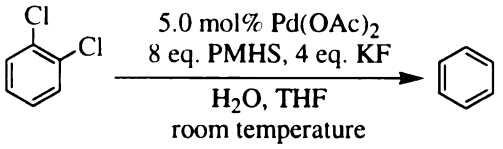
1-Chloro-4-iodobenzene and 4-iodotoluene were reduced following general procedure B using 1.0 equiv. 1-chloro-4-iodobenzene (1.0 mmol, 0.238 g) and 1.0 equiv. 4-iodotoluene (1.0 mmol, 0.218 g) for 24 hours, with 85% conversion to chlorobenzene and 49% conversion to toluene as determined by GC analysis. GC conditions: starting temperature (30°C), ramp rate (10°C/m), final temperature (250°C), R.T. = 7.7, 8.6 (S.M.), 2.22, 3.14 (P).



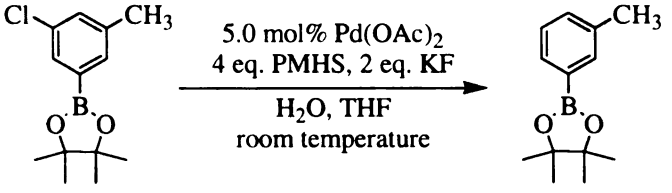
Reduction of 1,4-dichlorobenzene: A round bottom flask (oven dried) was charged with 1.0 equiv. 1,4-dichlorobenzene (1.0 mmol, 0.147 g) in 5.0 mL THF (0.2 M solution, based on halide) and 0.05 equiv. of $Pd(OAc)_2$ (0.05 mmol, 0.011 g). The flask was sealed with a septum and flushed with nitrogen. While flushing the reaction, 4.0 equiv. of KF (4.0 mmol, 0.232 g) in 2 mL of degassed water was introduced via syringe. 8.0 equiv of PMHS (8.0 mmol, 0.48 mL) was then injected dropwise into the reaction mixture. The reaction was stirred for 3 hours until complete as judged by disappearance of the starting material (GC analysis), yielding 98% benzene. Yield was determined by NMR using an internal standard (CH_2Cl_2) in THF-d_8.



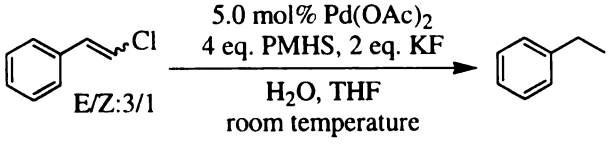
Reduction 1,3-dichlorobenzene: A round bottom flask (oven dried) was charged with 1.0 equiv. 1,3-dichlorobenzene (1.0 mmol, 0.114 mL) in 5.0 mL THF (0.2 M solution, based on halide) and 0.05 equiv. of $Pd(OAc)_2$ (0.05 mmol, 0.011 g). The flask was sealed with a septum and flushed with nitrogen. While flushing the reaction, 4.0 equiv. of KF (4.0 mmol, 0.232 g) in 2 mL of degassed water was introduced via syringe. 8.0 equiv of PMHS (8.0 mmol, 0.48 mL) was then injected dropwise into the reaction mixture. The reaction was stirred for 6 hours until complete as judged by disappearance of the starting material (GC analysis), yielding 98% benzene. Yield was determined by NMR using an internal standard (CH_2Cl_2) in THF-d_8.



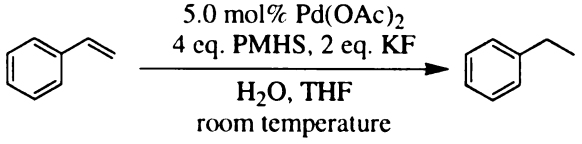
Reduction of 1,2-dichlorobenzene: A round bottom flask (oven dried) was charged with 1.0 equiv. 1,2-dichlorobenzene (1.0 mmol, 0.1125 mL) in 5.0 mL THF (0.2 M solution, based on halide) and 0.05 equiv. of $Pd(OAc)_2$ (0.05 mmol, 0.011 g). The flask was sealed with a septum and flushed with nitrogen. While flushing the reaction, 4.0 equiv. of KF (4.0 mmol, 0.232 g) in 2 mL of degassed water was introduced via syringe. 8.0 equiv of PMHS (8.0 mmol, 0.48 mL) was then injected dropwise into the reaction mixture. The reaction was stirred for 18 hours until complete as judged by disappearance of the starting material (GC analysis), yielding 98% benzene. Yield was determined by NMR using an internal standard (CH_2Cl_2) in THF-d_8.



3-Chloro-5-methylphenyl-pinacolborane[33] was reduced following general procedure B using 1.0 equiv. (1.0 mmol, 0.108g) for 6 hours, yielding 0.0557 g (85%) of 3-methylphenyl-pinacolborane, as a light yellow oil. The crude material was purified by silica plug with hexanes/EtOAc (80/20). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.66 (m, 2 H), 7.31 (m, 2 H), 2.38 (s, 3 H), 1.37 (s, 12 H).

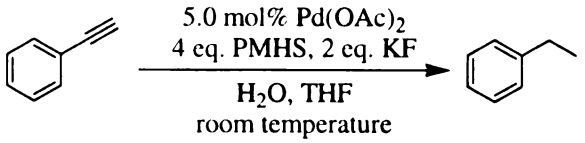


β-Chlorostyrene (E/Z: 3/1) was reduced following general procedure B using 1.0 equiv. (1.0 mmol, 0.124 mL) for 3 hours, to yield 99% ethylbenzene. Yield was determined by NMR using an internal standard (CH_2Cl_2).

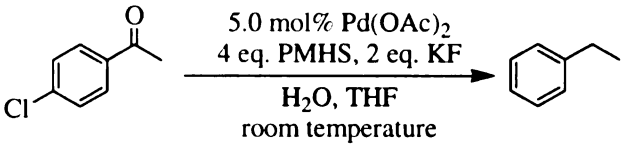


Styrene was reduced following general procedure B using 1.0 equiv. (1.0 mmol, 0.115 mL) for 45 minutes, to yield 100% ethylbenzene. Yield was determined by NMR using an internal standard (CH_2Cl_2).

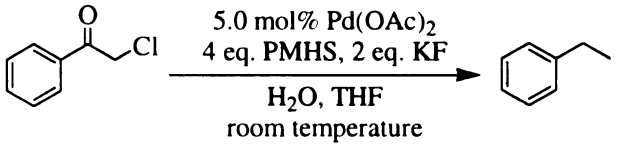
Hydrogenation of styrene: A round bottom flask (oven dried) was charged with 1.0 equiv. styrene (5.0 mmol, 0.573 mL) in 25.0 mL THF (0.2 M solution) and 0.05 equiv. of $Pd(OAc)_2$ (0.25 mmol, 0.056 g). The flask was sealed with a septum and flushed with nitrogen. While flushing the reaction, 2.0 equiv. of KF (10.0 mmol, 0.581 g) in 10.0 mL of degassed water was introduced via syringe. 4.0 equiv of PMHS (20.0 mmol, 1.2 mL) was then injected dropwise into the reaction mixture. The reaction was stirred until complete as judged by disappearance of the starting material (GC analysis). Upon complete reduction, 10.0 mL of a 3 M NaOH solution was added to the reaction mixture. After stirring 24 hours to hydrolyze unreacted PMHS, the mixture was extracted several times with Et_2O. The combined organics were dried over $MgSO_4$ and concentrated, affording 0.254 g (47.8%) of ethylbenzene as a clear liquid. ^1H NMR (300 MHz, $CDCl_3$) δ 7.33 – 7.21 (m, 5 H), 2.68 (q, J = 7.69 Hz, 2 H), 1.26 (t, J = 7.4 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 144.01, 128.10, 127.65, 125.38, 28.71, 15.44. Product data was identical to that from an authentic commercial sample.



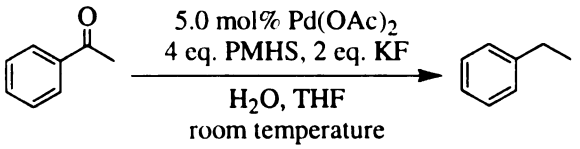
Phenyl acetylene was reduced following general procedure B using 1.0 equiv. (1.0 mmol, 0.11 mL) for 1 hour, to yield 100% conversion to ethylbenzene as determined by GC.



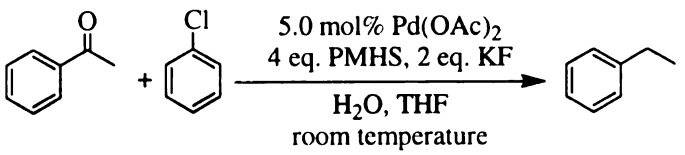
4'-Chloroacetophenone was reduced following general procedure B using 1.0 equiv. (1.0 mmol, 0.130 mL) for 3 hours, to yield 97% ethylbenzene. Yield was determined by NMR using an internal standard (CH_2Cl_2).



2-Chloroacetophenone was reduced following general procedure B using 1.0 equiv. (1.0 mmol, 0.155 g) for 45 minutes, to yield 99% ethylbenzene. Yield was determined by NMR using an internal standard (CH_2Cl_2).

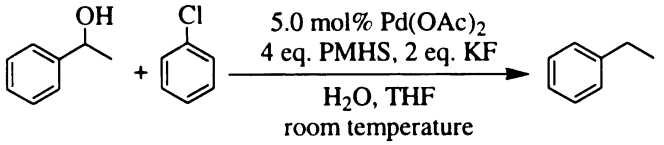


Acetophenone was reduced following general procedure B using 1.0 equiv. (1.0 mmol, 0.117 mL) for 20 hours, yielding trace amounts of ethylbenzene as determined by GC analysis.

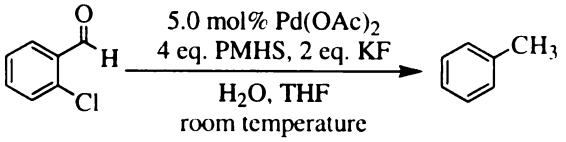


Acetophenone and chlorobenzene were reduced following general procedure B using 1.0 equiv. acetophenone (1.0 mmol, 0.117 mL) and 1.0 equiv. chlorobenzene (1 mmol, 0.102 mL) for 1 hour, to yield 96% ethylbenzene. Yield was determined by NMR using an internal standard (CH_2Cl_2).

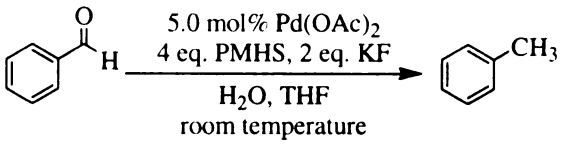
Deoxygenation of acetophenone with chlorobenzene: A round bottom flask (oven dried) was charged with 1.0 equiv. acetophenone (5.0 mmol, 0.583 mL) and 0.1 equiv. chlorobenzene (0.5mmol, 0.051 mL) in 25.0 mL THF (0.2 M solution) and 0.05 equiv. of $Pd(OAc)_2$ (0.25 mmol, 0.056 g). The flask was sealed with a septum and flushed with nitrogen. While flushing the reaction, 2.0 equiv. of KF (10.0 mmol, 0.581 g) in 10.0 mL of degassed water was introduced via syringe. 4.0 equiv of PMHS (20.0 mmol, 1.2 mL) was then injected dropwise into the reaction mixture. The reaction was stirred until complete as judged by disappearance of the starting material (GC analysis). Upon complete reduction, 10.0 mL of a 3 M NaOH solution was added to the reaction mixture. After stirring 24 hours to hydrolyze unreacted PMHS, the mixture was extracted several times with Et_2O. The combined organics were dried over $MgSO_4$ and concentrated, affording 0.306 g (57.6%) of ethylbenzene as a clear liquid. Product data was identical to that from an authentic commercial sample.



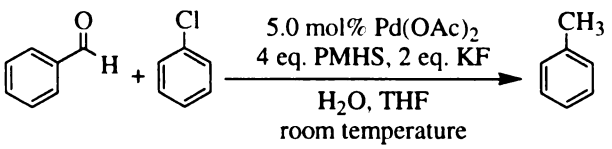
***sec*-Phenethyl alcohol and chlorobenzene were reduced following general procedure B** using 1.0 equiv. *sec*-phenethyl alcohol (1.0 mmol, 0.121 mL) and 1.0 equiv. chlorobenzene (1 mmol, 0.102 mL) for 30 minutes, to yield 100% ethylbenzene. Yield was determined by NMR using an internal standard (CH_2Cl_2).



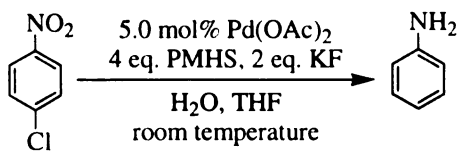
2-Chlorobenzaldehyde was reduced following general procedure B using 1.0 equiv. (1.0 mmol, 0.113 mL) for 1.75 hours, to yield 96% toluene. Yield was determined by NMR using an internal standard (CH_2Cl_2).



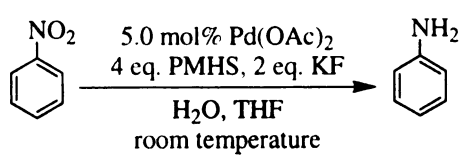
Benzaldehyde was reduced following general procedure B using 1.0 equiv. (1.0 mmol, 0.102 mL) for 5 hours, yielding trace amounts of toluene as determined by GC analysis.



Benzaldehyde and chlorobenzene were reduced following general procedure B using 1.0 equiv. benzaldehyde (1.0 mmol, 0.102 mL) and 1.0 equiv. chlorobenzene (1 mmol, 0.102 mL) for 30 minutes, to yield 100% toluene. Yield was determined by NMR using an internal standard (CH_2Cl_2).

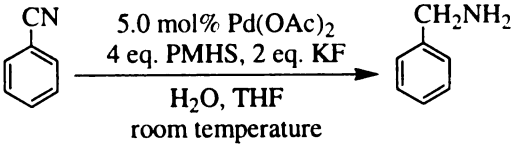


1-Chloro-4-nitrobenzene was reduced following general procedure B using 1.0 equiv. (1.0 mmol, 0.157 g) for 24 hours, to yield 97% aniline. Yield was determined by NMR using an internal standard (CH_2Cl_2).



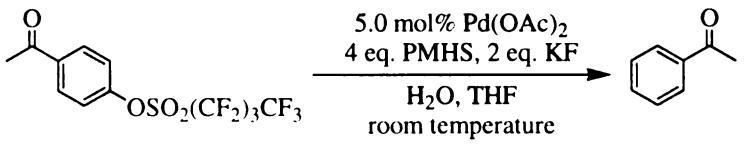
Nitrobenzene was reduced following general procedure B using 1.0 equiv. (1.0 mmol, 0.103 mL) for 1 hour, to yield 99% aniline. Yield was determined by NMR using an internal standard (CH_2Cl_2).

Reduction of nitrobenzene: A round bottom flask (oven dried) was charged with 1.0 equiv. nitrobenzene (5.0 mmol, 0.514 mL) in 25.0 mL THF (0.2 M solution) and 0.05 equiv. of $Pd(OAc)_2$ (0.25 mmol, 0.056 g). The flask was sealed with a septum and flushed with nitrogen. While flushing the reaction, 2.0 equiv. of KF (10.0 mmol, 0.581 g) in 10.0 mL of degassed water was introduced via syringe. 4.0 equiv of PMHS (20.0 mmol, 1.2 mL) was then injected dropwise into the reaction mixture. The reaction was stirred until complete as judged by disappearance of the starting material (GC analysis). Upon complete reduction, 10.0 mL of a 3 M NaOH solution was added to the reaction mixture. After stirring 24 hours to hydrolyze unreacted PMHS, the mixture was extracted several times with Et_2O. The combined organics were dried over $MgSO_4$ and concentrated. The crude material was taken up in CCl_4/hexanes (1/1) placed on a column, flushed with an initial elution of CCl_4/hexanes (100 mL) followed by 100 mL of EtOAc. The EtOAc fraction was concentrated affording 0.439 g (94.2%) of a pure clear liquid. ^1H NMR (300 MHz, $CDCl_3$) δ 7.15 (t, J = 7.9 Hz, 2 H), 6.75 (t, J = 7.3 Hz, 1 H), 6.67 (d, J = 8.2 Hz, 2 H), 3.59 (s, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 146.23, 129.01, 118.12, 114.82. Product data was identical to that from an authentic commercial sample.



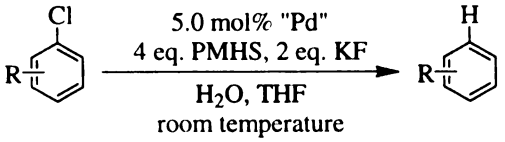
Reduction of benzonitrile: A round bottom flask (oven dried) was charged with 1.0 equiv. benzonitrile (5.0 mmol, 0.51 mL) in 25.0 mL THF (0.2 M solution) and 0.05

equiv. of $Pd(OAc)_2$ (0.25 mmol, 0.056 g). The flask was sealed with a septum and flushed with nitrogen. While flushing the reaction, 2.0 equiv. of KF (10.0 mmol, 0.581 g) in 10.0 mL of degassed water was introduced via syringe. 4.0 equiv of PMHS (20.0 mmol, 1.2 mL) was then injected dropwise into the reaction mixture. The reaction was stirred for 24 hours, at which point 10.0 mL of a 3 M NaOH solution was added to the reaction mixture. After stirring 24 hours to hydrolyze unreacted PMHS, the mixture was extracted several times with Et_2O. The combined organics were dried over $MgSO_4$ and concentrated, affording 0.455 g of crude material that was a mixture of benzonitrile (0.257 g, 50.4 %) and benzylamine (0.18 g, 33.5%) based on NMR.



4-acetylphenyl nonaflurobutanesulfonate was reduced following general procedure B using 1.0 equiv. (1.0 mmol, 0.418 g) for 1 hour, affording 97% conversion to acetophenone with 2.5% conversion to ethylbenzene, as determined by GC.

General Procedure C: "Pd"-catalyzed dehalogenation



A round bottom flask (oven dried) was charged with 1.0 equiv. chloroarene (1.0 mmol) in 5.0 mL THF (0.2 M solution, based on halide) and 0.05 equiv. "Pd"-catalyst (0.05 mmol). The flask was sealed with a septum and flushed with nitrogen. While flushing the reaction, 2.0 equiv. of KF (2.0 mmol, 0.116 g) in 2 mL of degassed water was introduced via syringe. 4.0 equiv of PMHS (4.0 mmol, 0.24 mL) was then injected

dropwise into the reaction mixture. The reaction was stirred until complete as judged by disappearance of the starting material (GC analysis).

Reaction of 4-chlorotoluene with $Pd(CN)_2$ following general procedure C using 1.0 equiv. (1.0 mmol, 0.118 mL) 4-chlorotoluene and 0.05 equiv. (0.05 mmol, 0.008 g) $Pd(CN)_2$ for 3 hours, yielded 0% toluene. Yield was determined by GC and NMR using an internal standard (CH_2Cl_2).

Reaction of 4-chlorotoluene with $Pd(NH_2)Cl_2$ following general procedure C using 1.0 equiv. (1.0 mmol, 0.118 mL) 4-chlorotoluene and 0.05 equiv. (0.05 mmol, 0.01 g) $Pd(NH_2)Cl_2$ for 3 hours, yielded 0% toluene. Yield was determined by GC and NMR using an internal standard (CH_2Cl_2).

Reaction of 4-chlorotoluene with $Pd(acac)_2$ following general procedure C using 1.0 equiv. (1.0 mmol, 0.118 mL) 4-chlorotoluene and 0.05 equiv. (0.05 mmol, 0.015 g) $Pd(acac)_2$ for 3 hours, yielded 72.7% toluene. Yield was determined by NMR using an internal standard (CH_2Cl_2).

Reaction of 4-chlorotoluene with Pd black following general procedure C using 1.0 equiv. (1.0 mmol, 0.118 mL) 4-chlorotoluene and 0.05 equiv. (0.05 mmol, 0.005 g) Pd black for 3 hours, yielded 93.7% toluene. Yield was determined by NMR using an internal standard (CH_2Cl_2).

Reaction of 4-chlorotoluene with $PdCl_2$ following general procedure C using 1.0 equiv. (1.0 mmol, 0.118 mL) 4-chlorotoluene and 0.05 equiv. (0.05 mmol, 0.008 g) $PdCl_2$ for 3 hours, yielded 76.7% toluene. Yield was determined by NMR using an internal standard (CH_2Cl_2).

Reaction of 4-chlorotoluene with $Pd_2(dba)_2$ following general procedure C using 1.0 equiv. (1.0 mmol, 0.118 mL) 4-chlorotoluene and 0.05 equiv. (0.05 mmol, 0.045 g) $Pd_2(dba)_2$ for 3 hours, yielded 96% toluene. Yield was determined by NMR using an internal standard (CH_2Cl_2).

Reaction of 4-chloroaniline with Pd black following general procedure C using 1.0 equiv. (1.0 mmol, 0.127 g) 4-chloroaniline and 0.05 equiv. (0.05 mmol, 0.005 g) Pd black for 30 minutes, yielded 96% aniline. Yield was determined by NMR using an internal standard (CH_2Cl_2).

Reaction of 4-chloroaniline with $PdCl_2$ following general procedure C using 1.0 equiv. (1.0 mmol, 0.127 g) 4-chloroaniline and 0.05 equiv. (0.05 mmol, 0.008 g) $PdCl_2$ for 30 minutes, yielded 96.4% aniline. Yield was determined by NMR using an internal standard (CH_2Cl_2).

Reaction of 4-chloroaniline with $Pd_2(dba)_2$ following general procedure C using 1.0 equiv. (1.0 mmol, 0.127 g) 4-chloroaniline and 0.05 equiv. (0.05 mmol, 0.045 g) $Pd_2(dba)_2$ for 30 minutes, yielded 73.6% aniline. Yield was determined by NMR using an internal standard (CH_2Cl_2).

Reaction of 2-chloropyridine with Pd black following general procedure C using 1.0 equiv. (1.0 mmol, 0.095 mL) 2-chloropyridine and 0.05 equiv. (0.05 mmol, 0.005 g) Pd black for 1.5 hours, yielded 0% pyridine. Yield was determined by GC and NMR using an internal standard (CH_2Cl_2).

Reaction of 2-chloropyridine with $PdCl_2$ following general procedure C using 1.0 equiv. (1.0 mmol, 0.095 mL) 2-chloropyridine and 0.05 equiv. (0.05 mmol, 0.008 g)

$PdCl_2$ for 1.5 hours, yielded 100% pyridine. Yield was determined by NMR using an internal standard (CH_2Cl_2).

Reaction of 2-chloropyridine with $Pd_2(dba)_2$ following general procedure C using 1.0 equiv. (1.0 mmol, 0.095 mL) 2-chloropyridine and 0.05 equiv. (0.05 mmol, 0.045 g) $Pd_2(dba)_2$ for 1.5 hours, yielded 75% pyridine. Yield was determined by NMR using an internal standard (CH_2Cl_2).

Reaction of 2-chloro-*m*-xylene with $PdCl_2$ following general procedure C using 1.0 equiv. (1.0 mmol, 0.095 mL) 2-chloro-*m*-xylene and 0.05 equiv. (0.05 mmol, 0.008 g) $PdCl_2$ for 14 hours, yielded 0% xylene. Yield was determined by GC and NMR using an internal standard (CH_2Cl_2).

Reaction of 2-chloro-*m*-xylene with $Pd_2(dba)_2$ following general procedure C using 1.0 equiv. (1.0 mmol, 0.095 mL) 2-chloro-*m*-xylene and 0.05 equiv. (0.05 mmol, 0.045 g) $Pd_2(dba)_2$ for 17 hours, yielded 50% xylene. Yield was determined by NMR using an internal standard (CH_2Cl_2).

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[19] Fluoride free reductions of β-bromostyrene and 2-bromoacetophenone saw yields drop by 60 and 40%, respectively.

[20] Substituting DMSO/MeCN for THF proved inefficient.

[21] Byproduct isolation proved difficult, but analysis of crude reaction mixtures suggests these minor constituents to be the result of condensation reactions.

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[23] β-Bromostyrene reductions under Pri-Bar and Buchman's conditions were repeated four times.

[24] Pri-Bar and Buchman assigned their reaction products by GC analysis. Though we do not know their GC parameters, retention times for styrene and PhEt on a 30 M x 0.32 mm SPB-5 fused silica GC column at 30–200 °C (increased 10 °C/min.) are similar. Thus absent additional analysis PhEt could be easily mis-assigned as styrene.

[25] One exception is β-chlorostyrene subjected to the $Cl_2Pd(PPh_3)_2$ conditions, resulting in 33% PhEt and 7% styrene, which is not that unusual for this facile vinyl halide.

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[29] % Conversion was determined by NMR and are the average of two runs.

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[31] These substrates could be reduced with 4 equivalents of PMHS per equivalent of arene, however these reactions took 2-4 times longer.

[32] 4-(4-Chlorophenyl)butan-2-one was prepared according to Buntin, S. A.; Heck, R. F. *Org. Synth.* **1983**, *61*, 82–84.

[33] 3-Chloro-5-methylphenylpinacolborane was prepared according to the general method of Cho, J.-Y.; Tse, M. K.; Holmes, D.; Maleczka, R. E., Jr.; Smith, M. R., III *Science* **2002**, *295*, 305-308.

[34] Even after 48 hours only chlorobenzene was present. Similar observations were made by Tashiro and co-workers during dehalogenations with metallic calcium in ethanol. See Mitoma, Y.; Nagashima, S.; Simion, C.; Simion, A. M.; Yamada, T.; Mimura, K.; Ishimoto, K.; Tashiro, M. *Environ. Sci. Technol.* **2001**, *35*, 4145–4148.

[35] A range of solvent systems were screened from hexanes and ethyl acetate to various combinations of the two.

[36] Phosphine bearing catalysts fail to reduce chloroarenes (reference 9).

[37] Bu_4NBr was tested as a bromide source in the hydrogenation of styrene in the $Cl_2Pd(PPh_3)_2$ system, resulting in the reaction mixture turning into a solid mass from polymerization.

[38] 3-Phenyl-1-propanol, 4-(4-chlorophenyl)-butan-2-one, and 4-heptanone all afforded starting material when subjected to the deoxygenation reaction conditions.

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